BEHAVIOR OF AN ALKYLTHIOACETALDEHYDE UNDER CONDITIONS OF THE MANNICH REACTION

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On the example of the 2-alkoxyacroleins it was shown [1] that substituted acrylic systems exist, for which electrophilic addition to the C = C bond in harmony with the Markovnikov rule is characteristic. As a continuation of these studies we undertook the preparation of the thio analog of a 2-alkoxyacrolein from an alkylthioacetaldehyde via the Mannich reaction. The use of thioaldehydes in the Mannich reaction has not been described

$$\operatorname{RSCH}_{2}\operatorname{CHO} + \operatorname{NHR}_{2} \cdot \operatorname{HCl} + \operatorname{CH}_{2}\operatorname{O} \xrightarrow{a} \left[\begin{array}{c} \operatorname{RSCHCHO} \\ | \\ \operatorname{CH}_{2} \\ | \\ \operatorname{NR}_{2} \cdot \operatorname{HCl} \\ \end{array} \right] \xrightarrow{b} \operatorname{RSCCHO} \\ \xrightarrow{b} \operatorname{RSCCHO} \\ \underset{CH_{2}}{\overset{\|}{\longrightarrow}} \\ \xrightarrow{c} \operatorname{CH}_{2} \\ \xrightarrow{c} \operatorname{C$$

The reaction was run under milder conditions than was required for the alkoxyacetaldehydes [2, 3]. Contrary to expectations, the sole reaction product that was isolated in 61% yield was the 2-formyl-2,5-dialkylthio-2,3-dihydro- γ -pyran (I), the dimer of the 2-alkylthioacrolein



As was shown by the GLC method, the starting alkylthioacetaldehyde disappears almost completely even in the first 10 min at 20°C, whereas for the ethoxyacrolein the reaction lasts for 20 min at 60° [4]. Attempts to record the appearance of the free 2-alkylthioacrolein by the TLC and GLC methods, and also by the precipitation of the crystalline 3,5-dinitrobenzoylhydrazide (3,5-DNBH) derivative, even with a possible retardation of the reaction (dilution, lowering of the temperature), failed to give positive results.

By analogy with the previously described 2-alkylthio-substituted acrylates and acrylonitriles [5], an increased capacity to dimerize could be expected for the alkylthioacrolein. Our data revealed that the 2-alkylthioacroleins enter into the diene condensation even more easily than the 2-alkoxyacroleins [6]. The degree of increase in the dimerization rate as a function of the substituent can be arranged in the following order: H < OR < OS. The formation of a product with a cyclic structure on the type of adducts of the Diels –Alder reaction is corroborated by the data for the oxime titration of the CHO group, the mercurimetric determination of the C=C bond, the preparation of the monoadducts with 2,4-dinitrophenylhydrazine and 3,5-dinitrobenzoylhydrazide, and also by the molecular weight determination and an analysis of the IR spectrum (C=O 1730, C=C 1630, C-O 1050 cm⁻¹). The starting alkylthioacetaldehydes were obtained by the scheme:

 $\operatorname{BrCH}_2\operatorname{CH}(\operatorname{OC}_2\operatorname{H}_5)_2 \xrightarrow[\operatorname{RSNa}]{\operatorname{RSCH}_2} \operatorname{RSCH}_2\operatorname{CH}(\operatorname{OC}_2\operatorname{H}_5)_2 \xrightarrow[\operatorname{H}_*O]{\operatorname{H}_*} \operatorname{RSCH}_2 - \operatorname{CHO}$

EXPERIMENTAL METHOD

<u>Dimer of 2-Butylthioacrolein</u>. A solution of 7.3 g of $(C_2H_5)_2$ NH · HCl and 20.2 g of 10% formalin solution was neutralized with 10% Na₂CO₃ solution to pH 7. With vigorous stirring, 8.9 g of butylthioacetaldehyde

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was added and the mixture was stirred at 20° for 1 h. Then the organic layer was separated, and the aqueous layer was extracted with ether. The combined extract and organic layer was dried over MgSO₄, and the ether was distilled off. Vacuum-distillation gave 5.9 g (61%) of 2-formyl-2,5-dibutylthio-2,3-di-hydro- γ -pyran, bp 119-121° (4 mm); n_D^{20} 1.5160; d_4^{20} 1.0686. Found: C 58.67; H 8.39; S 22.22%; MR 81.75; mol. wt. 300 (±5%) (reverse ebullioscopy [7]). $C_{14}H_{24}O_2S_2$. Calculated: C 58.3; H 8.32; S 22.2%; MR 81.83.

Using the procedure given in [8], the oxime titration of 0.3044 g of the butylthioacrolein dimer with 0.96 N NaOH solution (1.05 ml) gave the amount of carbonyl groups as equal to 91.5%.

The mercurimetric determination of the double bond was run as described in [9]. The potentiometric titration of 0.2065 g of the dimer for a day required 0.7 ml of 0.96 N NaOH solution, which corresponds to an unsaturation of 93.8%.

The reaction of 0.1201 g of the product with 0.12 g of 2,4-DNPH in alcohol solution, in the presence of catalytic amounts of HCl, gave 0.0428 g of the hydrazone with mp 87-88°. Found: N 12.12; S 13.41%. $C_{20}H_{28}O_5N_4S_2$. Calculated: N 11.95; S 13.6%.

The reaction of 0.3977 g of the product with 0.21 g of 3,5-DNBH, with heating in alcohol solution, gave 0.2576 g (56%) of the corresponding hydrazone, mp 133°. Found: N 11.12%. $C_{22}H_{28}O_6N_4S_2$. Calculated: N 11.28%.

<u>Dimer of 2-Ethylthioacrolein</u>. The reaction was run by the above described method: from 12.2 g of $(C_2H_5)_2NH \cdot HCl$, 32.6 g of formaldehyde (10% solution), and 11.7 g of ethylthioacetaldehyde. In contrast to the reaction with butylthioacetaldehyde, a substantial heat effect was observed during the addition of the ethylthioacetaldehyde, for which reason the reaction mixture was cooled in cold water. After the usual workup we obtained 8 g (61.5%) of 2-formyl-2,5-diethylthio-2,3-dihydro- γ -pyran, bp 145° (6 mm); n_D^{20} 1.5400; d_4^{20} 1.1442. Found: C 52.03; H 6.91; S 27.70%; MR 63.67. $C_{10}H_{16}O_2S_2$. Calculated: C 51.7; H 6.89; S 27.61%; MR 63.26. The 2,4-dinitrophenylhydrazone was obtained in 56% yield, mp 117°. Found: C 46.48; H 4.79; S 15.29; N 13.82%. $C_{16}H_{20}O_5N_4S_2$. Calculated: C 46.6; H 4.84; S 15.5; N 13.58%.

Diethyl Acetal of Butylthioacetaldehyde. To a mixture of 280 ml of absolute alcohol and 75.7 g of butyl mercaptan was added 19.3 g of Na metal in portions. After all of the Na had reacted, the temperature of the reaction mixture was raised to 70° and 163.3 g of the diethyl acetal of bromoacetaldehyde was added dropwise in 2 h. The mixture was refluxed for 2.5 h and allowed to stand overnight. The reaction mixture was decomposed with 400 ml of water, the organic layer was separated, and the aqueous layer was extracted with ether (6 × 50 ml). The combined extract and organic layer was dried over MgSO₄. After removal of the ether the residue was vacuum-distilled. We obtained 150 g (90%) of the diethyl acetal of butylthioacetaldehyde, bp 78° (2 mm); n_D^{20} 1.4490; d_4^{20} 0.9276. Calculated: C 57.81; H 11.37; S 15.82%; MR 59.59. $C_{10}H_{22}O_2S$. Calculated: C 58.25; H 10.67; S 15.55%; MR 59.35.

Diethyl Acetal of Ethylthioacetaldehyde. Obtained in the same manner as above in 92.4% yield, bp 60° (7 mm); n_{D}^{20} 1.4470; cf. [10].

Butylthioacetaldehyde. A mixture of 100 g of the diethyl acetal of butylthioacetaldehyde, 47 ml of conc. HCl, 281 ml of water, and a little hydroquinone was refluxed for 2 h, cooled, the organic layer was separated, and the aqueous layer was extracted with ether (6×50 ml). The combined extract and organic layer was dried over MgSO₄. After distilling off the ether the residue was vacuum-distilled. We obtained 37.5 g (58.5%) of butylthioacetaldehyde, bp 53° (3 mm); n_D^{20} 1.4715; d_4^{20} 0.9720. Found: C 54.42; H 9.33%; MR 37.95. $C_6H_{12}OS$. Calculated: C 54.50; H 9.15%; MR 37.61.

Ethylthioacetaldehyde. Obtained in the same manner as above. For the experiment we took 86 g of the acetal, 50 ml of conc. HCl, and 330 ml of water. We obtained 22.4 g (43%) of ethylthioacetaldehyde, bp 40° (10 mm); n_D^{20} 1.4750; cf. [11].

CONCLUSIONS

Alkylthioacetaldehydes under the conditions of the aminomethylation reaction give α -alkylthioacroleins, which under the synthesis conditions are dimerized to 2-formyl-2,5-dialkylthio-2,3-dihydro- γ pyrans.

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