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Preview

Metal-Free Routes From Carbon Monoxide to Ketenes

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SUMMARY

In this preview, we highlight the recent findings of Gessner and co-workers on the direct access to ketenes from carbon monoxide as a C1 source under transition metal free conditions via ketenyl anions.

Keywords: ketenyl anion, ynoate, phosphorus ylide, ketene, CO insertion

INTRODUCTION

Ketenes ($R_2C=C=O$) are versatile intermediates in organic synthesis and readily undergo electrophilic attack at the *sp*-hybridised carbon centre with nucleophiles such as alcohols, carboxylic acids, and amines. They are also employed in a broad range of cycloaddition reactions.¹ Although synthetically very useful, their high reactivity makes them inherently unstable and as a consequence they are often formed *in situ* and directly consumed. The widely used traditional methods for the generation of highly reactive ketenes are from acids and their derivatives, diazo ketones, metalated carbenes or pyrolysis of diones. However, most of the reaction conditions suffer from the instability of starting materials, the use of stoichiometric metals, high temperatures, a narrow substrate scope, poor yields, and/or selectivity issues. Therefore, the development of an atom economical and more sustainable synthetic methodology is highly desirable to address the issues associated with the traditional methods.

Carbon monoxide (CO), a readily accessible C1 source available from biomass or fossil energy resources, is an important small molecule building block to design many molecular architectures in organic synthesis.² The reactions of CO with transition metals are well-documented, and the bonding of CO to transition metals is a key component of undergraduate chemistry courses. Indeed, metal carbonyls are employed in many carbonylation reactions in industry such as the Fischer–Tropsch and Monsanto processes. Recently, the involvement of *s* and *p* block elements in the synthesis of carbonyl coupled complexes from CO has sparked interest from the chemical community to expand the scope of metal free CO activation.³ However, despite substantial improvement in the field, there is still a lack of chemical space relating to the selective incorporation of CO as a C1 building block.

In a recent publication in *Science*, Gessner and co-workers highlight a novel transition metal free route to ketenyl anions from carbon monoxide and alkali metalated ylides **1** (Figure 1A).⁴ The ylide **1** can be considered as a phosphine-stabilised carbynyl anion **1'** which should undergo phosphine displacement with CO to form a ketene in analogy to that observed with transition metal carbynes. The newly discovered ketenyl anion **2**, formed from the reaction of the metalated ylide and CO, is an excellent synthon for ketene formation, and could be successfully isolated and characterised. This high yielding route to stable ketenyl anions could unlock new reactivities in ketene chemistry and their applications. Various alkali metalated ylides⁵ could be employed as a precursor for the CO insertion reaction including phosphine sulfide, phosphine oxide, diphenyl phosphane, and tosyl containing metalated (potassium or sodium) ylides. For instance, the stepwise synthesis of phosphine sulfides containing potassium ylides from triphenylphosphine via methyltriphenylphosphonium iodide, sulfuration, and finally metalation by benzyl potassium or standard MHMDS bases, led to the isolable ketenyl anion or ynoate in the presence of 1 atm CO. In the reaction the ketenyl anion **2** precipitated out as a colourless solid by displacement of the phosphine from the metalated ylide when reacted with 1 atm CO in toluene. Remarkably, **2** was stable under an inert atmosphere and storable for weeks. The scaled-up synthesis (2.8 g scale) of the

ketenyl anion showed 88% yield for **2a** (Figure 1c) which could be beneficial for potential future industrial applications.

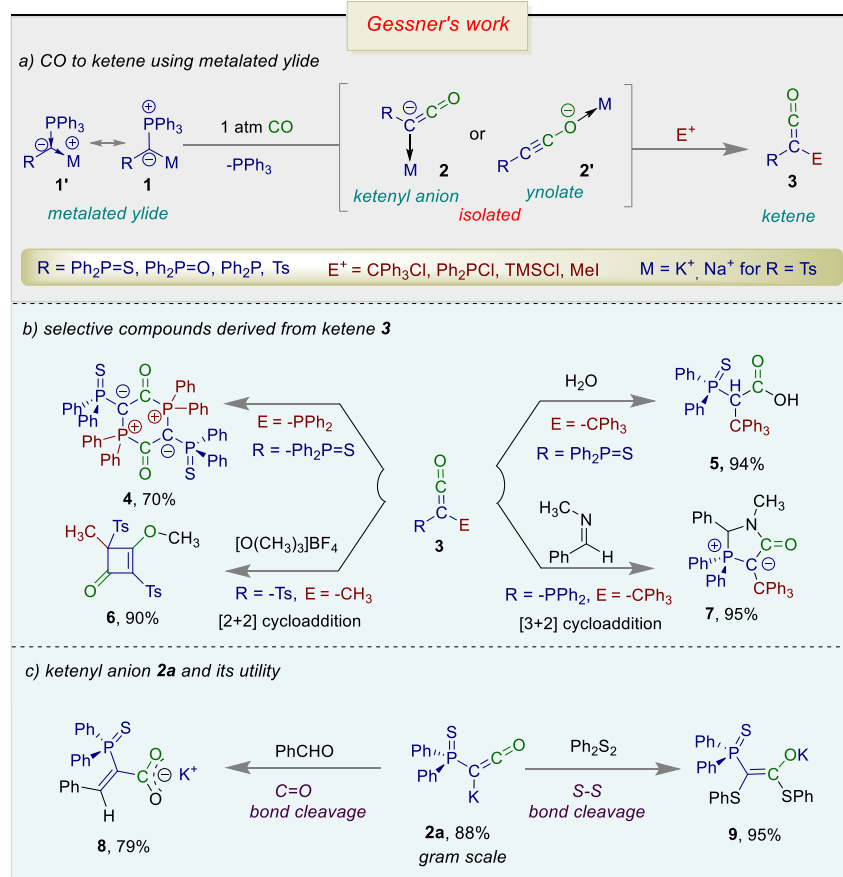


Figure 1. Carbon Monoxide to Ketene via a Ketenyl Anion as an Accessible Synthon: (A) CO to ketene via an isolable ketenyl anion using a metalated ylide. (B) Selective compounds derived from ketene **3**. (C) Follow up reactions of ketenyl anion **2** with an aldehyde and diphenyl disulphide to achieve compounds **8** and **9**.

The structure and properties of the ketenyl anion were compared to previously reported systems,⁵⁻⁷ and were investigated by NMR chemical shifts, IR stretches, X-ray diffraction analysis, and computational studies. The isolated anionic ketene was characterized with the assistance of ³¹P NMR spectroscopy and was compared to previous reports.⁷ The typical C=C=O stretching vibration of **2a** was also visible in the infrared spectrum at 2086 cm⁻¹, which is in the range of ketenes. Interestingly, the anionic ketene **2a** displayed a polymeric structure in the solid-state between two units through both metal (K)-carbon and metal-oxygen atoms in newly formed C=C=O linkage. The polymeric structure of **2a** could be converted into the monomeric unit in the presence of 18-crown-6 where only the metal-carbon interaction was detected in the solid-state structure. In DFT studies, Natural Bond Orbital (NBO) calculations using Wiberg Bond Indices indicated that the C₁ carbon atom has a higher negative charge than the O atom, although it is partially delocalised towards C–O. Comparative Molecular Orbital studies were also undertaken between the ketenyl anion, ketene, and ethynol suggesting the electron density in the C–C bond steadily increases from ketene to ketenyl and ethynol.⁹ Taken together the IR spectroscopic, X-ray, and computational studies helped to rationalise the structure of the anionic ketene. Collectively these suggested an intermediate electronic structure between the ketenyl anion **2** and the ethynolate **2'** (Figure 1A).

These newly identified ketenyl anions displayed a broad range of reactivity towards various electrophiles including trityl chloride, chlorosilane, chlorophosphine, and alkyl iodide derivatives to form the corresponding ketenes with good to excellent yields (up to 95% isolated yield). Selected ketenes were then further converted to other important molecules

(Figure 1B). Phosphorus heterocycle **4** with 70% yield was observed from the dimerisation of the corresponding ketene. The acid **5** could be derived from the corresponding ketene in 94% yield in the presence of water. Surprisingly, the tosyl substituted ketenyl anion transformed to a cyclic ketone and enol ether derivative **6** through carbometallation, [2+2] cycloaddition followed by methylation. Diphenyl phosphine-based ketenyl anion, which formed the corresponding ketene with trityl chloride, could be further converted to lactam **7** by a [3+2] cycloaddition with (*E*)-*N*-methyl-1-phenylmethanimine. For compound **2a**, an unusual reactivity pattern of the ketenyl anion with diphenyl disulfide and aldehydes was observed showing S–S and C=O bond cleavage producing compounds **8** and **9** with 79% and 95% yields, respectively (Figure 1C).

In summary, Gessner and co-workers have discovered a direct and transition metal free route to ketene formation from ylides and carbon monoxide as a C₁ source through the isolation of a ketenyl anion intermediate. The newly identified ketenyl anions are formed in high yields and are stable and storable under an inert atmosphere for weeks. Importantly these compounds could be scaled up to a gram. Furthermore, the post-synthetic transformations of the ketenyl anions demonstrate the applicability of this methodology. Overall, we foresee that this discovery will broaden the synthetic chemist's toolbox in both academic and industrial research by bridging organic and inorganic chemistry.

Lead Contact

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AUTHOR CONTRIBUTIONS

M.P. and R.L.M. jointly wrote and edited the article.

DECLARATION OF INTERESTS

The authors declare no competing financial interests. R.L.M. is a member of the journal's advisory board.

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