A Convenient One-Pot Synthesis of Ketene Dithioacetals

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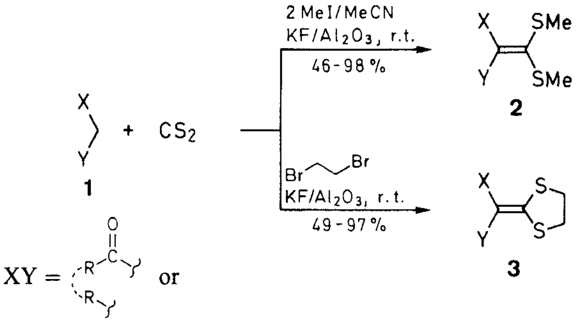
An easy synthesis of ketene dithioacetals **2** and **3** by the condensation of carbon disulfide and active methylene compounds **1** with subsequent alkylation in the presence of potassium fluoride is described.

Ketene dithioacetals are very versatile and useful intermediates in organic synthesis,[1] because the double bonds present in them are amenable for both nucleophilic as well as electrophilic attack. Functionalized ketene dithioacetals and particularly α-oxoketene dithioacetals[2] are used in the synthesis of heterocyclic compounds.[3] Ketene dithioacetals were generally prepared by bisalkylation of dithioacid salts.[4] The dithioacid salts were obtained by the condensation of carbon disulfide with active methylene compounds in the presence of a strong, hindered base. Many hindered bases were used for this condensation, e.g. sodium *tert*-amylate,[5] sodium 2,6-di-*tert*-butyl-4-methylphenoxide,[6] lithium dialkylamide,[7] and potassium *tert*-butoxide.[8]

We report here on the use of potassium fluoride on alumina[9] for the preparation of ketene dithioacetals **2** and **3** from ketones, esters, nitriles and a lutidinium salt **1** (Tables 1 and 2).



X = COR; Y = H, Ph or
XY = COR, CO_2R', CN
(see Table 1 for the individual substrates used)

Table 1. Ketene Dithioacetals **2** Prepared

	Substrate **1**	Product **2**	Yield (%)	Appearance	mp (°C) (solvent) or bp (°C)/Torr	Molecular Formula[a] or Lit. mp (°C) or bp (°C)/Torr
a	acetone	4,4-bis(methylthio)-3-buten-2-one	58	yellow solid	67 (cyclohexane)	66–67[5]
b	acetophenone	3,3-bis(methylthio)-1-phenyl-2-propen-1-one	76	yellow solid	90 (MeOH)	90[5]
c	cyclopentanone	2-[bis(methylthio)methylene]cyclopentanone	84	yellow solid	32 (Et_2O)	32–33[5]
d	cyclohexanone	2-[bis(methylthio)methylene]cyclohexanone	68	orange liquid	143–145/0.3	123–124/0.1[5]
e	cycloheptanone	2-[bis(methylthio)methylene]cycloheptanone	54	yellow liquid	188–190/15	112/0.2[5]
f	1-indanone	2-[bis(methylthio)methylene]-1-indanone	81	yellow solid	123–124 (EtOH)	124–125[10]
g	camphor	3-[bis(methylthio)methylene]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one	46	yellow liquid	125–127/0.3	117–118/0.2[5]
h	anthrone	10-[bis(methylthio)methylene]anthrone	94	yellow solid	137 (EtOH)	$C_{17}H_{14}OS_2$[b] (298.4)
i	2,4-pentandione	3-[bis(methylthio)methylene]-2,4-pentandione	85	orange solid	60 (MeOH)	59–60[11]
j	1,3-diphenyl-1,3-propanedione	2-[bis(methylthio)methylene]-1,3-diphenyl-1,3-propanedione	68	yellow solid	66 (MeOH)	66–67[14]
k	5,5-dimethyl-1,3-cyclohexanedione	2-[bis(methylthio)methylene]-5,5-dimethyl-1,3-cyclohexanedione	72	yellow solid	84 (EtOH)	86–87[15]
l	diethyl malonate	diethyl 2-bis[(methylthio)methylene]propandioate	94	orange liquid	130–132/0.3	193–195/12[12]
m	*N*-methyl-2,6-lutidinium iodide	*N*-methyl-2,6-bis[bis(methylthio)methylene)] lutidinium iodide[c]	98	green solid	160–162 (acetone)	$C_{14}H_{18}INS_4$ (455.6)
n	benzyl cyanide	β,β-bis(methylthio)-α-phenylacrylonitrile	84	red solid	50 (MeOH/Et_2O)	49–51[11]

[a] Satisfactory microanalyses obtained: C, H, S ±0.30.

[b] Reported mp 174 °C.[13] Due to the large difference in the mp between found and reported values, the purity of our product was checked by elemental analyses and found to be acceptable. IR (Nujol): $\nu = 1665, 1510\ cm^{-1}$.
^{1}H-NMR ($CDCl_3$/TMS): $\delta = 2.3$ (s, 6H, CH_3), 7.4–7.8 (m, $4H_{arom}$), 8.0–8.4 (m, $4H_{arom}$). MS (70 eV): m/z (%) = 298 (M^+, 77), 283 (36), 268 (16), 236 (100).

[c] IR (Nujol): $\nu = 1475\ cm^{-1}$.
^{1}H-NMR ($CDCl_3$/TMS): $\delta = 2.50, 2.65$ (2S, 6H each, $4\times CH_3$), 4.30 (s, 3H, NCH_3), 6.55 (S, 2H, $2\times{=}CH$), 7.80–8.45 (m, $3H_{arom}$).

Table 2. 1,3-Dithiolane-2-ylidenes **3** Prepared

	Substrate **1**	Product **2**	Yield (%)	Appearance	mp (°C)	
					found (solvent)	reported
a	acetone	3-(1,3-dithiolan-2-ylidene)-2-propanone	68	yellow-orange solid	74–76 (Et_2O)	74–75[12]
b	acetophenone	2-(1,3-dithiolan-2-ylidene)-1-phenylethanone	50	orange solid	81–82 ($EtOH/Et_2O$)	82–83[12]
f	1-indanone	2-(1,3-dithiolan-2-ylidene)-1-indanone	88	orange solid	168–170 (EtOH)	170–172[10]
h	anthrone	10-(1,3-dithiolan-2-ylidine)anthrone	90	yellow-orange solid	165 (EtOH)	166[13]
i	2,4-pentandione	3-(1,3-dithiolan-2-ylidene)-2,4-pentanedione	80	yellow solid	138 (MeOH)	136–137[16]
k	5,5-dimethyl-1,3-cyclohexanedione	2-(1,3-dithiolan-2-ylidene)-5,5-dimethyl-1,3-cyclohexanedione	76	yellow orange solid	200 (MeCN)	201–202[16]
n	benzyl cyanide	*β*-(1,3-dithiolan-2-ylidene)-*α*-phenylacrylonitrile	87	red solid	50 (Et_2O)	50–51[12]
o	malonodinitrile	2-(1,3-dithiolan-2-ylidine)propanedinitrile	53	orange solid	200–202 (EtOH)	203–204[12]
p	ethyl cyanoacetate	ethyl (1,3-dithiolan-2-ylidene)cyanoacetate	96	yellow solid	104 (EtOH)	105–106[12]
q	ethyl acetoacetate	ethyl 2-(1,3-dithiolan-2-ylidene)-3-oxobutanoate	90	orange solid	81 ($MeOH/Et_2O$)	81.5–82[12]
r	fluorene	2-(fluorene-9-ylidene)-1,3-dithiolane	50	yellow-orange solid	120 (EtOH/benzene)	121–122[12]
s	phenol	4-(1,3-dithiolan-2-ylidene)-2,5-cyclohexydien-1-one	49	yellow-orange solid	194 (DMF)	196[13]
t	*β*-naphthol	1-(1,3-dithiolan-2-ylidene)-2(1*H*)-naphthalenone	97	yellow-orange solid	152 (EtOH)	152[13]

The use of solid potassium fluoride on alumina allows easy preparation of these functionalized alkenes. This method does not require expensive organometallic, tedious alkoxides, highly purified solvent or low temperature. Small quantities of solvent (tetrahydrofuran, acetonitrile) only are used for the dissolution of reactants. The reaction is smooth and takes place at room temperature, yields are excellent, and the workup is very easy. Potassium fluoride on alumina is easily prepared from potassium fluoride and chromatography alumina.[8] The reagent is stable and can be stored in a closed flask without alteration.

In conclusion this new method for the preparation of ketene dithioacetals is easy, efficient, and inexpensive.

Preparation of Potassium Fluoride on Alumina:

KF (20 g) is dissolved in water (200 mL) and mixed with neutral chromatographic alumina (Woelm-N, 2087; 30 g). The slurry is evaporated using a rotary evaporator under vacuum at 100 °C. The moisture in the reagent is coevaporated with EtOH (4 × 50 mL). The white solid obtained is dried in an oven at 110 °C for 24 h. The reagent is kept in a closed flask and can be stored for a longer period of time without decomposition.

Ketene Dithioacetals 2 and 3; General Procedure:

Method A, *for Solid Substrates:* To a solution of the appropriate solid substrate **1** (5 mmol) in MeCN (10 mL) and CS_2 (456 mg, 6 mmol) in a 50 mL round-bottom flask is added KF in alumina (4 g) at r.t. The flask is closed with a stopper and the mixture is magnetically stirred for 1 h. To this mixture is added MeI (1.45 g, 10.2 mmol) or 1,2-dibromoethane (0.98 g, 5.2 mmol) and the contents of the flask is well mixed by stirring. After keeping the mixture in the closed flask for 16 h, it is extracted with MeCN (20 mL), the organic extract is filtered through Celite and the solvent evaporated *in vacuo*. Solid products are purified by recrystallization from suitable solvents and liquid products are distilled (Tables 1 and 2).

Method B, *for Liquid Substrates:* A solution of the appropriate liquid substrate **1** (5 mmol) in CS_2 (476 mg, 6 mmol) is absorbed on KF on alumina (4 g) in a 50 mL round-bottom flask and the mixture is kept closed at r.t. for 1 h. MeI (1.45 g, 10.2 mmol) or 1,2-dibromoethane (0.98 g, 5.2 mmol) is added and the contents of the flask is mixed well. The workup is carried out as described under Method A (Tables 1 and 2).

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