Energy considerations require that the $C_5H_9$ radical be cyclic, since the 112 kcal./mole available for reaction (2) is insufficient to open the cyclopentane ring simultaneously with the splitting off of a hydrogen atom—an additional confirmation of the identification of the $C_{10}H_{18}$ product with cyclopentylcyclopentane.

In view of the small quantity of polymer formed in the long exposure runs it is not necessary to account for its formation in the main mechanism; it seems probable that it is formed by secondary reactions of the products.

## Conclusions

The reaction of Hg $6(^3P_1)$ atoms with cyclopentane bears great resemblance to the reactions of Hg $6(^3P_1)$ atoms with the lower paraffins[2-8,25] (with the exception of methane and neopentane). It differs markedly from those of the olefins which have been investigated to date in that cyclopentane shows no evidence of reacting *via* an excited molecule. Furthermore, the mercury photosensitized reaction of cyclopentane is shown to contrast strongly with the thermal reaction of cyclopentane, where the products are hydrogen and cyclopentadiene, or alternatively ethylene and propylene.

Further investigations of the mercury photosensitized reactions of cyclopentane and other cyclic paraffins are now in progress in the laboratories of one of us (H. E. G.).

**Acknowledgment.**—It is a sincere pleasure for the authors to acknowledge their indebtedness to Mr. G. P. Happ and the Eastman Kodak Company and to Drs. Fred L. Mohler and Vernon H. Dibeler of the National Bureau of Standards for performing a number of very helpful mass spectrometric analyses in connection with this investigation.

## Summary

An investigation has been made of the reaction of cyclopentane with mercury $6(^3P_1)$ atoms in a static system at 30°, over the pressure range from 5–200 mm.

The products of the reaction are hydrogen, cyclopentene and cyclopentylcyclopentane.

The linear pressure decrease observed is attributed to the condensation of the cyclopentylcyclopentane.

Both the nature of the products formed and the quantum yield suggest that the mercury photosensitized decomposition of cyclopentane strongly resembles those of the lower paraffins.

A mechanism is proposed, involving the formation of cyclopentyl radicals, which is consistent with the data observed.

RECEIVED JANUARY 3, 1950

(25) B. de B. Darwent and E. W. R. Steacie, unpublished data.

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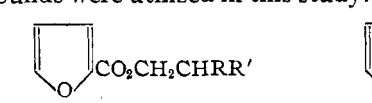
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF IOWA STATE COLLEGE]

# The Preparation of Some *exo*-Nitro Derivatives of Substituted 5-Nitrofurans[1,2]

BY HENRY GILMAN AND HARRY L. YALE

The preparation of several new *exo*-nitro-5-nitrofurans was undertaken in order to evaluate them as explosives. Three types of furan compounds were utilized in this study.



R or R′ = H, OH, $CH_2Cl$ or $CH_3$

I

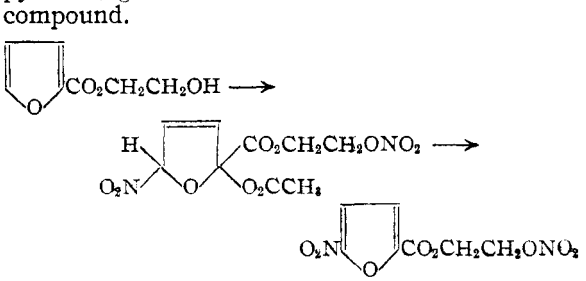
R″ = H or alkyl

II

R‴ = H or alkyl

III

The esters represented by Type I were prepared by the reaction between furoic acid and ethylene oxide, epichlorohydrin or propylene oxide in the presence of catalytic amounts of anhydrous ferric chloride. Nitration of these esters by means of nitric acid (d. 1.5) in acetic anhydride proceeded smoothly through the intermediate nitro compound[3] which, after treatment with pyridine, gave the desired *exo*-nitro-5-nitrofuran compound.



The amides represented by Type II were best prepared by the reaction of the acid chloride and the amine or ammonia. When N-methyl-5-nitrofuramide was treated with distilled white fuming nitric acid at 0° there was obtained a 65.3% yield of N-methyl-N,5-dinitrofuramide.

(1) The work reported here was done under the auspices of a contract between O. S. R. D. and Iowa State College.

(2) Drs. Crane and Capell of *Chemical Abstracts* have suggested the nomenclature used in this paper.

(3) Freure and Johnson, THIS JOURNAL, **53**, 1142 (1931). The most recent paper on the structure of the intermediate nitration product of furan is by Clauson-Kaas and Fakstorp, *Acta Chem. Scand.*, **1**, 210 (1947).

Anomalously, however, none of the other amides prepared, 5-nitrofuramide, N-methylfuramide, N-butyl-5-nitrofuramide, furan-2,5-dicarboxamide and furan-2,5-N-methyldicarboxamide, gave nitramides under the same conditions. When other nitration procedures were employed, extensive decomposition occurred.[4]

Furohydroxamic acid, 5-nitrofurohydroxamic acid, 5-nitrofuro-O-methylhydroxamate, bis-(5-nitrofuro)-O-methylhydroxamate, 2,5-furodihydroxamic acid and furylacrylohydroxamic acid were decomposed by fuming nitric acid even at 0° and no *exo*-nitro derivatives could be prepared.

## Experimental

**2-Hydroxyethyl Furoate.**—A mixture of 80.4 g. (0.72 mole) of furoic acid and 26.4 g. (0.6 mole) of ethylene oxide was cooled in an ice-salt-bath and 0.5 g. of anhydrous ferric chloride was added with stirring. After standing overnight, the solid product was dissolved in 100 ml. of ether and the ether solution was washed with water, 5% aqueous sodium bicarbonate solution, dried, concentrated and distilled to give 12 g. (12.9% yield) of product, b. p. 161–162° (15 mm.), m. p. 63–65°.

*Anal.* Calcd. for $C_7H_8O_4$: C, 53.85; H, 5.17. Found: C, 53.70; H, 5.17.

**3-Chloro-2-hydroxypropyl Furoate.**—The above procedure gave this product in 56.3% yield, b. p. 191° (15 mm.), $n^{25}D$ 1.5191.

*Anal.* Calcd. for $C_8H_9O_4Cl$: Cl, 17.33. Found: Cl, 17.61.

**2-Hydroxypropyl Furoate.**—From propylene oxide, furoic acid and anhydrous ferric chloride, there was obtained a mixture of liquid and solid products, b. p. 155–165° (23 mm.). The mixture could not be separated and the ester could not be obtained pure. In the subsequent nitration, however, a pure product was obtained.

*Anal.* Calcd. for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 54.80; H, 5.43.

**2-Nitratoethyl 5-Nitrofuroate.**—To a mixture of 40 ml. of acetic anhydride and 18.3 g. of nitric acid (d. 1.5), at −10 to −5°, was added 7.8 g. (0.05 mole) of 2-hydroxyethyl furoate in 40 ml. of acetic anhydride. Subsequently, stirring continued for three hours during which time the temperature rose to 0°. The reaction mixture was poured on ice. The oil which separated soon solidified and was filtered; it weighed 6.0 g. and after recrystallization from methanol melted at 124–125°. Repeated crystallization from methanol had no effect on the m. p. Analyses showed that the intermediate nitro compound crystallized with one molecule of methanol.

*Anal.* Calcd. for $C_7H_6N_2O_8 \cdot CH_3CO_2H \cdot CH_3OH$: N, 8.28. Found: N, 8.18, 8.28.

The above intermediate was dissolved in pyridine, the solution kept at room temperature five days, then diluted with water. The solid which separated was recrystallized from methanol to give an 86.5% yield of product, m. p. 81–82°. Another crystallization from methanol was without effect on the m. p. This compound also crystallized with one molecule of methanol.

*Anal.* Calcd. for $C_7H_6N_2O_8 \cdot CH_3OH$: N, 10.07. Found: N, 10.20.

**3-Chloro-2-nitratopropyl 5-Nitrofuroate.**—In the nitration of 3-chloro-2-hydroxypropyl furoate, as above, the intermediate product was an oil and was, therefore, treated directly with pyridine to give the desired product, m. p. 73–74°, after recrystallization from petroleum ether.

*Anal.* Calcd. for $C_8H_7N_2O_8Cl$: N, 9.51; Cl, 12.04. Found: N, 9.65; Cl, 12.38.

**2-Nitratopropyl 5-Nitrofuroate.**—Nitration of the crude 2-hydroxypropyl furoate followed by the pyridine treatment gave the product, m. p. 70–71°, after recrystallization from petroleum ether.

*Anal.* Calcd. for $C_8H_8N_2O_8$: N, 10.90. Found: N, 11.10.

**N-Methyl-5-nitrofuramide.**—A solution of 3.51 g. (0.02 mole) of 5-nitrofuroyl chloride[4] in 25 ml. of ether was stirred and treated dropwise with 1.86 g. of methylamine in 33% aqueous solution. The yield of amide was quantitative. The analytical sample was twice recrystallized from ethanol, m. p. 202–203°.

*Anal.* Calcd. for $C_6H_6N_2O_4$: N, 16.47. Found: N, 16.22.

**Furan-2,5-N-methyldicarboxamide.**—Aqueous methylamine and furan-2,5-dicarbonyl chloride[5] gave a 46.7% yield of the product, m. p. 97° after recrystallization from acetone.

*Anal.* Calcd. for $C_8H_{10}N_2O_3$: N, 15.35. Found: N, 15.15.

**N-Butyl-5-nitrofuramide.**—The mixing of 3.14 g. (0.02 mole) of 5-nitrofuroic acid and 1.5 g. (0.02 mole) of *n*-butylamine resulted in a vigorous reaction. When this had subsided, 2.0 g. of $POCl_3$ was added and the whole heated in an oil-bath at 140° for two hours. The cooled mixture was extracted with ether and the ether extracts were dried, concentrated and distilled to give 1.0 g. (23.6%) of product, b. p. 190° (10 mm.), m. p. 89–90° after recrystallization from petroleum ether.

*Anal.* Calcd. for $C_9H_{12}N_2O_4$: N, 13.20. Found: N, 13.20.

The same compound was prepared in 73% yield by refluxing for one-half hour, 3.51 g. of 5-nitrofuroyl chloride, 2.92 g. of *n*-butylamine and 25 ml. of benzene, evaporating the benzene, and recrystallizing the residue from petroleum ether.

**5-Nitrofuramide.**—This compound was prepared from 5-nitrofuroyl chloride and aqueous ammonia; it melted at 161° after recrystallization from ethanol.[6]

**N-Methylfuramide.**—A mixture of 26 g. (0.2 mole) of methyl furoate and 25 g. of 33% aqueous methylamine was refluxed eight hours, cooled, saturated with sodium chloride and extracted with ether. The ether extracts yielded 12 g. of product, b. p. 144–145° (18 mm.), m. p. 60°.[7]

**Furan-2,5-dicarboxamide.**—This compound was prepared from furan-2,5-dicarbonyl chloride and aqueous ammonia. It was recrystallized from hot water, m. p. above 220°.[8]

**N-Methyl-N,5-dinitrofuramide.**—Water-white fuming nitric acid was prepared by distilling concentrated nitric acid from concentrated sulfuric acid in an all glass apparatus. To 10 ml. of this acid was added a few crystals of urea, the whole cooled to 0° and 2.0 g. of N-methyl-5-nitrofuramide added in small portions. Subsequently, the flask was removed from the ice-bath and after six minutes the mixture was poured on ice. The precipitated solid weighed 1.65 g. (65.3% yield), m. p. 89–90°, and was practically pure nitramide.

*Anal.* Calcd. for $C_6H_5N_3O_6$: N, 19.53. Found: N, 19.25, 19.25.

**Furohydroxamic Acid.**—The preparation was carried out between ethyl furoate, hydroxylamine and sodium ethoxide[9]; since furohydroxamic acid is quite soluble in water, its presence is to be avoided. The yield of product,

(4) Gilman and Young, THIS JOURNAL, **56**, 464 (1939), were unable to obtain identifiable nitro compounds from the nitration of N-2,4,6-tribromophenylfuramide or N-methyl-N-phenylfuramide.

(5) Klinkhardt, *J. prakt. Chem.*, [2] **25**, 46 (1882).

(6) Marquis, *Compt. rend.*, **137**, 520 (1903), prepared this compound, m. p. 161°, using dry ammonia in ether with 5-nitrofuroyl chloride.

(7) Wheeler and Atwater, *Am. Chem. J.*, **23**, 145 (1900), report a m. p. of 64°.

(8) Klinkhardt, ref. 5, prepared this compound using dry ammonia in ether.

(9) Yale, *Chem. Rev.*, **33**, 209 (1944).

m. p. 121–122°, after recrystallization from acetone, was 47.2%.[10]

**5-Nitrofurohydroxamic Acid.**—To 21 g. (0.3 mole) of hydroxylamine hydrochloride in 100 ml. of methanol was added 12.0 g. of sodium hydroxide in 60 ml. of methanol, the whole was heated to boiling, cooled, and stirred while 13 g. (0.074 mole) of 5-nitrofuroyl chloride in 50 ml. of ether was added dropwise. Stirring continued for five hours, the reaction mixture was filtered and the filtrate concentrated to dryness. The residue was washed with ether, then extracted in a Soxhlet extractor with ethyl acetate. The ethyl acetate extracts yielded 7.1 g. (56.0%) of product, m. p. 169° (dec.).

*Anal.* Calcd. for $C_5H_4N_2O_6$: N, 16.28. Found: N, 15.95, 16.00.

**5-Nitrofuro-O-methylhydroxamate and Bis-(5-nitrofuro)-O-methylhydroxamate.**—A solution of 13.0 g. (0.074 mole) of 5-nitrofuroyl chloride in 100 ml. of absolute ether was added with vigorous stirring to 10 g. (0.212 mole) of O-methylhydroxylamine and the whole allowed to stand overnight. The insoluble material was filtered and extracted with chloroform. The combined chloroform extracts and ether filtrate were concentrated to dryness. The residue, 13 g., was recrystallized successively from 40 ml. and 20 ml. of acetone. The material from the second recrystallization was pure 5-nitrofuro-O-methylhydroxamate, m. p. 151–152°.

(10) Pickard and Neville, *J. Chem. Soc.*, **79**, 847 (1901), prepared this compound, m. p. 124°, without employing sodium ethoxide.

*Anal.* Calcd. for $C_6H_6N_2O_5$: N, 15.05. Found: N, 15.24.

The acetone filtrates from the above compound were evaporated to dryness and the residue recrystallized from methanol to give bis-(5-nitrofuro)-O-methylhydroxamate, m. p. 105.6–106.0°.

*Anal.* Calcd. for $C_{11}H_7N_3O_8$: N, 12.92. Found: N, 13.30, 13.30.

**2,5-Furodihydroxamic Acid.**—This compound was prepared in 60.2% yield by the same procedure used for 5-nitrofurohydroxamic acid. It was recrystallized from hot water and melted above 250°.

*Anal.* Calcd. for $C_6H_6N_2O_5$: N, 15.05. Found: N, 15.13.

**Furylacrylohydroxamic Acid.**—This compound was prepared in similar fashion in 46.2% yield, m. p. 137–138° (with dec.) after recrystallization from ethyl acetate.

*Anal.* Calcd. for $C_7H_7NO_3$: N, 9.15. Found: N, 9.07.

## Summary

The preparation of several *exo*-nitro derivatives of 5-nitrofuran has been described.

The preparation of a number of amides and hydroxamic acids of furan has also been described.

AMES, IOWA RECEIVED NOVEMBER 7, 1949

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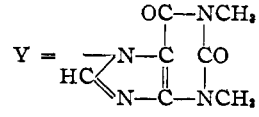
[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF LAKESIDE LABORATORIES, INC.]

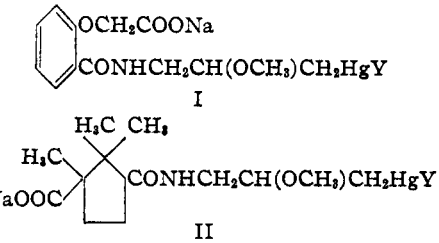
# Mercurial Diuretics. I. Addition of Mercuric Acetate to Allyl Urea[1]

BY R. L. ROWLAND, WENDELL L. PERRY, E. LEON FOREMAN[2] AND HARRIS L. FRIEDMAN

Organic mercury compounds have been generally accepted as the most efficient therapeutic agents for stimulation of urine production. This diuretic effect is utilized for the relief of edema, *e. g.*, in treatment of congestive heart failure.[3] The organic mercurial diuretics in accepted clinical use in this country exhibit a similar chemical structure. Salyrgan-theophylline (Mersalyl-Theophylline, U.S.P.) (I),[4] mercuzanthin (Mercurophylline, U.S.P.) (II)[5] and mercuhydrin (Meralluride, N.N.R.) (III)[6] possess the basic structure $RCONHCH_2CH(OCH_3)CH_2HgY$, wherein R includes a carboxyl group. Although the mercurial diuretics originally were utilized in the form of the hydroxymercuri compounds (Y = OH), for the last decade the hydroxy mercurials have been mixed with excess theophylline, presumably with formation of the compound in which



Recently a diuretic has been studied in which Y is a carboxymethylmercapto radical (II, Y = $SCH_2COOH$).[7]



I



II

$NaOOCCH_2CH_2CONHCONHCH_2CH(OCH_3)CH_2HgY$

III

In the course of a study of variation of toxicity and diuretic effect with changes in chemical structure, it was noted that the products obtained from the addition of mercuric acetate to allylurea in methyl alcohol effected in the dog a three- to five-fold greater diuretic response than that resulting

(1) Presented before the Medicinal Division of the American Chemical Society, Atlantic City, September, 1949.

(2) E. S. Miller Laboratories, Los Angeles, Calif.

(3) A recent summary of mercurial diuretics is presented by Ray and Burch, *Am. J. Med. Sci.*, **217**, 96 (1949).

(4) Bockmühl and Schwartz, U. S. Patent 1,693,432 (1948); Bockmühl, Middendorf and Fritzsche, U. S. Patent 2,213,457 (1940).

(5) Molnar, U. S. Patent 2,117,901 (1938).

(6) Geiger, Vargha and Richter, U. S. Patent 2,208,941 (1940). In this reference the structure of the product from addition of mercuric acetate to N-(allylcarbamyl)-succinamic acid in methyl alcohol is reported to be N-(3-hydroxy-2-hydroxymercuripropylcarbamyl)-succinamic acid. The formula presented for mercuhydrin in figure III is based upon unpublished studies of D. E. Pearson and Max V. Sigal, Vanderbilt University.

(7) Lehman, *Proc. Soc. Exp. Biol. Med.*, **64**, 428 (1947); Lehman, Taube and King, *ibid.*, **71**, 1 (1949).