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REACTION OF 2-CHLORO-5-(CHLOROMETHYL)THIOPHENE WITH MONOETHANOLAMINE VINYL ETHER

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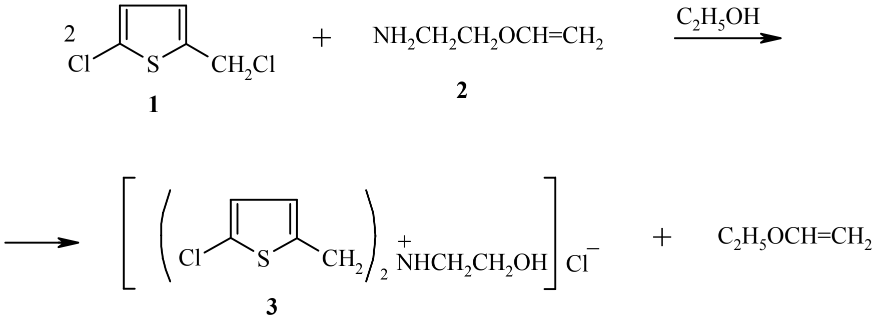
At the alkylation of monoethanolamine vinyl ether with 2-chloro-5-(chloromethyl)thiophene in ethyl alcohol (60-70°C) a product of disubstitution and transvinylation, viz. N,N-bis(5-chloro-2-thienylmethyl)-N-(2-hydroxyethyl)ammonium chloride is formed. The analogous reaction in the absence of solvent proceeds with the formation of N-(5-chloro-2-thienylmethyl)-N-(2-vinyloxyethyl)amine.

Keywords: monoethanolamine vinyl ether, N-(5-chloro-2-thienylmethyl)-N-(2-vinyloxyethyl)amine, N,N-bis(5-chloro-2-thienylmethyl)-N-(2-hydroxyethyl)ammonium chloride, 2-chloro-5-(chloromethyl)thiophene, reactions.

It is known that the condensation of monoethanolamine vinyl ether with propargyl bromide leads to the formation of the corresponding dipropargylamine [1].

We have established that ammonium salt **3** is formed on alkylation of monoethanolamine vinyl ether (**2**) with 2-chloro-5-(chloromethyl)thiophene (**1**) in ethyl alcohol at 60-70°C. This is the product of substitution of two hydrogen atoms of the amino group by the alkylating agent and transvinylation of ethyl alcohol (ethyl vinyl ether was detected in the reaction mixture).



The reaction of compounds **1** and **2** in the absence of solvent occurs at 50-70°C with the formation of N-(5-chloro-2-thienylmethyl)-N-(2-vinyloxyethyl)amine (**4**).

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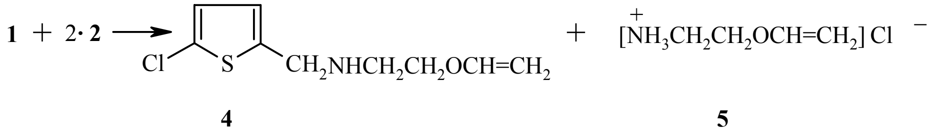

With an equimolar ratio of reactants the reaction does not proceed to completion. The conversion of chloride **1** was ~50%, and the yields of compounds **4** and **5** were 35 and 65% respectively. For the complete conversion of chloride **1** a 2-3 fold excess of amine **2** is necessary, which combines with hydrogen chloride evolved. The synthesized compounds **3** and **4** are potentially biologically active substances.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 instrument (400 MHz for ^1H and 100 MHz for ^{13}C), internal standard was HMDS. The mass spectra were taken on an LKB-2091 chromato-mass spectrometer with direct insertion of samples into the ion source at 300°C. Ion source temperature was 230°C and ionizing voltage was 60 eV.

N,N-Bis(5-chloro-2-thienylmethyl)-N-(2-hydroxyethyl)ammonium Chloride (3). Mixture of chloro compound **1** (14.4 g, 86 mmol) and amino ether **2** (7.5 g, 86 mmol) in ethanol (22-25 ml) was stirred with heating to 60-70°C. After 6 h the reaction mixture was poured into diethyl ether. The precipitated crystals were separated on a Schott funnel, then dissolved with heating in methanol and precipitated once again with ether. Product **3** (4.84 g, 31.4%) was obtained as a grayish powder, soluble in ethanol and somewhat less in water; mp 175-176°C. ^1H NMR spectrum ($(CD_3)_2SO$), δ, ppm, *J* (Hz): 7.27 (2H, d, *J* = 4.0, two 4-H); 7.05 (2H, d, *J* = 4.0, two 3-H); 4.45 (4H, s, two Het–CH_2); 3.77 (2H, t, CH_2O); 3.04 (2H, t, $N\underline{H_2}CCH_2$). ^{13}C NMR spectrum ($(CD_3)_2SO$), δ, ppm, *J* (Hz): 50.76 (^1J = 144.1, Het–CH_2); 52.68 (^1J = 141.16, $N\underline{C}H_2CH_2$); 55.83 (^1J = 144.11, CH_2OH); 126.5 ($C_{(4)}$); 131.7 ($C_{(3)}$); 130.37 ($C_{(5)}$); 131.46 ($C_{(2)}$). Mass spectrum, *m/z*: 321 $[M\text{-}HCl]^+$; 290 $[M\text{-}HCl\text{-}CH_2OH]^+$; 131 $[ClC_4H_2SCH_2]^+$. Found, %: C 40.1; H 3.54; Cl 29.67; N 3.94; S 18.48. $C_{12}H_{14}Cl_3NOS_2$. Calculated, %: C 40.16; H 3.91; Cl 29.70; N 3.91; S 17.85. Inorganic chlorine: found 10.57%, calculated 9.90%.

N-(5-Chloro-2-thienylmethyl)-N-(2-vinyloxyethyl)amine (4). Mixture of chloride **1** (2.8 g, 17 mmol) and amino ether **2** (3.8 g, 45 mmol) was heated without solvent at 65-70°C for 8 h. After cooling, the reaction mixture was treated with water to dissolve salt **5**. The organic mass was extracted with ether, and with dichloromethane. The combined extract was dried over $CaCl_2$, evaporated, and the residue distilled in vacuum. Product **4** (2.1 g, 57%) was obtained; bp 140-141°C (4 mm Hg), n_D^{20} 1.5405. ^1H NMR spectrum ($CDCl_3$), δ, ppm, *J* (Hz): 1.90 (1H, s, NH); 2.81 (2H, t, $^3J_{CH_2CH_2}$ = 5.3, $NC\underline{H_2}CH_2$); 3.87 (2H, d, $^4J_{NCH_2C=CH}$ = 0.9, N–$C\underline{H_2}$–Het); 3.74 (2H, t, $^3J_{NCH_2CH_2O}$ = 5.3, CH_2O); 3.98 (1H, dd, ^4J = 6.8, *cis*-$H_{=CH_2}$); 4.16 (1H, dd, ^4J = 14.6, *trans*-$H_{=CH_2}$); 6.43 (1H, dd, $^4J_{cis}$ = 6.8, $^4J_{trans}$ = 14.6, =CH); 6.64 (1H, dt, $^3J_{3\text{-}4}$ = 3.7, $^4J_{CH=CCH_2N}$ = 0.9, 3-H); 6.69 (1H, d, $J_{4\text{-}3}$ = 3.7, 4-H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 86.73 (=CH_2); 151.56 (=CH); 67.22 (CH_2O); 47.56 ($N\underline{C}H_2CH_2$); 48.50 (Het–CH_2N); 143.46 ($C_{(2)}$); 123.81 ($C_{(3)}$); 125.49 ($C_{(4)}$); 128.32 ($C_{(5)}$). Found, %: C 49.60; H 5.55; Cl 16.57; N 6.23; S 14.53. $C_9H_{12}ClNOS$. Calculated, %: C 49.65; H 5.51; Cl 16.32; N 6.43; S 14.71.

(2-Vinyloxyethyl)ammonium Chloride (5). Chloride **1** (4.2 g, 25 mmol) and amino ether **2** (2.2 g, 25 mmol) were mixed without a solvent. The reaction proceeded with self-heating to 50°C and was completed after 6 h. The resulting glass-like mass was covered with diethyl ether. On standing bright beige crystals were precipitated. Salt **5** (2 g, 65%) was obtained; mp 40-41°C, readily soluble in water and chloroform. ^1H NMR spectrum ($CDCl_3$), δ, ppm, *J* (Hz): 3.03 (2H, t, $^3J_{CH_2CH_2}$ = 5.3, $NC\underline{H_2}CH_2$); 3.90 (2H, t, $^3J_{CH_2CH_2}$ = 5.3, CH_2O); 4.03 (1H, dd, ^4J = 6.6, *cis*-$H_{=CH_2}$); 4.20 (1H, dd, ^4J = 14.3, *trans*-$H_{=CH_2}$); 6.49 (1H, dd, $^4J_{cis}$ = 6.6, $^4J_{trans}$ = 14.3, =CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 88.38 (=CH_2); 150.88 (=CH); 63.58 (CH_2O); 39.18 ($N\underline{C}H_2CH_2$).

The molecular ion was not recorded in the mass spectrum, the fragment ions were *m/z* 30 (CH_2O), 42 (C_2H_2O), 61 ($NH_3CH_2CH_2O$). Found, %: C 38.79; H 8.27; Cl 28.89; N 11.25. $C_4H_{10}ClNO$. Calculated, %: C 38.86; H 8.09; Cl 28.74; N 11.33.

Salt **5** was unstable and on standing for 8-10 days melted and was converted into a brown oil. Unreacted chloride **1** and amine **4** were detected in the ether mother liquor by chromato-mass spectrometry and NMR.

REFERENCES

1. B. A. Trofimov, *Heteroatomic Derivatives of Acetylene* [in Russian], Nauka, Moscow (1981), p. 114.