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The synthesis and properties of twelve 2-substituted 3,5-dinitrofurans are described. These derivatives include bromo-, iodo-, azido-, hydroxy-, amino-, 3,5-dinitro-2-furanyl-, 5-nitro-2-furanyl-, acetamido-, and carbamate compounds.

J. Heterocyclic Chem., **16**, 477 (1979).

Introduction.

The nitration of furan and its derivatives is complicated by the susceptibility of the furan nucleus to the oxidizing and acidic properties of many nitrating agents. For the preparation of mononitrofurans, acetyl nitrate is the usual nitrating agent and often the furan starting materials contain electronegative substituents which stabilize the furan ring toward oxidizing and acidic reagents (1) (2). Although the stabilizing effect of the nitro group on the nucleus of mononitrofurans allows further nitration with stronger nitrating agents (3), extremely few dinitrofurans have been reported in the literature. Efforts at this laboratory have produced a number of new dinitrofurans whose synthesis and properties are described in this paper (4).

Results and Discussion.

A. Preparation of 2-Bromo-3,5-dinitrofuran.

Nitration of 2-bromo-5-nitrofuran gave 2-bromo-3,5-dinitrofuran, although in low yield, presumably due to oxidation of the furan nucleus by the nitrating medium (large amounts of bromine were liberated during the course of the reaction). The structure assignment for I, with the entering nitro group adjacent to the bromine atom, is based on literature assignments for products resulting from electrophilic attack on 2,5-disubstituted

furans containing one positive and one negative substituent. Many such products have been described, and in all cases, the entering electrophilic group occupies the position adjacent to the positive, *o,p*-directing substituent (5). For example, the nitrations of 5-methyl-2-furoic acid and 5-methyl-2-nitrofuran gave the products with the nitro group adjacent to the methyl substituent (6) (3).

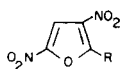
B. 3,5-Dinitrofuran Derivatives Prepared from 2-Bromo-3,5-dinitrofuran.

2-Iodo-3,5-dinitrofuran (II) and 2-azido-3,5-dinitrofuran (III) were prepared by treatment of I with potassium iodide and sodium azide, respectively. Both I and II were converted to 3,3',5,5'-tetranitro-2,2'-bifuran (IV) *via* the Ullmann reaction but the yields with II are considerably better. Nitration of 5,5'-dinitro-2,2'-bifuran gave the trinitro derivative, 3,5,5'-trinitro-2,2'-bifuran (V) (7), but further nitration of V to IV could not be accomplished.

C. Reaction of 2-Bromo-3,5-dinitrofuran on Silica Gel.

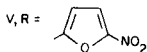
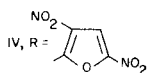
The bromodinitrofuran I, when adsorbed on silica gel, is slowly converted to a bright yellow product that can be removed with acetone. The product is an acidic, water soluble compound that is very sensitive to impact and explodes without melting in the vicinity of 140°. A freshly prepared sample of the yellow product showed only one spot by tlc analysis (benzene-ether-ethanol, 50/30/20) but after standing for several hours (in the dark) it was no longer totally soluble in acetone or methanol, and tlc of the solution showed origin material in addition to the main spot (8). The infrared spectrum of the yellow product shows a strong carbonyl peak at 1745 cm^{-1} along with a medium to weak hydroxyl absorption at 3700-3400 cm^{-1} . The nmr spectrum (methanol- d_4) consists of only a singlet (7.70 ppm); presumably the acidic proton in the yellow product would exchange with the water present in the nmr solvent and not be observed separately.

It may be speculated that the yellow product formed from I is the hydrolysis product, 2-hydroxy-3,5-dinitrofuran (VI), or one of its tautomeric keto forms (VIa, VIb). In general both 2- and 3-hydroxyfurans have a strong tendency to exist in the keto form (9). However, this tendency can be reversed if the enol form is stabilized by

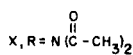
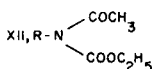


I, R = Br

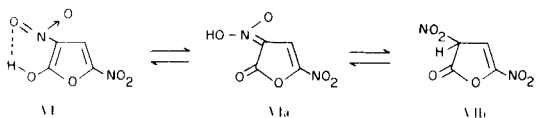
II, R = I

III, R = N₃

VI, R = OH

VII, R = NH₂VIII, R = NHCOOC₂H₅IX, R = NHCOO *t*-ButylXI, R = NHCOCH₃

hydrogen bonding of the hydroxyl hydrogen to an adjacent group (10). Although stabilization by hydrogen bonding appears possible for VI, the infrared spectrum of the yellow product shows carbonyl absorption which would suggest the presence of at least some keto form (VIa or VIb).



D. 3,5-Dinitro-2-furanamine. Its Precursors and Derivatives.

The synthesis and physical properties of 3,5-dinitro-2-furanamine (VII) have not been reported in the literature although physiological properties of this compound have been described (11). We had hoped to prepare VII from ethyl (3,5-dinitro-2-furanyl)carbamate (VIII), a compound described in the literature (12), but attempts to hydrolyze VIII to VII were unsuccessful. However, the analogous *t*-butyl derivative, *t*-butyl (3,5-dinitro-2-furanyl)carbamate (IX), is readily hydrolyzed to give VII. The carbamate (IX) was prepared by nitration of *t*-butyl (5-nitro-2-furanyl)carbamate, which was obtained from thermolysis of 5-nitro-2-furoyl azide in *t*-butyl alcohol. Compound IX sinters at 130-140° and then melts at 154°, the same melting point as for crude VII. Tlc analysis of a sample of IX which had been heated at 130-140° showed it was converted to VII, apparently by loss of carbon dioxide and isobutylene.

In company with other known furanamines, VII did not undergo many of the normal reactions of aromatic amines (13); 2,3,5-trinitrofurane could not be prepared from VII by the usual diazotization or oxidation methods. With acetic anhydride (pyridine as catalyst), VII readily forms the diacetyl derivative (X) along with the expected monoacetyl compound (XI). Similarly, the ethyl carbamate (VIII) under the same conditions forms the acetyl derivative XII.

EXPERIMENTAL

Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. The nmr spectra were determined on a Varian HA 100 spectrometer and the chemical shifts are relative to tetramethylsilane. The melting points are uncorrected.

2-Bromo-3,5-dinitrofurane (I).

The procedure of Nazarova and Novikov (14) was used for the preparation of 2-bromo-5-nitrofurane from 5-bromofuroic acid (100 g.). The reaction mixture was poured onto ice and the 2-bromo-5-nitrofurane was extracted with 3 x 200 ml. of methylene chloride. The combined methylene chloride extracts were washed with water (400 ml.) and then stirred with 500 ml. of water while 60 g. of sodium bicarbonate was added in portions. The methylene chloride layer was dried over magnesium sulfate, filtered, and cooled in ice. The ice cold solution was added with good stirring over a 20 minute period to a mixture of 150 ml. of 90% nitric acid and 150 ml. of concentrated sulfuric acid cooled at -10°. The mixture was stirred at -8 to -5° for 1 hour and then poured onto ice. The dark red brown methylene chloride layer was dried over magnesium sulfate, filtered, and

placed in the hood to allow the solvent to evaporate (15). The liquid residue (62 g.) was stirred vigorously with 200 ml. of distilled water while cooling in ice. An exothermic reaction (with evolution of brown fumes) slowly began which raised the temperature to 20° (16). When the temperature began to fall (after ca. 15 minutes), the ice bath was removed and the mixture was stirred rapidly at 20-22° for 3.5 hours. The insoluble semisolid material was removed and stirred with 20 ml. of methanol at ambient temperature for 10 minutes. Dilute hydrochloric acid (40 ml.) was slowly added and the insoluble material was removed from the cooled mixture and washed with cold water to give 12.4 g. of product, m.p. 55-60°. The product was dissolved in 700 ml. of boiling hexane, the hot solution was decanted from a small amount of insoluble material and cooled to give 8.6 g. of cream colored crystals, m.p. 78-80° (14% yield from 2-bromo-5-nitrofurane) (17). Recrystallization from hexane raised the melting point to 81-82°; nmr (benzene): δ 6.38 (s); ms: 238, 236 (M^+ , bromine isotopes).

Anal. Calcd. for $C_4HBrN_2O_5$: C, 20.27, H, 0.42; N, 11.82; Br, 33.72. Found: C, 20.30; H, 0.47; N, 11.71; Br, 33.61.

2-Iodo-3,5-dinitrofurane (II).

2-Bromo-3,5-dinitrofurane (3.0 g.) in 20 ml. of acetic acid was stirred with 3 g. of potassium iodide at 65-70° for 10 minutes. To the cooled mixture was added 100 ml. of ice cold water with stirring. The precipitated material was washed with cold water to give 3.4 g. (94%) of cream colored solid, m.p. 109-111°. Crystallization from benzene-hexane raised the melting point to 111-112°; nmr (benzene): δ 6.41 (s); ms: 284 (M^+).

Anal. Calcd. for $C_4HI N_2 O_5$: C, 16.92; H, 0.35; N, 9.87; I, 44.69. Found: C, 17.06; H, 0.42; N, 10.02; I, 44.89.

2-Azido-3,5-dinitrofurane (III).

Caution! The azido compound (III) is very sensitive to impact!

To a solution of 120 mg. of 18-crown-6 in 10 ml. of methylene chloride was added 237 mg. of 2-bromo-3,5-dinitrofurane and 195 mg. of sodium azide. The mixture was stirred in a stoppered flask for 3 hours, an additional 100 mg. of 18-crown-6 was added, and stirring was continued for 2 more hours. The deep red reaction mixture was filtered through a silica gel pad to give a light yellow filtrate. The solvent was allowed to evaporate in the hood to give a cream colored crystalline residue (98 mg.) which was crystallized from benzene-hexane to give 65 mg. of crystals, m.p. 105-106°; nmr (benzene): δ 6.64 (s); ir (potassium bromide): 2160 (N_3) cm^{-1} . Because of its extreme sensitivity to impact, the azido compound was not submitted for elemental analysis.

3,3',5,5',-Tetranitro-2,2'-bifurane (IV).

A vigorously stirred mixture of 1.0 g. of 2-iodo-3,5-dinitrofurane and 0.8 g. of copper (Venus Natural Copper Fine No. 44, American Bronze Powder Co., Flemington, N.J.) in 8 ml. of dry nitrobenzene was heated at 135-140° for 7 minutes. The hot mixture was filtered through a glass fiber filter pad and the insoluble material was washed with 10 ml. of hot benzene. Additional benzene (15 ml.) was added to the filtrate to precipitate 260 mg. of crystals, m.p. 274-276°. An additional 220 mg. of crystals m.p. 274-276°, was obtained by extracting the nitrobenzene insoluble material with 100 ml. of boiling acetone. The total yield (480 mg.) is 86.8% of the theoretical. Recrystallization from acetone-benzene gave the analytical sample, m.p. 275-276°; nmr (DMSO): δ 8.70 (s); ms: 314 (M^+).

Anal. Calcd. for $C_8H_2N_4O_{10}$: C, 30.59; H, 0.64; N, 17.84. Found: C, 30.63; H, 0.67; N, 17.73.

3,5,5'-Trinitro-2,2'-bifurane (V).

To 30 ml. of 90% nitric acid stirred at 5-10° was added 3.0 g. of 5,5'-dinitro-2,2'-bifurane (18) in portions over a 15 minute period. The solution was stirred at 22-23° for 30 minutes and then poured into ice-water to precipitate 1.6 g. of product, m.p. 155-170°. Two crystallizations from acetone gave 1.25 g. of crystals, m.p. 211-212°; nmr (acetone): δ 8.25 (s, 1H), 8.00 (d, 1H), 7.76 (d, 1H); ms: 269 (M^+).

Anal. Calcd. for $C_8H_3N_3O_9$: C, 35.70; H, 1.12; N, 15.61. Found: C, 35.77; H, 1.17; N, 15.53.

t-Butyl (5-Nitro-2-furanyl)carbamate.

5-Nitro-2-furoic acid (125.6 g.; 0.8 mole) was converted to the acid chloride by refluxing in 120 ml. of thionyl chloride (2 ml. of dimethylformamide as catalyst) for 3.5 hours. The thionyl chloride was removed under reduced pressure and the residue was dissolved in 800 ml. of ether and added in 100 ml. portions to a solution of 104 g. of sodium azide in 400 ml. of water cooled at 20°. After 25 minutes, the ether layer was washed with water, dried over sodium sulfate and filtered. The ether filtrate was cooled in a dryice-acetone bath to give 132.6 g. of 5-nitro-2-furoyl azide, m.p. 65-67°; lit. m.p. 66.5-67.5° (19). (**Caution! the acyl azide is impact sensitive**). The acyl azide was refluxed with 700 ml. of *t*-butyl alcohol for 6.5 hours. The hot solution was filtered to remove some dark insoluble material and the solvent was removed from the filtrate. The residue was dissolved in 300 ml. of hot benzene and the solution was decanted from insoluble tar, treated with charcoal and filtered. The filtrate was cooled to give 86.6 g. of yellow crystals, m.p. 114-118°. Two additional crystallizations raised the melting point to 120-122°; nmr (acetone): δ 7.52 (d, 1H), 6.38 (d, 1H), 1.49 (s, 9H), NH not observed.

Anal. Calcd. for $C_8H_{12}N_2O_5$: C, 47.36; H, 5.30; N, 12.28. Found: C, 47.54; H, 5.43; N, 12.32.

3,5-Dinitro-2-furanamine (VII).

A mixture of carbon tetrachloride (77 ml.) and acetic anhydride (30 ml.) was stirred at -5° during the dropwise addition of 52 ml. of 90% nitric acid. The mixture was kept at -5° for 15 minutes before 40 g. of *t*-butyl (5-nitro-2-furanyl)carbamate was added in small portions over a 20 minute period with cooling at -15 to -10°. After 15 minutes at -10°, the mixture was poured into ice-water and the yellow insoluble product was removed and washed with cold water. Tlc analysis of the product (18.3 g.) showed approximately equal amounts of the dinitrocarbamate (IX) and the dinitrofuraminine (VII). The product was stirred with 200 ml. of concentrated hydrochloric acid at ambient temperature for 70 minutes, then 100 ml. of ice-water was added. The insoluble material was removed and washed with cold water to give 8.3 g. (27%) of yellow solid, m.p. 155° dec. Crystallization from methanol or dilute hydrochloric acid raised the melting point to 158° dec.; nmr (acetone): δ 8.75 (broad s, NH_2), 7.86 (s, furan H); ir (potassium bromide): 3510, 3340 (NH_2) cm^{-1} ; ms: 173 (M^+).

Anal. Calcd. for $C_6H_8N_2O_5$: C, 27.76; H, 1.75; N, 24.28. Found: C, 27.77; H, 1.74; N, 24.13.

t-Butyl (3,5-Dinitro-2-furanyl)carbamate (IX).

A 22.4 g. sample of *t*-butyl (5-nitro-2-furanyl)carbamate was nitrated according to the procedure described for 3,5-dinitro-2-furanamine (VII). The product (6.1 g.) by tlc analysis (silica gel 60, benzene-ethyl acetate 80/20) contained ca. equal amounts of VII and IX. The product was stirred for 16 hours with 60 ml. of benzene at ambient temperature and the insoluble material (5 g.) was removed by filtration. The filtrate was concentrated and cooled to give 350 mg. of yellow-orange crystals, m.p. 154° dec. with sintering at 130-140° (IX is converted to VII by heating, see text); nmr (acetone): δ 8.02 (s, 1H), 1.53 (s, 9H), the N-H was not observed; ir (potassium bromide): 3380 (NH), 1770 (C=O) cm^{-1} .

Anal. Calcd. for $C_8H_{11}N_3O_7$: C, 39.56; H, 4.06; N, 15.38. Found: C, 39.62; H, 4.08; N, 15.25.

2-Acetamido-3,5-dinitrofurans (XI) and *N,N*-Diacetyl-3,5-dinitro-2-furanamine (X).

A solution of 590 mg. of 3,5-dinitro-2-furanamine in 12 ml. of acetic anhydride was stirred at 25° during the dropwise addition of 0.3 ml. of pyridine. After 40 minutes, 75 ml. of ice cold water was added and the mixture was stirred until the red brown oil turned to a gray solid. The solid (637 mg.), which contained ca. equal amounts of XI and X by tlc analysis was dissolved in 20 ml. of boiling benzene. The benzene solution was treated with charcoal, filtered, and the filtrate cooled to give 330 mg. of yellow crystals (XI), m.p. 146-148°. Recrystallization from methanol did not raise the melting point and the crystals showed only one spot by tlc analysis (20); nmr (acetone): δ 8.02 (s, 1H, furan H), 2.37 (s, 3H, CH_3),

2.83 (broad, 1H, NH); ir (potassium bromide): 3400 (NH), 1755 (C=O) cm^{-1} .

Anal. Calcd. for $C_8H_8N_3O_6$: C, 33.50; H, 2.34; N, 19.53. Found: C, 33.40; H, 2.40; N, 19.49.

Addition of hexane to the benzene mother liquor precipitated a small additional amount of XI. The solvent was removed yielding a residue which was crystallized from methanol to give 160 mg. of white crystals (X), m.p. 122-123°; nmr (acetone): δ 8.16 (s, 1H, furan H), 2.44 (s, 6H, CH_3); ir (potassium bromide): no NH peak, 1755 with shoulder at 1740 (C=O) cm^{-1} .

Anal. Calcd. $C_8H_7N_3O_7$: C, 37.36; H, 2.74; N, 16.34. Found: 37.50; H, 2.75; N, 16.42.

N-Carbethoxy-*N*-acetyl-3,5-dinitro-2-furanamine (XII).

To a stirred solution of 456 mg. of ethyl (3,5-dinitro-2-furanyl)carbamate in 5 ml. of acetic anhydride was added 0.3 ml. of pyridine dropwise. After 20 minutes the reaction mixture was poured into ice water with stirring to give a dark insoluble oil which was extracted into 15 ml. of benzene. The benzene solution was treated with magnesium sulfate and charcoal, then concentrated and hexane was added to give 94 mg. of white crystals, m.p. 69-70°; nmr (chloroform): δ 7.73 (s, 1H, furan H), 4.28 (q, 2H, CH_2) 2.67 (s, 3H, CH_3), 1.21 (t, 3H, CH_3); ir (potassium bromide): no NH peak, 1775 and 1745 (C=O) cm^{-1} .

Anal. Calcd. for $C_{10}H_{11}N_3O_7$: C, 37.64; H, 3.16; N, 14.63. Found: C, 37.71; H, 3.23; N, 14.64.

REFERENCES AND NOTES

- (1) R. C. Elderfield and T. N. Dodd, Jr., in "Heterocyclic Compounds," Vol. 1, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, p. 142.
- (2) A. P. Dunlop and F. N. Peters, "The Furans," Reinhold Publishing Corp., New York, N. Y., 1953, p. 141.
- (3) Reference 2, p. 147.
- (4) The preparation and properties of 2,5-dipicryl-3,4-dinitrofurans have been described in a previous paper: J. C. Dacons and M. E. Sitzmann, *J. Heterocyclic Chem.*, **14**, 1151 (1977).
- (5) Reference 1, p. 158.
- (6) Reference 1, p. 159.
- (7) The structure assignment for V is analogous to that for I.
- (8) This instability of the yellow product as well as its sensitivity to heat and impact precluded an elemental analysis.
- (9) Reference 2, p. 171.
- (10) The fact that 2,5-dicarbethoxy-3,4-dihydroxyfuran exists mainly in the enol form is attributed to stabilization of this form by hydrogen bonding between the hydroxyl hydrogen and the carbonyl portion of the ester group: Reference 2, p. 181.
- (11) S. S. Novikov, V. N. Solov'ev, K. E. Ovcherov, L. I. Khmel'nitskii, T. S. Novikova, G. A. Konyaev and N. N. Borisova, *Nitro Compounds. Proc. Inter. Symp. Warsaw*, 519 (1963); L. I. Khmel'nitskii, T. S. Novikova, S. S. Novikov, K. E. Ovcharov and N. N. Borisova, "Fiziol. Aktiv. Veshchesta Ikh Primen. Rastenievod.," Dokl. Nauch. Konf., Vilnyus 1963, p. 215 (Published 1965); V. N. Solov'ev, G. A. Konyaev, S. S. Novikov, L. I. Khmel'nitskii and T. S. Novikova, *Farmakol. i Toksikol.*, **28**, 316 (1965).
- (12) S. S. Novikov, L. I. Khmel'nitskii, and T. S. Novikova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 103 (1965).
- (13) Reference 1, p. 182.
- (14) Z. N. Nazarova and V. N. Novikov, *Metody Poluch. Khim. Reakt. Prep.*, **17**, 20 (1967); *Chem. Abstr.*, **70**, 114901v (1969). These authors had earlier reported a more complicated procedure: *Zhur. Obshchei Khim.*, **31**, 263 (1961). **Caution! 2-Bromo-5-nitrofurans is a powerful skin irritant. Gloves should be worn when handling this compound or its solutions.**
- (15) Since a substantial amount of bromine is formed during the reaction, the workup should be performed in a hood.
- (16) The nature of this reaction is not understood although the evolu-

tion of brown fumes suggests that a species is present that can be hydrolyzed to form nitrous acid.

(17) The yield of 2-bromo-5-nitrofurane from 5-bromofuroic acid is 47%: Reference 14.

(18) R. Grigg, J. A. Knight and M. V. Sargent, *J. Chem. Soc. C*, 980 (1966).

(19) M. Amorosa and L. Lipparini, *Ann. Chim. (Rome)*, **46**, 343 (1956).

(20) In reference 12, the authors give m.p. 146-148° for unrecrystallized

N-acetyl-3,5-dinitro-2-furanamine but state that after several crystallizations from absolute methanol the compound has m.p. 157.5° dec. This agrees with a prior literature m.p. of 155° with a decomposition temperature of 160° [T. Sasaki, *Bull. Inst. Chem. Res., Kyoto Univ.*, **33**, 39 (1955)]. However, it should be noted that the parent compound, 3,5-dinitro-2-furanamine, melts in the region of 155° to 160° with decomposition.