N_2 and irradiated for 1.5 h (95% of the 18DAF was converted into products). The mass spectrum of the insertion product **5** formed in this irradiation indicates that only 2.3% of crossover product was formed.

Sensitization of 18DAF in Cyclohexane with Styrene. Six samples were prepared; each contained 2.4×10^{-3} M 18DAF and 2.6×10^{-2} M benzil in 5 mL of cyclohexane. The samples also contained a variable amount of styrene (0–1.06 M). The solutions were purged with argon and irradiated (Oriel lamp) and then analyzed by GC with methyl stearate added as internal standard. The reaction products and their yields are reported in Table II.

Photolysis of 18DAF in Benzene. A 5×10^{-3} M solution of 18DAF in benzene was purged with Ar and irradiated (Rayonet). The ^{1}H NMR spectrum of the crude reaction mixture showed that the yield of **6** was ca. 75%. This product was isolated by chromatography on silica gel: ^{1}H NMR δ 3.95 (q, J = 2.0 Hz, 2 H), 6.15 (m, 2 H), 6.50 (q, J = 2.0 Hz, 2 H), 7.20 (dd, J = 7.5, 3.0 Hz, 2 H), 7.95 (dd, J = 7.5, 1.5 Hz, 2 H), 8.60 (dd, J = 3.0, 1.5 Hz, 2 H); exact MS for **6** calcd for $C_{17}H_{12}N_2$ m/e 244.0984, found 244.0992.

Reaction of 18DAF with α-Methylstyrene in the Presence of Benzil as a Sensitizer. A 5.15×10^{-3} M solution of 18DAF in benzene containing 1.0 M α-methylstyrene and 4.7×10^{-2} M benzil was purged with argon and irradiated (Oriel lamp) until 90% of 18DAF had disappeared (by GC analysis). Analysis of the reaction mixture by ^{1}H NMR spectroscopy showed that the yield of **6** was <5% and that of **7** was 85%. Compound **7** was isolated from the reaction mixture by chromatography on silica gel eluting with benzene–ether (1:2 v/v): ^{1}H NMR δ 2.0 (s, 3 H), 2.5 (d, 1 H), 2.8 (d, 1 H), 7.1–7.5 (m, 8 H), 8.0 (m, 2 H), 8.5 (m, 1 H); MS (EI), m/e 284.0; exact MS calcd for $C_{20}H_{16}N_2$ m/e 284.1315, found 284.1314.

A similar experiment in which the deuterated α-methylstyrene (0.47 M) was used gave **7** with total randomization of stereochemistry.

Direct Photolysis of 18DAF in Methyl Alcohol. (A) A 3.6×10^{-3} M solution of 18DAF in neat methyl alcohol was purged with argon and irradiated (Rayonet) until 95% of 18DAF was converted into products. ^{1}H NMR spectral analysis gave the yields of the three major products as 1,8-diazafluorene, 16%, the methyl ether **1**, 42%, and dimer **2**, 32%. These products were separated on silica gel eluted with an acetonitrile–ethyl acetate mixture (1:1, v/v). The ^{1}H NMR spectrum ($CDCl_3$) for **1**: δ 3.90 (s, 3 H), 5.10 (s, 1 H), 7.33 (m, 2 H), 7.89 (m, 2 H), 8.59 (m, 2 H). ^{1}H NMR ($CDCl_3$) for **2**: δ 8.30 (m, 2 H), 7.90 (m, 2 H), 7.30 (m, 2 H), 3.10 (s, 3 H); exact MS calcd for $C_{24}H_{18}N_4O_2$ m/e 394.1430, found 394.1428.

(B) A 5.0×10^{-3} M solution of 18DAF was purged with Ar and irradiated for 2 h. The reaction mixture was chromatographed on silica gel eluted with a benzene–acetonitrile mixture (7:3, v/v). This procedure gave 20% of diazirine **4**. This compound has the same GC retention time, mass spectrum, and molecular weight (osmetric) as 18DAF but a different behavior on TLC and a different ^{1}H NMR spectrum. **4** ($CDCl_3$): δ 8.50 (m, 2 H), 8.10 (m, 2 H), 7.38 (m, 2 H). A solution of the purified diazirine in methyl alcohol was heated at 80 °C for 20 min. Analysis of this reaction by ^{1}H NMR spectroscopy showed that **4** had been completely reconverted to 18DAF.

(C) A solution of 18DAF (250 mg in 250 mL of methyl alcohol) was purged with Ar and irradiated at 350 nm. Samples were withdrawn after 5, 10, and 20 min of irradiation and then at 30-min intervals for 6 h. The product yields were determined by analysis of the ^{1}H NMR spectra and are shown on Figure 1.

(D) Several attempts were made to isolate or characterize the unstable product from direct photolysis of 18DAF in methyl alcohol that is responsible for the absorption at δ 3.70. A solution of 18DAF (5×10^{-3} M) in methyl alcohol was irradiated to partial conversion (90 min). At this time the δ 3.70 product reaches its maximum concentration. The solvent was removed under vacuum and chromatographic separation attempted under a variety of conditions. All attempts led to destruction of the desired compound. Related efforts to purify this unstable compound by extraction met with similar failures. Attempted methylation with methyl iodide also failed.

Triplet Sensitization of 18DAF in Methyl Alcohol. A solution of 18DAF in methyl alcohol (5×10^{-3} M, 25 mg) containing 4.7×10^{-2} M benzil was purged with Ar and irradiated with light (>380 nm) until >95% 18DAF had been consumed. The ^{1}H NMR spectrum of the reaction mixture showed that 1,8-diazafluorene was the only product and that its yield was almost quantitative.

Acknowledgment. The 4,7-phenathroline-5,6-dione used in the preparation of 18DAF was a gift from CIBA-Geigy in Basel for which we are very grateful. This work was supported by a grant from the National Science Foundation and a fellowship to Y.-Z.L. from the Ministry of Education of the People's Republic of China.

Registry No. **1**, 103621-87-0; **2**, 103621-88-1; **3**, 244-50-8; 18DAF, 1807-47-2; **4**, 103621-89-2; **5**, 103621-83-6; **6**, 103639-24-3; **7**, 103621-86-9; **9**, 103621-84-7; **13**, 103621-85-8; **3** (ketone), 54078-29-4; 18DAF (carbene), 103621-90-5; 18DAF·$ZnCl_2$, 103621-82-5; DAF, 832-80-4; $ZnCl_2$, 7646-85-7; $C_6H_5CH{=}CH_2$, 100-42-5; $C_6H_5C(CH_3){=}CH_2$, 98-83-9; $H_2NNHC_6H_{11}$·HCl, 24214-73-1.

Nitronium Acetate Adducts of Furan Derivatives

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An improved procedure for the isolation of the main addition products of the reaction between nitronium acetate and furfural diacetate or methyl 2-furoate is described. The kinetics of the deacetylation of the diastereomeric 1,4-adducts in buffer solutions revealed a substantial primary hydrogen isotope effect. Mild acid-induced alcoholysis transformed the adducts into 2,5-dialkoxy-2,5-dihydrofurans. The reaction chemistry of the furan adducts is compared with the solvolytic pathways reported for ipso nitronium acetate adducts formed from alkylbenzenes.

During the past decade it has become a relatively routine matter to prepare and isolate ipso adducts such as **1** by nitration of the appropriate aromatic in acetic anhydride solvent systems.[1] The current view is that such adducts

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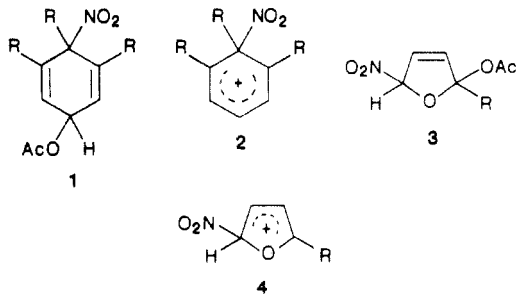


are formed by nucleophilic trapping of ipso ions **2**. Related adducts obtained by nitration of furan and its derivatives, though reported as early as the turn of the century, have been less thoroughly studied.[2] These furan adducts, usually represented as 1,4-adducts, **3**, have been used as intermediates in the synthesis of nitrofurans, which often are not readily accessible by direct nitration in strongly acidic media owing to the sensitivity of the furan ring to strong acids and oxidants.[3-6]

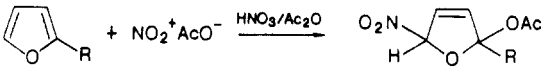
The formation of nitronium acetate adducts of furan indicates that the nitrooxacyclopentenyl cation **4** has sufficient lifetime to be intercepted. For this condition to hold, proton loss to yield a nitrofuran must be relatively slow with respect to nucleophilic capture.

There are formal analogies between nitronium acetate adducts of arenes and furans and there are also differences in behavior that might be anticipated. This investigation is part of an attempt to gain a more general perspective of the chemistry of nitronium acetate adducts of aromatic molecules. While this work was in progress, Venter and co-workers reported new investigations of furan adducts,[7,8] and Greene and Lewis studied the acid-catalyzed solvolysis of a furfural adduct.[9] Recently, Kolb and co-workers identified several adducts of methyl 2-furoate by analysis of their ^{1}H NMR spectra.[10]

Results

The reactions of nitronium acetate with furan, 2-methylfuran, 2,5-dimethylfuran, furufural, and methyl 2-furoate were surveyed. In all cases, NMR spectra of crude product mixtures indicated adduct formation. However, the lability of furan and methyl furan adducts prompted us to investigate initially those of furfural and methyl 2-furoate, adducts which proved to be relatively stable and isolable in crystalline form.

Nitration of furfural or furfural diacetate in acetic anhydride yields a nitronium acetate adduct of furfural diacetate, **5**, in about 80% yield. The ^{1}H NMR resonances

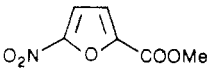


5, R = $CH(OAc)_2$; *Z* and *E*
6, R = $COOCH_3$; *Z* and *E*

of **5** at 7.21 and 7.31 ppm indicate two isomeric adducts. We found that the pure isomers of **5** could be isolated by a modification of the procedure of Srogl and Peterek.[11] During the course of the reaction at −5 °C, spontaneous crystallization occurs, permitting the separation of a fraction composed predominantly (90%) of the higher melting isomer. The pure isomer **5a** (mp 106–107 °C) is usually obtained after one crystallization of this fraction. The filtrate from the separation of the original crystalline fraction yields a second crystalline crop, which is enriched up to 60% in the other isomer, **5b**. More elaborate fractional crystallization steps are often necessary to isolate pure **5b** (mp 96–98 °C). The distribution of **5a** and **5b** in the combined product fractions was 70:30, which is close to the 67:33 ratio for the isomers in the liquid crude product obtained via the Srogl–Peterek method employing an ether extraction of the reaction product from ice–water.

The scatter of reported melting points for **5a** (99–115 °C) in the literature[12] deserves some comment. On occasion, we have isolated **5a** as crystals melting at 115–116 °C, although the lower melting point range (106–107 °C) is more common. The existence of dimorphism of **5a** was first recognized by Kimura, who designated the different crystalline forms as β-crystals (mp 106–107 °C) and α-crystals (mp 114–115 °C).[12] The two forms are interconverted readily. There is no evidence of the interconversion of isomer **5a** and **5b** during isolation and purification, as judged by the differences in the NMR spectra of the isomers.

Nitration of methyl 2-furoate in acetic anhydride is not accompanied by spontaneous crystallization and partitioning of the diastereomers.[13] The procedure of Freure and Johnson[14] results in a combination of a crystalline crude product and a complex, viscous oil fraction. ^{1}H NMR of the crystalline product indicates the presence of isomers of an acetyl nitrate adduct (**6**) and smaller quantities of methyl 5-nitrofuran-2-carboxylate (**7**). Additional



7

low intensity peaks in the acetyl methyl and methoxy carbonyl region suggest the presence of methyl 4-acetoxy-5-nitro-4,5-dihydrofuran-2-carboxylate isomers[10] and of methyl 2,5-diacetoxy-2,5-dihydrofuran-2-carboxylate isomers.[7]

A higher melting diastereomer of **6** is the major component in the crystalline fraction. A lower melting isomer is enriched in the oil fraction together with increased concentrations of the nitrofuran ester **7** and 4,5-dihydrofuran-type adducts.[15] Separation of the constituents of

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(12) See, for example: ref 8, mp 105–107 °C; ref 9, mp 99–104 °C; ref 11, mp 102 °C. Holly et al. (Holly, S.; Troth, G.; Varsanyi, G. *Acta Chim. Acad. Sci. Hung.* **1969**, *61*, 45), mp 109–111 °C; Kimura (Kimura, R. *J. Pharm. Soc. Jpn.* **1955**, *75*, 424), mp 114–115 °C.

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Table I. ^{1}H NMR Chemical Shifts[a] of 1,4-Adducts of Furfural and Methyl 2-Furoate with Nitronium Acetate

		δ							coupling constants J, Hz (1st order)		
compd[b]	mp, °C	$OC(O)CH_3$	$CH(OC(O)CH_3)_2$	$CH(OAc)_2$	$C(O)OCH_3$	3-H	4-H	5-H	J_{34}	J_{45}	J_{35}
5a	107–109	2.06	2.09, 2.13	7.21		6.37	6.55	6.43	5.88	1.47	1.84
5a–d	107–109	2.07	2.11, 2.14	7.23		6.38	6.56		5.88		
5b	98–100	2.10	2.11, 2.14	7.34		6.69[c]	6.50[c]	6.24	5.88	1.84	1.84
6a	99–101	2.18			3.82	6.46	6.52	6.41	5.83	1.46	1.46
6b	75–77	2.14			3.85	6.64	6.47	6.47	6.00	*d*	*d*

[a] Recorded at 250 MHz in $CDCl_3$. [b] Ring protons of **5a,b** and **6a** produce 11 line spectra, which were analyzed as ABX systems (Garbisch, E. W. *J. Chem. Educ.* **1968**, *45*, 311). [c] Tentative assignments for 3-H and 4-H. [d] The ABC spectrum of **6b** could not be resolved completely owing to similar chemical shifts of 4-H and 5-H.

Table II. ^{13}C NMR Chemical Shifts (δ)[a] of 1,4-Nitronium Acetate Adducts of Furfural and Methyl 2-Furoate

	compd			
	5a	**5b**	**6a**	**6b**
C-2	113.55	112.98	108.32	110.55
C-3[b]	130.08	128.97	130.00	129.06
C-4[b]	130.72	132.59	133.32	133.72
C-5	110.81	109.18	110.01	110.28
$CH_3C(O)O$	21.73	21.23	20.52	20.66
$CH_3C(O)O$	168.10	168.14	169.00	169.19
$(CH_3C(O)O)_2CH$	20.51	20.50		
$(CH_3C(O)O)_2CH$	167.94	168.03		
$(CH_3C(O)O)_2CH$	85.74	85.74		
$CH_3OC(O)$			53.62	53.45
$CH_3OC(O)$			165.44	164.85

[a] Recorded at 22.63 MHz in $CDCl_3$. [b] Tentative assignment.

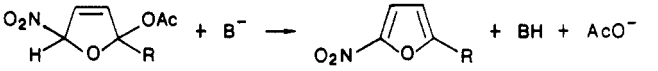
the oil was found to be difficult. Fractional crystallization procedures when applied to the crude crystalline fraction gave isomers **6a** and **6b** with the melting points of 100–101 and 75–76 °C, respectively.

The ^{1}H and ^{13}C NMR data for the isomers of **5** and **6** are collected in Tables I and II.[16]

Thin-layer chromatography of the diastereomers of **5** or **6** on silica gel causes their transformation into 5-nitrofurfural diacetate or **7**, respectively. The deacetylation reaction can be largely suppressed by deactivating the plates through exposure to aqueous acetic acid vapors for 20 h prior to chromatographic development. After evaporation of the solvent, the adduct spots are nearly invisible under UV light but show up gradually and gain in intensity as the conversion to the nitrofuran progresses on the silica layer.

The isomers of **5** and **6** are sufficiently stable to permit crystallization from methanol or ethanol. However, solutions of the adducts in these and other polar solvents exhibit a steady increase of their UV absorption due to the slow transformation into nitrofurans and acetic acid.[17] We noticed, however, that the presence of very small quantities of sulfuric acid (10^{-3}–10^{-5} M) in these solvents effectively inhibited the deacetylation.

The kinetics of deacetylation of the isomers of **5** and **6** was investigated in phosphate and tris buffers. Kinetic data are presented in Tables III and IV.

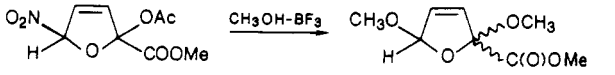


5a,b, R = $CH(OAc)_2$
6a,b, R = $COOCH_3$

Replacement of hydrogen by deuterium at C5 in **5a** reduced the rate markedly. The observed isotope effect, k_H/k_D, ranges from 5 to 8, depending upon the buffer system used. As expected, the reaction rate was found to increase with the pH. General base catalysis was demonstrated for **6** by a buffer dilution plot of k_{obsd} vs. phosphate buffer concentration at constant pH and ionic strength. At pH 7.11, the second-order rate constant $k_{HPO_4^{2-}}$ for **6a** and **6b** was found to be 1.8×10^{-2} and 4.1×10^{-2} M^{-1} s^{-1}, respectively. It should also be noted that the reaction rate was quite sensitive to the nature of the buffer system with approximately threefold rate enhancements on going from phosphate to tris buffers at the same pH. The progress of the elimination can be readily monitored by ^{1}H NMR spectroscopy of a solution of **6a** in acetone-d_6/D_2O containing some pyridine. However, no exchange of 5-H by deuterium and formation of diastereomeric **6b** could be verified in this medium.

The stability of **5a** and **6a** in pure solvents was also examined at higher temperatures (Table V).

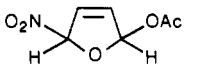
Acid-catalyzed alcoholysis of adducts **5** and **6** results in formation of 2,5-dialkoxy-2,5-dihydrofuran derivatives. We found that boron trifluoroide (10%) in methanol is an effective reagent at room temperature for converting **6a** into the diastereomers of methyl 2,5-dimethoxy-2,5-dihydrofuran-2-carboxylate (**8**). ^{1}H NMR analysis allowed



6a **8**, *Z* and *E*

configurational assignments of the isomers and proved the preponderance of the *Z* isomer analogous to the results reported by Greene and Lewis for **5a**.[9] GLC analysis of **8** gave 2.6/1.0 for the proportions of *Z*/*E*. The mass spectrum of **8** conformed to the fragmentation pattern characteristic of 2,5-dihydrofurans.[18]

Solvolysis of the highly reactive, noncrystalline nitronium acetate adduct of furan, 2-acetoxy-5-nitro-2,5-dihydrofuran (**9**), did not require an acid catalyst. Reaction of **9** in methanol–water (2:1) at room temperature gave



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(15) Kolb et al. have demonstrated the formation of diastereomeric 4,5-dihydrofuran-type adducts as minor products during this nitration by flash chromatography of the oil and ^{1}H NMR analysis of the fractions obtained.[10]

(16) ^{13}C NMR and ^{1}H NMR spectra (analyzed as an AMX system) of **5a** have been reported (Gaset, A.; Gorrichon, J. P. *Org. Magn. Reson.* **1981**, *16*, 239) and are in accord with our data. ^{1}H NMR δ values for **6a** and **6b** are close to those of Kolb et al.[10] However, use of a Laocoon program provided Kolb with more precise coupling constants for **6a** and **6b** than those given in Table I. Kolb also assigned a negative sign to J_{35} to optimize the simulated spectrum.

(17) k_{obsd} for **6a** in CH_3OH (10^{-3} M) was of the order of 10^{-5} s^{-1} by using the method of initial rates. **6a** also reacted with apolar aprotic solvents such as THF but was stable in acetic acid at room temperature. Faster rates were observed in polar aprotic solvents (acetonitrile, Me_2SO). ^{1}H NMR of solutions of **5a** or **6a** in Me_2SO-d_6 indicated only the presence of acetic acid and the respective furans after extended heat treatment (75 °C, 16 h).

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Table III. Rates of Solvolysis of 2-Acetoxy-5-nitro-2,5-dihydrofurans (10^4k, s^{-1}) at 26.5 °C

	buffer[a]					
	$HPO_4^{2-}/H_2PO_4^-$			tris		
compd	pH 7.11	pH 7.36	pH 7.20[b]	pH 7.11	pH 7.29	pH 7.20[b]
5a	7.51 ± 0.21	8.98 ± 0.15	6.7	28.8 ± 0.6	49.3 ± 0.2	25
5b	15.5 ± 2.0	17.0 ± 1.7		33.9 ± 1.4	62.0 ± 2.4	
5a-d	1.55 ± 0.10	1.82 ± 0.06		3.52 ± 0.09	6.61 ± 0.09	
6a		11.5 ± 0.4	7.8			31.7
6b		20.4 ± 0.8	14.2			36.7
$k_H/k_D = k_{5a}/k_{5a-d}$	4.84 ± 0.34	4.93 ± 0.18		8.18 ± 0.27	7.46 ± 0.11	

[a] Buffer solutions were prepared without any added neutral salt to produce an ionic strength of $I = 0.10$. (*Biochemists Handbook*, Long, C., Ed.; Van Nostrand: Princeton, 1961). [b] 2.84 mL of methanolic substrate solution was added to 20.0 mL of a buffer, raising (phosphate) or lowering (tris) the pH of the mixture to 7.20. The presence of methanol (12.4%) lowered reaction rates relative to those measured in aqueous systems given in the other columns.

Table IV. Activation Parameters[a] of 6a and 6b

	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, cal deg^{-1} mol^{-1}
6a	16.2 ± 0.4	−18.3 ± 1.3
6b	17.0 ± 0.9	−14.3 ± 3.1

[a] Computed from linear least-squares analysis of rate constants (mean values of five determinations each) measured at 22.5, 25.0, 27.5, 30.0, and 35.0 °C. Errors represent standard deviations from the least-squares analysis. Composition of the phosphate buffers used was computed for each temperature. For all buffer solutions ionic strength ($I = 0.115$), pOH (6.81), and $[HPO_4^{2-}]$ (0.2884 M) were kept constant by adjustment of $[H_2PO_4^-]$ and [KCl].

Table V. Solvolysis of 5a and 6a in Selected Solvents

adduct	solvent	temp, °C	reacn, time, h	product mp, °C	conversion to Nitrofuran derivative, mol %
5a	acetonitrile	82	21.0	93–95	<2
6a	acetonitrile	82	21.5	84–88	18[a]
6a	ethanol	78	21.0	85–94	16[a]
6a	ethanol	78	2.0	97	<1[a]
6a	toluene	111	6.0	93–95	<2[a]
6a	Me_2SO-d_6	75	2.2		32[b,c]
5a	Me_2SO-d_6	75	1.0		10[b]

[a] Reaction rate is strongly dependent upon purity of adduct. Samples of **6a** of slightly lower mp (93–95 °C) were deacetylated to give pure **7** within 21.0 h. [b] Solvolysis was conducted in a NMR tube. Product was not isolated but directly analyzed by NMR. [c] Batches of **6a**, mp 93–95 °C, underwent deacetylation in this solvent already at room temperature.

52% of pure 2,5-dimethoxy-2,5-dihydrofuran. Integration of the methine proton peaks indicated a Z/E ratio of 69:31. The IR spectrum was identical with that of a commercial product of similar composition (Z/E = 66:34). Yields upon alcoholysis of **9** with other alcohols were found to be lower. In the case of ethanol, for example, only 32% of the diastereomers of 2,5-diethoxy-2,5-dihydrofuran was isolated.

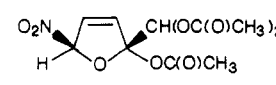
Reaction of **5** and **6** in strong acid gave only recovered starting material. (In some cases, e.g., CF_3COOH, breakdown of the adduct and release of NO_2 vapor was noted.) Thus, stirring a solution of **6a** in $CHCl_3$ with 80% H_2SO_4 failed to induce elimination of acetic acid to give **7**. Instead, the adduct could be recovered in 71% yield. (The stability of **7** in this system was confirmed by a control experiment allowing 87% recovery of **7**.) The balance, presumed to consist of water-soluble ring fission products, was not isolated. Results with **5a** (recovery 39%) were less conclusive, since the potential solvolysis product, 5-nitrofurfural diacetate, was unstable under these reaction conditions. **6a** was also unreactive in THF or acetic acid containing 10% H_2SO_4. Further, the acidic proton at C5 of adduct **6a** in a $CH_3CN/D_2O/D_2SO_4$ solvent failed to undergo isotopic exchange.

Both **5a** and **6a** remained unchanged in the presence of hydrogen chloride in ether/pentane and were recovered quantitatively. However, reaction with hydrogen bromide in methylene chloride proceeded rapidly with the liberation of bromine. With **5a**, the product consisted of large quantities of insoluble black material and was not investigated further. Adduct **6a** and HBr gave a product mixture of methyl 2-furoate and methyl 5-bromo-2-furoate (**10**), based on NMR, HPLC, and TLC data. In the course of product isolation, the spontaneous evolution of both HBr and bromine upon vacuum evaporation of the solvent suggested dibromodihydrofuran derivatives as intermediates. No evidence could be adduced for the presence of **7** or of methyl 2-bromo-5-nitro-2,5-dihydrofuran-2-carboxylate. Reaction of hydrogen iodide with **6a** in methylene chloride gave methyl 2-furoate as the principal product.

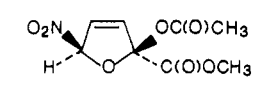
Discussion

The nitronium acetate adducts of furan derivatives have generally been assigned 2,5-dihydrofuran structures.[19] Recently, ^1H NMR data of regioisomeric 1,2-adducts of methyl 2-furoate have been reported by Kolb et al.[10] Adducts resulting from 1,2-addition are formed as minor products only and proved difficult to purify by chromatographic methods due to silica-catalyzed elimination.[10] This discussion is concerned in the main with the crystalline nitronium acetate adducts of furfural and methyl furoate formed by the favored 1,4-addition mode. Three features will be considered: the structure and stereochemical assignment of these adducts, their solvolytic reactivity, and comparisons with the well-known reaction chemistry of nitronium adducts of arenes.

Structure and Stereochemistry. Recent X-ray structures for **5a** and **6a** reported by Venter and confirmed for **6a** by Kolb are in accord with the 2,5-dihydrofuran structural assignments to adducts **5a** and **6a**.[10,20,21] The X-ray data show **5a** to be the E isomer and **6a** to be the Z isomer. Are **5b** and **6b** the corresponding Z and E isomers, respectively? Venter reported the isolation of



5a

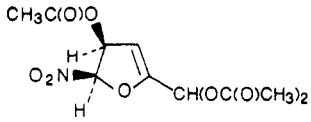


6a

products from the nitration of furfural (or furfural diacetate) and methyl 2-furoate whose properties correspond very closely to those found for **5b** and **6b** in this study.[7,8]

(19) Clauson-Kaas, N.; Fakstorp, J. *Acta. Chem. Scand.* **1947**, *1*, 210.
(20) Mishnev, A. F.; Bleidelis, J. J.; Venter, K. K. *Tetrahedron* **1980**, *36*, 1817.
(21) Venter, K. K.; Kemme, A. A.; Bleidelis, J. J. *Latv. PSR Zinat. Akad. Vestis.* **1980**, *No. 4*, 479.

Venter's group assigned the 4,5-dihydrofuran structures (11 and 12) to these compounds, although the evidence for this assignment does not appear compelling. There are



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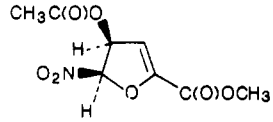
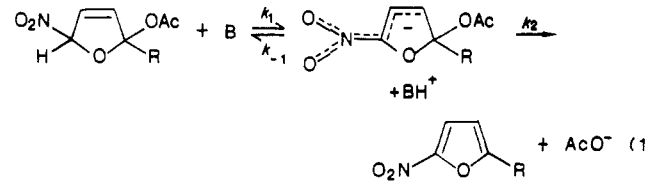


12

several lines of evidence that suggest strongly that **5b** and **6b** are geometric isomers of **5a** and **6a**. The similarity of the ^{13}C NMR resonances for adducts **5a** and **5b** and **6a** and **6b** (Table II) indicate a diastereomeric relation between them. Furthermore, chemical shift correlations support the assignment of both pairs as 2,5-dihydrofurans. Thus, the ^{13}C chemical shifts of carbon atoms in **5a,b** and **6a,b** show little variation. The unsubstituted olefinic carbon atoms C3 and C4 absorb within the range of 130.8 ± 1.8 ppm. Also, the resonances assigned to C2 of these adducts are of low intensity owing to their quaternary character and are found in the 108–113 ppm region. A 4,5-dihydrofuran structure with the olefinic bond between C2 and C3 would have a substantially larger chemical shift for C2 than can be found in the spectra of **5b** and **6b**.[22] Similarly, the close correspondence of the ABX or ABC coupling constants of protons assigned to C3–5 of the adduct isomers (Table I) speaks to diastereomeric relationships. Finally, absence of any allylic coupling between the acylal proton and the C3 proton in **5b** (and insignificant variation of the absorption maximum of **5a**/**5b** and **6a**/**6b** in the UV) support the assignment of **5b** and **6b** as stereomers of **5a** and **6a**, respectively.

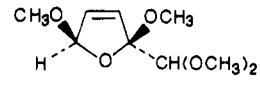
Elimination and Substitution Reactions of 5 and 6. The deacetylation of the nitronium acetate adducts is formally a conjugate, 1,4-elimination (E2′) of the elements of acetic acid to yield aromatic nitrofurans that has been exploited for some time.[3-6] A careful study of the base-induced elimination of **5a** was reported by Michels and Hayes.[23] With the use of a series of carboxylic acid buffers, they demonstrated general base catalysis with a β-value of 0.67. The work reported here is limited to the use of phosphate and tris buffers in the 7.0–7.6 pH range. General base catalysis was demonstrated for the isomers of **6** by linear plots of k_{obsd} vs. phosphate buffer concentration with a value of k_{OH^-} estimated to be 2×10^3 M^{-1} s^{-1}, comparable to that of Michels and Hayes found for **5a**.[23] Within experimental error k_{OH^-} is independent of the stereochemistry of **6**, although the catalysis by hydrogen phosphate is considerably more effective for **5b** and **6b** than it is for their respective stereomers.[24] It is noteworthy that the faster solvolysis rate of the *E* isomer of **6** in phosphate buffer must be attributed to a less negative activation entropy, whereas $\Delta H^{\ddagger}$ of both isomers is similar and even slightly larger for **6b** (Table IV).

The deacetylation may proceed via a stepwise $(ElcB)_I$ elimination which would be facilitated by NO_2 as an EWG combined with activation of H5 and stabilization of the allylic carbanion and by acetate as a fair leaving group[25a]

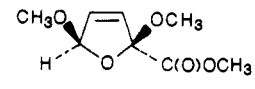


(eq 1). Such a mechanism would be consistent with our findings of lack of deuterium exchange, a sizeable primary deuterium isotope effect, general base catalysis, and small differences between the rate constants of the diastereomers. However, these observations do not rule out a concerted E2 mechanism associated with a driving force by the aromatizing elimination. Studies to provide additional structure–reactivity parameters especially with respect to the sensitivity of the reaction to the pK_a of different leaving groups are planned to distinguish an $(ElcB)_I$-type path from a concerted elimination mechanism.[25]

Solvolysis of **9** occurs under mild conditions in aqueous alcohols at room temperature to yield 2,5-dialkoxy-2,5-dihydrofurans. By contrast, adducts like **5** and **6** bearing an EWG in the 2-position require catalytic amounts of strong acids. Greene and Lewis have explored many aspects of the reaction of **5a** with methanolic hydrogen chloride.[9] They isolated a 3:1 mixture of the *Z* and *E* isomers of 2,5-dimethoxy-2,5-dihydrofurfural dimethyl acetal and assigned the *Z* configuration (**13**) to the more prevalent diastereomer on the basis of chemical shift relationships.[9,26] Since **5a** was assumed to be the *Z* isomer



13



8a

(contrary to Venter's more recent X-ray diffraction data[20]) the moderately stereoselective formation of the *Z* diastereomer **13** was ascribed to an S_N2-type replacement process of both the nitro and acetate groups. Under more vigorous conditions these authors isolated complex mixtures generated from a combination of ring-opening, subsequent rearrangement, and ring-closure steps.[9] We employed boron trifluoride (10%) in methanol as an effective Lewis acid for conversion of **6a** into the diastereomers of methyl 2,5-dimethoxy-2,5-dihydrofuran-2-carboxylate (**8**) at room temperature. The isomers can also be obtained by refluxing of **6a** in methanol/HCl[27] and by electrolytic methoxylation of methyl 2-furoate.[28,29] Sizeable chemical shift differences of the corresponding methoxy protons of **8** permitted the configurational assignment for the isomers.[30] ^1H NMR and GLC analysis of the mixture confirmed again stereoselectivity in favor of the *Z* isomer **8a** analogous to the isomeric distribution of the product obtained from **5a**.[9] Occurrence of small amounts of **7** suggests

(22) Oakes, F. T.; Sebastian, J. *J. Org. Chem.* **1980**, *45*, 4595.
(23) Michels, J. G.; Hayes, K. J. *J. Am. Chem. Soc.* **1958**, *80*, 1114.
(24) Since the faster rate in the diastereomeric pairs is associated with the *Z* isomer of **5** (**5b**) and the *E* isomer of **6** (**6b**) no simple correlation between configuration and k_{obsd} is apparent. It should be noted that **5b** and **6b** both represent the lower melting isomer of each *Z*/*E* pair formed as the minor 1,4-addition product.
(25) For a discussion of distinguishing between $(ElcB)_I$ and E2 mechanisms, see: (a) Bordwell, F. G. *Acc. Chem. Res.* **1972**, *5*, 374. (b) Saunders, W. H. *Acc. Chem. Res.* **1976**, *9*, 19. (c) Keeffe, J. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1983**, *105*, 265.
(26) For other configurational assignments of diastereomeric 2,5-dimethoxy-2,5-dihydrofurans utilizing NMR proximity effects, see: (a) Gagnaire, D.; Vottero, P. *Bull. Soc. Chim. Fr.* **1963**, *2779*. (b) Aito, Y.; Matsuo, T.; Aso, C. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 130. (c) Ross, S. D.; Finkelstein, M.; Uebel, J. J. *J. Org. Chem.* **1969**, *34*, 1018. (d) Achmatowicz, O.; Bukowski, P.; Grynkiewicz, G.; Szechner, B.; Zamojski, A.; Zwierzchowska, Z. *Roczn. Chem.* **1972**, *46*, 879.
(27) Lolya, D. O.; Venter, K. K. *Khim. Geterotsikl. Soedin.* **1977**. *No. 2*, 1600.
(28) Clauson-Kaas N.; Limborg, F. *Acta. Chem. Scand.* **1952**, *6*, 551.
(29) Srogl, J.; Liska, F. *Collect. Czech. Chem. Commun.* **1964**, *29*, 1277.
(30) Since 2-methoxy of the *E* isomer is cis oriented to 5-*H* it should absorb upfield from the 2-OCH_3 signal of the *Z* isomer which is faced by its 5-OCH_3.

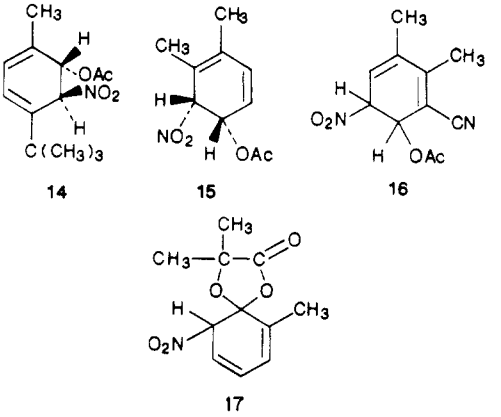
the generation of cation 4 as an intermediate in the methanolysis.

On the basis of these data the reactions of the furan adducts with alcohols under acidic conditions can be viewed as processes involving displacement of both the acetate and the nitro group functions by the nucleophilic reagent. The absence of stereospecificity implies a cationic intermediate in at least one of the stages of the displacement sequence, and the presence of 7 as a byproduct may implicate ions similar to 4.

Adducts 5 and 6 are remarkably resistant toward strong acids if no effective nucleophiles are present. Thus, treatment of **6a** with 80% H_2SO_4 in $CHCl_3$ failed to give 7 by acid-induced elimination of acetic acid. Similarly, attempts to obtain the epimer **6b** in acetic acid/H_2SO_4 were unsuccessful. A complex reaction was observed upon reaction of 5 and 6 with hydrogen bromide instead of HCl gas, which was found to be unreactive. In case of the reaction of HBr with **6a**, a mixture of methyl 2-furoate and 10 was isolated, but 7 was not detected. A reasonable pathway consistent with this result would involve dissociation of cation 4 into NO_2^+ and methyl 2-furoate followed by rapid oxidation of HBr to the halogen. Subsequent addition of bromine to the furan ring would form labile 1,2- and/or 1,4-adducts, which have been reported to aromatize fast at ambient temperature,[31] eliminating hydrogen bromide and bromine during the workup. (Direct electrophilic attack of bromine at the 5-position of methyl 2-furoate is, of course, a competing, parallel pathway to form 10.) The observation that reaction of hydrogen iodide with **6a** produces only methyl 2-furoate is in accord with this view.

Adducts of Furans and Arenes. The extensive studies of Fischer and co-workers have shown that nitronium acetate adducts of arenes can exhibit a very wide range of chemical reactivity which depends greatly on the nature of the substituent group.[32] While the furan adducts investigated here were selected on the basis of their stability and are not necessarily representative of the range of furans, a brief comparison of the chemistry of furan adducts 5 and 6 with that of adducts of arenes is instructive.

The furan adducts are formed regioselectively so that the nitro group is attached to a ring carbon (C5) bearing a hydrogen, i.e., a secondary carbon.[33] This may be contrasted with the adducts of arenes, where the nitro group is fixed at tertiary carbon, with the substituent typically an alkyl group (ipsonitration).[34] Secondary adducts in the benzene series are not observed since the initially formed nitrocyclohexadienyl cation eludes trapping by acetate through rapid deprotonation.[35] Recently, however, Fisher and Bapat have discovered such secondary adducts following thermal rearrangement of tertiary adducts in carbon tetrachloride.[36] Compounds **14–17** are representative. The relative stability of these secondary adducts is related



to steric hindrance around the secondary carbon bearing the nitro group. 1,2-Elimination of acetic acid from 14 requires sodium hydroxide solution. Reaction in more weakly basic systems results in preferential elimination of nitrous acid. The less sterically hindered adduct 15, however, reacts rapidly in methanol to yield the corresponding nitroarene by elimination of acetic acid, and 16 can only be detected in the NMR spectrum at limited concentration.

For the nitronium acetate adducts of furan, furfural, and methyl 2-furoate, which possess a secondary nitro group but unlike 14 lack bulky alkyl substituents close to C5, no enhanced stability with respect to elimination is expected. Solutions of 5 and 6 in polar solvents undergo aromatization very gradually at room temperature by solvolytic loss of acetic acid and are more stable than their counterparts in the arene series such as 15. However, much faster rates are observed in solvents containing significant concentrations of weak bases. Our data indicate that $(ElcB)_I$- and/or E2-like mechanisms account for the 1,4-elimination of acetic acid from 5 and 6. Likewise, a variable E2 transition state has been proposed by Bapat for the ring-opening mechanism of the secondary arene adduct 17.[36b] Tertiary adducts of arenes, however, due to their structural limitations give rise to an entirely different reaction chemistry. Since the nitro group is ipso to methyl instead of a proton, no elimination of acetic acid is feasible.[37] Instead, solvolysis of simple adducts such as 1 in aqueous ethanol will quickly give phenyl acetates via 1,4-elimination of the elements of nitrous acid. Under the conditions of study, the 1,4-elimination in 1 appears to follow an E1 mechanism with no significant involvement of the carbon–hydrogen bond cleavage in the rate-limiting step.[1c] The lability of adducts such as 1 in aqueous systems has impeded detailed study of base-induced eliminations.

Relatively little is known about the mechanistic details and stereochemical preferences of conjugate 1,4-eliminations.[38] The availability of several 1,4-adducts of the furans make future studies of the base-catalyzed 1,4-elimination of acetic acid and other leaving groups attractive.

Significantly, there is no evidence of acid-promoted intramolecular nitro group migration with adducts 5 or 6 under any reaction conditions investigated. It will be of interest to search for this reaction with tertiary adducts derived from furan systems carrying less deactivating substituents at both the 2- and 5-positions of the ring.

(31) Baciocchi, E.; Clementi, S.; Sebastiani, G. V. *J. Chem. Soc., Chem. Commun.* **1975**, 875.

(32) (a) Fischer, A.; Craig, C. C. *Can. J. Chem.* **1978**, *56*, 1063. (b) Fischer, A.; Seyan, S. S. *Can. J. Chem.* **1978**, *56*, 1348.

(33) Nucleophilic interception of the Wheland intermediate 4 at the nonequivalent allylic positions 2 and 4 would account for the distribution of 1,4- and 1,2-adducts as major and minor regioisomers.

(34) Addition of acetate to intermediate 2 forms exclusively 1,4-nitrocyclohexadienyl acetates unless steric crowding of the substrate makes 1,2-addition competitive resulting in a mixture of both types of adducts.[1f]

(35) Cross, G. G.; Fischer, A.; Henderson, G. N. *Can. J. Chem.* **1984**, *62*, 2803.

(36) (a) Bapat, G. S.; Fisher, A.; Henderson, G. N.; Raymahasay, S. *J. Chem. Soc., Chem. Commun.* **1983**, 119. (b) Bapat, G. S. Ph.D. Dissertation, University of Victoria, Victoria, B. C., Canada, 1983.

(37) Protonation of a tertiary adduct in strong acid, however, induces departure of the acetate function and the incipient cation 2 is aromatized to a nitro arene after migration of the nitro group to an unsubstituted carbon and elimination of a proton.[1b,32a]

(38) (a) Overton, K. H. *Chem. Soc. Rev.* **1980**, 447. (b) Hill, R. K.; Bock, M. G. *J. Am. Chem. Soc.* **1978**, *100*, 637. (c) Tuschka, T.; Katsuyuki, N.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 70. (d) Moss, R. J.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 3694.

Experimental Section

Materials. Methyl 2-furoate,[39] methyl 5-bromo-2-furoate,[40] furfural diacetate,[41] and 2-furfuraldehyde diethyl acetal[42] were prepared by the literature procedures. 2-furfuraldehyde-*5-d* was obtained by lithiation of 2-furfuraldehyde diethyl acetal and subsequent reaction with deuterium oxide following the procedure of Chadwick.[43]

General Methods. Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Infrared spectra were taken on a Beckman Acculab 2 infrared spectrometer. Routine ^1H NMR spectra were recorded on Varian Associates spectrometers, Models A-60, T-60, and EM 360L. High-resolution ^1H NMR spectra were obtained on a Bruker WM-250 spectrometer, and ^{13}C NMR spectra on a Bruker WH 90 spectrometer. The chemical shifts are reported in ppm (units) relative to internal $SiMe_4$ in $CDCl_3$ solution. UV absorption measurements were made on a Cary 118 spectrometer. Thin-layer chromatography was performed on commercial plates (E. Merck Silica Gel 60 F-254 and Baker Si-C_{18}-F). Visualization was accomplished with ultraviolet light and/or 2,4-dinitrophenylhydrazine in aqueous hydrochloric acid. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

Kinetic Measurements. Phosphate and tris buffer solutions were made up from the buffer species alone to give an ionic strength of 0.10. Reactions were initiated by injecting 1 μL of the THF solution of the substrate into the thermostated quartz cuvette containing 3.0 mL of the buffer. The appearance of the nitrofuran absorptions was followed at 303 and 309 nm for the isomers of **6** and **5**, respectively. Pseudo-first-order rate constants were computed from the slopes of log $(A_\infty - A_t)$ vs. time or from Guggenheim plots. Linear slopes of the data were achieved over four to five half-lives.

2-Acetoxy-5-nitro-2,5-dihydrofurfural Diacetate (5). Isolation of Stereoisomers 5a and 5b. A 250-mL three-neck flask equipped with a stirrer, thermometer, and a dropping funnel was charged with 40.0 mL of acetic anhydride. To the cooled (−5 °C), well-stirred liquid was added dropwise a mixture of nitric acid (7.0 mL, 0.105 mol, 70 wt %) and sulfuric acid (0.04 mL) over 12 min. A solution of redistilled furfural (8.2 mL, 0.099 mol) in 20 mL of acetic anhydride was dropped into the cooled (−3 to −6 °C), stirred mixture over 70 min. Stirring at −5 °C was then continued for 4 h. The crystalline precipitate was collected by suction filtration, washed with ice–water, and dried in a desiccator over KOH at 5 °C to yield crude **5a**, 10.4 g (34%), mp 97–100 °C. NMR spectra indicated the presence of 8% **5b**. Recrystallization of 5.18 g of **5a** from methanol (83 mL) afforded 3.79 g of pure **5a**: mp 107–109 °C (lit.[11,23] mp 107–108, 105–107 °C); IR (KBr) 3140, 1790, 1780, 1640, 1585, 1444, 1380, 1225, 1152, 1138, 1098, 1065, 1040, 1027, 948, 862, 830, 800, 777 cm^{-1}; UV (THF) 287 nm (ϵ 74 M^{-1} cm^{-1}).

Isomer **5b** was isolated from the filtrate of the reaction mixture. This filtrate was poured on 100 g of ice and 100 mL of water and stirred for 15 h at 5 °C. Filtration of the crystalline product gave 13.2 g (44%) of crude product, mp 69–74 °C, which by NMR consisted of 45% **5a** and 55% **5b**. Fractional crystallization of 2.09 g of **5b** from 10.0 mL of ethanol–methanol (1:1) with cooling to room temperature and filtration after about 20% of the material had crystallized gave 0.399 g of purified **5b**: mp 96–102 °C; IR(KBr) 3135, 1785, 1775, 1632, 1580, 1442, 1382, 1252, 1205, 1145, 1097, 1045, 1022, 945, 932, 852, 826, 790 cm^{-1}; UV (THF) 295 nm (ϵ 130 M^{-1} cm^{-1}). Anal. Calcd for $C_{11}H_{13}NO_9$: C, 43.57; H, 4.32; N, 4.62. Found: C, 43.57; H, 4.28; N, 4.63.

A run conducted at five times this scale gave comparable results, 83% of crude **5a** and **5b**. The Srogl–Peterek procedure[11] employing ether extractions produced a viscous yellow oil from which **5a**, mp 115–118 °C, was isolated. The ^1H NMR spectra of the two samples of **5a** isolated by different methods were identical. Small amounts of 5-nitro-2-furfural diacetate and other impurities were noted in the crude fraction containing **5b** and in the oil product isolated by the Srogl–Peterek method. Nitration of furfural diacetate (19.8 g, 0.10 mol) in 20.0 mL of acetic anhydride in place of furfural reduced the yield of the crude fraction of **5a** to 20% (mp 101–103 °C) but increased the fraction of crude **5b** to 53% (mp 72–78 °C).

Methyl 2-Acetoxy-5-nitro-2,5-dihydro-2-furancarboxylate (6). Isolation of isomers 6a and 6b. Nitric acid (14.0 mL, 0.30 mol, 90 wt %) was added dropwise with mechanical stirring to a cooled (0 °C) 60-mL sample of acetic anhydride. A solution of methyl 2-furoate (25.2 g, 0.20 mol) in 40 mL of acetic anhydride was added over 45 min to the stirred mixture at −28 to −30 °C. Stirring was continued at −30 °C for 130 min. The solution was poured on 250 g of ice in 500 mL of water and stirred for 25 min. The supernatant aqueous liquid was decanted and the residue stirred with 400 mL of water. The semisolid precipitate was separated from a heavy oil by filtration, triturated with cyclohexane, and air-dried: 24.5 g, mp 65–84 °C. Recrystallization from methanol (65 mL) gave 11.2 g, mp 96–98 °C. A second crystallization from ethanol afforded 9.6 g of **6a**: mp 99–101 °C (lit.[7] mp 99–101 °C); IR (KBr) 3125, 1775, 1755, 1625, 1570, 1453, 1435, 1372, 1290, 1270, 1220, 1190, 1142, 1115, 1038, 1020, 939, 908, 842, 802, 767, 700 cm^{-1}; UV (AcOH) 285 nm (ϵ 92 M^{-1} cm^{-1}); (10^{-3} M H_2SO_4, CH_3OH) 285 (ϵ 101 M^{-1} cm^{-1}). The methanolic filtrate from crude **6a** was cooled to −25 °C. After 15 h, a crystalline precipitate (5.3 g, mp 88–92 °C) was filtered off, and the filtrate was evaporated at reduced pressure to give an oil (6.9 g). The oil was dissolved in a mixture of methanol (10 mL) and ethanol (15 mL) and stored at −25 °C. After 4.5 h, the crystalline deposit was filtered, washed (cold ethanol), and dried to yield 2.23 g of crystalline material, mp 69–73 °C. Recrystallization from methanol (6.0 mL) gave 1.12 g, mp 75–77 °C of isomer **6b**. Additional **6b** (0.75 g) was recovered by chilling the filtrate to −25 °C: IR (KBr) 3100, 1755, 1745, 1626, 1572, 1495, 1448, 1436, 1370, 1299, 1267, 1238, 1200, 1160, 1110, 1053, 1015, 986, 920, 851, 825, 797, 779, 766 cm^{-1}; UV (AcOH) 283 nm (ϵ 84 M^{-1} cm^{-1}), (10^{-3} M H_2SO_4, CH_3OH) 283 (ϵ 77 M^{-1} cm^{-1}). Anal. Calcd for $C_8H_9NO_7$: C, 41.56; H, 3.92; N, 6.06. Found: C, 41.52; H, 3.81; N, 5.98.

2-Acetoxy-5-nitro-2,5-dihydrofufural-*5-d* Diacetate (5a-*d*). The procedure employed followed the outline given for **5a** except that furfuraldehyde-*5-d* (8.6 g, 0.0885 mol) in 20.0 mL of acetic anhydride was added. Crude product, **5a**-*d*, 9.7 g, mp 97–100 °C, was isolated, and recrystallization of 4.58 g of this material from 37 mL of methanol gave 3.65 g of **5a**-*d*: mp 107–109 °C; IR (KBr) 3140, 1790, 1780, 1635, 1580, 1444, 1379, 1225, 1205, 1140, 1095, 1060, 1046, 1025, 970, 945, 908, 823, 790, 760 cm^{-1}. Anal. Calcd for $C_{11}H_{12}DNO_9$: C, 43.42; H + D, 4.64; N, 4.61. Found: C, 43.37; H + D, 4.38; N, 4.65.

Formation of 5-Nitrofurfural Diacetate from 5. Triethylamine (1.6 mL, 12 mmol) was added dropwise to a stirred solution of 3.0 g of **5a** (5 mmol) in 15.0 mL of acetone at 0 °C. After 30 min the solution was added in small portions to 60 mL of water at 0 °C. After 1 h, the precipitate was filtered, washed with ice–water, and dried: 2.14 g (88%), mp 91–92 °C (lit.[4] mp 92.5 °C). By a similar procedure 5-nitrofurfural diacetate was obtained in 87% and 74% yields from crude fractions of **5a** and **5b**, respectively.

Formation of Methyl 5-Nitrofuran-2-carboxylate (7) from 6. Triethylamine (1.0 mL, 7 mmol) was added to 1.15 g (5 mmol) of **6a** in 3.0 mL of methanol. Dilution with water (10 mL) after 2 h afforded **7** (0.80 g, 94%), mp 80–81 °C. Recrystallization from methanol gave the material: mp 81–82 °C (lit.[14] mp 81.6 °C); ^1H NMR ($CDCl_3$) δ 3.98 (s, 3 H, COOMe), 7.30, 7.35 (dd, 2 H, J_{AB} = 3.6 Hz), 3-H, 4-H). **7** was also obtained from **6b** and the crude product in yields of 63% and 72%, respectively.

Pyridine-Catalyzed Formation of 7. 6a (50 mg, 2.2 mmol) was dissolved in a mixture of 0.30 mL of acetone-d_6 and 0.05 mL of D_2O. Deacetylation was initiated by addition of 1 drop of pyridine, and the progress of the reaction was monitored by NMR. Peaks of equal intensity developed at 2.02 and 3.98 ppm (AcOH and **7**) in step with decreasing peak heights of the CH_3 singlets of **6a**. Isomerization and H/D exchange indicating the presence of **6a**-d_5 and **6b**-d_5 was not observed.

Reaction of Adducts with Organic Solvents. Samples of **5a** or **6a** (ca. 90–120 mg) were refluxed in 5.0 mL of solvent, which

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was then evaporated in vacuo. Acetic acid was removed from the product (20-h storage in desiccator over NaOH) before mp and ^{1}H NMR were taken. Results for selected solvents are shown in Table V.

Reactions of Adducts with Sulfuric Acid. (a) Isomer **6a** (0.216 g) was dissolved in 8.0 mL of chloroform and stirred magnetically with 5.0 mL of 75 wt % of sulfuric acid at room temperature. After 30 min, the mixture was poured on 30 g of ice. The chloroform solution was washed twice with water, dried (Na_2SO_4), and evaporated at reduced pressure: 0.110 g (51%), mp 97–99 °C, with an NMR spectrum identical with that of **6a**. (b) Stirring of 0.259 g of **6a** in 6 mL of CH_2Cl_2 with 6.0 mL of 80 wt % sulfuric acid at 0 °C for 5 min resulted in recovery of 0.184 g (71%) of **6a**. (c) Methyl 5-nitrofuroate (**7**) (0.216 g) in 5.0 mL of chloroform was subjected to the same reaction conditions as in a, resulting in recovery of 0.189 g (87%), mp 80–81 °C, of starting material. (d) **6a** (96 mg) was dissolved in a solution of 3.0 mL of acetonitrile and 1.0 mL of D_2O. After addition of 0.08 mL of D_2SO_4 the solution was kept at ambient temperature for 22 h. Workup gave 74 mg (77%) of **6a**, mp 95–98 °C. (e) **6a** (129 mg) was dissolved in 2.0 mL of acetic acid. The solution was acidified by adding 0.20 mL of concentrated H_2SO_4 at 0 °C. The cold solution was quenched after 6 min with 4 mL of brine solution and extracted with methylene chloride. Workup gave 110 mg (85%) of **6a**, mp 98–100 °C. (f) The reaction of **5a** (0.304 g) in 5.0 mL of chloroform and 5.0 mL of 75 wt % of sulfuric acid with normal workup gave 0.118 g (39%), mp 111–114 °C, with NMR indicating unchanged **5a**. (g) Application of the same procedure to 0.243 g of 5-nitrofurfural diacetate gave 0.074 g of a mixture of 5-nitrofurfuraldehyde as the major product together with some unreacted starting material as analyzed by NMR.

Reactions of 5a and 6a with Hydrogen Halides. (a) A suspension of **6a** (0.295 g) in 4 mL of ether and 16 mL of pentane was treated with a stream of hydrogen chloride at −5 °C for 20 min. After 1 h the mixture was allowed to reach room temperature, and the solvent was evaporated at reduced pressure to yield 0.287 g (97%), mp 99–100 °C, of recovered **6a**. (b) Similarly, reaction of 0.460 g of **5a** gave 0.416 g (90%), mp 108–109 °C, of unchanged starting material. (c) A slow stream of hydrogen bromide was passed through a solution of **6a** (0.753 g) in 15 mL of methylene chloride at −5 °C (15 min). The brown solution was stored at ambient temperature for 10 min, poured on ice, and washed with sodium bicarbonate solution and water. The solution was dried (sodium sulfate) and evaporated at reduced pressure at room temperature. The residue evolved hydrogen bromide and bromine vapor (positive fluorescein test). After additional pumping 0.627 g was isolated. The ^{1}H NMR spectrum of the oil showed the superimposed signals of methyl 2-furoate and methyl 5-bromo-2-furoate (**10**) as the only major constituents. TLC (silica gel, 4:1 cyclohexane/ether) confirmed the NMR spectrum. No methyl 5-nitro-2-furoate (**7**) could be detected. Preparative TLC allowed the separation and identification of **10** by NMR. (c) Hydrogen iodide (generated from hydroiodic acid and phosphorus pentoxide) and argon was passed into a solution of **6a** (0.304 g) in methylene chloride (15 mL) at −5 °C for 20 min. The solution turned brown rapidly and was kept in an ice–salt bath for 90 min. After additional 3.5 h at room temperature the solution was poured on ice and washed with sodium bicarbonate, sodium bisulfite, and brine solutions. The usual workup gave 0.156 g of an oil. IR and NMR spectra of this substance were identical with those of methyl 2-furoate.

Preparation and Methanolysis of 2-Acetoxy-5-nitro-2,5-dihydrofuran (9). Isolation of (*E*)- and (*Z*)-2,5-Dimethoxydihydrofuran. Acetoxy-5-nitro-2,5-dihydrofuran was prepared by addition of 14 mL of 90% nitric acid (21.0 g, 0.30 mol) with vigorous stirring to 60 mL of acetic anhydride at 4 °C. Next, the temperature was lowered to −18 °C (dry ice) and a solution of furan (20.4 g, 0.30 mol) was added with stirring over a period of 1.5 h while the temperature was maintained between −20 and −25 °C. The solution was poured on 250 g of ice in 500 mL of water and stirred for 30 min. The supernatant aqueous phase was decanted, and the heavy oil was taken up in ether, neutralized with sodium bicarbonate solution, and washed with water. After drying (magnesium sulfate), the solution was concentrated at reduced pressure (water aspirator vacuum, then 5 torr) to yield 28.8 g of an orange colored oil. Ether extraction of the aqueous phase gave additional product (10.5 g). On standing at room temperature, the adduct decomposes, giving off vapors of nitrogen dioxide.

Treatment of **9** (20.1 g, 0.116 mol) with 100 mL of methanol and 50 mL of water for 5 days at room temperature gave, upon workup by dilution with water and extraction with methylene chloride, followed by washing with sodium bicarbonate solution, 10.9 g of a yellow oil. Distillation gave 7.6 g (50.4%) of a clear oil: bp 62–63 °C (20 torr), n^{23}_D 1.4331 [lit.[44] bp 80–82 °C (50 torr), n^{25}_D 1.4333]; ^{1}H NMR ($CDCl_3$) δ 3.23 (s, 6 H, OCH_3 *E*), 3.26 (s, 6 H, OCH_3 *Z*), 5.42 and 5.65 (s, 2 H, methine hydrogens of *Z* and *E* isomers), 5.83 (s, 2 H, 3-H, 4-H). The integrals of the well-separated methine signals gave a ratio of *Z* to *E* isomers equal to 69:31. At the end of the distillation a slightly higher boiling cut (0.50 g) showed the expected enrichment of the higher boiling *E* isomer.

Methanolysis of Methyl 2-Acetoxy-5-nitro-2,5-dihydro-2-furancarboxylate (6a) in the Presence and Absence of Boron Trifluoride. Isolation of (*E*)- and (*Z*)-Methyl 2,5-Dimethoxy-2,5-dihydro-2-furancarboxylate. Diastereomer **6a** (6.35 g) was added to 62 mL of methanol solution containing boron trifluoride (10%), and the mixture was kept for 3 days at room temperature. Within 20 h all crystals of **6a** had dissolved. After 3 days 6.0 mL of triethylamine was added to the stirred solution at 0 °C (in 0.5 mL increments). The neutralized solution was concentrated at reduced pressure, and the residue was dissolved in 25 mL of brine solution, which was then extracted four times with 25-mL portions of ethyl ether. The usual workup gave 4.9 g of an oil, which was purified by distillation to give a main fraction: 3.6 g, bp 86–87 °C (1 torr), n^{25}_D 1.4477; fraction 2, 0.41 g, bp 87–89 °C (1 torr), n^{25}_D 1.4500 [lit.[28] bp 119–121 °C (13–14 torr), n^{25}_D 1.4476]; total yield 77%. Analysis by capillary gas chromatography at 125 °C gave the following distributions of the diastereomers: main fraction, Z/E = 72.2/27.8; fraction 2, Z/E = 74.4/25.6; NMR ($CDCl_3$) δ 3.25 (s, 3 H, 5-OCH_3 *E*), 3.31 (s, 3 H, 5-OCH_3, *Z*), 3.41 (s, 3 H, 2-OCH_3 *E*), 3.53 (s, 3 H, 2-OCH_3, *Z*), 3.80 (s, 3 H, $COOCH_3$), 5.65–6.3 (m, 3 H, 4-H, 5-H); IR (neat) 3100, 2830, 1753, 1745, 1630, 1440, 1375, 1340, 1275, 1195, 1060, 1030, 830, 800, 760, 720 cm^{-1}; mass spectrum, *m/e* (relative intensity) 188 (M^+, 0.1), 157 (34), 130 (7), 129 (100), 113 (7), 102 (4), 101 (65), 98 (19), 83 (14), 69 (6), 59 (15), 55 (20), 45 (4).

Diastereomer **6a** (0.699 g) was dissolved in a mixture of 12 mL of methanol and 8 mL of water. The solution was stored at room temperature for 4 days. Evaporation of the solvent resulted in recovery of unchanged starting material.

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Registry No. **5a**, 75631-81-1; **5a**-*d*, 103752-24-5; **5b**, 75631-82-2; **6a**, 57505-57-4; **6b**, 57505-58-5; **7**, 1874-23-3; **8a**, 103752-25-6; **8b**, 103752-26-7; **9**, 28104-26-9; **10**, 2527-99-3; furfural, 98-01-1; methyl 2-furoate, 1334-76-5; furfuraldehyde-5-*d*, 38443-19-5; 5-nitrofurfural diacetate, 92-55-7; furan, 110-00-9; (*E*)-2,5-dimethoxydihydrofuran, 5143-08-8; (*Z*)-2,5-dimethoxydihydrofuran, 5143-07-7.

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