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Sodium carbonate as a solid-phase reagent for the generation of acetylketene

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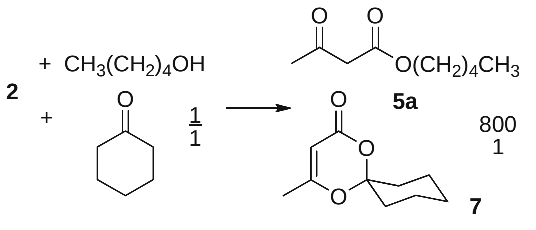
ABSTRACT

Reaction of a toluene solution of 3-oxobutanoyl chloride (**14**) with Na_2CO_3 in the presence of a catalytic amount of triethylamine at −78 °C generates a solution of acetylketene (**2**), the dimer of which was isolated. Acetylketene (**2**) was trapped with 2-propanone, 2-propanol, and ethyl vinyl ether.

1. Introduction

Acetylketene (**2**) is a versatile synthetic intermediate.[1–7] It can readily be generated by the thermolysis or photolysis (Scheme 1). Common precursors include dioxinones (e.g., **1**),[1] β-ketoesters[2,3] (**4** via the enol **5**), and diazodiketones[2,3] (**6**, via Wolff rearrangement). There are limitations to these reactions, however. The first two of these reactions are reversible; successful trapping of **2** requires that the byproducts (acetone or alcohol, respectively) be less reactive than the trapping reagent of interest.[4] The deazetization of **6** is irreversible; however, diazo compounds can be explosives. While **2** can be observed in low temperature matrices, in the absence of trapping reagents, it rapidly dimerizes at room temperature to form **3**.[2]

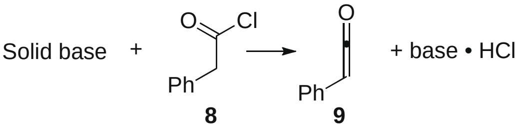
Despite its reactivity, **2** shows useful chemo-, regio-, and stereoselectivity (Eq. 1).[1–7] In competition experiments where **2** was generated in the presence of equimolar cyclohexanone and 1-pentanol, **2** reacted selectively to form **5a** in preference to **7** (800:1, Eq. 1).[4] This also highlights a limitation of this chemistry; if **5a** were used to generate **2** it could not be trapped to give **7**, because back reaction with the byproduct alcohol would be faster. On the other hand, when formed from **1**, **2** can undergo stereoselective cycloadditions, reacting for example with 3-phenyl-2-butanone to give mostly the Felkin–Anh product (6.3:1.0 selectivity).[5]



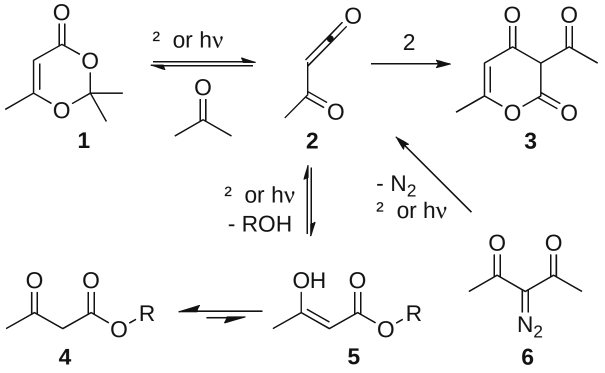
(1)

The reactions of acetylketene (**2**) and related α-oxoketenes are also of theoretical interest, as they are often pseudopericyclic.[6,8,9] Thus, the reactions can have planar transition states and lower barriers than comparable pericyclic reactions. As part of our longstanding interest in these reactions,[4–9] we sought a simple, irreversible method for the generation of **2** in solution.

In a creative approach to the generation of solutions of ketenes (e.g., **9**), Leckta has reported that passing a solution of an acid chloride (e.g., **8**) through a −78 °C column containing an excess of a solid base leads to elimination of HCl and generation of ketene (Eq. 2).[10–12] This method has the advantage that the column eluent contains the ketene free of other reactants. Although early reports utilized an expensive triaminophosphoamide imine (BEMP) resin,[10,11] more recent work utilized simpler reagents, including $NaHCO_3$, in conjunction with a catalytic amount of a soluble shuttle base.[12]



(2)



Scheme 1.

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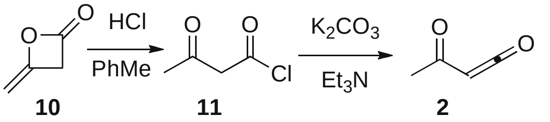
Acetylketene **2** is significantly more reactive than ketenes such as **9**.[2,3] We wondered if similar solid-phase reaction conditions could be utilized to generate **2** from the corresponding acid chloride **11** (3-oxobutanoyl chloride) that can, in turn, be generated from the readily available ketene dimer **10**.[13] Analogously, solution-phase reactions have been proposed.[14,15] We now report that this is indeed possible when a toluene of **11** is reacted with solid sodium carbonate in the presence of catalytic triethylamine at −78 °C (Eq. 3). Simple filtration gives a solution of acetylketene (**2**) that can readily be reacted with a wide variety of trapping agents.



(3)

2. Experimental

3-Oxobutanoyl chloride (**11**) was prepared by the reaction of anhydrous HCl with diketene (**10**).[13] Diketene (**10**, 6.4 mL, 83 mmol) was dissolved in 9.6 mL of toluene in a flask equipped with a gas inlet below the level of the toluene and connected to a nitrogen line equipped with a bubbler. The flask was cooled to −30 °C. Dry HCl was generated by the addition of concentrated sulfuric acid (15 mL) to ammonium chloride (15 g) and bubbled into the reaction mixture over 3 h. The 3-oxobutanoyl chloride (**11**) solution could be stored at −78 °C for one to two days.

Acetylketene (**2**) was generated by the elimination of HCl from 3-oxobutanoyl chloride (**11**) using the apparatus shown in Figure 1. Based on the design of Lectka,[10–12] this consists of a jacketed column fitted with a fritted glass disk and a three-way stopcock at the bottom. A round-bottomed flask was connected to the outlet and a pressure of dry nitrogen could be applied to the bottom of the flask. The top of the column could be vented or connected to nitrogen pressure. The column was oven dried, evacuated, and filled with nitrogen. After having been dried by heating under vacuum, K_2CO_3 (8.5 g, 0.084 mol) was added to the column. Then, dry toluene (15 mL, distilled from Na) was added. A sufficient pressure of nitrogen was applied to the stopcock and the top was vented, so that the flow of nitrogen through the apparatus prevented the toluene from dripping through the frit. Next, the column was cooled with dry ice/acetone, and then a portion of the above-mentioned toluene solution of 3-oxobutanoyl chloride (**11**, 4 mL, 0.021 mol) was added, followed by the addition of triethylamine (0.29 mL, 0.0021 mol) dropwise. The upward flow of nitrogen was continued, mixing the heterogeneous mixture for 10 min. Then, the nitrogen pressure differential was reversed and the solution of acetylketene (**2**) was allowed to flow into the receiving flask that contained an excess of the trapping agent. This was stirred for 4 h at −78 °C, then allowed to warm to room temperature. The products were isolated as described below, and the results are summarized in Table 1.

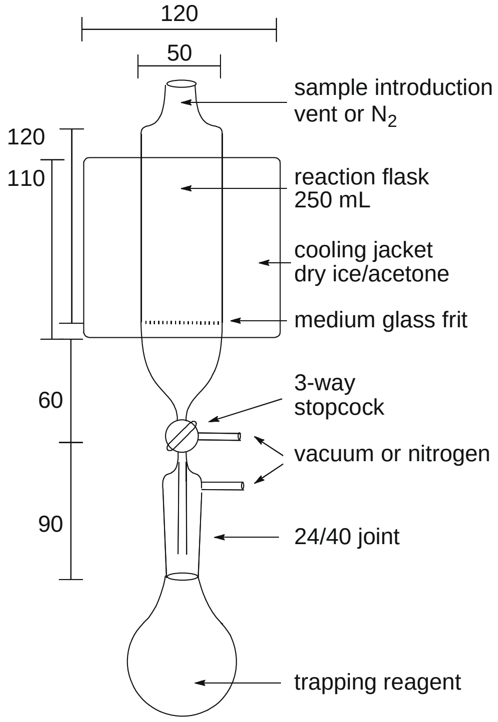
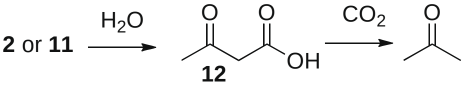


Figure 1. Apparatus for the low-temperature, solid-phase generation of acetylketene (**2**). Dimensions are expressed in mm.

Table 1
Trapping of acetylketene (**2**) with various reagents

Reagent	Product	Yield (%)	Purification
None (dimer)	**3**	12	Crystallization
Acetone	**1**	83	Column chromatography 4:6 hexane:ethyl acetate
2-Propanol	**5b** (R = 2-Pr)	82	Column chromatography 2:1 hexane:ethyl acetate
Ethyl vinyl ether	**16**	5.4	Column chromatography 1:9 hexane: ethyl acetate, then methanol

One additional aspect of this reaction sequence is noteworthy. If any of the acid chloride (**11**) or the acetylketene (**2**) fails to react as desired, this will reduce the overall yield but does not necessarily lead to impurities in the product. Both **2** and **11** react with water to give the carboxylic acid **12** (Eq. 4). However, **12** was not observed, presumably because it decarboxylated to form acetone, which is conveniently removed with the toluene solvent.



(4)

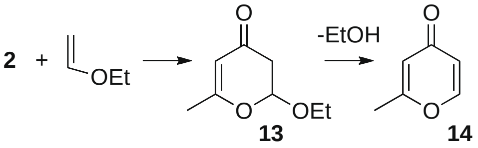
3. Results and discussion

We first sought to determine if acetylketene (**2**) is generated under these reaction conditions. Simply collecting the solution from the column, allowing it to warm to room temperature and analyzing the products addresses this question. As expected, the dimer **3**[1,2] precipitated from the toluene solution, and was isolated by filtration (0.21 g, 12% yield). The yield was not further optimized. Rather, this result was taken as evidence that **2** was indeed formed; the acid chloride **11** is not expected to give **3**. However, this does not address the question as to whether **3** is formed in the cold column or whether **2** survives in solution long enough to exit the column and react in the bottom flask.

In the next experiment, an excess of acetone was added as the trapping reagent to the bottom. 2,2,6-Trimethyl-*4H*-1,3-dioxan-4-one (**1**, 2.48 g)[1,3,4] was obtained in 83% yield after column chromatography. This product is known to form from the reaction of **2** with acetone, but would not be expected from the reaction of the acid chloride **11**. Since acetone was only present in the bottom flask, acetylketene (**2**) must have been formed in the upper flask and furthermore must have survived at −78 °C until transferred to the bottom to react with acetone.

In view of this, it was not surprising that 2-propanol was also able to function as the trapping reagent. After adding the solution of **2** to an excess of 2-propanol, the ester **5b** was isolated in 82% yield (2.48 g) following column chromatography.[2,4] Of course, the ester is the expected product from the reaction of either acid chloride **11** or acetylketene (**2**) with 2-propanol, but the above results are consistent with the initial formation of **2**, followed by its reaction with 2-propanol.

Finally, an attempt was made to react **2** with ethyl vinyl ether (10 mL, 104 mmol). A small amount of 2-methyl-4*H*-pyran-4-one (**14**,[16] 0.49 g, 5.4%) was obtained, presumably by initial [4+2] cycloaddition to form **13**, followed by elimination of EtOH to form **14** (Eq. 5).



(5)

Acknowledgments

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