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MOLECULAR AND CRYSTALLINE STRUCTURE OF FURFURAL DIACETATE NITRATION INTERMEDIATE

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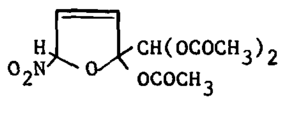
Abstract—X-ray crystallography established the structure of the acetyl nitrate adduct to furfural diacetate (H. Gilman and G. F. Wright (1930)) as *trans*-2-acetoxy-5-nitro-2,5-dihydro-2-furfural diacetate (**1a**). The furanoid ring is essentially planar, its geometry being similar to that of 2,5-dihydrofuran molecule, except for the interatomic distance C(3)–C(4) which is shorter than the corresponding length of double C–C bond in alkenes. The C(5)–N 1.52 Å bond significantly exceeds the standard C–N bond lengths in nitroalkanes and nitrobenzene.

Until recently it was assumed that the addition of acetyl nitrate to C=C double bonds leading to the formation of stable adducts takes place exclusively in the case of alkenes and furan derivatives, whereas aromatics produce only substitution products.[1,2] However, these opinions have changed since it was established that many alkylbenzenes form similar adducts with acetyl nitrate.[3,4] Following this discovery, an extensive investigation of the structure and properties of these compounds has been made resulting in new important theoretical concepts concerning the mechanism of aromatic nitration.[5]

The nitration of furfural diacetate (or furfural) by acetyl nitrate yields as the main product a crystalline "nitration intermediate" (m.p. 106–107°), corresponding in its composition to the adduct of acetyl nitrate and furfural diacetate.[6] The latter has been extensively studied but conflicting structures have been reported (1,[7] 2,[6] 3,[8] 4[9] and 5[10]) supported only by chemical, spectroscopic and polarographic investigations:



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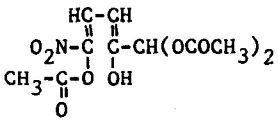

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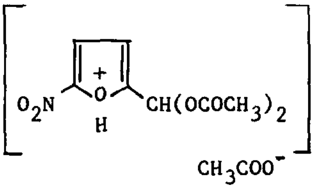

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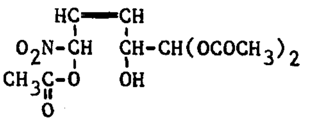

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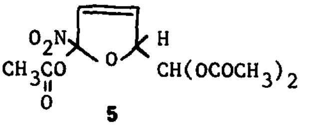

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The most feasible structure appears to be that of 2 - acetoxy - 5 - nitro - 2,5 - dihydro - 2 - furfural diacetate (1),[7,8,11-14]

The interest in the structure of this adduct is due to the fact that the nitration of furfural diacetate by acetyl nitrate is a key process in the manufacture of a wide variety of chemotherapeuticals.[15]

The present X-ray study of the adduct reveals its molecular and crystalline structure and provides clearcut evidence concerning the geometry, configuration, and conformation of the molecule.

RESULTS AND DISCUSSION

Crystals of the adduct are monoclinic, space group $P2_1/n$, with $a = 8.067(3)$, $b = 16.051(8)$, $c = 11.303(4)$ Å, $\beta = 107.43(3)°$, $Z = 4$. Final positional and anisotropic thermal parameters for the non-H atoms are given in Table 1. Interatomic distances and bond angles are given in Table 2. Figure 1 shows a stereoview of the final structure of the adduct and also shows the atom labelling scheme.

The furanoid ring appears to be planar within ± 0.05 Å range. The presence of bulky substituents at C(2) and C(5) leads to slight deformation of the ring. As a result C(2) and C(5) are located on the one side but O(1), C(3) and C(4)—on the other side of the median plane of the heterocycle.

The geometry of the 5-membered heterocycle corresponds, within experimental error, basically to that of the 2,5-dihydrofuran molecule,[16] except for the interatomic distance C(3)–C(4) which is reduced by 0.06 Å in the adduct equalling 1.29 Å. This is also shorter than the length of double C–C bond in alkenes. The endocyclic bond angle at the furanoid O(1) (111.0°) in the adduct is close to the corresponding value in 2,5-dihydrofuran (112°).

Table 1. Final positional and thermal parameters

Atoms	X	Y	Z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C(1)	0.3278(7)	0.3985(4)	0.7351(6)	1.8(3)	4.6(3)	4.5(3)	−0.1(2)	0.7(2)	−0.1(3)
C(2)	0.3275(7)	0.3522(3)	0.5317(5)	1.5(2)	3.7(3)	3.6(3)	0.3(2)	0.7(2)	0.4(2)
C(3)	0.1334(7)	0.3584(4)	0.4671(5)	1.6(3)	4.0(3)	4.4(2)	−0.2(2)	1.2(2)	0.2(2)
C(4)	0.0975(7)	0.4301(4)	0.4152(6)	1.5(3)	4.7(3)	4.7(3)	0.2(2)	0.9(2)	0.3(3)
C(5)	0.2596(8)	0.4815(3)	0.4400(6)	2.7(3)	3.2(3)	4.6(3)	0.5(2)	0.3(2)	0.6(2)
C(6)	0.3956(9)	0.3746(5)	0.8675(6)	4.3(4)	7.4(4)	4.2(3)	0.8(3)	0.4(3)	0.5(3)
C(7)	0.4229(7)	0.2809(4)	0.4932(5)	1.7(3)	3.9(3)	4.3(3)	0.1(2)	0.9(2)	0.2(2)
C(8)	0.5009(9)	0.2877(5)	0.1932(7)	4.9(4)	8.9(5)	5.7(4)	1.0(4)	3.1(3)	−0.4(4)
C(9)	0.5453(9)	0.2991(4)	0.3268(7)	3.8(4)	5.0(4)	5.3(4)	0.7(3)	2.4(3)	0.4(3)
C(10)	0.4469(9)	0.1365(4)	0.5369(6)	4.1(4)	3.6(3)	4.7(3)	0.4(3)	0.8(3)	0.1(2)
C(11)	0.3550(9)	0.0637(4)	0.5660(7)	4.9(4)	3.8(3)	6.3(4)	0.3(3)	1.6(3)	0.8(3)
O(1)	0.3940(4)	0.4275(2)	0.5017(3)	1.4(2)	3.4(2)	4.6(2)	0.3(1)	0.3(2)	0.6(2)
O(2)	0.3710(7)	0.4680(3)	0.2689(4)	5.9(3)	6.4(3)	5.3(3)	0.2(2)	2.3(2)	−0.1(2)
O(3)	0.2080(7)	0.5725(3)	0.2755(5)	5.5(3)	6.6(3)	7.8(3)	1.2(2)	1.2(2)	3.4(3)
O(4)	0.3714(5)	0.3416(2)	0.6616(4)	2.4(2)	4.0(2)	3.9(2)	0.8(2)	0.8(2)	0.3(2)
O(5)	0.2467(6)	0.4602(3)	0.6976(4)	3.9(2)	5.9(3)	5.3(2)	2.3(2)	0.9(2)	0.1(2)
O(6)	0.3474(5)	0.2073(2)	0.5202(4)	2.1(2)	3.3(2)	5.9(2)	0.3(1)	1.2(2)	0.4(2)
O(7)	0.5906(6)	0.1383(3)	0.5261(5)	2.5(2)	5.1(3)	11.8(4)	1.0(2)	2.4(2)	0.3(2)
O(8)	0.3996(5)	0.2830(2)	0.3657(4)	1.7(2)	4.9(2)	4.1(2)	−0.1(2)	1.1(2)	−0.3(2)
O(9)	0.6807(6)	0.3192(3)	0.3983(5)	2.3(2)	8.0(3)	6.6(3)	−0.4(2)	1.7(2)	−0.2(2)
11	0.2843(7)	0.5085(4)	0.3177(5)	3.1(3)	4.6(3)	4.4(3)	−0.6(2)	−0.3(2)	0.7(2)

Table 2. Bond lengths (d, Å) and bond angles (ω, degrees)

Atoms	d	Atoms	ω
C(2)–O(1)	1.41(1)	C(2)–O(1)–C(5)	111.0(4)
C(5)–O(1)	1.40(1)	C(2)–C(3)–C(4)	109.7(5)
C(2)–C(3)	1.52(1)	C(3)–C(4)–C(5)	110.1(5)
C(4)–C(5)	1.50(1)	C(4)–C(5)–O(1)	104.7(5)
C(3)–C(4)	1.29(1)	O(1)–C(5)–N	109.7(5)
C(2)–O(4)	1.41(1)	C(4)–C(5)–N	109.4(5)
C(1)–O(4)	1.35(1)	C(5)–N–O(2)	121.1(5)
C(1)–O(5)	1.19(1)	C(5)–N–O(3)	114.1(5)
C(1)–C(6)	1.48(1)	O(2)–N–O(3)	124.8(6)
C(2)–C(7)	1.51(1)	O(1)–C(2)–C(7)	108.5(4)
C(7)–O(6)	1.40(1)	O(4)–C(2)–C(7)	102.6(4)
C(10)–O(6)	1.37(1)	C(3)–C(2)–O(4)	114.1(5)
C(10)–O(7)	1.20(1)	C(3)–C(2)–O(1)	104.0(4)
C(10)–C(11)	1.47(1)	O(1)–C(2)–O(4)	111.0(4)
C(7)–O(8)	1.40(1)	C(7)–C(2)–C(3)	116.8(5)
C(9)–O(8)	1.40(1)	C(2)–O(4)–C(1)	121.9(5)
C(8)–C(9)	1.46(1)	O(4)–C(1)–O(5)	124.0(6)
C(9)–O(9)	1.19(1)	O(4)–C(1)–C(6)	111.2(5)
C(5)–N	1.52(1)	O(5)–C(1)–C(6)	124.8(6)
O(3)–N	1.22(1)	C(2)–C(7)–O(8)	110.9(5)
O(2)–N	1.20(1)	C(2)–C(7)–O(6)	106.4(5)
		C(7)–O(8)–C(9)	117.6(5)
		O(8)–C(9)–O(9)	121.5(6)
		O(8)–C(9)–C(8)	109.5(6)
		O(9)–C(9)–C(8)	129.0(7)
		C(7)–O(6)–C(10)	116.9(5)
		O(6)–C(10)–O(7)	120.6(6)
		O(6)–C(10)–C(11)	112.0(6)
		O(7)–C(10)–C(11)	127.4(7)

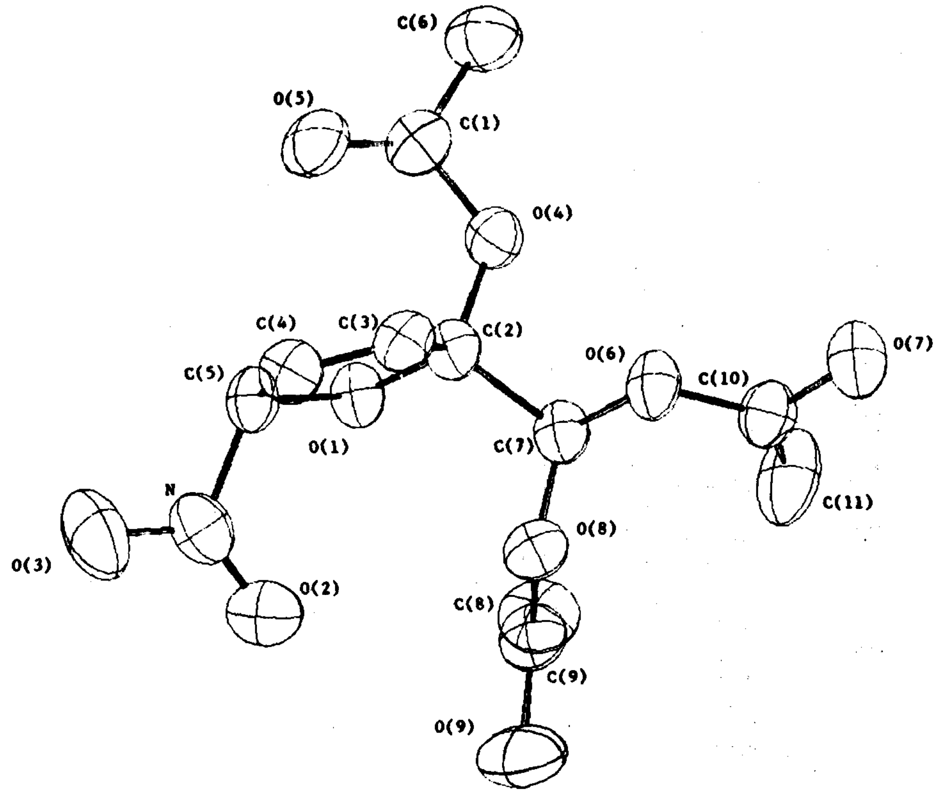
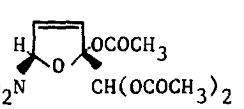


Fig. 1. Structure of adduct **1a**.

The furanoid C–O 1.40 Å distance in the adduct lies between the corresponding values found in furan (1.36 Å) and in 2,5-dihydrofuran (1.43 Å).

The N atom is distorted out of the average plane of the dihydrofuran ring by 1.16 Å in the opposite direction with respect to acetoxy group. Thus, nitro- and acetoxy-groups are *trans*-located with regard to the heterocycle plane. Consequently, the compound has, in fact, the structure of *trans* - 2 - acetoxy - 5 - nitro - 2,5 - dihydro - 2 - furfural diacetate (**1a**).



1a

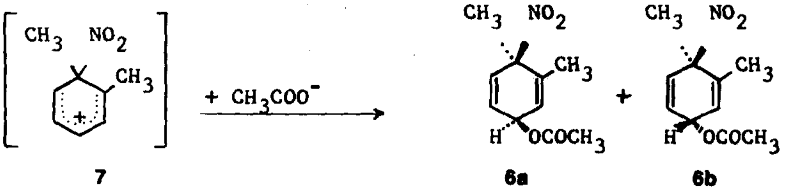
The molecule fragment C(5)–N–O(2)–O(3) is planar and forms a dihedral angle of 69.8° with the dihydrofuran ring. The C(5)–N 1.52 Å bond is considerably longer than the appropriate bonds in nitromethane, nitroethylene and nitrobenzene (1.46, 1.47 and 1.486 Å respectively[17]). This feature is an indication of the weakness of the C–N bond in the adduct **1a** which agrees with its chemical properties. For example, the nitro group in this compound can be readily replaced by a OMe group upon heating an acidified methanolic solution.[14] The average length of N–O(2) and N–O(3) bonds in adduct **1a** is equal 1.21 Å which corresponds to the common length of such bonds in nitro compounds.

The plane molecular fragment C(2)–O(4)–C(7) forms with the dihydrofuran ring a dihedral angle 89.5°. The atoms O(4) and C(7) have an out-of-plane distortion from the average plane of the dihydrofuran ring by −1.19 Å and 1.08 Å respectively. The C–C and C=O bonds in the side chain have standard values, whereas C–O bonds can be divided into two groups: one of them contains typical ester C–O bonds with average length of 1.40 Å, the other one includes shorter bonds (about 1.37 Å).

Intramolecular interaction is effected at distances equal to or exceeding the corresponding sums of van der Waals radii.

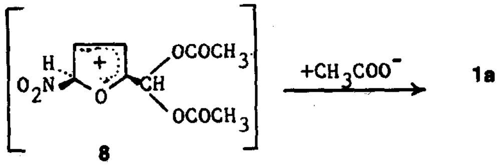
Direct evidence obtained from the X-ray study confirms the structure **1a** for the adduct thus rejecting the structures **2** ÷ **5** proposed earlier.

The addition of acetyl nitrate to aromatic or heteroaromatic compounds almost invariably yields a mixture of *cis*- and *trans*-adducts.[3] In the case of *o*-xylene nitration a mixture of *cis*- and *trans* - 1 - acetoxy - 4 - nitro - 3,4 - dimethyl - 2,5 - cyclohexadienes (**6a** and **6b**) is obtained. It is suggested that these compounds are formed through the carbcation **7** (Wheland intermediate) involving further capture of a nucleophile (CH_3COO^-) to give the diene adducts:



7 **6a** **6b**

The nitration of furfural diacetate with acetyl nitrate predominantly yields the *trans*-adduct **1a**[†]. This is, most likely, due to steric hindrance in the postulated intermediate carbcation **8** (induced by the bulky methanediol diacetate group) diminishing the *cis*-addition of the acetoxy group.



Similar steric specificity for the site of acetyl nitrate attachment was observed during the nitration of 4 - butyl - 1,2 - dimethylbenzene[18] and 1 - phenyl - cyclopentene[19] where *trans*-diastereomers of 1 - acetoxy - 4 - nitro - 1 - butyl - 3,4 - dimethyl - 2,5 - cyclohexadiene and 1 - acetoxy - 2 - nitro - 1 - phenylcyclopentane were obtained as the main products. The preference of *trans*-addition of the acetyl nitrate was also observed in the nitration of 1- phenylcyclohexene (the ratio of *trans*- to *cis* - 1 - acetoxy - 2 - nitro - 1 - phenilcyclohexanes is 3 : 1).[19] These examples of selective *trans*-addition of the acetoxy group is observed, especially at the C atom bearing a rather bulky substituent.

EXPERIMENTAL

The adduct of furfural diacetate and acetyl nitrate[6] was obtained by nitration of furfural diacetate with a mixture of nitric acid and Ac_2O (with H_2SO_4 as catalyst).[20] Isolation and purification of the adduct was performed according to the method described.[13] According to NMR data the purified sample of the adduct (m.p. 109.0–110.5°) contained only a single diastereomer. Single crystals of this compound were obtained from benzene.

Diffraction data were collected at room temp on a Syntex $P2_1$ diffractometer using CuK_α radiation and graphite monochromator. The $\theta/2\theta$ method was used to collect 1669 reflections with $I > 2\sigma$ (σ-standard deviation) from a crystal with dimensions $0.15 \times 0.15 \times 0.30$ mm. $2\theta_{max} = 150°$, μ $CuK_\alpha = 11.3\ cm^{-1}$. No absorption correction were applied.

The structure was solved by direct methods. Eight sets of phases were generated by MULTAN programme. The best E map revealed the positions of all non-H atoms ($R = 0.386$). Full-matrix least-squares isotropic refinement reduced R to 0.178. Two cycles of anisotropic refinement brought this value down to $R = 0.117$.

Difference synthesis yielded coordinates of all H atoms. Those in their turn ($B = 6$ Å) were used for obtaining more accurate data on non-H atoms, yielding $R = 0.103$.

The final refinement (1537 reflections restricted by $\sin 0/\lambda < 0.6$) with a weighting scheme of $w = 1/(\sigma_F{}^2 + 0.0001\ F^2_{obs})$ reduced R to 0.079.

[†] PMR spectra of the crude adduct (m.p. 97–102°) revealed the presence of small amounts (about 12%) of another diastereomer, apparently, *cis* - 2 - acetoxy - 5 - nitro - 2,5 - dihydro - 2 - furfural diacetate.

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