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Mercuration-Demercuration of 2-Prop-2-ynyloxymethyltetrahydrofuran

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Abstract—Mercuration-demercuration of 2-propyl-2-ynyloxymethyltetrahydrofuran with various nucleophiles has been investigated. Formation of products of hydration, alkylation at the substituted carbon atom of the triple bond, subsequent prototropic isomerization or intramolecular cyclization (giving diastereomeric dihydrofuran derivatives), and demercuration by hydrochloric acid has been demonstrated.

Keywords: mercuration, demercuration, furan derivatives, intramolecular cyclization, diastereomer, tautomer

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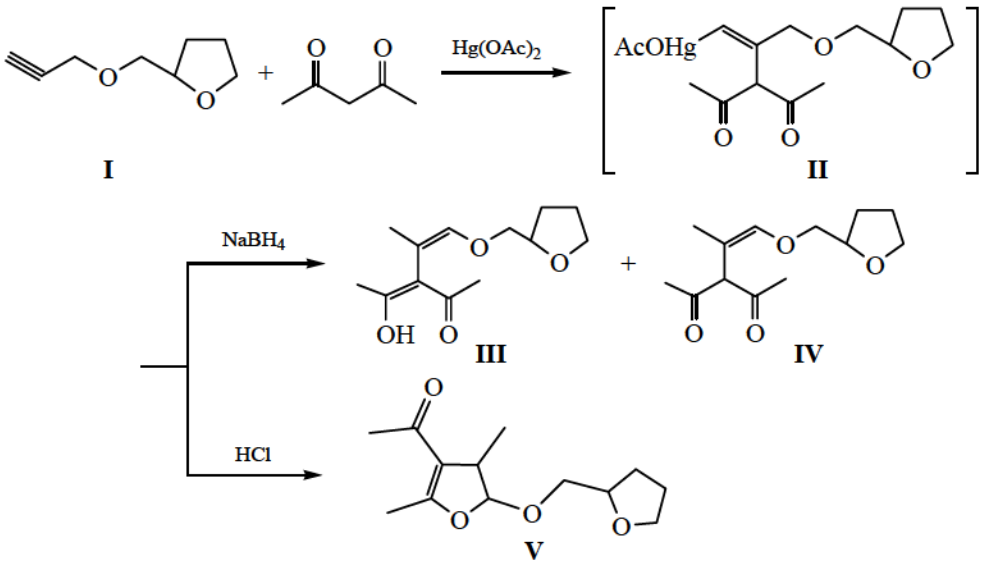
Recently, one-pot synthetic methods based on mercuration of terminal triple bond have been developed, and the reasons of formation of furan derivatives along with linear vinylation products have been rationalized [1–6].

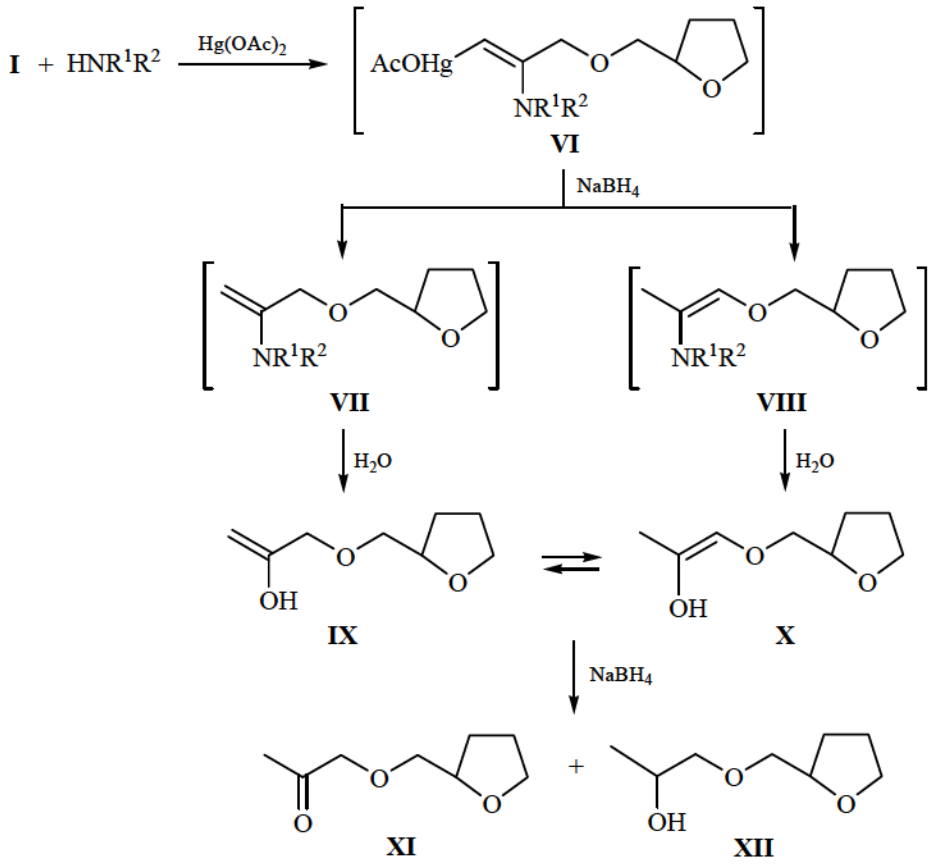
Extending the research in this area, herein we report on mercuration-demercuration of 2-prop-2-ynyloxymethyltetrahydrofuran with various CH and NH nucleophiles. The substrate contained both terminal acetylene and tetrahydrofuran fragments likely affecting regiochemistry of the studied reaction.

2-Prop-2-ynyloxymethyltetrahydrofuran reacted with sodium acetylacetonate in the presence of mercury(II) acetate in dioxane, the subsequent demercuration with

Scheme 1.



Scheme 2.



NR^1R^2 = morpholine, NEt_2.

sodium borohydride giving a mixture of enol and ketone, 4-hydroxy-3-[1-methyl-2-(tetrahydrofuran-2-ylmethoxy)vinyl]pent-3-en-2-one **III** and 3-[1-methyl-2-(tetrahydrofuran-2-ylmethoxy)vinyl]pentane-2,4-dione **IV**, in a ratio of 65:35 (NMR). Prolonged heating of the mixture allowed shifting the equilibrium towards formation of diketone **IV** (GLC) (Scheme 1).

Demercuration of the reaction mixture with 20% hydrochloric acid led to formation of 1-[2,4-dimethyl-5-(tetrahydrofuran-2-ylmethoxy)-4,5-dihydrofuran-3-yl]ethanone **V**.

Likely, enol **III** was also formed, but under conditions of electrophilic catalysis and due to electron-donating effect of tetrahydrofuranylmethyloxy group it underwent intramolecular cyclization to form a diastereomeric mixture of 1-[2,4-dimethyl-5-(tetrahydrofuran-2-ylmethoxy)-4,5-dihydrofuran-3-yl]ethanone **V** in a ratio of 1 : 1.

Further, reactions of 2-prop-2-ynyloxymethyltetrahydrofuran with morpholine and diethylamine in the presence of mercury(II) acetate in dioxane were studied. Similarly to the reported elsewhere [8], solvolysis un the presence of sodium borohydride did not yield products of *N*-alkylation of the terminal triple bond. According to the NMR spectra, a mixture of 1-(tetrahydrofuran-2-ylmethoxy)propan-2-one **XI** and 1-(tetrahydrofuran-2-ylmethoxy)propan-2-ol **XII** was formed (Scheme 2).

Probably, the reaction proceeded via the intermediate formation of enamines **VII** and **VIII**, undergoing hydrolysis to give unstable unsaturated alcohols **IX** and **X**. The latter were easily transformed into a mixture of 1-(tetrahydrofuran-2-ylmethoxy)propan-2-one **XI** and 1-(tetrahydrofuran-2-ylmethoxy)propan-2-ol **XII** in a ratio of 65 : 35. The ratio of the reaction products was determined by ^{1}H NMR spectroscopy.

Prolonged heating of the mixture in the presence of excess of the reducing agent shifted the reaction equilibrium towards formation of the derivative **XII**.

We failed to perform direct hydration (without the participation of the amine) of 2-propyl-2-ynyloxymethyltetrahydrofuran in the presence of mercury(II) acetate.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra (300.07 and 75.46 MHz respectively) of the solutions in DMSO-d_6–CCl_4 (1 : 3) were recorded with a Varian Mercury-300 VX spectrometer at 303 K relative to internal TMS. The reaction progress was monitored by TLC using Silufol UV-254 plates, developing with $KMnO_4$ and iodine vapor. GLC analysis was performed using a LHM-80MD instrument (model 3) (1.5 m column, AW-NMDC sorbent soaked with 10% Sarbovax-20M, rate of carrier gas 40 mL/min, detector temperature 250°C, evaporator temperature 200°C).

2-Prop-2-ynyloxymethyltetrahydrofuran was prepared as described in [8].

Reaction of 2-prop-2-ynyloxymethyltetrahydrofuran with acetylacetone. *a*. 7 g (0.05 mol) of 2-prop-2-ynyloxymethyltetrahydrofuran was added dropwise to a solution of 8 g (0.025 mol) of mercury(II) acetate in 50 mL of dioxane. The mixture was stirred during 1 h at 25°C. In a separate vessel, a mixture of 20 mL of acetylacetone and 1.2 g (0.05 mol) of sodium in 10 mL of dioxane was stirred for 30 min. Next, the both mixtures were combined. After stirring during 12 h at 25°C, 1.2 g (0.03 mol) of powdered sodium borohydride and 50 mL of water were subsequently added to the mixture. The mixture was stirred for another 30 min, extracted with diethyl ether, dried over magnesium sulfate, and concentrated. The residue was distilled in vacuum. Yield 6.91 g (54%) of the mixture of 4-hydroxy-3-[1-methyl-2-(tetrahydrofuran-2-ylmethoxy)vinyl]pent-3-en-2-one **III** [R_f 0.63 (Et_2O–hexane, 1 : 1)] and 3-[1-methyl-2-(tetrahydrofuran-2-ylmethoxy)vinyl]pentane-2,4-dione **IV** [R_f 0.72 (Et_2O–hexane, 1 : 1)], bp 90–92°C (5 mmHg). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.75 s (3H, CH_3C=), 1.7–1.9 m (4H, CH_2, furan), 2.15 s (6H, CH_3C=O), 3.8 m (2H, CH_2O, furan), 4.01–4.12 m (3H, OCH_2, OCH, furan), 6.23 br.s (1H, =CH), 16.37 s (1H, OH).

b. 4 g (0.029 mol) of 2-prop-2-ynyloxymethyltetrahydrofuran was added dropwise to a solution of 9.28 g (0.029 mol) of mercury(II) acetate in 50 mL of DMSO. The mixture was stirred during 1 h at 25°C. In a separate vessel, a mixture of 3 mL of acetylacetone, 0.67 g (0.029 mol) of sodium, and 10 mL of DMSO was stirred for 30 min. Next, the both mixtures were combined. After stirring during 12 h at 25°C, 16 mL of 20% hydrochloric acid was added. The mixture was stirred for another 30 min, extracted with diethyl ether, dried over magnesium sulfate, and concentrated. The residue was distilled in vacuum to give **1-[2,4-dimethyl-5-(tetrahydrofuran-2-ylmethoxy)-4,5-dihydrofuran-3-yl]ethanone (V)** as a 1 : 1 mixture of diastereomers in yield of 2.784 g (40%), bp 149°C (3 mmHg), R_f 0.41 (Et_2O–hexane, 3 : 1). ^{1}H NMR spectrum, δ, ppm: 1.14 d and 1.14 d (3H, CH$\underline{CH}_3$, *J* 7.1 Hz), 1.80–1.98 m and 1.51–1.73 m (4H, CH_2CH_2), 2.17 s and 2.17 s (3H, $COCH_3$), 2.21 d and 2.22 d (3H, =CCH_3, *J* 1.1 Hz), 2.89–2.99 m (1H, $\underline{CH}CH_3$), 3.47–3.52 m (1H, OCH_2), 3.59–3.71 m (2H, OCH_2), 3.74–3.82 m (1H, OCH_2), 3.90–3.99 m (1H, OCH), 5.06 d and 5.07 d (1H, OCHO, *J* 10.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 191.5 and 191.5 (C=O), 163.5 (=$\underline{C}CH_3$), 117.6 (=$\underline{C}CO$), 110.8 and 110.6 (O$\underline{C}$HO), 76.9 and 76.5 (OCH), 70.3 and 69.9 (OCH_2), 67.3 and 67.1 (OCH_2), 43.1 and 43.0 ($\underline{C}HCH_3$), 28.5 ($CO\underline{C}H_3$), 27.7 and 27.5 (CH_2), 25.2 and 24.9 (CH_2), 17.3 (CH_3CH), 14.6 (=CCH_3).

Reaction of 2-prop-2-ynyloxymethyltetrahydrofuran with amines. A mixture of 8.1 g (0.025 mol) of mercury(II) acetate and a solution of 7 g (0.05 mol) of 2-prop-2-ynyloxymethyltetrahydrofuran in 20 mL of dioxane was stirred at 25°C for 30 min. Then 0.05 mol of diethylamine or morpholine was added dropwise to the resulting complex of mercury(II) acetate. After stirring during 48 h at 25°C, 1 g (0.026 mol) of sodium borohydride was added, and the mixture was stirred for another 1 h. Next, 25 mL of water was slowly added. After stirring during 30 min, the mixture was extracted with diethyl ether, dried over magnesium sulfate, and concentrated. The residue was distilled in vacuum to yield 3.87 g of a mixture of 1-(tetrahydrofuran-2-ylmethoxy)propan-2-one **XI** and 1-(tetrahydrofuran-2-ylmethoxy)propan-2-ol **XII**, bp 92–99°C (3 mmHg).

1-(Tetrahydrofuran-2-ylmethoxy)propan-2-one (XI). R_f 0.65. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.7–1.9 m (4H, CH_2, furan), 2.12 s (3H, CH_3C=O), 3.4–3.6 m (2H, OCH_2), 3.8–4.12 m (3H, OCH_2, OCH, furan), 4.53 s (2H, OCH_2C=O).

1-(Tetrahydrofuran-2-ylmethoxy)propan-2-ol (XII). R_f 0.55. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm:

1.21–1.22 m (3H, CH_3), 1.7–1.9 m (5H, CH_2, furan, OH), 3.4–3.8 m (5H, OCH_2, CH), 3.8–4.12 m (3H, OCH_2, OCH, furan), 4.13 m (1H, OCH, furan).

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