

# Application of Commercially Available Anhydrous Potassium Fluoride for a Convenient Synthesis of Ketene Dithioacetals†

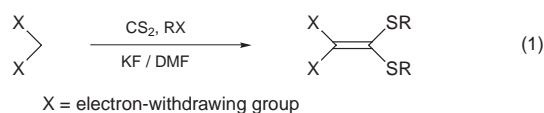
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Commercially available anhydrous KF without activation or solid support promotes condensation between active methylene compounds, carbon disulfide and an alkylating agent in dry DMF to allow the preparation of a variety of ketene dithioacetals in fair to good yields under ambient conditions.

Ketene dithioacetals are versatile synthons in the area of C–C bond formation, functional group manipulations and in the synthesis of carbo- and heterocyclic systems.<sup>1</sup> A general procedure for preparing ketene dithioacetals is based on the condensation of carbanions with CS<sub>2</sub>, followed by *in situ* bis-thioalkylations of the resultant ketene dithiolate anions. These condensations have been described using a variety of basic reagents, which include potassium hydroxide, sodium hydride, potassium *tert*-butoxide, sodium *tert*-amylate, *n*-butyllithium, lithium diisopropylamide (LDA), lithium dicyclohexylamide and lithium hexamethyldisilazide.<sup>2</sup> In addition, Lawesson and coworkers<sup>3</sup> have reported the synthesis of ketene dithioacetals of some active methylene compounds under phase transfer catalysis. However, lack of sufficient generality, variable yields and instabilities of ketene dithioacetals under strong basic conditions are limitations of many of these procedures.

In recent years, ionic fluoride salts, either alone or in the form of coated reagents or in combination with complexing agents such as crown ethers, have found increasing applications in organic synthesis through the intermediacy of carbanions and heteroatom nucleophiles.<sup>4,5</sup> Being mild and non-nucleophilic in nature, the fluoride ion methodology appeared to us of interest for preparing ketene dithioacetals. Indeed, Villemin and Abdelkrim<sup>6</sup> have reported the application of activated anhydrous KF supported on alumina for the synthesis of ketene dithioacetals. Curiously, these authors either failed to study or report if KF directly, without activation or solid support, could be used to promote these reactions. During the course of our work, we have been able to define conditions that allow, without prior activation or solid support, the direct use of commercial anhydrous KF for preparing ketene dithioacetals as shown in the generalized reaction (1).



As a test case, we studied the conversion of dibenzoylmethane **1** into the corresponding dimethylketene dithioacetal **7** (Table 1) in different solvents such as 1,4-dioxane, THF, CH<sub>3</sub>CN and DMF at room temperature. The reaction mixture, which consisted of 10 mmol of **1**, excess of CS<sub>2</sub> and 20 molar equivalents of commercial grade anhydrous KF, was initially stirred in the aforementioned solvents for 10 min at room temperature and for a further

period of up to 20 h after the addition of *ca.* 2.5 equiv. of methyl iodide. Of the various solvents examined, we found anhydrous DMF to be a solvent of choice in terms of high efficiency and yield (2 h for complete conversion, 77% isolated yield of **7**). In contrast, the same reaction in 1,4-dioxane, THF or CH<sub>3</sub>CN showed relatively poor conversions (12–30%) even after 20 h under ambient conditions.

To demonstrate the generality of our procedure, the synthesis of a number of ketene dithioacetals was attempted with KF/DMF. Our results, collected in the Table 1, clearly show that a variety of active methylene compounds, such

**Table 1** Preparation of ketene dithioacetals using anhydrous KF/DMF system<sup>a</sup>

Entry	Active methylene compound	Alkylating agent (RX)	Time (t/h)	Product <sup>b</sup>	Yield <sup>c</sup> (%)	Mp (T/°C)
1		CH <sub>3</sub> I	2		<b>7</b> 77	62–64(66) <sup>6</sup>
2		C <sub>2</sub> H <sub>5</sub> I	4		<b>8</b> 71	76–78
3		PhCH <sub>2</sub> Cl	3		<b>9</b> 60	142–144
4		CH <sub>2</sub> =CHCH <sub>2</sub> Cl	3		<b>10</b> 40	70–72(74) <sup>3</sup>
5			CH <sub>3</sub> I		2	<b>11</b> 65
6	PhCH <sub>2</sub> Cl		3	<b>12</b> 57	106–108	
7		BrCH <sub>2</sub> CH <sub>2</sub> Br <sup>d</sup>	4		<b>13</b> 50	135–38(138) <sup>6</sup>
8					CH <sub>3</sub> I	4
9	PhCH <sub>2</sub> Cl	6		<b>15</b> 25	oil	
10		PhCH <sub>2</sub> Cl	6		<b>16</b> 40	88–89(87) <sup>8</sup>
11					PhCH <sub>2</sub> Cl	4
12		CH <sub>3</sub> I		3		<b>18</b> 52
13		CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> Br	6	<b>19</b> 79		94–96
14		PhCH <sub>2</sub> Cl	8	<b>20</b> 60		126–128

<sup>a</sup>Except where mentioned otherwise, all reactions conducted at room temperature (2–8 h) using 10 mmol of active methylene compound and 10–12 mmol of alkylating agent as described in the general procedure. <sup>b</sup>All known products were fully characterized by physical and spectral data which agree with the literature values. <sup>c</sup>Yields refer to pure products. <sup>d</sup>5 mmol of dibromoethane used.

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**Table 2** Analytical and spectral data for the new ketene dithioacetals

Compound	Formula	Found(required)(%)				$\nu_{\max}/\text{cm}^{-1}$	$\delta_{\text{H}}(\text{CDCl}_3)$
		C	H	N	S		
<b>8</b>	C <sub>20</sub> H <sub>20</sub> O <sub>2</sub> S <sub>2</sub>	67.21 (67.38)	5.89 (5.65)	– –	18.22 (17.99)	1720, 1680, 1560	1.1 (6H, t, CH <sub>3</sub> CH <sub>2</sub> –), 2.7 (4H, q, CH <sub>3</sub> CH <sub>2</sub> –), 7.2–8.1 (10H, m, arom.)
<b>9</b>	C <sub>30</sub> H <sub>24</sub> O <sub>2</sub> S <sub>2</sub>	74.78 (74.97)	5.29 (5.03)	– –	13.62 (13.34)	1660, 1640, 1600	3.9 (4 H, s, –SCH <sub>2</sub> ), 7.0–8.05 (20 H, m, arom.)
<b>12</b>	C <sub>18</sub> H <sub>20</sub> O <sub>2</sub> S <sub>2</sub>	65.39 (65.03)	5.89 (6.06)	– –	19.02 (19.29)	1720, 1682, 1663	2.1 (6 H, s, –SCH <sub>3</sub> ), 4.1 (4 H, s, PhCH <sub>2</sub> –), 7.2 (10 H, m, arom.)
<b>15<sup>a</sup></b>	C <sub>18</sub> H <sub>14</sub> N <sub>2</sub> S <sub>2</sub>	66.77 (67.05)	4.65 (4.38)	8.60 (8.69)	19.62 (19.89)	1580, 1504, 1083	4.45 and 4.50 (2 H, s, each, –SCH <sub>2</sub> –), 7.44 and 7.5 (5 H, s, each H arom.)
<b>19</b>	C <sub>16</sub> H <sub>18</sub> O <sub>2</sub> S <sub>2</sub>	62.71 (62.73)	6.13 (5.93)	– –	20.66 (20.89)	1678, 1621, 1606	1.0 (6 H, t, CH <sub>3</sub> CH <sub>2</sub> –), 1.7 (4 H, t, –SCH <sub>2</sub> CH <sub>2</sub> –), 3.1 (4 H, t, –SCH <sub>2</sub> CH <sub>2</sub> –), 7.6 (H, m, H arom.)
<b>20</b>	C <sub>24</sub> H <sub>18</sub> O <sub>2</sub> S <sub>2</sub>	71.39 (71.61)	4.28 (4.51)	– –	16.22 (15.93)	1703, 1677, 1600	4.3 (4 H, s, SCH <sub>2</sub> –), 7.2 (10 H, s, H arom.), 7.7–7.9 (4 H, m, H arom.)

<sup>a</sup>IR band for the CN group either absent or too weak to be detected.

as dibenzoyl methane, acetyl acetone, dimedone, 1,3-indanedione, diethyl malonate and malononitrile, successfully participate in the reaction, giving fair to good yields of ketene dithioacetals. The structural characterization for unknown ketene dithioacetals is based on elemental analysis and spectral data (Table 2). However, attempts to effect the synthesis of ketene dithioacetals derived from simple aliphatic or aromatic ketones were unsuccessful<sup>2,6</sup> presumably because of the failure of these ketones to undergo deprotonation under the present conditions.

The sharp signals and the simplicity of the <sup>1</sup>H NMR spectra (Table 2) suggest the presence of either a single predominant conformation or fast equilibria involving different conformers for these ketene dithioacetals. The otherwise symmetrical oxo-ketene dithioacetals (Table 2; compounds **8**, **9**, **12**, **19** and **20**) were all found to display split absorption bands for the carbonyl groups in their IR spectra. Such splittings, which find ample precedence in the literature,<sup>9</sup> may be attributed to the vibrational coupling of carbonyl functions with either the fundamental vibration of the  $\pi$ -bond or Fermi resonance.<sup>10</sup>

In summary, we have described a procedure for the direct application of commercially available anhydrous KF, without the need of activation or solid support, for the preparation of a variety of ketene dithioacetals of active methylene compounds in fair to good yields in what appears to be a simpler and more convenient alternative to other available methods.<sup>2,3,6</sup>

## Experimental

Melting points (uncorrected) were determined on a Gallenkamp melting point apparatus. IR spectra were recorded on a Shimadzu FTIR-4200 spectrophotometer either as oil films or KBr discs. <sup>1</sup>H NMR spectra were recorded on a Varian EM-360L (60 MHz) spectrometer with TMS as internal standard.

*General Procedure for the Preparation of Ketene Dithioacetals.*—To a vigorously stirred solution of dibenzoyl methane (**1**) (2.24 g, 10 mmol) in dry DMF (20 ml) were added, at room temperature, commercial grade dry KF (12 g), freshly distilled CS<sub>2</sub> (0.8 ml, 12 mmol) and methyl iodide (1.3 ml, 20 mmol). The initial yellow reaction mixture, which rapidly turned red in colour, was stirred for a period of 2 h. At this point the reaction mixture was diluted with water,

extracted with ethyl acetate (3 × 25 ml) and the extract washed several times with water. Finally, the extract was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to give a yellow solid which upon crystallization from ethanol provided 2.5 g (77% yield) of ketene dithioacetal **7**, mp 62–64 °C (lit.<sup>6</sup> mp 66 °C).

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