# A facile route to ketene-functionalized polymers for general materials applications

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Function matters in materials science, and methodologies that provide paths to multiple functionality in a single step are to be prized. Therefore, we introduce a robust and efficient strategy for exploiting the versatile reactivity of ketenes in polymer chemistry. New monomers for both radical and ring-opening metathesis polymerization have been developed, which take advantage of Meldrum's acid as both a synthetic building block and a thermolytic precursor to dialkyl ketenes. The ketene-functionalized polymers are directly detected by their characteristic infrared absorption and are found to be stable under ambient conditions. The inherent ability of ketenes to provide crosslinking via dimerization and to act as reactive chemical handles via addition, provides simple methodology for application in complex materials challenges. Such versatile characteristics are illustrated by covalently attaching and patterning a dye through microcontact printing. The strategy highlights the significant opportunities afforded by the traditionally neglected ketene functional group in polymer chemistry.

A pplications for functional materials that possess tailor-made properties have been expanding significantly with the development of nanotechnology and the growing need to address resource, health and energy issues<sup>1</sup>. A constant in all of these studies is the need for control of functional groups and for these functional groups to perform multiple roles, such as crosslinking, light harvesting and ligation. In addition to these issues, practical use demands that functional groups be incorporated via robust high-yielding chemistry<sup>2</sup>. Addressing these seemingly contrasting challenges requires the development of powerful methodology for macromolecular systems.

Accordingly, thermolytic generation of reactive groups provides the advantages of reagent-free, fast and efficient generation of functional polymers in both solution and the bulk. A classic example of the thermal generation of highly reactive species is *o*-quinodimethane, which is obtained from the corresponding precursor benzocyclobutene (BCB)<sup>3</sup>. This robust and efficient ring-opening reaction has been successful in the formulation of thermosetting materials<sup>4,5</sup>, intramolecularly collapsed nanoparticles<sup>6–8</sup>, selective crosslinking of polymer matrices<sup>9,10</sup> and synthesis of C<sub>60</sub>-fullerene-grafted polymers<sup>11</sup>. The BCB system, however, is inherently limited owing to the synthetic difficulty in monomer preparation and its reliance on a transient reactive intermediate, which restricts its applications to a single (crosslinking) function. To overcome these limitations, a robust and modular approach to the generation of ketene-functionalized materials is presented.

The selection of ketenes as a target functional group is governed by its rich history in organic chemistry and versatile reactivity. Although it has been over a century since the discovery of ketenes by Staudinger in 1905<sup>12</sup> and its synthetic use has been well demonstrated in complex small-molecule syntheses<sup>13,14</sup>, the value of this versatile functional group in polymer and materials chemistry has yet to be fully exploited<sup>15</sup>. Early efforts to this end constituted the direct polymerization of ketenes<sup>16,17</sup>, and Endo has recently furthered such efforts in realizing the living anionic polymerization of stable ketenes to produce novel polyesters<sup>18,19</sup>. Ketenes as functional groups have been limited to the generation of transient species and the concomitant trapping by nucleophiles. The well known diazonapthoquinone (DNQ) moiety has been used as a precursor for ketene intermediates via the Wolff rearrangement<sup>20</sup> and has found applications in photoactivated solubility modification for photoresists<sup>21</sup> and supramolecular assembly disruption<sup>22,23</sup>. Yagci has also recently investigated the photolytic generation of transient  $\alpha$ -oxoketene species from benzodioxinone and its use as a highly reactive electrophile<sup>24–26</sup>.

Herein, we present a range of ketene precursors based on the modular chemistry of Meldrum's acid<sup>27</sup>, which allows for the synthesis of monomers for both radical and ring-opening metathesis polymerization (ROMP) mechanisms. The observed thermal generation and subsequent reaction of ketene intermediates under ambient conditions are exploited to provide crosslinking via dimerization and functionalization via nucleophilic addition in both solution and the solid state. Above all, the versatility of this approach and the fertile chemistry of ketenes are combined to provide methodology applicable to a variety of functionalized polymeric materials.

#### **Results and discussion**

The synthetic route to ketene derivatives involves thermal treatment of 5,5-dialkyl-2,2-dimethyl-1,3-dioxa-4,6-dione (or 5,5-dialkyl Meldrum's acid) **1**. Traditionally, this reaction is performed under flash vacuum pyrolysis conditions (500 °C, 0.01 torr) to give the dialkyl ketene **2** after loss of acetone and carbon dioxide<sup>28-30</sup>. However, model studies (Supplementary Information) with dibenzyl Meldrum's acid (R = R' = benzyl, **1**) showed that heating at 200 °C or above resulted in highly efficient formation of ketene **2**, which in the absence of nucleophiles underwent dimerization to 2,2,4,4-tetraalkyl-1,3-cyclobutanedione, **3** (ref. 30). In the presence of nucleophiles (NuH) such as amines or alcohols, the ketene intermediate was trapped as the expected amide or ester, **4** (Fig. 1).

Coupled with the highly efficient generation of 2 from 1, Meldrum's acid is also an attractive monomer building block

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**Figure 1** | **Thermolysis of 5,5-dialkyl Meldrum's acid to a ketene, and subsequent reactivity.** Meldrum's acid thermolyses through the loss of acetone and  $CO_2$  to form the ketene **2**, which has two paths of reactivity: (1) dimerization to the cyclobutanedione, **3**, or (2) addition in the presence of a nucleophile to afford the corresponding ester or amide, **4**.

owing to its commercial availability and rich chemistry associated with the acidic methylene group. The latter allows a wide variety of derivatives to be prepared in high yields under mild conditions. To demonstrate this feature, two different strategies were developed that allowed monomers to be prepared based on styrene and norbornene, which are suitable for either radical or ring opening polymerization procedures (Fig. 2).

Starting from Meldrum's acid, 5, a novel, room temperature Knoevenagel condensation and reduction allows access to the monoalkylated derivative, 6, which can then be readily alkylated under mild conditions with 4-vinylbenzyl chloride to give the desired styrenebased monomer 7 in approximately 90% yield. Condensation of 5 with formaldehyde in pyridine leads to the zwitterionic adduct 8 (ref. 31), and trapping with cyclopentadiene affords the norbornene system 9 in only two steps. Homopolymerization of 7 under normal and controlled radical polymerization conditions gives the corresponding polymer of 10, whereas copolymerization of 7 with styrene under controlled radical polymerization conditions was shown to be a facile process leading to a range of materials with varying amounts of Meldrum's acid units along the backbone. For example, copolymerization of a 19:1 mixture of styrene and 7 under standard atom transfer radical polymerization (ATRP) conditions<sup>32</sup>—(1-bromoethyl)benzene, CuBr, 4,4'-dinonyl-2,2'dipyridyl, 110 °C (see Supplementary Information for details)-was shown to be a living process giving the corresponding copolymer of 10, with incorporation of 7 consistent with initial stoichiometry  $(M_{\rm n} = 21.0 \text{ kg mol}^{-1}, 74\% \text{ conversion, PDI } (M_{\rm w}/M_{\rm n}) = 1.12)$  (Fig. 3).

The critical step for materials functionalization is the efficient and quantitative formation of the intermediate ketene derivative **11**. This was initially explored by thermal gravimetric analysis (TGA), which shows a significant mass loss beginning at 180 °C corresponding to approximately 28 wt% of the homopolymer. Based on the repeat unit structure, full conversion of the Meldrum's acid groups to ketene functionalities via loss of acetone and CO<sub>2</sub> leads to a theoretical value of 29.1 wt%, in close agreement with the experimentally observed value. Definitive evidence for the loss of acetone and CO<sub>2</sub> was obtained by TGA-mass spectrometry (Fig. 4a), which showed molecular ion peaks for CO<sub>2</sub> (m/z = 44) and acetone (m/z = 58).

With quantitative data supporting the loss of acetone and  $CO_2$  from **10** at elevated temperatures, identification of the actual ketene intermediate was investigated by Fourier transform infrared spectroscopy. A representative set of spectra is shown in Fig. 4b with the original polymer **10** showing a strong absorbance at 1,738 cm<sup>-1</sup>, corresponding to the C=O stretching mode of the diester derived from Meldrum's acid. Of particular note is that heating results in the appearance of a strong absorbance at 2,103 cm<sup>-1</sup>, corresponding to the typical absorbance for ketenes<sup>13</sup>. The emergence of the ketene peak is coupled with a decrease in intensity for the ester absorbance at 1,738 cm<sup>-1</sup>, and further heating shows a reduction in the intensity of the ketene peak and the appearance of a new peak at 1,810 cm<sup>-1</sup>.

This final absorbance is explained by the propensity of dialkyl ketenes to undergo [2+2] dimerization to form cyclobutane-1,3diones, as shown in **12**. This expected sequence of reactions, diester to ketene to cyclobutane-1,3-dione, was fully consistent with model studies using small molecules and was similarly observed at lower temperatures/longer heating times. As a control, the polymer was shown to be stable at the experimental temperatures by isothermal TGA (Supplementary Information). To the best of our knowledge, this infrared data is the first observation of a ketene polymer system stable at room temperature<sup>33</sup>.

The dual role of ketenes to provide both crosslinking and a reactive chemical handle was explored in solution experiments. Thermolysis with a monomer incorporation of only 2 mol% to styrene produced a crosslinked polymer, which was evidenced by the observation of gel formation and swelling in an appropriate solvent. Conversely, no crosslinking was observed when the polymer was heated in the presence of a secondary amine; instead, quantitative formation of the amide from the thermolytically generated ketenes provided efficient polymer backbone functionalization (Supplementary Information). A kinetic argument explains such observations, as nucleophilic addition of amines to ketenes is much faster than ketene dimerization<sup>34</sup>. A detailed kinetic study on this dual-purpose functional group in macromolecular systems will be reported in due course.

To demonstrate the versatility and potential for ketene-functionalized materials in high-value applications, the observed stability of dialkyl ketenes under ambient conditions was exploited in the creation of functionalized nanopatterned surfaces. In this case, the generated ketene-containing thin film (that is, **11**) serves both to crosslink the polymer layer and to allow residual ketene groups to be covalently modified. Such reactivity would prove useful in surface patterning of biomolecules or materials for chemical/biological sensing as traditional methods rely on either non-covalent adsorption<sup>35,36</sup>, or on multistep reactions for molecular recognition<sup>37</sup> or functionalization<sup>38</sup>. As initial evidence of the persistence of ketenes in the solid state, cooling the polymer films to room temperature after thermolysis (that is, at maximum ketene levels) revealed that the ketene absorbance persists for extended periods under ambient conditions (approximately 90+% remaining after 12 hours).

This stability suggests that the ketene could be synthetically accessible after crosslinking. To demonstrate this novel feature,



**Figure 2** | Synthesis of Meldrum's-acid-containing monomers for radical and ring-opening methathesis polymerizations. The rich chemistry of Meldrum's acid is used as a starting point for both monomers in this study. The styrenic-type monomer, **7**, was generated by a reductive alkylation with benzaldehyde (54%) followed by alkylation with 4-vinylbenzyl chloride under mildly basic conditions (86%). The norbornene monomer was prepared via a formylation to provide zwitterionic **8** (96%), which reacted smoothly with the dienophile cyclopentadiene in a Diels-Alder reaction to afford **9** (61%).

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**Figure 3** | **Synthesis of Meldrum's-acid-containing polymer 10 and its thermolytic properties.** The styrene monomer **7** can be polymerized by a variety of free radical techniques, including atom transfer radical polymerization, to form polymer **10**, which is quantitatively converted to **11** upon thermolysis. Subsequent ketene dimerization provides crosslinking, and unreacted ketenes can be trapped with nucleophiles to give **13**. The balance between dimerization and addition can be controlled by thermolysis time and order of addition of the nucleophile.



**Figure 4** | **Spectroscopic evidence for the formation of a ketene from 10. a**, TGA and TGA-mass spectrometry data for **10** show the loss of acetone and  $CO_2$  with a corresponding mass loss of 28 wt% upon thermolysis. TGA was obtained at a heating rate of 10 °C min<sup>-1</sup> under nitrogen. **b**, Infrared spectra of the film of polymer **10** after heating at 240 °C for varying times. Samples were cooled to room temperature, and the spectra were obtained under ambient conditions. The infrared absorption at 2,103 cm<sup>-1</sup> is that of the ketene, which is stable at room temperature. The spectra were normalized against the aromatic C-H stretching peak (3,030 cm<sup>-1</sup>).

microcontact printing ( $\mu$ CP)<sup>39</sup> was used to pattern an aminefunctional fluorescent dye, tetramethylrhodamine-5-carboxamide cadaverine (TAMRA cadaverine), onto a polymer thin film<sup>40</sup>. In the control system, a thin film of the Meldrum's-acid-functionalized derivative **10** was microcontact printed with the dye without heat treatment. As can be seen in Fig. 5, transfer of the fluorescent pattern could be observed (Fig. 5a), however gentle rinsing with water resulted in complete removal of the dye (Fig. 5b). In direct contrast, if the thin film of **10** was heated at 225 °C for two minutes, cooled to room temperature and microcontact printed with the dye, the pattern was persistent before and after extensive rinsing with a variety of solvents, demonstrating covalent attachment of the dye (Fig. 5d). Furthermore, to probe the stability of the films, the control sample and crosslinked system were sonicated in aqueous solution for five minutes. The control film showed significant cracking and loss of film integrity, whereas the thermally treated film was not affected by sonication (Supplementary Information). Similarly, washing with organic solvents led to complete dissolution of the control sample whereas the thermolysed system retained a uniform surface with the printed fluorescent pattern still present. These  $\mu$ CP results illustrate the power of ketenes in materials chemistry; their reactivity towards soft nucleophiles combined with their propensity towards dimerization provides both a reactive surface for the attachment of a variety of substrates and a stabilized crosslinked thin film.



**Figure 5** | **Covalent attachment of fluorescent dye on \muCP surface.** An amine-functionalized fluorescent dye was patterned to the surface of polymer **10** by microcontact printing ( $\mu$ CP). **a**,**b**, Non-heat-treated films, which have no surface reactive groups, are shown before (**a**) and after (**b**) rinsing with water. The water-soluble fluorescent dye is easily removed from the surface. **c**,**d**, Heat-treated films, which contain surface reactive ketenes, are shown before (**c**) and after (**d**) rinsing with water. The retention of the pattern illustrates the covalent attachment of the fluorescent dye under the mild conditions used for  $\mu$ CP.



Figure 6 | Synthesis of Meldrum's-acid-containing polynorbornene. Norbornene monomer 9 undergoes ring opening metathesis polymerization (ROMP) to form the Meldrum's-acid-containing polymer 14, and subsequent thermolysis provides the ketene-containing polymer, 15. The Meldrum's-acid-containing polymer is also easily extended into block copolymer 16 by sequential addition of 9 and norbornene. EVE, ethyl vinyl ether.

The versatility of this strategy is further demonstrated by the synthesis of a norbornene-derived Meldrum's acid monomer **9** (refs 41,42), which was prepared by the Diels-Alder reaction between cyclopentadiene and the methylidene-Meldrum's acid-pyridine adduct **8** (Fig. 2). Ring-opening metathesis polymerization using the third-generation Grubbs catalyst (Grubbs-III)<sup>43</sup> proceeded smoothly at room temperature, providing Meldrum's-acid-containing polynorbornene **14** (PMANB) with accurate molecular weight and polydispersity control (that is,  $M_n = 11.2 \text{ kg mol}^{-1}$ , PDI  $(M_w/M_n) = 1.06)$  (Fig. 6). TGA analysis of **14** showed 46.1% weight loss with an onset temperature of 150–160 °C, closely matching the theoretical weight loss for acetone and CO<sub>2</sub> (45.9%), and provides evidence for the formation of **15**. Generation of the ketene functionality was also verified by observing the diagnostic

ketene peak at 2,106 cm<sup>-1</sup> in the Fourier transform infrared spectrum of heat-treated films of PMANB, **14** (see Supplementary Information). These results indicate that ketene generation from **14** occurs at significantly lower temperatures than from **10**, which we attribute to the favourable release of spiro-ring strain upon thermolysis of **14**. Further reductions in the temperature of ketene generation will significantly expand the potential applications of this methodology. Efforts to this end are underway in our laboratory and will be reported in a future manuscript. The block copolymer PMANB-*b*-PNB (**16**) could be also synthesized by the successive feeding of two monomers, **9** and norbornene, at different temperatures (room temperature for **9** and -20 °C for norbornene). The resulting PMANB-*b*-PNB showed the targeted molecular weight (22.9 kg mol<sup>-1</sup>-*b*-23.2 kg mol<sup>-1</sup>) with a narrow polydispersity (PDI = 1.20).

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In conclusion, ketenes formed by the thermolysis of modular Meldrum's acid derivatives have been demonstrated to have significant potential for general materials functionalization with the approach being versatile in both monomer and polymer backbone selection. The inherent chemistry of ketenes, specifically the ability to provide crosslinking, act as a reactive chemical handle, or both, allows this simple and modular chemistry to be applied to a variety of challenges in materials, including covalent microcontact printing of crosslinked thin films. This strategy highlights the robust, efficient and orthogonal nature of Meldrum's acid as a monomer building block and the significant opportunities afforded by the traditionally neglected ketene functional group in polymer chemistry.

#### Methods

Diels-Alder reaction for the synthesis of 2',2'-dimethyl-spiro[bicyclo[2.2.1]hept-5-ene-2,5'-[1,3]dioxane]-4',6'-dione (9). To a solution of freshly cracked cyclopentadiene (820 mg, 12.4 mmol) in CH<sub>3</sub>CN (10 ml) was added actic acid (750 mg, 12.5 mmol). To the solution was added a suspension of 1-[(6-hydroxy-2,2dimethyl-4-oxo-4H-1,3-dioxin-5-yl)methyl]pyridinium hydroxide, inner salt (8) (1.95 g, 8.30 mmol) in CH<sub>3</sub>CN (20 ml) at 0 °C. The yellow colour gradually disappeared upon addition. After stirring for 1 h at 0 °C, water (30 ml) was added and the mixture was extracted with EtOAc (3 × 100 ml). The combined ether layer was dried over MgSO<sub>4</sub>, filtered and concentrated in vacuo to yield a crude product as a yellowish white solid (2.38 g). The crude product was further purified by flash column chromatography to afford the desired product **9** as a white solid. All new compounds were fully characterized (see Supplementary Information).

**Copolymerization of 7 with styrene via ATRP.** The statistical copolymerization of 7 with styrene is illustrated by conditions that provide a polymer containing 2 mol% of 7 to styrene. ATRP initiator (1-bromoethyl)benzene (16.9 mg, 0.091 mmol), styrene (2.50 g, 24.5 mmol), 5-benzyl-2,2-dimethyl-5-(4-vinylbenzyl)-[1,3]dioxane-4,6-dione (7) (175 mg, 0.50 mmol), and 4,4'-dinonyl-2,2'-bipyridine (74.4 mg, 0.18 mmol) were added to a 20 ml scored ampule and the solution was deoxygenated by freezing in liquid nitrogen under vacuum and subsequent thawing to room temperature. This process was repeated twice, the ampule was filled with nitrogen and CuBr (13 mg, 0.091 mmol) was added. The ampule was again frozen by liquid nitrogen under vacuum and subsequently thawed to room temperature. This process was repeated twice, the ampule was guaced in an oil bath at 110 °C for 17 hours. The viscous solution was quenched by exposing to air, diluted with 15 ml THF, and precipitated into 200 ml methanol. The resulting product was a white powder (conversion = 74%,  $M_n = 23.7$  kg mol<sup>-1</sup>, PDI = 1.12).

Synthesis of polymer PMANB (14) by ROMP. A vial was charged with Grubbs catalyst III (9 mg, 11  $\mu$ mol) and 1 ml of dry CH<sub>2</sub>Cl<sub>2</sub> under nitrogen atmosphere. A solution of monomer 9 (100 mg, 0.45 mmol) in 3 ml of dry CH<sub>2</sub>Cl<sub>2</sub> was added at room temperature. After 30 min, the reaction was quenched by adding excess ethyl vinyl ether (~10 equivalents). The solution was dripped into methanol to precipitate the desired polymer. The resulting product was a white powder. Yield: 92%, conversion: 100%,  $M_{\rm n}$ : 11,200 g mol<sup>-1</sup>, PDI: 1.06.

 $\mu$ CP of TAMRA cadaverine fluorescent dye. A thin film of 10 was prepared by spin casting a 20 wt% solution of 10 onto an 18 × 18 mm<sup>2</sup> glass slide (spin rate = 1,500 rpm for 45 seconds). A poly[(mercaptopropyl)methylsiloxane] stamp was fabricated by previously reported procedures<sup>39</sup>. The stamp was immersed in a 0.02 M solution of TAMRA cadaverine in deionized water to ink for three minutes. The stamp was removed from the solution, dried under a stream of nitrogen, placed in conformal contact and pressed against the polymer surface for two minutes. The stamp was observed to stick to the glass slide and was carefully peeled off. The polymer film used as a control was stamped after spin casting. In order to prepare a reactive surface of ketenes for covalent attachment of TAMRA cadaverine, a polymer film was placed on a microscope hot stage for two minutes at 225 °C. Fluorescence images were obtained after printing. The slides were immersed in water under slight convection (60 rpm) for 12 hours. The slides were removed from water, dried and reimaged.

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#### Author contributions

F.A.L., B.M., M.K. and C.J.H. developed the concept and conceived the experiments. F.A.L., M.K., B.M., M.H. and J.K. performed the laboratory experiments and analysed the results. L.C. and N.G. provided expertise in  $\mu$ CP and fluorescence microscopy, respectively. F.A.L., B.M. and C.J.H wrote the manuscript.

#### Additional information

The authors declare no competing financial interests. Supplementary information and chemical compound information accompany this paper at www.nature.com/ naturechemistry. Reprints and permission information is available online at http://npg.nature. com/reprintsandpermissions/. Correspondence and requests for materials should be addressed to B.M. and C.J.H.