

STUDIES IN THE THIOPHENE SERIES. III.*

ANODIC OXIDATION OF 2-THENYL ALCOHOL

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During anodic oxidation of 2-thenyl alcohol in methanol, using sulfuric acid as electrolyte, dimethyl acetal of 2-thiophenecarbaldehyde is formed as the main product; this is analogous to the oxidation of benzyl alcohol from which benzaldehyde was isolated in high yield. Electrochemical EC_BEC_N -type of mechanism is proposed for this reaction in contrast to the more common course of the anodic oxidation in the furan and thiophene series, characterised by common intermediary stages of the EC_NEC_N type.

As part of our systematic investigation of the course of anodic oxidation in thiophene series¹ we described now the course of this reaction in the case of 2-thenyl alcohol (*I*).

For the preparation of compound *I* we made use of the Vilsmeier-Haack formylation of thiophene² and subsequent reduction with lithium aluminum hydride. The electrochemical oxidation proper was carried out in methanol containing acid. Gas chromatographic analysis of the reaction mixture has shown that it contained four components (*A—D*) of which the following were isolated: *B*, representing 70%, and *C*, representing over 10% of the reaction mixture. In the spectrum of component *B* the following signals were observed (values in p.p.m. units): multiplets of three protons, centered at 7.37 and 7.12, a singlet of one proton at 5.67, and a singlet at 3.34, corresponding to six protons of two OCH_3 groups. Hence, this spectrum indicates the structure of the dimethyl acetal of 2-thiophenecarbaldehyde. The PMR spectrum of component *C* contains the following signals: a singlet at 9.92, a doublet at 7.78, and a triplet at 7.22 (relative ratio of integrals 1 : 2 : 1); it indicates the structure of 2-thiophenecarbaldehyde. Its identity was proved by reduction of compound *C* with lithium aluminum hydride, affording 2-thenyl alcohol. Standards for the isolated compounds were prepared by other routes: 2-thiophenecarbaldehyde by formylation of thiophene; subsequent reaction with methyl orthoformate gave corresponding dimethyl acetal. The identity of these standards with compounds *B* and *C* was proved by IR and PMR spectroscopy as well as by the mixture melting point of their 2,4-dinitrophenylhydrazones. Substance *D* was the unreacted 2-thenyl alcohol (yield 7.60%).

The course of the anodic oxidation of 2-thenyl alcohol, leading to 2-thiophenecarbaldehyde and its dimethyl acetal is the first observed case in the thiophene series in which sulfur is not eliminated during the electrolytic process and in which the

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loss of electrons is eventually observed in the side chain. In the literature a precedent may be found, *i.e.* the oxidation of *p*-methoxybenzyl alcohol, affording *p*-methoxybenzaldehyde³. The reaction was carried out in 0.5M sodium perchlorate in acetonitrile in the presence of pyridine as proton acceptor, without which the reaction practically did not take place. The authors propose a mechanism which is initiated by the abstraction of the electron on the benzene carbon atom carrying the alcoholic function. Thus the radical-cation of quinoid character formed is stabilised after another loss of electron from the same carbon atom by the splitting off of two protons from the alcoholic function of the side chain. In connection with this work we tried to carry out the anodic oxidation with benzyl alcohol under the conditions used for 2-thenyl alcohol, *i.e.* in methanol containing sulfuric acid. A chromatographic analysis of products, using standards for comparison, showed that benzylaldehyde was the main product (87.8%), but that by-products were also formed (9.3 and 3.6%). From the comparison of this result with the mentioned study of the oxidation of *p*-methoxybenzyl alcohol it follows that on oxidation of benzyl alcohol under the conditions mentioned by us the splitting off of protons is spontaneous and does not require the presence of an additional proton acceptor in the reaction mixture.

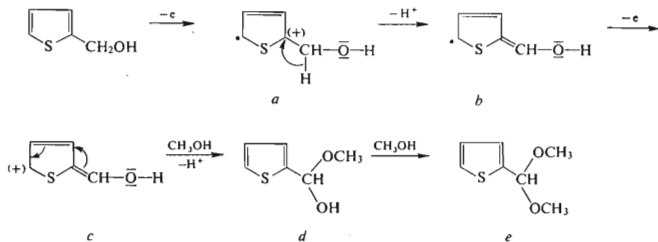
When comparing the oxidation of 2-thenyl alcohol with that of benzyl alcohol an interesting feature may be observed, *i.e.* that the fraction of dimethyl acetal formed from the thiophene derivative is much more pronounced than in the case of the benzene analogue, in which the corresponding acetal could not be isolated at all. Therefore we followed the formation of 2-thiophenecarbaldehyde and benzaldehyde acetals under the conditions analogous to those occurring during the anodic oxidations, *i.e.* under the effect of methanol and 1% of sulfuric acid, in the cold. It was found that in contrast to benzaldehyde, which did not afford the acetal, the ratio of the acetal and the free aldehyde corresponds in the case of thiophenecarbaldehyde to the proportional representation of these substances in the reaction mixture after oxidation of 2-thenyl alcohol. From this it may be concluded that acetalisation is subsequent to the originally formed 2-thiophenecarbaldehyde, which is similar to the behaviour of the furan analogue^{4,5}.

For the oxidation of 2-thenyl alcohol we propose the mechanism represented in Scheme 1 comprising the abstraction of electron in α -position. Of the alternative positions, 2 and 5, we chose position 5 on the basis of the HMO calculation *a*) mentioned farther on. Later, instead of an alcoholic attack the formation of a conjugated double bond under departure of a proton *b*) takes place in contrast to the cases described so far in the thiophene series¹. The cation formed *c*) by a subsequent loss of electron is transformed under the effect of anion OCH_3^- on a conjugated system to the hemiacetal of 2-thiophenecarbaldehyde *d*) by EC_BEC_N mechanism.* The final

* E the electrochemical step of the reaction, C the chemical step. Index B deprotonation, index N a nucleophilic attack.

product, dimethyl acetal of 2-thiophenecarbaldehyde, is then formed from the semi-acetal by reaction with methanol.

When HMO method was applied to the anodic oxidation of 2-thenyl alcohol and 2-furyl alcohol the following parameters were employed^{6,7}: π -electronic energy of the highest occupied π -molecular orbital k_1 of the furan model $F k_1 = 0.3793$, for the thiophene model $T k_1 = 0.3727$; empirical parameters: $X = O$, $\delta_X = 2.0$, $\rho_{CX} = 0.8$; $X = S$, $\delta_X = 1.0$, $\rho_{CX} = 0.8$; $Y = CH_2OH$, $\delta = 1.0$, $\rho_{CY} = 0.7$. Indexes of chemical reactivity, *i.e.* π -electronic density q and nucleophilic superdelocalisability S_N were computed for the given models both in the basic state and for the radical cation. From values q (for model F, position 2, $q = 0.959$, position 5, $q = 1.078$; for model T, position 2, $q = 1.014$, position 5, $q = 1.110$) it follows that the abstraction of the first electron from position 5 is more probable. The difference between $EC_N EC_N$ and $EC_B EC_N$ mechanisms lies in the second step, *i.e.* in the disposition of the primarily formed radical cation; it can be formulated as a competition between the nucleophilic intervention of the methanol anion in the α -position of the nucleus and the splitting off of proton from the side chain. The measure of the participation of the $EC_N EC_N$ mechanism may be judged from the values of S_N^+ indices. The latter agree with experimental values, *i.e.* in model T the inclination for a "normal" nucleophilic attack by methanol (S^+ for T in the position 2 = 1.284, and position 5 = 1.466) is lower in comparison with F (S^+ for F in position 2 = 1.364, and position 5 = 1.612).



SCHEME 1

It is interesting to compare the results of anodic oxidation in the series 2-furyl alcohol, 2-thenyl alcohol, benzyl alcohol. In the case of the five-membered oxygen-containing heterocycle anodic oxidation is connected with the loss of electrons in α -position in combination with solvolytic processes ($EC_N EC_N$ mechanism) under formation of 2,5-dihydro-2,5-dimethoxy-2-hydroxymethylfuran⁵. In the case of thiophene analogue a loss of electrons, also on α -carbon atoms of the cycle, is supposed, but it is connected with the departure of a proton from the CH_2OH group. The splitting off of this proton is a characteristic of the electrochemical oxidation of the benzene series analogue. As present results of anodic oxidation in the thiophene series are connected with $EC_N EC_N$ mechanism¹, the results of this work place thiophene between the furan and benzene series.

EXPERIMENTAL

Melting points and boiling points were not corrected. Solid substances were dried at room temperature and 0.5 Torr for 8 hours for analysis. The IR spectra were measured on a UR 10 (Zeiss, Jena) spectrophotometer, within the $700\text{--}3700\text{ cm}^{-1}$ range, in a CCl_4 solution. The PMR spectra were measured on a Tesla BS 477 apparatus in deuteriochloroform. Electrochemical oxidation was carried out on an apparatus⁸ the cathode of which was constructed of two concentric cylinders connected with a riveted nickel band. The exterior was made of stainless steel AKV and its diameter was 53 mm, its height 343 mm, while the interior was of pure nickel, diameter 43 mm, height 240 mm. The anode was of graphite, diameter 28 mm, height 360 mm. The electrolyser was placed in a cylinder containing the cooling mixture, butanol with solid CO_2 . The calculations for the HMO method were carried out, using a standard program, on an Elliot 503 computer.

2-Thenyl Alcohol

A solution of 70 g (0.675 mol) of 2-thiophenecarbaldehyde, prepared by formylation of thiophene², in 250 ml of ether was added dropwise into a mixture of 19 g (0.5 mol) of lithium aluminium hydride in 350 ml of ether cooled with a mixture of ice and water. The reaction mixture was stirred at room temperature for one hour, then cooled with ice and mixed by dropwise addition with 19 ml of water, 19 ml of a 15% NaOH solution, and 57 ml of water. Stirring was continued for another 20 minutes at room temperature, the precipitate was filtered off and washed with ether. After evaporation of the solvent the product was distilled. Yield 63.8 g (89.7%) of 2-thenyl alcohol, b.p. $91^\circ\text{C}/8\text{ Torr}$. For $\text{C}_5\text{H}_6\text{OS}$ (114.2) calculated: 52.60% C, 5.30% H, 28.08% S; found: 52.95% C, 5.41% H, 28.27% S.

Electrochemical Oxidation of 2-Thenyl Alcohol

A solution of 22.4 g (0.2 mol) of 2-thenyl alcohol and 1 ml of conc. sulfuric acid in 300 ml of methanol was electrolysed at 4.2 A, 25 V, and -20 to -30°C for 8 hours. The reaction mixture was neutralised with a solution of 0.96 g of sodium in 20 ml of methanol. Methanol was evaporated under reduced pressure and the residue extracted with ether (200 ml). After drying over magnesium sulfate ether was distilled off and the residue distilled to afford 9.20 g of a fraction of b.p. 91 to $98^\circ\text{C}/14\text{ Torr}$. Gas chromatographic analysis (on polypropylene sebacate on celite, 160°C , nitrogen as carrier gas, column length 160 cm, diameter 6 mm) showed that the fraction contained two main components. Using preparative gas chromatography (Carbowax 20 M on Chromosorb W, 135°C , column length 6 m, column diameter 8 mm, carrier gas nitrogen), of components indicated according to their increasing elution times by letters A–D the components B and C could be isolated in a 95% purity. Component B was identified as dimethyl acetal of 2-thiophenecarbaldehyde on the basis of its IR and PMR spectra which were identical with those of a substance prepared from 2-thiophenecarbaldehyde and methyl orthoformate. With 2,4-dinitrophenylhydrazine component B afforded 2,4-dinitrophenylhydrazone of 2-thiophenecarbaldehyde; red crystals, m.p. $230\text{--}231^\circ\text{C}$ (nitromethane). For $\text{C}_{11}\text{H}_8\text{N}_4\text{O}_4\text{S}$ (292.3) calculated: 45.21% C, 2.76% H, 19.06% N, 10.97% S; found: 45.52% C, 2.29% H, 19.57% N, 11.37% S.

Component C was identified on the basis of PMR spectra as 2-thiophenecarbaldehyde. Its structure was corroborated by comparison of its spectra with those of 2-thiophenecarbaldehyde prepared by formylation of thiophene; the values of the chemical shifts were identical with those in the catalogue of PMR spectra⁹. 2,4-Dinitrophenylhydrazone, m.p. $231\text{--}232^\circ\text{C}$. For $\text{C}_{11}\text{H}_8\text{N}_4\text{O}_4\text{S}$ (292.3) calculated: 45.21% C, 2.76% H, 19.06% N, 10.97% S; found: 45.59% C, 2.96% H, 19.49% N, 11.03% S. In a repeated experiment an 8 hours anodic oxidation of 22.8 g (0.2 mol) of 2-thenyl alcohol gave, according to gas chromatography on a Carlo Erba apparatus (filled with Carbowax 20 M on Chromosorb W, temperature 162°C , column length 250 cm, diameter 2 mm, carrier gas nitrogen, shift of the paper 0.254 cm/min), the following mixture (component, elution time in cm, % of the component in the mixture): A, 0.77, 1.85%; B, 1.35,

72.92%; C, 1.85, 11.58%; D, 7.27, 6.43%; unreacted 2-thenyl alcohol 7.23%. On oxidation of 11.4 g (0.1 mol) of 2-thenyl alcohol for 4 hours the following mixture was formed: A, 0.69%; B, 74.70%; C, 11.05%; D, 5.70%; unreacted 2-thenyl alcohol 7.86%.

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