STUDIES IN THE FURAN SERIES

XLVII. Syntheses Based on 3, 4-Bis(chloromethyl)furan*

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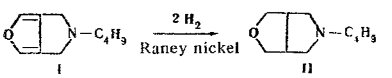
A study was made of certain transformations of the bicyclic compounds of the furan series synthesized from 3,4-bis(chloromethyl)furan, N-butyl-4H, 6H-furo[3, 4-c]pyrrole and 4H, 6H-thieno[3, 4-c]furan. On the basis of the same dichloride, 3,4-dimethyl furan and furan-3,4-dialdehyde were synthesized.

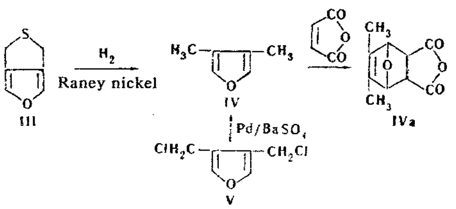
It has previously been established that the reaction of 3, 4-bis(chloromethyl)furan with primary amines [1] and with sodium sulfide [2] leads to the formation of the new bicyclic structures, N-alkyl-4H, 6H-furo[3, 4-c]pyrroles and 4H, 6H-thieno(3, 4-c)furan, respectively.

This communication describes a study of certain transformations of these new compounds which confirm their structure.

On hydrogenation of N-butyl-4H, 6H-furo[3, 4-c]pyrrole (I) in presence of Raney nickel, N-butylfuranidino[3, 4-c]pyrrolidine (II), characterized also by the formation of picrate, was obtained with a yield of 73%.

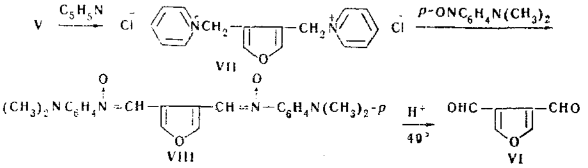


Desulfurization of 4H, 6H-thieno[3, 4-c]furan (III) in the presence of a large excess of Raney nickel leads to the formation of 3, 4-dimethylfuran (IV), characterized by formation of an aduct (IVa) with maleic anhydride.

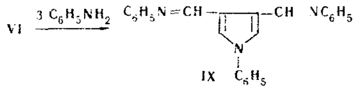


The constants of 3, 4-dimethylfuran (apart from the boiling point [3]) were not previously known. This compound has also been synthesized by us by the reduction of 3, 4-bis(chloromethyl)furan (V) in the presence of palladium in barium sulfate. The 3, 4-dimethylfurans obtained by the two different pathways were found to be identical.

When the study of the reactions of 3, 4-bis(chloromethyl)furan (V) was continued, this dischloride was converted into furan-3, 4-dialdehyde (VI)** by using a previously described method [4]. 3, 4-Bis(chloromethyl)furan (V) reacts with pyridine with the formation of the 3, 4-bispyridinal salt VII. By the action of n-nitrosodimethyl alanine, the bispyridinal salt was converted into the substituted bisnitrofuran-3, 4-dialdehyde VIII, the hydrolysis of which led to the formation of furan-3, 4-dialdehyde. Yield 23%, calculated for 3, 4-bis(chloromethyl)furan:



Furan-3, 4-dialdehyde reacted with aniline in an unusual manner and led to the formation of a compound which contained no oxygen. According to the data of the elementary analysis, this compound corresponded to the Schiff's double base from aniline and N-phenylpyrrole-3, 4-dialdehyde, N-phenyl-3, 4-bis(phenylazomethine)pyrrole IX. Such a compound may be formed on account of the opening of the furan ring* and subsequent recyclization into N-phenylpyrrole under the action of aniline.



A study was made in this laboratory of the PMR spectra of the N-alkylfuropyrroles Ia and b [1] and thieno-furan III [2], and also of the previously synthesized [1, 2] tricyclic systems (diazetines Xa, b and dithiezine XI and the 3, 4-disubstituted furans, bis(aminomethyl (XIIa, b and bis(alkylmercaptomethyl)furans (XIII).

The values for the chemical displacement of α-furan protons of these compounds and also 3, 4-bis(chloromethyl)furan are presented in the table.

It follows from the data in the table that the signals of α-furan protons of the bicyclic compounds I, III (Ha) are displaced into the region of stronger fields ($\delta \sim$ $\sim$ 7.00 m. d.) in comparison with the corresponding signals (Ha) of the tricyclic (X, XI) and 3, 4-disubstituted

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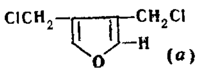
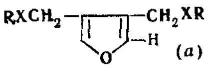
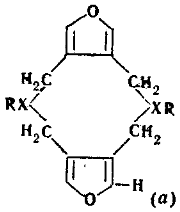
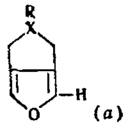
*For part XLVI, see [10].

**This compound has recently been synthesized by the reduction of the dinitrite of furan-3, 4-dicarboxylic acid [5, 6].

*The opening of the furan ring in furan-3, 4-dialdehyde under the action of potassium hydroxide [5, 6] has recently been described.

Values of the Chemical Displacements δ (ppm) of α-Furan Protons in Compounds of the Furan Series

Compound	XR	δH_a
		7.45
	XIIa NHC_4H_9 XIIb NHC_3H_7 XIII SC_2H_5	7.23 7.20 7.27
	Xa NC_4H_9 Xb NC_3H_7 XI S	7.21 7.20 7.37
	Ia NC_4H_9 Ib NC_3H_7 III S	7.01 7.00 7.08

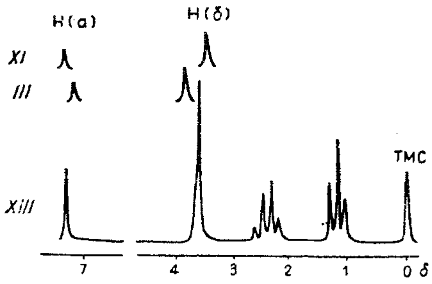


Fig. 1. PMR spectra of Compounds III, XI, and XIII.

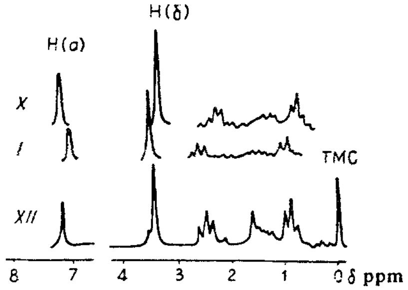


Fig. 2. PMR spectra of Compounds I, X, XII.

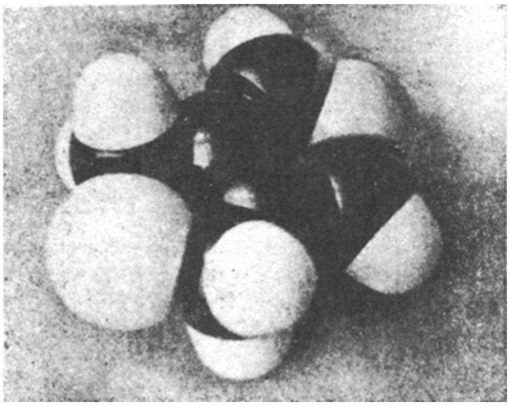


Fig. 3. Molecular model (according to Stuart and Brigleb) of 4H, 6H-thieno[3, 4-c]furan (III).

(XII, XIII) furan oompounds (δ ~ 7,25 ppm). Also the difference in the values of the chemical displacements (Δδ 0.25 ppm) is reproduced in the series of these compounds with great accuracy.

When our data is compared with that in the literature, for example, the values of chemical displacements of the α-protons of unsubstituted furan (δ_H 7.42 [7]) and the proton situated at the double bond, and, for example, in vinylallyl ether (δ_H 6.45 [7]), it follows that the closure of the new five-membered ring with the formation of the bicyclic structure weakens the aromatic and intensifies the diene properties of the furan nucleus. An analogous pattern is found in the PMR spectrum of 1H, 3H-thieno[3, 4-c]thiofuran [8].

The α-protons of the furan nucleus and protons of the methylene groups of bicycles (H_b) each give one resonance peak (their area is in the ratio of 1 : 2,) which indicates the complete symmetry of the molecules of these compounds (Fig. 1 and 2).

The construction of the molecular models of the bicyclic compounds (according to Stuart-Brigleb) indicates that they are flat and somewhat strained structures (Fig. 3).

EXPERIMENTAL

N-Butylfuranidino[3, 4-c]pyrrolidine (II). A solution of 2 g (0.012 mole) of compound I in 20 ml absolute alcohol was hydrogenated in the presence of 4 g Raney nickel in a shaking autoclave (145 ml in volume) at 100°C and 100 atm for 2.5 hr. On cooling the catalyst was removed by filtration, washed with absolute alcohol, and the alcohol was removed by distillation. A 1.5 g (73%) quantity of compound **II** was obtained. Colorless liquid, bp 82–83° C (1 mm), n_D^{20}, 1.4658, d_4^{20} 0.9444. Found,%: C 70.95, 70.98; H 11.28, 11.34; N 7.85, 7.77; MR_D 49.62. Calculated for $C_{10}H_{19}NO$,%: C 70.95; H 11.32; N 8.28; MR_D 49.57. Picrate, mp 121–122° C (from alcohol). The sample of the mixture with picric acid gives a depression. Found,%: C 48.43, 48.46; H 5.78, 6.00. Calculated for $C_{10}H_{19}NO \cdot C_3H_3N_3O_7$,%: C 48.26; H 5.57.

3, 4-Dimethylfuran. A) A 5 g quantity of freshly prepared palladium in barium sulfate [9] in 10 ml of 80% acetone was shaken in the hydrogenation apparatus at room temperature until hydrogen ceased to be absorbed. A solution of 5 g (0.03 mole) of 3, 4-bis(chloromethyl)furan (V) in 25 ml of 80% acetone and 3.7 g potassium hydroxide in 25 ml 80% acetone was then added and hydrogenated at room temperature. The theoretical quantity of hydrogen (1320 ml) was adsorbed within 70 min. The catalyst was removed by filtration, washed with ether, and the filtrate treated with 120 ml of a 40% solution of sodium bisulfite. After 12 hr the resulting precipitate was removed by filtration, washed with ether, the filtrate was extracted with ether, and the combined ethereal extracts were washed with a standard solution of sodium bicarbonate and water and dried with calcined magnesium sulfate. After the ether had been removed by distillation, 1.1 g (38%) of 3, 4-dimethylfuran (IV) and 0.9 g of a fraction with a bp of 54° C (10 mm) and an unestablished structure were obtained. 3, 4-Dimethylfuran is a colorless, highly volatile liquid, bp 52–53° C (200 mm), n_D^{20} 1.4436; d_4^{20} 0.9085. Found,%: C 75.38, 75.55; H 8.69, 8.76; MR_D 28.09. Calculated for $C_6H_8OF_2$,%: C 74.96; H 8.39; MR_D 28.42.

When compound **IV** was chromatographed in a thin layer of aluminum oxide, a single spot was obtained (R_f, 0.5 in petroleum ether, 0.9 in benzene).

An adduct with maleic anhydride **IVa** was obtained under the following conditions. A mixture of 170 mg of **IV** in 0.5 ml absolute ether and 190 mg of maleic anhydride in a minimum quantity of absolute ether was maintained for 6 hr at room temperature. The crystals formed were removed by filtration and washed with ether. A 300 mg (87%) quantity of the adduct was obtained. Coloreless crystals, mp 141–142° C (in a sealed capillary). Found, %: C 61.78, 61.62; H 5.29, 5.12. Calculated for $C_{10}H_{10}O_4$: C 61.85; H 5.19.

B) A solution of 2.5 g (0.02 mole) of 4H, 6H-thiano[3, 4-c]furan (III) in 15 ml absolute ether was added dropwise to 30 g of Raney nickel (which had been carefully washed with methanol, ether, and absolute ether) in 100 ml absolute ether at 30° C. The reaction mixture was boiled for 2 hr, cooled, the ethereal layer was decanted and the catalyst was washed several times with ether. After distillation 0.9 g of a fraction was obtained with a bp of 53–54° C (185 mm), n_D^{20} 1.4370, d_4^{20} 0.8810, in which, in addition to 3, 4-dimethylfuran, there was also an impurity of an unknown compound. During thin layer chromatography on aluminum oxide, the single spot corresponded to 3, 4-dimethylfuran (R_f 0.5 in petroleum ether and 0.9 in benzene), and the impurity remained at the starting point. 3, 4-Dimethylfuran was identified in the form of an adduct with maleic anhydride. mp 141–142° C (in a sealed capillary). The sample of the mixture does not produce a depression with the adduct obtained in the previous experiments.

Furan-3, 4-dialdehyde. A 36 ml volume of pyridine was added to a solution of 26 g (0.16 mole) of 3, 4-bis(chloromethyl)furan (V) in 35 ml absolute alcohol, and the mixture was heated for 1 hr on a boiling water bath. During this procedure crystals of the bispyridinal salt **VII** were formed. After cooling the crystals were rapidly filtered by suction, washed with absolute acetone, absolute ether, and dried in a vacuum over calcium chloride. A 47 g (92%) quantity of the bipyridine salt **VII** was obtained. Colorless and very hygroscopic crystals*. Found, %: C 56.88, 56.84; H 5.48, 5.45. Calculated for $C_{16}H_{16}Cl_2N_2O \cdot H_2O$,%: C 56.34; H 5.31.

A solution of 47 g (0.14 mole) of the bispyridinal salt **VII** in 75 ml water was added to a solution of 42 g (0.28 mole) of n-nitrosodimethylaniline in 1000 ml alcohol, and then 300 ml of a 1 N solution of sodium hydroxide, heated to 40° C was added to the mixture. After 10 hr the precipitate was removed by filtration, washed with 50% alcohol, and dried. A 31 g (55%) quantity of bisnitron **VIII** was obtained. Yellow crystals, mp. 234–235° C (from alcohol). Found, % : C 66.78, 66.99; H 6.19, 6.00. Calculated for $C_{22}H_{24}N_4O_3$,%: C 67.33; H 6.17%.

A 22 g (0.056 mole) quantity of bisnitron **VIII** was dissolved in 660 ml of 1 N sulfuric acid, heated to 40° C, and the resulting precipitate was removed by filtration and extracted with ether (20 times with 50-ml portions). The ethereal extracts were washed with water and dried with anhydrous magnesium sulfate. After removing the ether by distillation 3.3 g (23%, calculated for the original 3, 4-bis(chloromethyl)furan) of furan-3, 4-dialdehyde (**VI**) was obtained. Light-yellow crystals, mp 77–78° C (after recrystallization from carbon tetrachloride and distillation under vacuum). Data in the literature [6]: mp 77–78°C, λ_{max} (CH_3CH) 251 nm, log ε 4.07. Found, %: C 58.17, 58.31; H 3.43, 3.41. Calculated for $C_6H_4O_3$,%: C 58.07; H 3.25. 2, 4-Dinitrophenylhydrazone: mp 280–282° C (from dimethyl formamide). Data in the literature [6] mp 280–282° C.

N-Phenyl-3, 4-bis(phenylazomethine)pyrrole (IX). A 125 mg quantity of furan-3, 4-dialdehyde (**VI**) in 15 ml absolute alcohol and 280 mg aniline were boiled for 2 hr. The reaction mixture was cooled, and 1 ml absolute ether was added and the resulting precipitate separated. A 255 mg (73%) quantity of the Schiff double base **IX** was obtained. mp 153–154° C (from alcohol); colorless crystals. Found, % : C 82.42, 82.70; H 5.74, 5.72; N 11.88, 11.67; Mol. wt. 349**. Calculated for $C_{24}H_{19}N_3$,%: C 82.49; H 5.48; N 12.03; Mol. wt. 394.4.

PMR spectra were recorded in a UNM-C60 (60 MHz) apparatus in carbon tetrachloride. The chemical displacements are presented in million parts in relation to the signal of tetramethylsilane, taken at 0**.

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*As the compound was very hygroscopic it was not possible to determine the melting point.

**According to mass spectrum data.

***We wish to express our thanks to Research worker IKhPS AN SSSR V. I. Sheichenko, for recording the PMR spectra.

REFERENCES

1. K. Yu. Novitskii, G. T. Khachaturova, and Yu. K. Yur'ev, KhGS, [Chemistry of Heterocyclic Compounds], 818, 1966.

2. K. Yu. Novitskii, G. T. Khachaturova, and Yu. K. Yur'ev, KhGS, [Chemistry of Heterocyclic Compounds], 822, 1966.

3. T. Reichstein and A. Grüssner, Helv. Chim. Acta. **16**, 28, 1933.

4. F. Kröhnke, Angew, Chem., **75**, 317, 1963.

5. S. Trofimenko, J. Am. Chem. Soc., **85**, 1357, 1963.

6. S. Trofimenko, J. Org. Chem., **29**, 3046, 1964.

7. N. S. Bhacca, L. F. Johnson and I. N. Shoolery, NMR-Spectra Catalog, National Press, New York, 1962.

8. H. Winberg and D. Zwanenburg, J. Org. Chem., **29**, 1919, 1964.

9. R. Mozingo, S. A. Harris, D. E. Wolf, C. E. Hoffhine, N. R. Easton and K. Folkers, J. Am. Chem. Soc., **67**, 2092, 1945.

10. K. Yu. Novitskii, L. V. Brattseva, G. I. Sazonova, and Yu. K. Yur'ev, KhGS, [Chemistry of Heterocyclic Compounds], 839, 1966.

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