Synthesis of α-alkylthioacroleins

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Monomeric α-alkylthioacroleins were obtained by the reaction of alkylthioacetaldehydes with formaldehyde and diethylamine hydrochloride. The structures of the α-alkylthioacroleins were confirmed by NMR spectroscopy and mass spectrometry as well as by chemical transformations of these compounds.

Key words: α-alkylthioacroleins, aminomethylation; diene synthesis; hydrazones; addition of thiols.

Alkylthiocrotonic aldehydes are stable as monomers.[1] Conversely, α-alkylthioacroleins **1** synthesized from alkylthioacetaldehydes **2** *via* aminomethyl-substituted derivatives **3** quite readily dimerize into 2,5-dialkylthio-2,3-dihydro-4*H*-pyrans **4**.[2] Attempts at synthesizing monomeric α-alkylthioacroleins[1] by other methods also gave cyclic dimers **4**.[3,4] Like α-alkylthioacroleins, isostructural α-methylselenoacrolein exists only at low temperatures (−40 °C) and undergoes total cyclodimerization at 20 °C (20 min).[6,7]

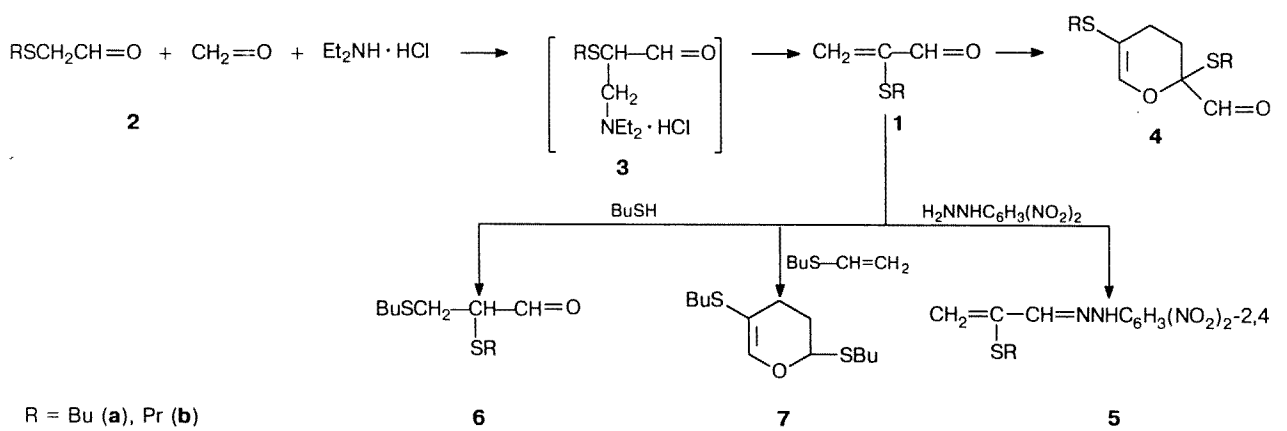
Using ^{1}H NMR spectroscopy, we previously detected short-lived butylthioacrolein.[5] However, to date no one has succeeded in detecting it in the form of a derivative.

In the present work we consider a method for synthesizing α-alkylthioacroleins **1** and some of their transformations. The method proposed is based on the reaction of equimolar amounts of alkylthioacetaldehyde, formaldehyde, and diethylamine hydrochloride in an aqueous-alcohol medium at room temperature (Scheme 1).

It is possible to increase the yields and lifetimes of the resulting α-alkylthioacroleins by adding a solvent immiscible with water (CCl_4 or ether) to the reaction mixture. This procedure is carried out when the hydrochloride of Mannich base **3** has already formed (the starting alkylthioacetaldehyde has disappeared) and its decomposition to give monomeric thioacrolein **1** has started. This process occurs simultaneously with extraction of the thioacrolein by the organic layer. Such an approach makes it possible to isolate aldehyde **1** (as a solution) from other components of the reaction mixture and to avoid its further transformations (dimerization and polymerization) for a period of several hours at room temperature.

The structures of α-alkylthioacroleins **1** were confirmed by spectral and chemical methods. For example, their reactions with 2,4-dinitrophenylhydrazine (2,4-DNPH) in a strongly acidic medium give hydrazones **5**. Unlike α-alkoxyacroleins,[8] α-alkylthioacroleins are not hydrolyzed under these conditions.

Scheme 1



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The reactions of α-alkylthioacroleins with excess mercaptan under Mannich condensation conditions give α,β-dialkylthiopropanals **6**.

In the reaction with excess butylvinylsulfide, α-butylthioacrolein serves as a diene to give stable 2,5-dibutylthio-2,3-dihydro-4*H*-pyran (**7**). In addition, a significant amount of cyclodimer **4a** was also obtained.

Experimental

Chromatographic analyses were carried out on a Tsvet-100 chromatograph (flame ionization detector, a 3000×4 mm column filled with SE-30 (5 %) on Chromaton N-AW-HMDS, helium as the carrier gas). NMR spectra were recorded on a Jeol FX-90Q spectrometer with working frequencies of 89.95 MHz (^{1}H) and 22.49 MHz (^{13}C) in $CDCl_3$, using HMDS as the internal standard. Mass spectra (EI, 70 eV) were obtained on a Hewlett-Packard chromato-mass spectrometer (an HP 5971A mass-selective detector and an HP 5890 chromatograph).

α-Butylthioacrolein (1a). A mixture of diethylamine hydrochloride (4.27 g, 0.039 mol), 34 % CH_2O (3.6 mL, 0.039 mol), and isopropyl alcohol (3.6 mL) was neutralized with 30 % NaOH to pH 7. Isopropyl alcohol (60 %, 60 mL) and butylthioacetaldehyde **3a** (5.1 g, 0.039 mol) were added, and CCl_4 (50 mL) was added 20 min later. The mixture was vigorously stirred for 2 h, and a sample was withdrawn from the lower layer of the reaction mixture. According to ^{1}H NMR spectral data, the **1a** : **4a** ratio was 7 : 3. ^{1}H NMR spectrum of compound **1a**, δ: 0.92 (t, 3 H, CH_3); 1.57 (m, 4 H, CH_2CH_2); 2.75 (t, 2 H, SCH_2); 6.05 (s, 1 H, CH_2=); 6.18 (s, 1 H, CH_2=); 9.51 (s, 1 H, CH=O). ^{13}C NMR, δ: 21.85 (CH_3); 29.34 and 29.79 (CH_2CH_2); 38.51 (SCH_2); 126.10 (H_2C=); 147.63 (=CSBu); 190.16 (CH=O). MS, *m/z* (I_{rel} (%)): 144 $[M]^+$ (83), 115 $[M-CH=O]^+$, 101 (11), 89 (23), 88 (35), 73 (42), 60 (31), 59 (71), 58 (58), 57 (54), 56 (43), 55 (52), 45 (32), 41 (100).

α-Butylthioacrolein 2,4-dinitrophenylhydrazone (5a). A solution of α-butylthioacrolein (**1a**) was obtained as described above, but ether (50 mL) was used instead of CCl_4. After the mixture was stirred for 2 h, an aliquot (6 mL) of the ethereal layer was added to 15 mL of freshly prepared (by the procedure reported previously[9]) H_2O—EtOH (3 : 10) solution of 2,4-DNPH (0.4 g, 0.002 mol) acidified with H_2SO_4 (2 mL). The hydrazone **5a** (0.25 g) that precipitated after 2 min was filtered off and washed with water, yield 35 % with respect to aldehyde **2a**. Compound **5a** was purified by column chromatography (silica gel L, 21×650 mm column, hexane—ether (2 : 3) as the eluent), m.p. 121—122 °C (decomp.). Found (%): C, 48.28; H, 4.90; N, 16.93; S, 9.74. $C_{13}H_{16}N_2O_4S$. Calculated (%): C, 48.16; H, 4.93; N, 17.27; S, 9.88. ^{1}H NMR, δ: 0.96 (t, 3 H, CH_3); 1.56 (m, 4 H, CH_2CH_2); 2.84 (t, 2 H, SCH_2); 5.47 (s, 1 H, CH_2=); 5.68 (s, 1 H, CH_2=); 7.81—8.50 (m, 3 H, Ar); 9.08 (d, 1 H, CH=N); 11.14 (s, 1 H, NH).

2,3-Dibutylthiopropanal (6a). Butane-1-thiol (4.2 mL, 0.039 mol) was added to a solution of α-butylthioacrolein (**1a**) obtained as described above, but with ether (50 mL) instead of CCl_4. The reaction mixture was vigorously stirred for 2 h and kept overnight. The ethereal layer separated and dried with $MgSO_4$. Molecular distillation *in vacuo* gave compound **8a** (1.8 g), yield 20 % with respect to the starting BuSH. Found (%): C, 56.31; H, 9.49; S, 27.37. $C_{11}H_{22}OS_2$ Calculated (%): C, 56.40; H, 9.39; S, 27.34. ^{1}H NMR, δ: 2.72 (d, 2 H, SCH_2CH); 3.23 (dt, 1 H, SCH); 9.12 (d, 1 H, CH=O); 2.33 (t, 2 H, $BuSCH_2$); 2.46 (t, 2 H, $BuSCH_2$); 1.36 (m, 8 H, CH_2 in C_4H_9); 0.80 (t, 6 H, CH_3 in C_4H_9). ^{13}C NMR, δ: 32.18 (SCH_2); 52.52 (SCH); 191.6 (CH=O); 31.43 ($BuSCH_2$); 31.26 ($BuSCH_2$); 29.90 (α-CH_2 in C_4H_9); 29.76 (α-CH_2 in C_4H_9); 21.79 (β-CH_2 in C_4H_9); 21.73 (β-CH_2 in C_4H_9); 13.47 (CH_3 in C_4H_9); 13.40 (CH_3 in C_4H_9). MS, *m/z* (I_{rel} (%)): 234 $[M]^+$ (15), 205 $[M-CH=O]^+$ (5), 177 (2), 146 (12), 145 (14), 117 (21), 116 $[CH_2CHSBu]^+$ (70), 103 (30), 101 (32), 61 (100), 41 (46).

2,5-Dibutylthio-2,3-dihydro-4*H*-pyran (7a). Butylvinylsulfide (4.92 g, 0.042 mol) was added to a solution of α-butylthioacrolein in ether obtained as described above. The reaction mixture was vigorously stirred for 2 h and kept overnight at room temperature. The unreacted butylvinylsulfide (4 g) was distilled off *in vacuo*. The remaining reaction mixture was chromatographed (silica gel L, 25×700 mm column, $CHCl_3$ as the eluent) to give 0.39 g of compound **7a**, yield 4 % with respect to the reacted butylvinylsulfide. Found (%): C, 60.02; H, 9.97; S, 25.06. $C_{13}H_{24}OS_2$. Calculated (%): C, 56.13; H, 9.23; S, 24.62. ^{1}H NMR, δ: 1.96—2.36 (m, 4 H, $C(3)H_2$, $C(4)H_2$); 5.23 (m, 1 H, C(2)H); 6.57 (s, 1 H, C(6)H); 0.90 (t, 3 H, CH_3); 1.43 (m, 4 H, CH_2CH_2); 2.50 and 2.69 (both t, 2 H, SCH_2). ^{13}C NMR, δ: 24.30 (C(3)); 32.49 (C(4)); 79.79 (C(2)); 106.62 (C(5)); 144.79 (C(6)); 32.04 and 31.58 (SCH_2); 28.26 and 30.41 (β-CH_2); 21.95 and 21.69 (γ-CH_2); 13.69 (CH_3). MS, *m/z* (I_{rel} (%)): 260 $[M]^+$ (35), 175 (24), 171 (8), 129 (16), 116 (80), 113 (31), 101 (79), 85 (100), 60 (73), 45 (50), 41 (97).

α-Propylthioacrolein (1b). A mixture of diethylamine hydrochloride (4.36 g, 0.04 mol), 34 % CH_2O (3.7 mL, 0.04 mol), and isopropyl alcohol (3.7 mL) was neutralized with 30 % NaOH to pH 7, and 60 % Pr^iOH (60 mL) and propylthioacetaldehyde (4.72 g, 0.04 mol) were added. After 20 min, CCl_4 (50 mL) was added, and the mixture was vigorously stirred for 2 h. After that, the ratio of compounds **1b** : **4b** in the lower layer was found to be 6 : 4 (^{1}H NMR data). ^{1}H NMR spectrum of compound **1b**, δ: 1.02 (t, 3 H, CH_3); 1.63 (m, 4 H, CH_2CH_2); 2.75 (t, 2 H, SCH_2); 6.07 (d, 1 H, CH_2=, J = 1.0 Hz); 6.20 (s, 1 H, CH_2=, J = 1.0 Hz); 9.52 (s, CH=O). MS, *m/z* (I_{rel} (%)): 130 $[M]^+$ (63), 115 $[M-15]^+$ (12), 101 $[M-CH=O]^+$ (15), 97 $[M-33]^+$ (11), 88 $[M-42]^+$ (27), 73 $[M-57]^+$ (31), 60 $[M-70]^+$ (43), 59 (100), 58 $(74)^+$, 45 (37), 43 (57), 41 (50).

α-Propylthioacrolein 2,4-dinitrophenylhydrazone (5b). The reaction mixture was prepared similarly to the above procedure, but 20 min after propylthioacetaldehyde dissolved completely, ether (50 mL) was added, and the mixture was vigorously stirred for 2 h. The procedure as described above for compound **5a** (see also Ref. 9) gave compound **5b** (0.21 g). The product was purified by column chromatography (see the synthesis of butylthioacrolein 2,4-dinitrophenylhydrazone **5a**); m.p. 110—111 °C after purification. Found (%): C, 46.58; H, 4.49; N, 17.59; S, 10.50. $C_{12}H_{14}O_4N_4S$. Calculated (%): C, 46.46; H, 4.51; N, 18.05; S, 10.33. ^{1}H NMR, δ: 1.08 (t, CH_3); 1.63 (m, CH_2CH_2); 2.82 (t, SCH_2); 5.47 (s, CH_2=); 5.69 (s, CH_2=); 7.85—8.40 (m, Ar); 8.90 (s, CH=N); 9.00 (s, CH=N); 10.95 (s, NH); 11.14 (s, NH).

3-Butylthio-2-propylthiopropanal (6b). A solution of diethylamine hydrochloride (15.3 g, 0.14 mol), 34 % CH_2O (12.92 mL), and isopropyl alcohol (12.9 mL) was neutralized

with 30 % NaOH, and 60 % Pr^iOH (60 mL), propylthioacetaldehyde (16.53 g, 0.14 mol), and butanethiol (15 mL, 0.14 mol) were added. The mixture was vigorously stirred for 2 h, and the reaction mixture was kept overnight at room temperature. The ethereal layer was separated and dried with $MgSO_4$, and the ether and ethylmercaptan were distilled off. Molecular distillation gave 4 g of compound **6b**, yield 13 %. Found (%): C, 54.21; H, 9.19; S, 29.31. $C_{10}H_{20}OS_2$. Calculated (%): C, 54.53; H, 9.08; S, 29.12. ^{1}H NMR, δ: 2.81 (d, 2 H, SCH_2, ^3J = 7.3 Hz); 3.34 (dt, 1 H, SCH); 9.22 (d, 1 H, CH=O, ^3J = 4.4 Hz); 2.40 (t, 2 H, BuSC$\underline{H}_2$); 2.58 (t, 2 H, BuSC$\underline{H}_2$); 1.53 (m, 8 H, CH_2 in C_4H_9); 0.95 (t, 6 H, CH_3 in C_4H_9). ^{13}C NMR, δ: 28.80 (SCH_2); 52.51 (SCH); 191.6 (CH=O); 31.55 (BuS$\underline{C}H_2$); 31.40 (Bu$\underline{S}CH_2$); 26.00 (α-CH_2 in C_4H_9); 26.71 (α-CH_2 in C_4H_9); 21.80 (β-CH_2 in C_4H_9); 22.50 (β-CH_2 in C_4H_9); 13.70 (CH_3 in C_4H_9). MS, m/z (I_{rel} (%)): 220 $[M]^+$ (3), 191 $[M-CH=O]^+$ (1), 146 (3), 145 (2), 103 (24), 102 $[CH_2CHSPr]^+$ (52), 61 (100), 60 (42), 45 (19), 41 (39).

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