# Crystal and Molecular Structure of the 1:1 Complex of Urea and *syn*-5-Nitro-2-furaldehyde Oxime

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The crystal structure of the title adduct has been determined by *X*-ray diffraction techniques. The crystals are monoclinic, space group $P2_1/c$, $Z = 4$, with unit-cell dimensions $a = 6{\cdot}571(2)$, $b = 17{\cdot}575(7)$, $c = 8{\cdot}472(3)$ Å, and $\beta = 104{\cdot}47(3)°$. The structure was determined by using a combination of symbolic addition and Patterson methods and was refined by full-matrix least-squares methods to $R$ 0·053 for 1215 observed reflections. The structure consists of hydrogen-bonded layers of nearly planar *syn*-5-nitro-2-furaldehyde oxime molecules and urea molecules. The distances in the furan ring together with the short C–N (nitro) distance suggest an interaction between the nitro-group and the ring. The absence of a urea adduct of the *anti*-isomer is discussed.

THE bacteriostatic action of derivatives of 5-nitrofuraldehyde is not well understood although evidence suggests that the production of coenzyme A is inhibited. Since the inhibition might involve a hydrogen-bonded species, we undertook an investigation of the 1:1 hydrogen-bonded adduct of urea with *syn*-5-nitro-2-furaldehyde oxime as part of a programme to correlate biological activity with hydrogen-bonding pattern.

## EXPERIMENTAL

The adduct was prepared by the method of Gever [1] as light yellow crystals from methanol.

*Crystal Data.*—$C_5H_4N_2O_4,CH_4N_2O$, $M = 216{\cdot}2$. Monoclinic, $a = 6{\cdot}571(2)$, $b = 17{\cdot}575(7)$, $c = 8{\cdot}472(3)$ Å, $\beta = 104{\cdot}47(3)$, $U = 947{\cdot}4$ Å$^3$, $D_m = 1{\cdot}47$ (by flotation), $Z = 4$, $D_c = 1{\cdot}515$, $F(000) = 448$. Space group $P2_1/c$ from systematic absences: $h0l$ for $l$ odd, $0k0$ for $k$ odd. Cu-$K_{\alpha 1}$ radiation, $\lambda = 1{\cdot}54051$ Å; $\mu$(Cu-$K_{\alpha 1}$) = 11·7 cm$^{-1}$.

Cell dimensions were determined from preliminary precession and Weissenberg photographs, followed by a least-squares fit of 27 high-angle reflexions measured with Cu-$K_\beta$ radiation ($\lambda = 1{\cdot}39217$ Å) on a General Electric XRD-6 diffractometer.

The intensity data were collected on a General Electric XRD-6 automatic diffractometer, equipped with a pulse-height analyser, by use of nickel-filtered Cu-$K_{\alpha 1}$ radiation and the stationary-crystal–stationary-counter method. A 20 s count was taken for each reflection. All reflections in the unique set for which $2\theta \leq 135°$ were measured and then the entire hemisphere with $2\theta \leq 90°$ was remeasured. The 4 standard reflections which were measured after every 100 reflections were used to correct the data for a slight decrease (max. 9%) in intensity with time. A total of 1643 unique reflections were obtained after averaging symmetry equivalent reflections. A background curve as a function of $2\theta$ was derived from measurement of backgrounds at various points in reciprocal space free from streaks or reflections. The 1215 reflections which were $>1{\cdot}2$ times the appropriate background counts were considered observed and used in the analysis. The remaining 428 were considered unobserved and entered as 0·1 times the local background and flagged with a minus sign. An empirical correction for the splitting of the $\alpha_1 - \alpha_2$ doublet was made. The intensity data were reduced to a set of structure amplitudes on an arbitrary scale in the usual manner.

*Structure Determination and Refinement.*—The structure was solved by a combination of symbolic-addition procedures [2] and Patterson methods. The computer programs FAME–MAGIC–LINK–SYMPL [3] were used to derive the most consistent set of signs. However, the resulting $E$-map had too many peaks to discern any reasonable structure. The probable cause of failure may be due to the location of the whole molecule approximately in the plane $x = \frac{3}{4}$. A three-dimensional sharpened Patterson function was computed and this in conjunction with the $E$-map was used in selecting the best possible positions of 9 atoms. All these atoms were given values $x = 0{\cdot}75$. Successive Fourier syntheses were used to locate the remaining atoms. The positional parameters, especially those of $x$, were refined by applying double shifts after each Fourier syntheses. At this point $R$ was 0·28.

Four cycles of refinement by full-matrix least-squares methods, using individual isotropic temperature factors reduced $R$ to 0·19. Another two least-squares cycles with anisotropic thermal parameters reduced $R$ to 0·11. The positions of all hydrogen atoms were now located in a difference Fourier synthesis. Three additional cycles of least-squares calculations were carried out in which all non-hydrogen atoms were refined with anisotropic thermal parameters and all hydrogen atoms with individual isotropic temperature factors. At this stage, the shifts in parameters of all non-hydrogen atoms were $<0{\cdot}2\sigma$ and therefore, the refinement was considered complete. The final $R$ for 1215 observed reflections was 0·053.

All calculations were carried out on an IBM-360 model 65 computer. The quantity minimized in the least-squares calculations was $\Sigma w(|F_o| - |F_c|)^2$. The weighting scheme employed was: $\sqrt{w} = |F_o|/4F_{min.}$ if $|F_o| < 4F_{min.}$, 1·0 if $4F_{min.} \leq |F_o| \leq 6F_{min.}$, and $6F_{min.}/|F_o|$ if $|F_o| > 6F_{min.}$, where $F_{min.}$ was 2·4. The scattering factors for all atoms were taken from ref. 4.

The final atomic parameters along with their estimated standard deviations are given in Tables 1 and 2.* The atomic numbering, bond distances, and estimated standard deviations are given in Figure 1. The bond angles are given in Table 3.

* Measured and calculated structure factors are listed in Supplementary Publication No. SUP 20347 (4 pp., 1 microfiche). For details see Notice to Authors No. 7 in *J. Chem. Soc. (A)*, 1970, Issue No. 20 (items less than 10 pp. are supplied as full size copies).

[1] G. Gever, *J. Org. Chem.*, 1955, **23**, 754.
[2] J. Karle and I. L. Karle, *Acta Cryst.*, 1966, **21**, 849.
[3] R. B. K. Dewar, A. L. Stone, and E. B. Fleischer, personal communication.
[4] 'International Tables for *X*-Ray Crystallography, vol. III, p. 202, Kynoch Press, Birmingham, 1962.

DISCUSSION

The crystal consists of layers of *syn*-5-nitro-2-furaldehyde oxime and urea molecules held together by strong hydrogen bonds. The arrangement of one layer is illustrated in Figure 2. The layers are stacked, with only the usual van der Waals forces between the layers.

TABLE 1

Final parameters ($\times 10^4$) of non-hydrogen atoms with their estimated standard deviations in parentheses *

| | $x$ | $y$ | $z$ | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ | $\beta_{12}$ | $\beta_{13}$ | $\beta_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| O(1) | 7510(3) | 4569(1) | 1188(2) | 266(7) | 17(1) | 136(4) | 4(4) | 124(8) | −1(3) |
| O(2) | 7564(5) | 3277(2) | 4273(2) | 723(15) | 25(1) | 232(6) | −14(6) | 94(14) | 72(4) |
| O(3) | 7578(5) | 4508(1) | 4286(3) | 739(14) | 24(1) | 158(5) | −7(6) | 193(13) | 2(3) |
| O(4) | 7329(4) | 6204(1) | −2339(3) | 471(10) | 28(1) | 112(4) | −31(5) | 227(9) | −1(3) |
| N(1) | 7552(5) | 3896(2) | 3604(4) | 425(12) | 23(1) | 170(6) | −2(6) | 82(13) | 27(4) |
| N(2) | 7410(4) | 5698(1) | −1071(3) | 263(10) | 25(1) | 116(4) | −8(5) | 148(13) | −3(4) |
| C(1) | 7397(5) | 4392(2) | −409(4) | 190(10) | 26(1) | 142(6) | −9(5) | 122(12) | −27(4) |
| C(2) | 7342(6) | 3629(2) | −623(5) | 311(13) | 23(1) | 202(8) | −13(6) | 167(16) | −51(5) |
| C(3) | 7408(6) | 3300(2) | 899(5) | 355(14) | 18(1) | 233(8) | 4(7) | 154(16) | −17(5) |
| C(4) | 7508(5) | 3883(2) | 1918(4) | 260(11) | 18(1) | 167(6) | 7(6) | 100(13) | 12(4) |
| C(5) | 7350(6) | 5011(2) | −1537(4) | 266(12) | 30(1) | 121(6) | −15(6) | 161(13) | −32(4) |
| O(5) | 7319(5) | 7438(1) | 3917(3) | 662(13) | 20(1) | 130(4) | 18(5) | 321(11) | −19(3) |
| N(3) | 7300(6) | 6174(2) | 4079(3) | 626(17) | 24(1) | 144(5) | 3(7) | 313(15) | 6(4) |
| N(4) | 8070(5) | 6749(2) | 1903(3) | 514(13) | 25(1) | 105(4) | 1(6) | 243(12) | −7(4) |
| C(6) | 7549(6) | 6818(2) | 3315(3) | 344(12) | 20(1) | 91(5) | −1(6) | 114(12) | −8(4) |

* The temperature factor is of the form $\exp\{-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)\}$.

The urea molecule is planar within experimental error (see Table 4). The mean C–N bond lengths are 1·332(5) Å, in excellent agreement with those found in urea [5] [1·356(7)] and in the urea adduct with α-D-glucose[6] [1·330(6) Å]. However, the C–O bond length [1·228(4)] is significantly shorter than that in urea [5] [1·268(7)] or in the urea adduct with α-D-glucose [6] [1·246(5) Å]. Although the oxygen atom of the urea molecule is involved in two hydrogen bonds in each case [two N–H · · · O hydrogen bonds of 2·985(6) and 3·040(7) in urea, two O–H · · · O hydrogen bonds of 2·694(3) and 2·704(4) in the α-D-glucose–urea adduct, and one O–H · · · O hydrogen bond of 2·614(3) and one N–H · · · O hydrogen bond of 2·840(4) Å in the present study], no definite conclusions regarding the effect of hydrogen bonding on the length of the C–O bond can be made. However, the C–O bond appears to be the shortest in the adduct, with the strongest hydrogen bonds to the oxygen atoms.

TABLE 2

Final parameters ($\times 10^3$) of the hydrogen atoms and their estimated standard deviations in parentheses

| | $x$ | $y$ | $z$ | $B$/Å$^2$ |
|---|---|---|---|---|
| H(1)[C(2)] * | 712(6) | 339(2) | −169(5) | 3·4(9) |
| H(2)[C(3)] | 727(6) | 278(2) | 109(4) | 2·9(9) |
| H(3)[C(5)] | 716(4) | 486(2) | −260(4) | 2·2(6) |
| H(4)[O(4)] | 727(6) | 674(3) | −191(5) | 3·6(9) |
| H(5)[N(3)] | 751(6) | 572(3) | 371(5) | 3·0(1·0) |
| H(6)[N(3)] | 726(8) | 617(3) | 509(7) | 5·0(1·3) |
| H(7)[N(4)] | 785(6) | 631(2) | 138(4) | 2·8(9) |
| H(8)[N(4)] | 804(5) | 715(2) | 124(4) | 2·5(8) |

* The atom in square brackets is that to which the hydrogen atom is bonded.

The furan ring is planar (see Table 4) and the nitro- and oxime groups are nearly coplanar with the ring, with angles 1·8 and 0·8°. The C–N(nitro) distance [1·422(4) Å] is one of the shortest such distances found in either an aromatic or heterocyclic ring system. A comparison of these distances in aromatic compounds suggests that the C–N bond is dependent upon the strength of the interaction between the nitro-group and the ring. Long C–N bonds are found in *m*-dinitrobenzene [7] (1·493) and in *m*-nitroperchlorylbenzene [8] (1·497 Å) where the interaction is expected to be weak. In contrast, short C–N distances are found in 1,3-diamino-2,4,6-trinitrobenzene [9]

TABLE 3

Bond angles (°) and their estimated standard deviations in parentheses

(*a*) Angles involving non-hydrogen atoms

| | | | |
|---|---|---|---|
| C(1)–O(1)–C(4) | 104·0(2) | C(4)–N(1)–O(2) | 116·5(3) |
| O(1)–C(1)–C(2) | 110·5(3) | C(4)–N(1)–O(3) | 119·0(3) |
| C(1)–C(2)–C(3) | 107·0(3) | O(2)–N(1)–O(3) | 124·5(3) |
| C(2)–C(3)–C(4) | 105·3(3) | C(1)–C(5)–N(2) | 121·2(3) |
| C(3)–C(4)–O(1) | 113·2(3) | C(5)–N(2)–O(4) | 112·2(3) |
| C(3)–C(4)–N(1) | 130·6(3) | | |
| O(1)–C(4)–N(1) | 116·2(3) | N(3)–C(6)–O(5) | 120·6(3) |
| O(1)–C(1)–C(5) | 118·0(3) | N(3)–C(6)–N(4) | 116·7(3) |
| C(2)–C(1)–C(5) | 131·6(3) | N(4)–C(6)–O(5) | 122·8(3) |

(*b*) Angles involving hydrogen atoms

| | | | |
|---|---|---|---|
| C(1)–C(2)–H(1) | 123(2) | C(6)–H(3)–H(5) | 124(3) |
| C(3)–C(3)–H(1) | 130(2) | C(6)–N(3)–H(6) | 121(3) |
| C(2)–C(3)–H(2) | 126(2) | H(5)–N(3)–H(6) | 113(4) |
| C(4)–C(3)–H(2) | 129(2) | C(6)–N(4)–H(7) | 119(3) |
| C(1)–C(5)–H(3) | 114(2) | C(6)–N(4)–H(8) | 121(2) |
| N(2)–C(5)–H(3) | 125(2) | H(7)–N(4)–H(8) | 114(4) |
| N(2)–O(4)–H(4) | 108(2) | | |

[5] A. Caron and J. Donohue, *Acta Cryst.*, 1964, **17**, 544.

[6] R. L. Snyder and R. D. Rosenstein, *Acta Cryst.*, 1971, *B*, **27**, 1969.

[7] J. Trotter and C. S. Williston, *Acta Cryst.*, 1966, **21**, 285.

[8] G. J. Palenik, J. Donohue, and K. N. Trueblood, *Acta Cryst.*, 1969, *B*, **24**, 1139.

[9] J. R. Holden, *Acta Cryst.*, 1967, **22**, 545.

(1·42 and 1·43 Å) and in potassium picrate [10] (1·436 and 1·437 Å) where the interaction of the nitro-group and the ring is significant.

The C–N and N–O bond lengths in the oxime group are in good agreement with the values given for other oximes.[11] However, the C(1)–C(5) bond [1·443(5) Å]

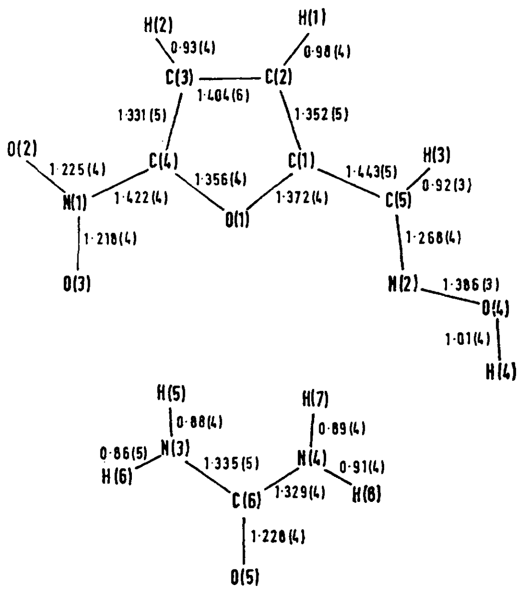


FIGURE 1 The atomic numbering and bond distances, with estimated standard deviations in parentheses

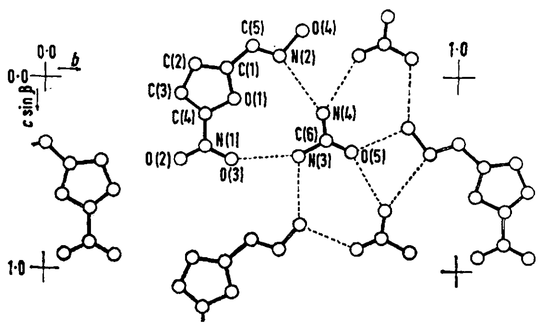


FIGURE 2 A section of the unit cell at $x = \frac{1}{4}$ showing the hydrogen-bonding arrangement in one layer; hydrogen bonds are shown by dashed lines, hydrogen atoms are omitted for clarity

from the ring to the oxime group is significantly shorter than the corresponding value in *syn-p*-chlorobenzaldehyde oxime [11] [1·486(9) Å] but agrees well with the value found in *anti*-2-furaldehyde oxime [12] [1·44(1) Å]. Since the C(5)–N(2) bond of 1·268(4) Å is very close to a pure C=N distance, the existence of double-bond character in the C(1)–C(5) bond is difficult to rationalize. Unfortunately the lack of precise structural data on an unconjugated oxime precludes any further discussion at this time.

A comparison of the bond distances in furan derivatives is presented in Table 5. There are three symmetrically substituted derivatives, three unsymmetrically substituted compounds as well as furan itself. The tentative conclusions based on the reported dimensions are that the symmetrically substituted derivatives are very similar to furan itself. However, asymmetric substitution introduces a definite asymmetry in the distances

TABLE 4

Equations of least-squares planes in the form $AX + BY + CZ = D$ where $X$, $Y$, and $Z$ are orthogonal co-ordinates in Å relative to ***a***, ***b***, ***c****. Distances (Å $\times 10^3$) of relevant atoms from the planes are given in square brackets

(*a*) 5-Nitro-2-furaldehyde oxime

| | $10^4A$ | $10^4B$ | $10^4C$ | $D$ |
|---|---|---|---|---|
| Plane (I): O(1)—(4), C(1)—(5), N(2) | 9761 | −97 | 2170 | 4·677 |
| [O(1) 28, C(1) 5, C(2) −11, C(3) −7, C(4) 18, C(5) −4, N(2) 10, O(4) −15, N(1) −3, O(2) −4, O(3) −16] | | | | |
| Plane (II): O(1), C(1)—(4) | 9784 | −231 | 2053 | 4·595 |
| [O(1) 1, C(1) −2, C(2) 2, C(3) −1, C(4) 0, C(5) −14, N(2) −21), O(4) −45, N(1) −38, O(2) −31, O(3) −72] | | | | |
| Plane (III): N(1), O(2), O(3) | 9735 | −42 | 2288 | 4·736 |
| [O(1) 13, C(1) −29, C(2) −54, C(3) −37, C(4) 3, C(5) −43, N(2) −18, O(4) −50] | | | | |
| Plane (IV): C(5), N(2), O(4) | 9806 | −150 | 1953 | 4·674 |
| [O(1) −11, C(1) −3, C(2) −8, C(3) −29, C(4) −29, N(1), −81, O(2) −88, O(3) −112] | | | | |
| (*b*) Urea | | | | |
| Plane (V): N(3), N(4), C(6), O(5) | 8769 | −104 | 4805 | 1·727 |
| [O(5) −1, N(3) −1, N(4) 1, C(6) 3] | | | | |

TABLE 5

Comparison of bond distances (Å) in various furan derivatives

| | O–C(1) | O–C(4) | C(1)–C(2) | C(3)–C(4) | C(2)–C(3) |
|---|---|---|---|---|---|
| Furan [a] | 1·371 | | 1·354 | | 1·440 |
| Furan-2-carboxylic acid [b] | 1·368 | 1·288 | 1·312 | 1·351 | 1·446 |
| Furan-α,α′-dicarboxylic acid [c] | 1·368 | | 1·354 | | 1·442 |
| Furan-β,β′-dicarboxylic acid [d] | 1·361 | | 1·351 | | 1·462 |
| Furantetracarboxylic acid [e] | 1·363 | 1·344 | 1·366 | 1·354 | 1·473 |
| *anti*-2-Furaldehyde oxime [f] | 1·389 | 1·376 | 1·364 | 1·346 | 1·432 |
| *syn*-5-Nitro-2-furaldehyde oxime [g] | 1·372 | 1·356 | 1·352 | 1·331 | 1·404 |

[a] B. Bak, L. Hansen, and J. Rastrup-Andersen, *Discuss. Faraday Soc.*, 1955, **19**, 30. [b] P. Hudson, *Acta Cryst.*, 1962, **15**, 919. [c] E. Martuscelli and C. Pedone, *Acta Cryst.*, 1968, *B*, **24**, 175. [d] O. E. Williams and R. E. Rundle, *J. Amer. Chem. Soc.*, 1964, **86**, 1660. [e] I. D. Paul, *Chem. Comm.*, 1964, 461. [f] Ref. 12. [g] Present work.

in the furan ring. Furthermore, the length of the C(1)–C(2) and C(3)–C(4) bonds indicates that furan is

[10] K. Maartmann-Moe, *Acta Cryst.*, 1969, *B*, **25**, 1452

[11] K. Folting, W. N. Lipscomb, and B. Jerslev, *Acta Cryst.*, 1964, **17**, 1263.

[12] B. Jensen and B. Jerslev, *Acta Chem. Scand.*, 1967, **21**, 730.

best regarded as a delocalized system. Although nitrofuran derivatives may be slightly perturbed furan systems, this perturbation does not appear a reasonable explanation for the biological activity. The hydrogen bonding capabilities of the nitro-group may be of more fundamental importance although this cannot be proven conclusively at present.

TABLE 6

Geometry of hydrogen bonds; distances (Å), angles (deg.)

| D–H ··· A | D–H | H ··· A | D ··· A | D–H–A |
|---|---|---|---|---|
| N(3)–H(5) ··· O(3) | 0·88(4) | 2·18(4) | 2·936(4) | 144(4) |
| N(3)–H(6) ··· O($4^{I}$) | 0·86(6) | 2·17(5) | 2·031(4) | 177(5) |
| N(4)–H(7) ··· H(2) | 0·89(4) | 2·29(4) | 3·066(4) | 146(3) |
| N(4)–H(8) ··· O($5^{II}$) | 0·91(4) | 2·03(4) | 2·840(4) | 147(3) |
| O(4)–H(4) ··· O($5^{II}$) | 1·01(4) | 1·61(4) | 2·614(4) | 175(4) |

Roman numerals as superscripts refer to the following equivalent positions relative to the reference molecule at $x, y, z$:

I $x, y, z + 1$
II $x, \frac{3}{2} - y, z - \frac{1}{2}$

All five hydrogen atoms capable of forming hydrogen bonds do form such intermolecular bonds. The pertinent distances and angles are shown in Table 6 and the hydrogen bonds in Figure 2. The urea and *syn*-5-nitro-2-furaldehyde oxime molecules are held together by a strong two-dimensional network of hydrogen bonds. The bonding between the layers was surveyed by calculating all intermolecular distances <3·8 Å, none of which corresponded to any unusual interaction. The *anti*-isomer would be incapable of forming hydrogen bonds from the nitro-group and oxime nitrogen atom to the urea molecule, hence a two-dimensional network seems less likely. This lack of a hydrogen-bonded network must explain the non-existence of a urea adduct with the *anti*-isomer.

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