A One-Pot Synthesis of Ketene Dithioacetals from Alkyl Halides

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Ketene dithioacetals have acquired considerable importance as versatile synthetic intermediates[1,2,3]. A host of methods have been developed for their preparation which vary widely in utility and the variety of starting materials employed. The usefulness of many of these methods has recently been reviewed[1], but none of the currently available syntheses utilize the simplicity and convenience of a one-pot preparation from a readily available class of starting materials which we now report. Our procedure involves the sequential transformation of

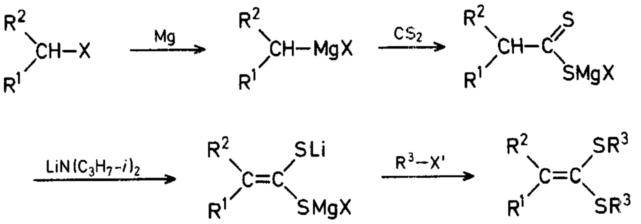

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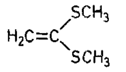
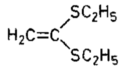
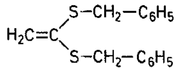
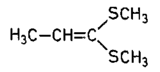
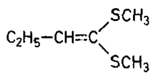
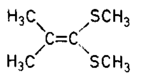
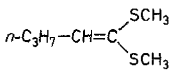
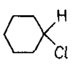
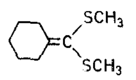
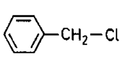
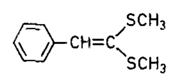
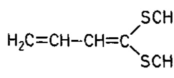
Table. Ketene Dithioacetals

Alkyl halide	Ketene *S,S*-acetal	Alkylating agent R^3—X′	Yield[a] [%]	b.p./torr [°C]	Molecular formula or b.p./torr reported
H_3C-Cl[b]	 $H_2C=C(SCH_3)_2$	dimethyl sulfate	80	76-80°/26	80°/10[7]
	 $H_2C=C(SC_2H_5)_2$	diethyl sulfate	72	95-100°/26	85°/10[6]
	 $H_2C=C(S-CH_2-C_6H_5)_2$	benzyl chloride	80[c]	—[e]	
H_3C-CH_2-Br[d]	 $H_3C-CH=C(SCH_3)_2$	dimethyl sulfate	70	87°/24	
n-C_3H_7-Cl	 $C_2H_5-CH=C(SCH_3)_2$	dimethyl sulfate	60	73-77°/7	$C_6H_{12}S_2$ (148.1)[f]
i-C_3H_7-Cl	 $(H_3C)_2C=C(SCH_3)_2$	dimethyl sulfate	65	67-72°/8	
n-C_4H_9-Cl	 *n*-$C_3H_7-CH=C(SCH_3)_2$	dimethyl sulfate	70	96-101°/13	
		dimethyl sulfate	5-10[c]	—[g]	77-78°/1.5[8]
		dimethyl sulfate	9	124-140°/2	94-96°/0.25[9]
$H_2C=CH-CH_2-Br$	 $H_2C=CH-CH=C(SCH_3)_2$[h]	dimethyl sulfate	—	—[g]	—

[a] Identity and purity (≥95%) of all products, except where indicated, were confirmed by ^{1}H-N.M.R. analysis.

[b] As commercially available methylmagnesium chloride in tetrahydrofuran.

[c] As calculated from the ^{1}H-N.M.R. spectrum.

[d] As commercially available ethylmagnesium bromide in ether.

[e] Product decomposed on attempted distillation.

[f] calc. C 48.60 H 8.16 S 43.24
found 48.36 8.47 42.98

[g] A complex mixture from which the ketene *S,S*-acetal could not be isolated.

[h] The expected product.

an alkyl halide to a Grignard reagent, a dithioic acid anion, a dithioic acid dianion, and finally a ketene dithioacetal.

Recently, we reported[4] one example of this strategy in an improved synthesis of ketene dimethyl dithioacetal monoxide, but other workers have also reported facets of this strategy such as the preparation of ketene dithioacetals from dithioic acids[5] or esters[6]. Our procedure differs from these earlier reports in utilizing the anions of such acids and esters as non-isolable intermediates resulting in improved yields and shorter preparation times of the desired ketene dithioacetals.

Yields of the prepared ketene dithioacetals varied considerably depending on the particular starting material and were calculated from the amount of alkyl halide if the Grignard reagent was prepared or from the amount of Grignard reagent when commercial (titrated) material was used. Satisfactory yields were obtained in the case of simple alkyl halides and the poor yields of ketene dithioacetals from cyclohexylmagnesium chloride and benzylmagnesium chloride were not unexpected in view of the reported low yields of methyl cyclohexyldithiocarboxylate[10] and methyl phenyldithioacetate (~3%)[11] obtained from the corresponding Grignard reagents. Similarly, the one-pot procedure failed altogether in the case of allylmagnesium bromide. In all three of these cases the major isolable product was methyl *N,N*-diisopropyldithiocarbamate[12], presumably formed by reaction of lithium diisopropylamide with carbon disulfide followed by alkylation of the intermediate adduct, indicating poor or no formation of the intermediate Grignard-carbon disulfide adducts.

The following procedure is an improvement over the reported procedure[4] for the preparation of ketene dimethyl dithioacetal. It should be noted that the viscosity of the intermediate dianion solution requires mechanical stirring and dilution with tetrahydrofuran.

Ketene Dithioacetals (Ketene *S,S*-Acetals); General Procedure:
Into a mechanically stirred 1 molar solution of the Grignard reagent (0.25 mol) in tetrahydrofuran or tetrahydrofuran/ether under nitrogen is added a solution of carbon disulfide (19.0 g, 0.25 mol) dissolved in an equal volume of tetrahydrofuran at a rate sufficient to increase the temperature of the reaction mixture to 40-45 °C and maintain this temperature during the remainder of the addition. After addition is complete the mixture is stirred for 2 h at 40-45 °C, diluted with tetrahydrofuran to give a 0.7 molar concentration of the Grignard-carbon disulfide adduct, and then cooled to −78 °C with a Dry Ice/acetone bath. Then, lithium diisopropylamide[4] (26.8 g, 0.25 mol) in tetrahydrofuran is added during 45-60 min and the mixture stirred for 45 min

after addition is complete. The mixture is allowed to warm to room temperature, stirred an additional 20 min, and a solution of the alkylating agent (2 equiv) in an equal volume of tetrahydrofuran is added at a rate sufficient to increase the temperature of the reaction mixture to 40 °C and maintain this temperature during the remainder of the addition. After addition is complete the reaction mixture is allowed to cool to room temperature, stirred for 2 h, and poured into excess 5% aqueous sodium hydrogen carbonate solution. The aqueous layer is extracted with ether (3 x 250 ml) and the combined ether extracts are added to the separated organic layer. The resulting organic solution is dried with magnesium sulfate and distilled of solvent on a rotary evaporator to give a residue of crude ketene dithioacetal which can be purified by distillation under reduced pressure.

In the case of alkylation with benzyl chloride the reaction mixture is heated 2 h at 40 °C after addition is complete and then stirred at room temperature overnight.

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[1] M. Kolb, *Ketene Thioacetals*, in: *The Chemistry of Ketene, Allenes, and Related Compounds*, Part 2, S. Patai, Ed., Interscience Publishers, New York, 1980, p. 669–699.

[2] R. K. Olsen, J. O. Currie, *The Chemistry of the Thiol Group*, Part 2, S. Patai, Ed., John Wiley & Sons, London, 1974.

[3] B. T. Gröbel, D. Seebach, *Synthesis* **1977**, 357.

[4] R. Kaya, N. R. Beller, *J. Org. Chem.* **46**, 196 (1981).

[5] F. E. Ziegler, C. M. Chan, *J. Org. Chem.* **43**, 3065 (1978).

[6] P. J. W. Schuijl, L. Brandsma, J. F. Arens, *Recl. Trav. Chim. Pays Bas* **85**, 1263 (1966).

[7] J. D. Kendall, H. D. Edwards, *U. S. Patent* 2493071 (1950), Ilford Ltd.; *C. A.* **44**, 7346 (1950).

[8] D. Seebach, M. Kolb, B. T. Gröbel, *Chem. Ber.* **106**, 2277 (1973).

[9] G. A. Russell, L. A. Ochrymowycz, *J. Org. Chem.* **35**, 764 (1970).

[10] J. Meijer, P. Vermeer, L. Brandsma, *Recl. Trav. Chim. Pays Bas* **92**, 601 (1973).

[11] M. S. Kharasch, O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, Englewood Cliffs, N. J., 1954, p. 1287.

[12] Identified by comparison to material prepared by a reported procedure; T. Tanaka, N. Watanabe, *Org. Mag. Res.* **6**, 165 (1974).

0039-7881/81/1032-0816 $ 03.00