# Brief Communications

## Synthesis and some transformations of N-cyclohexyl-3(4)-chloro-4(3)-methylthiobutyramides

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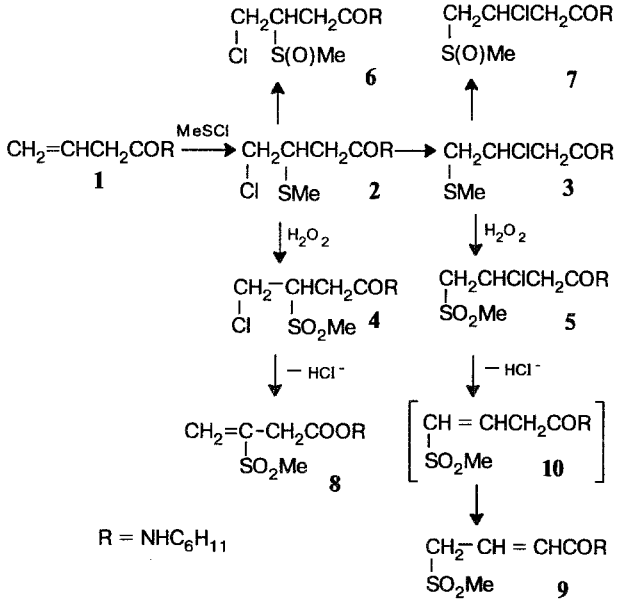
Addition of methylsulfenyl chloride to N-cyclohexyl-3-butenamide yields N-cyclohexyl-4-chloro-3-methylthiobutyramide. Isomerization, oxidation of the latter, and β-elimination were studied.

**Key words**: N-cyclohexyl-3-butenamide, addition of methylsulfenyl chloride, isomerization of N-cyclohexyl-γ-chloro-β-methylthiobutyramide, N-cyclohexyl-γ-chloro-β-methylsulfinylbutyramide, N-cyclohexyl-γ-chloro-β-methylsulfonylbutyramide.

Addition of various sulfenyl chlorides to β,γ-unsaturated acids and derivatives thereof affords a number of adducts that are of interest as biologically active compounds and as valuable intermediates for further syntheses.[1,2] In the present work we report that addition of methylsulfenyl chloride to N-cyclohexyl-3-butenamide (**1**) yields a 4-chloro-3-methylthio-derivative (**2**). The latter is isomerized on heating in nitromethane to give the corresponding 3-chloro-isomer (**3**).




4-Chloro-3-methylthio- and 3-chloro-4-methylthio-derivatives (**2** and **3**) were oxidized with 30% $H_2O_2$ in glacial acetic acid into the corresponding N-cyclohexyl-4-chloro-3-methylsulfonyl- (**4**) and -3-chloro-4-methylsulfonylbutyramides (**5**).

Oxidation of sulfides **2** and **3** with bromine in the presence of $KHCO_3$ was carried out to obtain the intermediate oxidation products, i.e., sulfoxides **6** and **7**. The oxidation products were identified by means of IR spectroscopy. In the spectra of sulfones there are strong bands in the regions of 1120—1155 and 1290—1360 $cm^{-1}$ which correspond to vibrations of the $SO_2$ group. In the spectra of sulfoxides the characteristic region is 1000—1050 $cm^{-1}$ corresponding to vibrations of the SO group. Sulfides **2** and **3** exhibit only weak bands in the regions mentioned above.

The methylsulfonyl derivatives **4** and **5** readily undergo β-elimination reactions. The reaction was carried out at room temperature in dioxane in the presence of triethylamine. In the case of cyclohexylamide **4**, the reaction gives N-cyclohexyl-3-methylsulfonyl-3-butenamide **8** as the final product. Cyclohexylamide **5** interacts with triethylamine to give N-cyclohexyl-4-methylsulfonyl-2-butenamide **9**, which is likely to be a product of prototropic rearrangement of the intermediate **10**.

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## Experimental

$^1$H NMR spectra were recorded on an R-22 spectrometer (90 MHz) using HMDS as an internal standard (δ, *J*, Hz).

**N-Cyclohexyl-3-butenamide (1).** To a solution of 0.1 mol of 3-butenoyl chloride in 50 ml of abs. ether was added dropwise at 0°C cyclohexylamine (0.2 mol) in 20 ml of abs. ether. The reaction mixture was kept for 10 h at ~20°C. The precipitate formed (cyclohexylamine hydrochloride) was filtered off, the filtrate was evaporated, and the residue was recrystallized from an ether — hexane mixture to give N-cyclohexyl-3-butenamide **1** in 80% yield, m.p. 58—60°C. Found, %: C 71.90; H 10.20; N 8.30. $C_{10}H_{17}NO$. Calculated, %: C 71.81; H 10.25; N 8.38.

**N-Cyclohexyl-4-chloro-3-methylthiobutyramide (2).** To a solution of N-cyclohexyl-3-butenamide (**1**) (0.01 mol) in 20 ml of $CCl_4$ was added dropwise at −20÷−25°C methylsulfenyl chloride (0.01 mol) in 10 ml of $CCl_4$. After the reaction was complete, the solvent was evaporated, and the residue was recrystallized from ether. The yield was 95%, m.p. 107—108°C. Found, %: C 53.07; H 8.06; Cl 14.16; N 5.74; S 12.70. $C_{11}H_{20}ClNOS$. Calculated, %: C 52.89; H 8.07; Cl 14.19; N 5.61; S 12.83. $^1$H NMR spectrum (acetone-$d_6$): 2.02 (s, $SCH_3$); 3.18 (m, CHS); 3.61 dd; 3.76 dd; ($J$ = 5, 7, 11, $CH_2Cl$).

**N-Cyclohexyl-3-chloro-4-methylthiobutyramide (3).** A solution of 0.1 mol of **2** in 100 ml of nitromethane was heated for 24 h at 50—60°C. The solvent was evaporated and the residue was recrystallized from $CCl_4$. The yield was 80%, m.p. 103—106°C. Found, %: C 53.11; H 7.50; Cl 13.23; N 5.70; S 11.97. $C_{11}H_{20}ClNOS$. Calculated, %: C 52.89; H 8.07; Cl 14.19; N 5.61; S 12.83. $^1$H NMR spectrum (acetone-$d_6$): 2.05 (s, $SCH_3$); 4.35 (m, CHCl); 2.80 (d; $J$ = 7, $CH_2S$.).

**N-Cyclohexyl-3(4)-chloro-4(3)-methylsulfonylbutyramides (4,5).** 0.01 mol of sulfide **2(3)** was dissolved in 50 ml of glacial acetic acid, then 10 ml of 30% $H_2O_2$ was added at 5°C. The reaction mixture was kept for 3—5 days at ~20 °C, then poured into ice water, and the precipitate formed was filtered off, dried, and recrystallized. Sulfone **4** was obtained in 60% yield, m.p. 156—160°C. Found, %: C 46.68; H 7.17; Cl 11.50; N 5.02. $C_{11}H_{20}ClNO_3S$. Calculated, %: C 46.88; H 7.15; Cl 12.58; N 4.97; S 11.38. $^1$H NMR spectrum (acetone-$d_6$, $CF_3COOH$): 3.01 (s, $SCH_3$); 3.40—4.15 (m, $CH_2Cl$—CHS). Sulfone **5** was obtained in 70% yield, m.p. 162—165°C (from acetone). Found, %: C 46.80; H 6.97; Cl 11.90; N 4.86; S 11.10. $C_{11}H_{20}ClNO_3S$. Calculated, %: C 46.88; H 7.15; Cl 12.58; N 4.97; S 11.38. $^1$H NMR spectrum (DMSO): 2.96 (s, $SCH_3$); 4.60 (m, CHCl).

**N-Cyclohexyl-3(4)-chloro-4(3)-methylsulfinylbutyramides (6,7).** To a solution of 0.005 mol of sulfide **2(3)** in 100 ml of methylene dichloride was added at 5°C 20 ml of a cooled 10% aqueous $KHCO_3$ solution. Under vigorous stirring a solution of 0.005 mol of bromine in 20 ml of methylene dichloride was added dropwise. The mixture was stirred for 1 h until the yellow color of bromine ceased, the organic phase was separated, the solvent was evaporated *in vacuo*, and the residue was recrystallized. Sulfoxide **6** was obtained in 60% yield, m.p. 112—114°C (from acetone). Found, %: C 49.64; H 7.50; Cl 13.23; N 5.20; S 11.97; $C_{11}H_{20}ClNO_2S$. Calculated, %: C 49.71; H 7.58; Cl 13.34; N 5.27; S 12.06. Sulfoxide **7** was obtained in 60% yield, m.p. 172°C (from methylene dichloride). Found, %: C 49.70; H 7.69; Cl 13.30; N 5.20; S 11.97. $C_{11}H_{20}ClNO_2S$. Calculated, %: C 49.71; H 7.58; Cl 13.34; N 5.27; S 12.06. $^1$H NMR spectrum (DMSO): 2.49 (s, $SCH_3$); 4.53 (m, CHCl).

**Interaction of N-cyclohexyl-3(4)-chloro-4(3)-methylsulfonylbutyramides (4,5) with triethylamine.** Sulfone **4** (0.005 mol) was dissolved in anhydrous dioxane and 0.01 mol of anhydrous triethylamine was added at 5°C. The precipitated $N(C_2H_5)_3 \cdot HCl$ was filtered off, dioxane was evaporated, and the residue was recrystallized. N-Cyclohexyl-3-methylsulfonyl-3-butenamide (**8**) was formed in 70% yield, m.p. 113—116°C (from benzene). Found, %: C 53.72; H 7.67; N 5.60; S 13.11; $C_{11}H_{19}NO_3S$. Calculated, %: C 53.85; H 7.80; N 5.71; S 13.07. $^1$H NMR spectrum (acetone-$d_6$): 2.88 (s, $SCH_3$); 3.28 (s, $CH_2CO$); 5.95 and 6.10 (br. s, $CH_2$=). N-Cyclohexyl-4-methylsulfonyl-2-butenamide (**9**) was formed in 90% yield, m.p. 233—235°C (from dioxane). Found, %: C 53.90; H 7.85; N 5.75; S 12.95. $C_{11}H_{19}NO_3S$. Calculated, %: C 53.85; H 7.80; N 5.71; S 13.07. $^1$H NMR spectrum (DMSO): 2.56 (s, $SCH_3$); 4.01 (d, $CH_2S$, $J$=7.2); 6.17 (d, =CHCO; $J$=15.5); 6.49 (d.t., CH=, $J$=15.5, 7.2).

## References

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