An unexpected synthesis of ketene monothioacetals†‡

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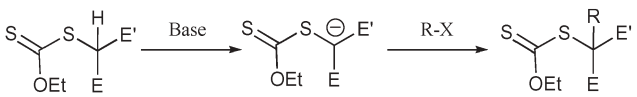
Some dithiocarbonates (xanthates) can be converted into ketene monothioacetals through extrusion of sulfur upon treatment with base and an alkylating agent.

As part of our ongoing work on the chemistry of dithiocarbonates (xanthates),[1] we required a convenient access to tertiary derivatives. These cannot normally be obtained by the common nucleophilic substitution of a leaving group with an *O*-alkyl xanthate salt, in contrast to primary and secondary analogues. In some cases, Michael addition of a xanthate salt to an electrophilic olefin under acidic conditions can be used to access tertiary xanthates.[2] Another route consists of the decarbonylation of *S*-acyl xanthates derived from tertiary carboxylic acids[3] or by reacting a diazo derivative with a bis-xanthate.[4] To expand the range of accessible tertiary derivatives, we considered the possibility of alkylating xanthates containing electron-withdrawing groups, as outlined in Scheme 1, a simple approach that had not apparently been used in the past.

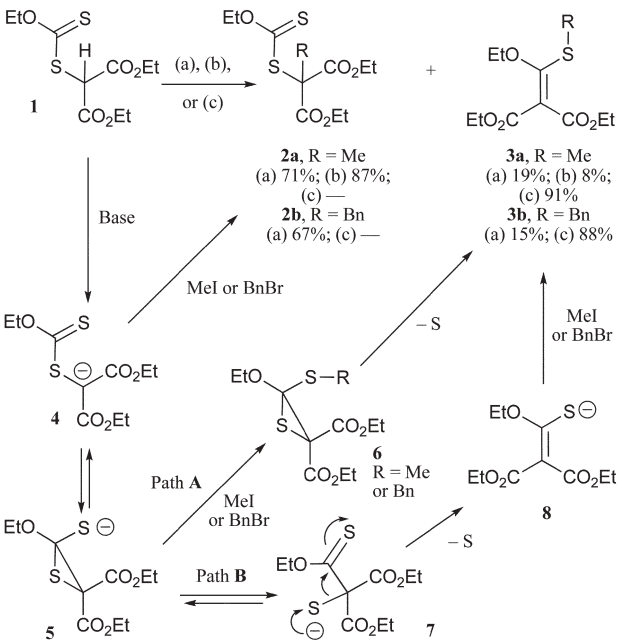
The malonyl derived xanthate **1** was readily prepared by reaction of commercially available diethyl chloromalonate with potassium *O*-ethyl xanthate.[5] When derivative **1** was treated with potassium carbonate and methyl iodide or benzyl bromide (1.2 equiv.) in acetone, the desired tertiary xanthates **2a** and **2b** were indeed produced in a synthetically useful yield (71 and 67% respectively). However, in both cases, a side product was formed which turned out unexpectedly to be ketene monothioacetals **3a** (19%) and **3b** (15%). The yield of **2a** could be increased to 87% by adding an excess of methyl iodide (5 equiv.) *before* incorporation of the potassium carbonate base. In contrast, exposure of the xanthate *first* to the carbonate and then to stoichiometric amounts of the alkylating agent led to the almost exclusive formation of ketene thioacetal **3a** (91%).

These observations can be rationalized by the mechanistic manifold in Scheme 2. The formation of the conjugate base **4** can be followed by direct alkylation to give **2a** or **2b**, depending on the alkylating agent used. This alkylation step is in competition with the reversible ring closure onto the thiocarbonyl group leading to the creation of episulfide **5**. This strained intermediate is then either alkylated to produce **6**, which furnishes **3a** or **3b** by loss of sulfur (path **A**), or opens reversibly into **7** followed by loss of sulfur to give **8** before the final alkylation (path **B**). The presence of excess methyl iodide upon generation of conjugate base **4** (conditions (b)) increases the chances of its direct methylation and a better yield of **2a** is obtained. In contrast, initial exposure to the carbonate in the absence of the alkylating agent allows **4** to undergo cyclisation into **5**, and **3a** and **3b** become essentially the only products of the reaction.

One previous report describes episulfides with *geminal* oxygen and sulfur substituents akin to structure **6**, and this may argue in favour of path **A** being the more likely route to the ketene thioacetals.[6] In any case, as far as we are aware, such a transformation has not been hitherto reported. Indeed, ketene monothioacetals such as **3a,b** are relatively rare, and their chemistry has remained largely unexplored.[7] The present process is straightforward and quite general, as indicated by the examples collected in the Table.§ Various alkylating agents can be used and the ester groups can be replaced by other electron-withdrawing



Scheme 1 Alkylation of a xanthate substituted anion.



Conditions: (a) MeI or BnBr (1.2 eq.), K_2CO_3, acetone; (b) MeI (5 eq.), acetone, then K_2CO_3; (c) K_2CO_3, acetone, then MeI or BnBr (1.2 eq.). Concentration in substrate **1** is 1M in all cases.

Scheme 2 Unexpected formation of a ketene thioacetal.

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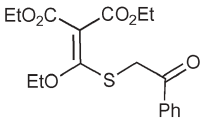
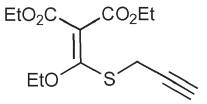
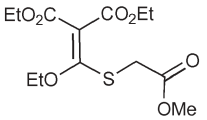
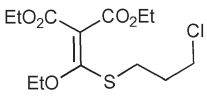
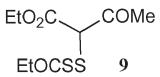
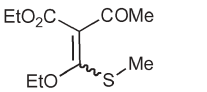
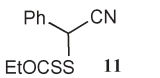
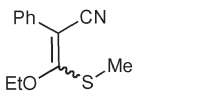
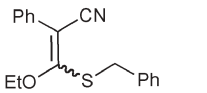
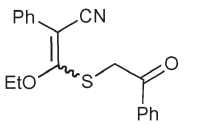
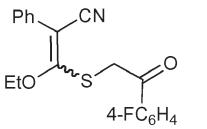
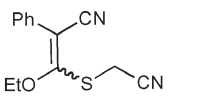
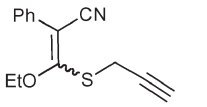
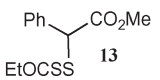
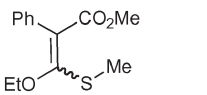
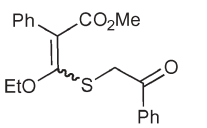
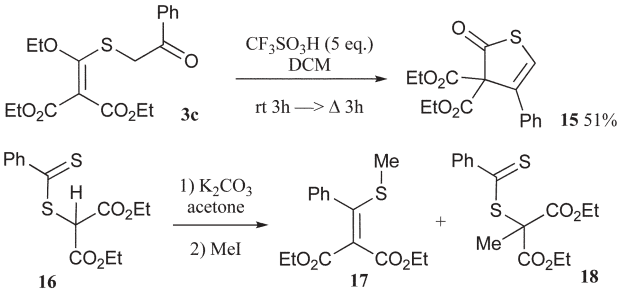
‡ This paper is dedicated with affection and respect to the memory of Professor Charles Rees.

Table 1 Synthesis of ketene monothioacetals from xanthates

Xanthate	R–X	Product	Yield (%)
1	$PhCOCH_2Br$		**3c** (92)[a]
1	$HCCCH_2Br$		**3d** (71)[a]
1	$MeOCOCH_2Br$		**3e** (71)[a]
1	$ClCH_2CH_2CH_2Br$		**3f** (83)[a]
 **9**	Mel		**10** (51)[a]
 **11**	Mel		**12a** (66)[b] 1 : 13
11	BnBr		**12b** (70)[c] 1 : 7
11	$PhCOCH_2Br$		**12c** (63)[b] 1 : 2
11	$4\text{-}FC_6H_4COCH_2Br$		**12d** (65)[b] 1 : 7
11	$NCCH_2Cl$		**12e** (61)[b] 1 : 9.5
11	$HCCCH_2Br$		**12f** (47)[b] 1 : 13
 **13**	Mel		**14a** (38)[b] 1 : 2
13	$PhCOCH_2Br$		**14b** (51)[b] 1 : 2

[a] K_2CO_3, acetone, rt, 30 min, then RX, rt, 30 min. [b] NaH, THF, 0 °C to rt, 30 min, then RX, rt, 30 min. [c] KOH, EtOH, reflux, 1 h, then RX, rt, 20 min.



Scheme 3 Further extensions.

entities. Inseperable mixtures of geometrical isomers were observed when two different electron-withdrawing groups were present in the starting xanthate (*e.g.* **9**, **11**, and **13**) but the geometry of the double bond could not be unambiguously established by NOE experiments. When one of the activating groups is a simple phenyl, then it is better to use the stronger sodium hydride or potassium hydroxide as the base. In these cases, potassium carbonate proved rather inefficient and the yields were significantly lower.

The products sometimes contain a useful combination of functionalities that can lend themselves to interesting further transformations. For example, exposure of compound **3c** to the action of trifluoromethanesulfonic acid in dichloromethane at room temperature results in the formation of the unusual thiolactone **15** in 51% yield through an internal aldol-dehydration reaction (Scheme 3).

The title transformation is not limited to xanthates. For instance, phenyldithioacetate **16** gave compound **17** upon treatment with potassium carbonate and methyl iodide. However, the reaction was sluggish, requiring 15 hours instead of 30 minutes as for the corresponding xanthate **1**, and the yield of product was modest (41%). When the reaction was stopped after 30 minutes, the yield of **17** dropped to 13% but, interestingly the *C*-alkylated derivative **18** could be isolated in 21% yield. This compound slowly decomposed, presumably through hydrolysis of the thiobenzoate, when the reaction time was very long.

These preliminary results highlight some of the synthetic possibilities attached to this new transformation, where a new carbon–carbon bond is formed under mild conditions. They also reveal yet another unexpected facet of the chemistry of xanthates and related derivatives.

We thank Rhodia for generous financial support to one of us (XV).

Notes and references

§ Typical experimental procedure: To a solution of xanthate **1** (205 mg, 0.73 mmol) in dry acetone (1.5 mL) was added solid K_2CO_3 (152 mg, 1.1 mmol). After stirring for 30 min at room temperature, benzyl bromide (104 mL, 0.88 mmol) was added. Stirring was continued for 30 min, the mixture was then filtered and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica (petroleum ether : ethyl acetate 9 : 1) to give the desired ketene monothioacetal **3b** as a pale yellow oil (218 mg, 88%). IR (CCl_4) ν_{max} (cm^{-1}): 1725 (CO), 1563 (C=C). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (bm, 6 H, 2 CH_3), 1.32 (t, J = 7 Hz, 3 H, CH_3), 4.04 (s, 2 H, SCH_2), 4.13 (q, J = 7.2 Hz, 2 H, OCH_2), 4.25 (bm, 4 H, 2 OCH_2), 7.20–7.40 (m, 5 H, ArH). ^{13}C-NMR (100 MHz, $CDCl_3$): δ (ppm) 13.9 (2 CH_3), 14.7 (CH_3), 35.4 (SCH_2), 60.8 (OCH_2 ester), 61.0 (OCH_2 ester), 70.8 (OCH_2 acetal), 111.6 (C=), 127.3, 128.4 and 128.7 (CH Ar), 136.2 (C Ar), 164.3 (CO), 164.6 (CO), 171.1 (C=). HRMS: calculated for $C_{17}H_{22}O_5S$: 338.1188. Found: 338.1187.

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