A New Method for the Synthesis of 1-Cycloalkenyl Alkyl Sulfides

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2-Isopropyl-5-methyl-1-cyclohexenyl alkyl sulfides were obtained in about a 60% yield by the reaction of 2-isopropyl-5-methylcyclohexanone with thioacetals or thiols in the presence of aluminum chloride. 1-Cycloalkenyl ethyl sulfides, $\overline{\text{-(CH}_2)_n\text{-C(R)=C-SEt}}$ (n=4, 5, or 6, R=H or alkyl) were obtained in good yields by the reaction of cycloalkanones with ethanethiol in the presence of diphosphorus pentaoxide. However, an attempt to apply this method to acyclic vinyl sulfides was unsuccessful.

Vinyl sulfides have been synthesized by the nucleophilic addition of thiols to acetylenic hydrocarbons[1-3] and by the reaction of α-halogenoalkenes with sodium ethanethiolate,[4] of cyclohexanethione with alkyl halides,[5] and of chloroalkyl sulfides with a base.[6,7]

Although the reaction of ketones with thiols in the presence of acids or metal salts have been reported to give bis(alkylthio)alkanes,[8-11] Mukaiyama *et al.* reported the synthesis of vinyl sulfides by the reaction of carbonyl compounds with thiols in the presence of titanium tetrachloride and triethylamine.[12] In our previous paper[13] the synthesis of substituted 1-cyclohexenyl alkyl sulfides by the reaction of substituted cyclohexanones with thiols or thioacetals in the presence of aluminum chloride was reported. In the present report a more convenient method for the synthesis of 1-cycloalkenyl ethyl sulfides by the reaction of cycloalkanones with ethanethiol in the presence of diphosphrus pentaoxide will be reported.

Results and Discussion

Reactions of Substituted Cyclohexanones with Thioacetals or Thiols in the Presence of Aluminum Chloride. The heating of a mixture of a thioacetal (0.02 mol), a substituted cyclohexanone (0.02 mol), and benzene (20 ml) under reflux for 15 min in the presence of a 1 mol equiv. $AlCl_3$ gave substituted 1-cyclohexenyl alkyl sulfide, as is shown in Table 1. The reaction using thiol instead of the thioacetal for 1 min gave the same product, but heating for 15 min caused the sulfide to disappear giving a resinous material. The different behaviors between the reaction using a thiol and that using a thioacetal are illustrated in Fig. 1.

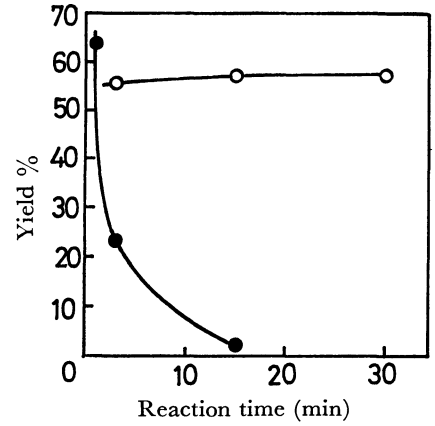
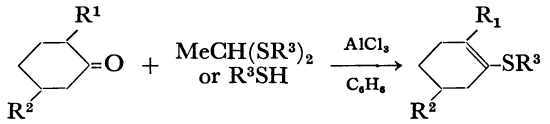


Fig. 1. Dependence of the yield of 2-isopropyl-5-methyl-1-cyclohexenyl propyl sulfide on the reaction time.
○: Reaction of menthone with $CH_3CH(SPr)_2$, ●: reaction of menthone with PrSH.

TABLE 1. YIELD OF SUBSTITUTED 1-CYCLOHEXENYL ALKYL SULFIDES



I: $R^1=CH_3$, $R^2=H$, $R^3=Et$
II: $R^1=CH_3$, $R^2=H$, $R^3=n$-Pr
III: $R^1=i$-Pr, $R^2=CH_3$, $R^3=Et$
IV: $R^1=i$-Pr, $R^2=CH_3$, $R^3=n$-Pr

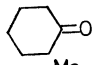
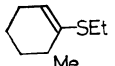
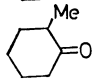
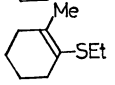
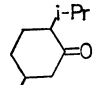
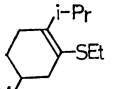
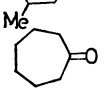
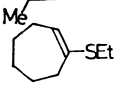
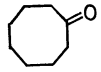
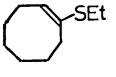
ketone	$R^3=SH$[a]	$MeCH(SR^3)_2$[b]	Remaining ketone (%)	Product	(%)
$R^1=CH_3$, $R^2=H$	$R^3=Et$		Trace	I	35
	$R^3=n$-Pr		4	II	29
		$R^3=Et$	7	I	25
		$R^3=n$-Pr	12	II	19
$R^1=i$-Pr, $R^2=CH_3$	$R^3=Et$		17	III	48
	$R^3=n$-Pr		13	IV	64
		$R^3=Et$	27	III	46
		$R^3=n$-Pr	29	IV	57

a) Reaction time: 1 min. b) Reaction time: 15 min.

In a similar reaction of cyclohexanone with thioacetals or thiols, a quick disappearance of 1-cyclohexenyl alkyl sulfide and the formation of a resinous material were observed. Thus, reactions using aluminum chloride are useful only for the synthesis of such sterically hindered vinyl sulfides as 2-isopropyl-5-methyl-1-cyclohexenyl alkyl sulfides. This limitation appears to be attributable to the stability of the product in the presence of aluminum chloride. The reaction of acyclic ketones with thiol or thioacetal in the presence of aluminum chloride gave a resinous material and unidentified oily products.

Reactions of Cycloalkanones with Ethanethiol in the Presence of Diphosphorus Pentaoxide. The heating of a mixture of ethanethiol (0.02 mol), a cycloalkanone (0.02 ml), and benzene (20 ml) under reflux for one hour in the presence of a 1 mol equiv. of diphosphorus pentaoxide gave 1-cycloalkenyl ethyl sulfide, as is shown in Table 2. Although the reaction of thiols carried out in the presence of aluminum chloride showed a rapid disappearance of the products (see Fig. 1), the reactions

Table 2. Yield of 1-cycloalkenyl ethyl sulfides[a)]

Starting ketone	Product	Remaining ketone (%)	Yield (%) of product
		5	43
		8	75
		36	42
		18	60
		12	81

a) Reaction time: one hour.

carried out in the presence of diphosphorus pentaoxide showed only a slight decrease in 1-cycloalkenyl ethyl sulfide on prolonged heating.

1-Cyclopentenyl ethyl sulfide was obtained in a low yield (less than 20%) by the reaction of cyclopentanone with ethanethiol in the presence of diphosphorus pentaoxide. Similar reactions of acyclic ketones gave bis(alkylthio)alkanes.

As is shown in Table 2, the yields of 1-cycloalkenyl ethyl sulfides are in the order: 1-cyclooctenyl>1-cycloheptenyl>1-cyclohexenyl. This reaction appears to be useful for the synthesis of large-membered 1-cycloalkenyl alkyl sulfides, $\overline{\text{—(CH}_2)_n\text{—C(R')=C—SR}}$ ($n \geqq 4$, R'=H or alkyl). Although the application of the method using diphosphorus pentaoxide has thus far been restricted to the synthesis of 1-cycloalkenyl alkyl sulfides, it appears to be more convenient than that using $TiCl_4$ and triethylamine.[12)]

Experimental

Materials. Commercially available cycloalkanones and thiols were used. 1,1-bis(ethylthio)ethane or 1,1-bis(propylthio)ethane was obtained by the reaction of acetaldehyde with ethanethiol or 1-propanethiol respectively in the presence of calcium chloride.

General Procedure. A mixture of thiol (or thioacetal) (0.02 mol), cycloalkanone (0.02 mol), an internal standard (hexamethylbenzene), and benzene (20 ml) was heated under reflux in the presence of aluminum chloride or diphosphorus pentaoxide (0.02 mol). At an appropriate time a small portion of the solution was sampled and washed with water, and then this solution was analyzed by GLC using an ethylene glycol adipate polyester, 20% on a chromosorb W column at 150 °C. The reaction times shown in Table 1 or 2 are nearly optimum ones.

For the purpose of the isolation of 1-cycloalkenyl sulfides, a mixture of 0.06 mol of each material in benzene (30 ml) was heated under reflux. At an appropriate time, which is shown in Table 1 or 2, the benzene solution was cooled and washed several times and then distilled under reduced pressure. Redistillation and separation by GLC each gave pure 1-cycloalkenyl alkyl sulfide.

Identification of 1-Cycloalkenyl Alkyl Sulfides. The structures of the 1-cycloalkenyl sulfides were established on the basis of the following data.

2-Methyl-1-cyclohexenyl Ethyl Sulfide. NMR (in CCl_4): δ 2.56 (2H, q, J=7 Hz; $-SC\underline{H}_2CH_3$), 1.85 (3H, s, CH_3–C=C), 1.96—2.4 and 1.5—1.76 (8H, m, ring protons), 1.2 (3H, t, J=7 Hz, $-SCH_2C\underline{H}_3$). IR (neat): 1620 cm^{-1} (very weak, C=C). Elementary analyses: Found: C, 68.89; H, 10.01; S, 20.61%. Calcd for $C_9H_{16}S$: C, 69.17; H, 10.32; S, 20.50%.

2-Methyl-1-cyclohexenyl Propyl Sulfide. NMR (in CCl_4): δ 2.51 (2H, t, J=7 Hz, $-SC\underline{H}_2CH_2CH_3$), 1.84 (3H, s, CH_3–C=C), 1.90—2.30 and 1.3—1.74 (10H, m, ring protons and $-SCH_2C\underline{H}_2CH_3$), 1.0 (3H, t, J=7 Hz, $-SCH_2CH_2C\underline{H}_3$). IR (neat): 1600 cm^{-1} (weak, C=C). Elementary analyses: Found: C, 70.38; H, 10.57; S, 18.61%. Calcd for $C_{10}H_{18}S$: C, 70.52; H, 10.65; S, 18.82%.

2-Isopropyl-5-methyl-1-cyclohexenyl Ethyl Sulfide. NMR (in CCl_4): δ 3.45 (1H, seven, J=7 Hz, $(CH_3)_2C\underline{H}$–C=C), 2.57 (2H, q, J=7 Hz, $-SC\underline{H}_2CH_3$), 1.55—2.40 (7H, m, ring protons), 1.2 (3H, t, J=7 Hz, $-SCH_2C\underline{H}_3$), 0.88—1.04 (9H, m; CH_3 attached to ring and $(C\underline{H}_3)_2CH$). IR (neat): 1618 cm^{-1} (very weak, C=C). Elementary analyses: Found: C, 72.45; H, 11.06; S, 16.34%. Calcd for $C_{12}H_{22}S$: C, 72.65; H, 11.17; S, 16.16%.

2-Isopropyl-5-methyl-1-cyclohexenyl Propyl Sulfide. NMR (in CCl_4): δ 3.48 (1H, seven, J=7 Hz, $(CH_3)_2C\underline{H}$–C=C), 2.50 (2H, q, J=7 Hz, $-SC\underline{H}_2CH_3$), 1.40—2.3 (9H, m, ring protons and $-SCH_2C\underline{H}_2CH_3$), 0.88—1.08 (12H, m, CH_3 attached to ring $(C\underline{H}_3)_2CH$, and $-SCH_2CH_2C\underline{H}_3$). IR (neat): 1600 cm^{-1} (weak, C=C). Elementary analyses: Found: C, 73.63; H, 11.69; S, 15.43%. Calcd for $C_{13}H_{24}S$: C, 73.51; H, 11.39; S, 15.10%.

1-Cyclohexenyl Ethyl Sulfide. NMR (in CCl_4): δ 5.5 (1H, m, >C=CH–), 2.62 (2H, q, J=7 Hz, $-SC\underline{H}_2CH_3$), 1.90—2.30 and 1.47—1.85 (8H, m, ring protons), 1.23 (3H, t, J=7 Hz, $-SCH_2C\underline{H}_3$). IR (neat): 1630 cm^{-1}. Elementary analyses: C, 67.40; H, 9.85; S, 22.26%. Calcd for $C_8H_{14}S$: C, 67.54; H, 9.92; S, 22.54%.

1-Cycloheptenyl Ethyl Sulfide. NMR (in CCl_4): δ 5.5 (1H, t, J=7 Hz, olefinic), 2.58 (2H, q, J=7 Hz, $-SC\underline{H}_2CH_3$), 2.04—2.30 and 1.36—1.90 (10H, m, ring protons), 1.28 (3H, t, J=7 Hz, $-SCH_2C\underline{H}_3$). IR (neat): 1632 cm^{-1}. Elementary analyses: Found: C, 69.10; H, 10.44; S, 20.84%. Calcd for $C_9H_{16}S$: C, 69.17; H, 10.32; S, 20.52%.

1-Cyclooctenyl Ethyl Sulfide. NMR (in CCl_4): δ 5.38 (1H, t, J=8 Hz, olefinic), 2.64 (2H, q, J=7 Hz; $-SC\underline{H}_2CH_3$), 2.04—2.40 and 1.40—1.90 (12H, m, ring protons), 1.28 (3H, t, J=7 Hz, $-SCH_2C\underline{H}_3$). IR (neat): 1619 cm^{-1}. Elementary analyses: Found: C, 70.36; H, 10.80; S, 19.08%. Cacld for $C_{10}H_{18}S$: C, 70.52; H, 10.65; S, 18.82%.

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