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Side-chain Reactions with Furans

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As part of attempts to transform furans into other aromatic systems 9 new α-substituted furans have been prepared.

In the course of attempts to transform furans into other aromatic systems [1-8] a number of new α-substituted furans (II—IV, VI, VIII, X—XIII) have been prepared by the reactions shown below. Further syntheses employing these compounds failed, but it was found worth while to publish directions for their preparation since all the compounds at any time may become of use for synthetic work in this field.

The acid chloride of 2,5-dimethoxy-2,5-dihydrofuroic acid (XI) was not isolated pure but identified by transformation to the corresponding methyl ester (IX).

EXPERIMENTAL

Microanalyses by E. Boss and K. Glens

2-(α-Oxo-β-bromoethyl)-furan (I) was prepared after Brown [9]. The yield was 51 % [b.p.$_{0.1}$ 66—67°; n_D^{25} 1.5718; m.p. 32—34° (Hershberg apparatus, corr.)]. Brown obtained 85 % of a product with b.p.$_{20}$ 121—123°; n_D^{25} 1.5783 and m.p. 36—37° (after two crystallizations from petroleum ether). (Found: C 38.4; H 2.9; Br 41.8. Calc. for $C_6H_5BrO_2$ (189.0): C 38.1; H 2.7; Br 42.3).

2-(α-Oxo-γ,γ-(dicarbomethoxy)-propyl)-furan (II). I (25.0 g, 0.13 mole) was dissolved in anhydrous ether (20 ml) and the solution added during 15 min with stirring to a suspension of sodium dimethyl malonate [from powdered sodium (3.22 g, 0.14 mole) and dimethyl malonate (19.4 g, 0.15 mole)] in anhydrous ether (140 ml) (gentle reflux). The reaction mixture was heated under reflux with stirring for 2 h and cooled. Cold water was added, the etheral layer separated, washed twice with cold water and dried. The ether was evaporated in a vacuum and the crystalline residue removed by filtration, washed with ether and dried. The yield was 16.7 g of II (white crystals, m.p. 67—69°). (Found: C 54.8; H 5.2; OCH_3 25.0. Calc. for $C_9H_6O_4(OCH_3)_2$ (240.2): C 55.0; H 5.0; OCH_3 25.8). After crystallization from ether the m.p. was 69—71°.

The filtrate from the above 16.7 g of II was distilled and the distillate (4.0 g, b.p.$_{0.1}$ 132—135°) crystallized from ether. Hereby another 3.2 g of II was obtained (white crystals, m.p. 68—70°). (Found: C 54.9; H 5.4; OCH_3 26.8). The total yield of II thus was 19.9 g (63 %).

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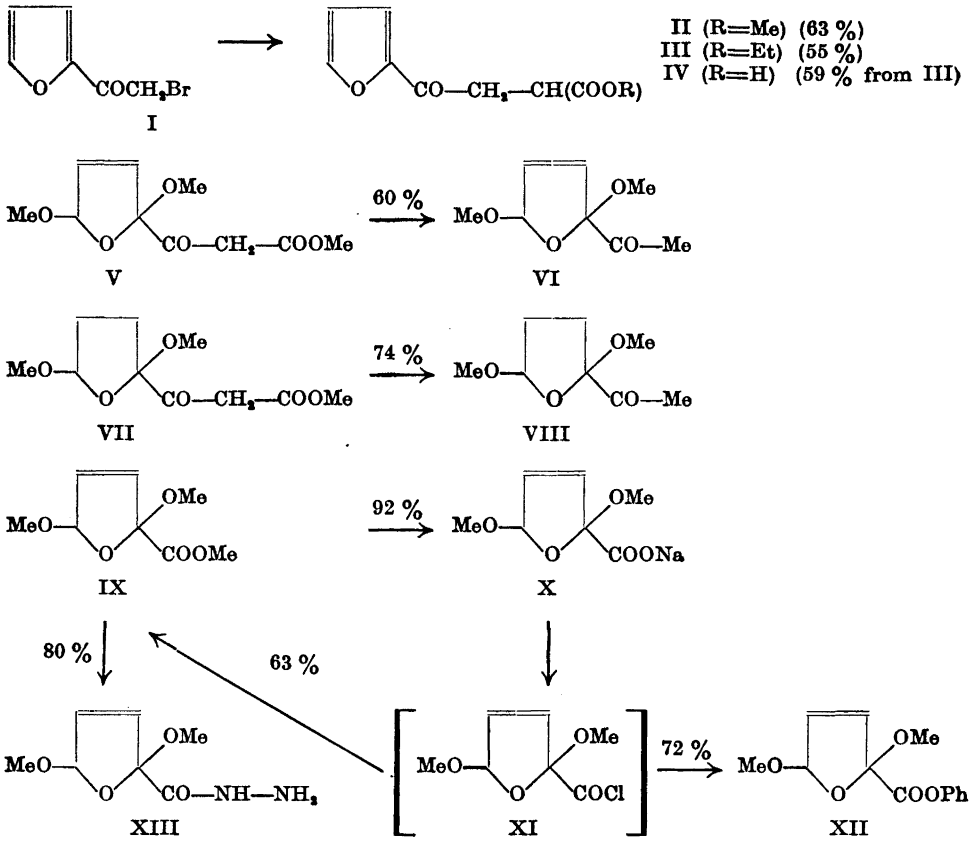

2-(α-Oxo-γ,γ-(dicarbethoxy)-propyl)-furan (III) was prepared from I (19.0 g), dissolved in 20 ml of anhydrous ether, and sodium diethyl malonate [from powdered sodium (2.30 g) and diethyl malonate (16.0 g) suspended in anhydrous ether (95 ml)] as described above for the preparation of II. The reaction product was isolated by distillation. The yield was 14.7 g (55 %) of III (colorless liquid; b.p.$_{0.1}$ 141—143°; n_D^{25} 1.4853). (Found: C 58.5; H 6.2; OC_2H_5 33.5. Calc. for $C_9H_8O_4(OC_2H_5)_2$ (268.3): C 58.2; H 6.0; OC_2H_5 33.6).

2-(α-Oxo-γ,γ-(dicarboxy)-propyl)-furan (IV). III (2.20 g) and a solution of potassium hydroxide (1.02 g) in methanol (20 ml) were heated under reflux (1 h). Water (5 ml) was added, the methanol distilled in a vacuum and the mixture adjusted to pH 3 with conc. hydrochloric acid. The precipitate formed was removed by filtration, washed twice with water and dried. The yield of crude IV was 1.49 g (86 %) [light-brown crystals; m.p. 158—161° (decomp.)]. Treatment with active carbon in methanol followed by crystallization from methanol-ether gave 1.02 g (59 %) of pure IV [white crystals, m.. 159—162° (decomp.)]. (Found: C 50.7; H 3.8; neut.equiv. (phenolphthalein indicator) 105.6. Calc. for $C_9H_8O_6$ (212.2): C 51.0; H 3.8).

2,5-Dimethoxy-2-(α-oxoethyl)-2,5-dihydrofuran (VI). V[5] (17.3 g) and a solution of potassium hydroxide (5 %, 200 ml) were mixed and heated under reflux (6 h). After cooling, the mixture was extracted continuously with ether and the etheral extract dried and distilled. The yield was 7.74 g (60 %) of VI (colorless liquid; b.p.$_{11}$ 91—94°;

n_D^{25} 1.4431). (Found: C 55.6; H 7.2; OCH_3 35.3. Calc. for $C_6H_6O_3(OCH_3)_2$ (172.2): C 55.8; H 7.0; OCH_3 36.0).

2,5-Dimethoxy-2-(α-oxoethyl)-tetrahydrofuran (VIII). VIII was prepared from VII[8] (4.64 g) as described for the preparation of VI. The yield was 2.57 g (74 %) of VIII (colorless liquid; b.p.$_{12}$ 92—93°; n_D^{25} 1.4347). (Found: C 55.3; H 8.1; OCH_3 34.8. Calc. for $C_6H_8O_2(OCH_3)_2$ (174.2): C 55.2; H 8.1; OCH_3 35.6).

Sodium 2,5-dimethoxy-2,5-dihydrofuroate (X). Methyl 2,5-dimethoxy-2,5-dihydrofuroate[10] (7.52 g, 0.040 mole) and sodium hydroxide (1.05 N, 40.0 ml, 0.042 mole) were mixed and heated under reflux (19 h). After cooling, the mixture was washed with ether, filtered and evaporated in a vacuum, at last for 4 h under 0.1 mm at 60—70°. The residue was pulverized in a mortar and dried further for 2 h. The yield was 7.24 g (92 %) of X (white powder with a yellow tinge). (Found: OCH_3 30.7. Calc. for $C_6H_7O_5Na(OCH_3)_2$ (196.1): OCH_3 31.6).

2,5-Dimethoxy-2,5-dihydrofuroyl chloride (XI). X (1.96 g, 0.010 mole), anhydrous benzene (10 ml) and a drop of pyridine were mixed and the mixture cooled to 0°. Oxalyl chloride (1.55 g, 0.012 mole) was added at 0° and the mixture shaken (20 min) at 0—10° and evaporated three times under 35 mm from a water bath of 20° with anhydrous benzene. A precipitate of sodium chloride was removed by filtration and washed with a little anhydrous ether. The slightly yellow filtrate consists of about equal parts of XI and solvent (benzene and ether) and is used directly for further syntheses without isolation of the acid chloride.

In order to identify XI the solution was added to a solution of sodium acetate (1.20 g) in anhydrous methanol (20 ml) during 10 min at 0°. After standing for 15 min without cooling anhydrous ether was added, the mixture filtered and the filtrate distilled. Hereby 1.18 g (63 %) of methyl 2,5-dimethoxy-2,5-dihydrofuroate (b.p.$_{14}$ 120—122°; n_D^{25} 1.4472; previously found[10] b.p.$_{13-14}$ 119—121°; n_D^{25} 1.4476) was obtained. (Found: C 51.5; H 6.7; OCH_3 48.1. Calc. for $C_6H_7O_3(OCH_3)_3$ (188.2): C 51.1; H 6.4; OCH_3 49.4).

Phenyl 2,5-dimethoxy-2,5-dihydrofuroate (XII). A solution of XI prepared as above was added to a solution of phenol (1.04 g, 0.011 mole) in pyridine (10 ml) during 10 min at −5°. After shaking for 2 h without cooling the mixture was evaporated partly in a vacuum and ether was added. A precipitate of pyridinium hydrochloride was removed by filtration and the filtrate washed with water, dried and distilled. The yield was 1.80 g (72 %) of XII (colorless liquid; b.p.$_{0.1}$ 129—132°; n_D^{25} 1.5076). (Found: C 62.3; H 5.8; OCH_3 24.3. Calc. for $C_{11}H_8O_3(OCH_3)_2$ (250.2): C 62.4; H 5.6; OCH_3 24.8).

2,5-Dimethoxy-2,5-dihydrofuroic acid hydrazide (XIII). Methyl 2,5-dimethoxy-2,5-dihydrofuroate[10] (3.76 g) and hydrazine hydrate (90 %, 7 ml) were mixed, the mixture left standing overnight and distilled. The yield was 3.01 g (80 %) of XIII (colorless liquid; b.p.$_{0.5}$ 140—145°; n_D^{25} 1.5008). (Found: C 44.7; H 6.5; N 15.0; OCH_3 32.4. Calc. for $C_6H_6N_2O_2(OCH_3)_2$ (188.2): C 44.7; H 6.4; N 14.9; OCH_3 33.0).

After standing for some days the sample crystallized completely (m.p. 60—75°). Crystallization from methanol-ether gave a product melting at 86—91°. (Found: C 44.6; H 6.7; N 14.8; OCH_3 32.4).

Three further crystallizations from methanol-ether gave products with the following m.p.'s: 86—90°, 100—102° and 105—106°. Probably all the products are mixtures of the *cis* and the *trans* isomer (*cf.*[10]).

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