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gem-Dichlorocyclopropanation of Dicarbonyl Derivatives

Gabriel M. F. Batista,[a] Pedro P. De Castro,[a] Arthur G. Carpanez,[a] Bruno A. C. Horta,*[b] and Giovanni W. Amarante*[a]

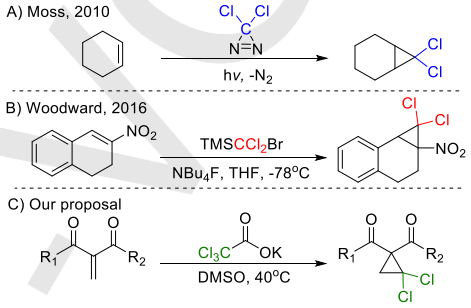
Abstract: A novel methodology for the 1,1-dichlorocyclopropanation of dicarbonyl conjugated olefins was hereby described. The developed protocol is simple and uses readily accessible starting materials, allowing the isolation of the desired adducts in moderate to excellent yields (up to 99%). Furthermore, the reaction tolerated well the scale up to a gram scale, highlighting the synthetic potential of this transformation. Control experiments and DFT studies revealed that the reaction proceeds through a Michael initiated ring closure process, in which reaction temperature play a crucial role. Finally, these *gem*-dichlorocyclopropanes were also employed in the preparation of a tri-substituted naphthyl derivative and a diastereoselective reduction was also demonstrated.

Introduction

The formation of carbon-carbon bonds is an essential synthetic transformation, especially those involving the formation of stereogenic centers.[1,2] In this context, the development of methods for the simple formation of cyclic compounds, notably cyclopropanes and cyclobutanes, is an area that still requires further development.[3–8] Moreover, these rings are intrinsically related to important pharmaceutical properties, such as the enhancement of drug potency, metabolic stability and the reduction of side-effects.[9]

Dihalo-substituted cyclopropanes have recently attracted great interest of the scientific community, mainly due to their versatile reactivity,[10] allowing their use as intermediates in a wide range of applications such as ring expansions, Friedel-Crafts and Doering–Moore–Skattebol reactions.[11] The *gem*-dihalocyclopropanes are also substrates in the preparation of monohalocyclopropanes, cyclopropenes, cyclopentane and a variety of other useful functional groups.[12]

Most methodologies used to access *gem*-dihalocyclopropanes involve the generation of a highly reactive carbene from different sources, such as dihalodiazirine and diazo compounds, that quickly reacts with electron-rich alkenes (Scheme 1A).[13,14] On the other hand, the *gem*-dihalocyclopropanation of electrophilic olefins requires alternative methodologies, commonly using stoichiometric amounts of the toxic Seyferth reagent or $TMSCCl_2Br$ (Scheme 1B).[15] Our research group recently described the use commercially available potassium trichloroacetate in the trichloromethylation of aldimines. Furthermore, we investigated by *ab initio* molecular dynamics simulations the decarboxylation of trichloroacetic acid, leading to the anion $^{-}CCl_3$ in dimethylsulfoxide (DMSO).[16,17] Thus, we envisioned that the reaction between this anion and dicarbonyl conjugated olefins would afford *gem*-dichlorocyclopropanes in a simple and inexpensive methodology (Scheme 1C).



Scheme 1. Previous studies and our proposal for the *gem*-dichlorocyclopropanation of olefins.

Results and Discussion

We started our investigation preparing substrate **1a** by the oxidation of a Morita-Baylis-Hillman (MBH) adduct employing Dess-Martin periodinane (DMP). This methodology was based on previous literature reports[18–20] employing hypervalent iodine reagents and allowed the access to the desired compound in excellent yield (99%) and without the need of purification by column chromatography. This dicarbonyl substrate was then reacted with potassium trichloroacetate in the presence of DMSO (Scheme 2), selectively leading to the 1,1-dichlorocyclopropyl adduct (product **2a**).

After observing that the optimal reaction temperature for the formation of **2a** was at 40-50°C, we proceed with further reaction optimization (Table 1). We observed that by lowering the salt loading (entries 5-7) the conversion considerably dropped. Moreover, when employing reaction times between 10-20 minutes, the isolated yields considerably dropped (entries 1-2), probably due to incomplete decarboxylation of the trichloroacetate salt. Thus, the best reaction condition was established as shown in entry **9**.

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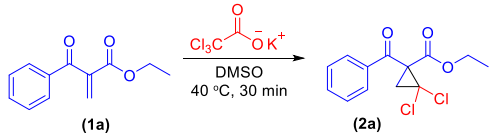
Table 1. Optimization of cyclopropanation reaction.

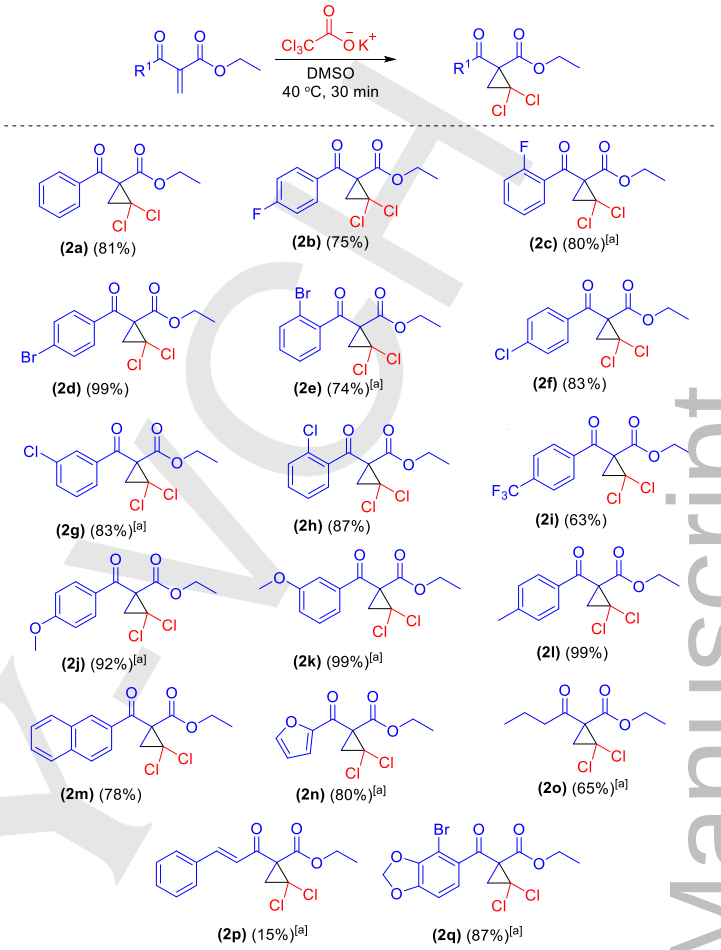


(1a) (2a)

Entry	Time (min.)	Concentration (M)	Salt (Eq.)	Conversion (%)[a]
1	10	0.50	2.00	82
2	20	0.50	2.00	94
3	30	1.00	2.00	51
4	30	0.75	2.00	40
5	30	0.50	1.25	82
6	30	0.50	1.50	95
7	30	0.50	1.75	97
8	60	0.50	2.00	99
9	30	0.50	2.00	99

[a] Conversion calculated by the analysis of the ^{1}H NMR data of the crude reaction mixture.

After the optimization, we turned our attention towards the reaction scope. A wide variety of substrates could be successfully employed under the optimized reaction conditions (Scheme 2). The methodology tolerated well the use of aryl groups containing electron withdrawing and donating aryl groups, including *p*- (such as compounds **2i** and **2k**), *m*- (derivatives **2g** and **2k**) and even sterically bulky *o*- substituents (compounds **2c** and **2e**), affording the desired adducts in good to excellent isolated yields (ranging from 63 to 99%). Furthermore, the alkyl substituted derivative **2o** could be obtained in 65% yield. Heterocycle-substituted adducts were also tolerated in the optimized reaction condition, resulting in compounds **2n** and **2q** in 80% and 87% yield respectively. Most interesting, the cyclopropanation regioselectively occurred at the more electrophilic olefin, affording compound **2p**.

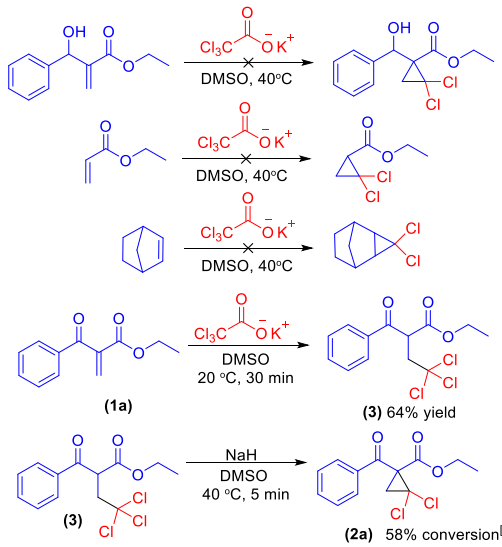


[a] Reaction carried out at 50 °C.

Scheme 2. Scope of the cyclopropanation reaction.

For the proposal of a plausible reaction mechanism, we carried out some control experiments (Scheme 3). Two plausible hypothesis were investigated: a Michael initiated ring closure (MIRC) process, in which initially a Michael-type addition occurs, followed by chlorine elimination or the decomposition of the CCl_3^- anion, generating CCl_2 carbene, that would then react with the olefin, affording the desired cyclopropane. Since it is well known that electron-rich alkenes readily react with carbenes, we carried out the reaction employing norbornene as olefin and no product formation was detected. Furthermore, the use of less electrophilic olefins, such as ethyl acrylate and Morita-Baylis-Hillman adducts also failed to provide the desired cyclopropane derivatives. Interestingly, by lowering the reaction temperature to 20 °C and employing substrate **1a** we observed the formation of a different product (compound **3**), formed by the insertion of trichloromethyl in the molecule. Finally, it is important to mention that when **3** was added in the presence of a base (sodium hydride), it readily converts into **2a** (58% conversion by the crude ^{1}H NMR analysis). This suggested that the mechanism proceed through a MIRC process, and that higher reaction temperatures are required for the chlorine elimination step.

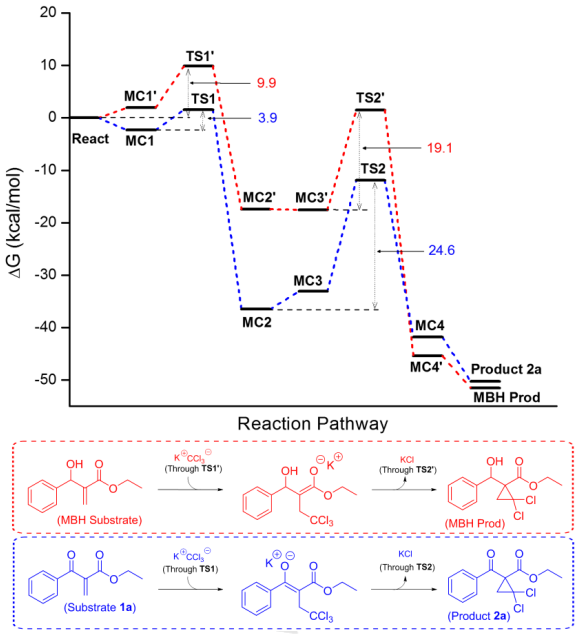
10.1002/chem.201904149



[a] Determined by the ^{1}H NMR analysis of crude reaction mixture.

Scheme 3. Control experiments for mechanistic investigation.

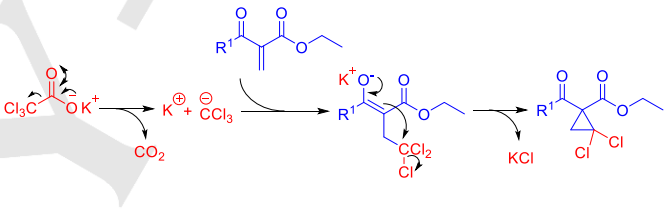
Aiming to better comprehend the reactivity profile of this transformation, we also decided to carry out DFT calculations of the cyclopropanation reaction for both substrate **1a** and a MBH adduct. The DFT calculations for the MBH adduct were performed in order to explain the need of the oxidation step. As shown in Figure 1, the initial step involves the Michael-type addition of the trichloromethyl group into the conjugated olefin. The reaction presents a significantly lower transition state barrier for substrate **1a** than for the MBH adducts ($\Delta\Delta G^{\ddagger}$=6.0 Kcal.mol^{-1}), which suggests that the oxidation step is required in order to obtain a more electrophilic olefin for the reaction with the anion. In the MBH case, although the $\Delta G^{\ddagger}$ can be considered low, the half-life of the trichloromethyl anion might be invoked to explain the absence of insertion product.



* React: isolated reagents; MC1: molecular complex of the reagents ($KCCl_3$ and substrate); TS1: transition state for the 1,4-addition reaction; MC2 and MC3: molecular complexes (two conformations) of the CCl_3^- insertion; TS2: transition state for the cyclopropanation step; MC4: molecular complex of the products (dichlorocyclopropane and KCl).

Figure 1. Reaction pathway for the dichlorocycloprapanation of substrate **1a** (blue) and of a MBH adduct (red).

Next, the reaction proceeds through a second transition state that is involved in the cyclopropane moiety formation. For substrate **1a** this is the rate-limiting step and presents a considerably high $\Delta G^{\ddagger}$ (24.6 Kcal.mol^{-1}), which perfectly explains the need of higher reaction temperatures (above 40 °C) to access the desired compound **2a**. Thus, the isolation of adduct **3** in lower temperatures might be related to the fact that, since the second reaction barrier is significantly high, the reactants at a lower temperature do not have enough energy to overcome it, following to another pathway that involves the α-protonation. This investigation strongly suggests a Michael-type addition followed by chlorine elimination as a mechanistic proposal, as depicted in Scheme 4. Moreover, in this methodology, the only side products are carbon dioxide and potassium chloride.



Scheme 4. Proposed reaction mechanism.

Finally, to highlight the synthetic applicability of the prepared dichlorocyclopropane adducts, we performed the reaction in a 1.5 grams scale (7.5 mmol), with no considerably loss in yield (74% isolated yield), what demonstrates the possibility of scaling-up this transformation (Scheme 5). We also demonstrated that in the presence of aluminum chloride compound **2a** could be converted into derivative **4** (48% yield) in a single step, through a Friedel-Crafts/cyclopropane ring-opening/aromatization cascade reaction. This hydroxylated naphthyl moiety has potential application in several transformations. [21-23] Moreover, a chemoselective ketone reduction of the final product **2a** lead to product **5** as a single diastereomer (d.r.>19:1).

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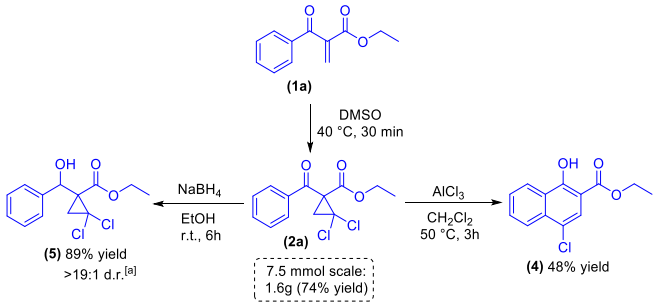

[a] Determined by the ^{1}H NMR analysis of crude reaction mixture.

Scheme 5. Applications of the obtained 1,1-dichlorocyclopropyl product.

Conclusions

In summary, a novel and simple methodology for the 1,1-dichlorocyclopropanation of dicarbonyl conjugated olefins has been described, affording the desired compounds in excellent yields (up to 99%). Several substituted aryl and heteroaryl groups were well tolerated, as well as alkyl analogues. Control experiments and DFT studies suggested a Michael initiated ring closure process, thus leading to the 1,1-dichlorocyclopropyl products. The final products were successfully employed in a cascade Friedel-Crafts/cyclopropane ring-opening/aromatization reaction, affording a tri-substituted naphthyl derivative in a single chemical step. Moreover, a highly diastereoselective and chemoselective reduction of ketone has been performed, giving the corresponding carbinol derivative as a single diastereomer.

Computational Methods

All calculations were performed in the Gaussian 09 package, at a pressure equal to 1 atm and temperature of 313.15 K.[24] All proposed molecules had their structure fully optimized in solution employing the Density functional theory (DFT) at the M06-2X/6-31++G(d,p) level of theory and the Solvation Model based on Density (SMD) for dimethylsulfoxide (DMSO).[25] The vibrational analysis has been carried out to check all stationary points and to obtain the Gibbs free energy corrections. The transition states (TS) were optimized using the Berny algorithm[26] and confirmed to be first-order saddle points. Intrinsic reaction coordinate[27] calculations also confirmed the obtained TS and are available in the Supporting information. The Gibbs free energy of each optimized structure was then calculated by the equation below, in which the terms are the electronic energy and the thermal correction to Gibbs free energy, respectively.

$$: G^{\circ}_{sol} = E_{sol} + G^{\circ}_{T}$$

Experimental Section

General Remarks: All purchased chemicals were employed without further purification and solvents dried following standard procedures. The reactions were followed by thin layer chromatography carried out on TLC plates (silica gel 60 F_{254}) and visualized by a UV lamp; column chromatography was performed employing 230− 400 mesh silica gel. Yields refer to chromatographically purified and spectroscopically pure compounds. Chemical shifts for ^{1}H were reported as δ (parts per million) relative to the signals of chloroform at 7.26 ppm (singlet). Chemical shifts for ^{13}C {^{1}H} NMR were reported as δ relative to the central line signal of the $CDCl_3$ triplet at 77 ppm. The ^{1}H NMR spectra were recorded at 500 MHz, and ^{13}C {^{1}H} NMR spectra were recorded at 125 MHz. Chemical shifts are reported employing the following peak abbreviations pattern: br, broad; s, singlet; d, doublet; dd, double doublet; t, triplet; dq, double quartet; q, quartet; m, multiplet. High resolution mass spectra were acquired in the positive ion mode using a time-of-flight (TOF) mass spectrometer equipped with an ESI source. Melting points were acquired on a melting point apparatus.

General procedure for the preparation of substrates 1a-1q: In a round bottom flask, a Morita-Baylis-Hillman adduct (5.0 mmol), 10.0 mL of dichloromethane and Dess-Martin periodinane (6.3 mmol, 1.25 eq.) were added. This mixture was kept under magnetic stirring at room temperature under stirring for 30 minutes. The crude reaction mixture was then filtrated for the removal of the excess of unreacted DMP. The dichloromethane was then removed under reduced pressure and the crude reaction mixture submitted to a liquid-liquid extraction employing diethyl ether and 5 aliquots of a $NaHCO_3$ water solution. The organic phase was then dried with sodium sulphate and the solvent removed under reduced pressure, affording the desired products (**1a**-**1q**).

Ethyl 2-benzoylacrylate (**1a**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1a** as a yellow oil (969 mg, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86 (m, 2H), 7.59 (m, 1H), 7.46 (m, 2H), 6.69 (s, 1H), 6.06 (s, 1H), 4.22 (q, *J* = 7.15 Hz, 2H), 1.19 (t, *J* = 7.15 Hz, 3H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ: 193.4, 164.5, 141.6, 136.4, 133.7, 131.5, 129.6, 128.7, 61.7, 14.1.

Ethyl 2-(4-fluorobenzoyl)acrylate (**1b**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1b** as a yellow oil (965 mg, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.89 (m, 2H), 7.14 (m, 2H), 6.69 (m, 1H), 6.06 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ: 191.7, 167.1, 164.1 (d, *J* = 106.7 Hz), 141.2, 132.7 (d, *J* = 2.8 Hz), 132.1 (d, *J* = 9.5 Hz), 131.4, 115.8 (d, *J* = 22.3 Hz), 61.6, 14.0.

Ethyl 2-(2-fluorobenzoyl)acrylate (**1c**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1c** as a yellow oil (810 mg, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.87 (m, 1H), 7.57 (m, 1H), 7.28 (m, 1H), 7.12 (m, 1H), 6.63 (m, 1H), 6.29 (m, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ: 189.6, 164.2, 161,8 (d, *J* = 254,6Hz), 143.4, 135.0 (d, *J* = 8,9 Hz), 131.0 (d, *J* = 2.0 Hz), 125.9 (d, *J* = 12.0 Hz), 124.6 (d, *J* = 3.4 Hz), 116.3 (d, *J* = 22.5 Hz), 61.4, 14.0.

Ethyl 2-(4-bromobenzoyl)acrylate (**1d**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1d** as an colorless oil (1089 mg, 77% yield). ^{1}H NMR (500 MHz,

$CDCl_3$) δ: 7.71 (m, 2H), 7.61 (m, 2H), 6.69 (s, 1H), 6.07 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 192.3, 164.2, 141.2, 135.2, 132.1, 131.9, 130.9, 129.0, 61.8, 14.1.

Ethyl 2-(2-bromobenzoyl)acrylate (**1e**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1e** as an colorless oil (1245 mg, 88% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.60 (m, 1H), 7.46 (m, 1H), 7.39 (m, 1H), 7.33 (m, 1H), 6.72 (m, 1H), 6.36 (m, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 192.8, 164.3, 141.7, 140.0, 135.5, 133.6, 132.2, 130.1, 127.4, 120.1, 61.6, 14.0.

Ethyl 2-(4-chlorobenzoyl)acrylate (**1f**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1f** as a yellow oil (1142 mg, 96% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.80 (m, 2H), 7.44 (m, 2H), 6.70 (s, 1H), 6.07 (s, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 192.1, 164.3, 141.3, 140.3, 134.8, 131.9, 130.9, 129.1, 61.8, 14.1.

Ethyl 2-(3-chlorobenzoyl)acrylate (**1g**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1g** as a yellow oil (916 mg, 77% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.83 (m, 1H), 7.71 (m, 1H), 7.55 (m, 1H), 7.41 (m, 1H), 6.72 (s, 1H), 6.09 (s, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 191.9, 164.0, 141.0, 137.9, 134.9, 133.5, 132.1, 129.9, 129.3, 127.5, 61.7, 14.0.

Ethyl 2-(2-chlorobenzoyl)acrylate (**1h**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1h** as a yellow oil (1178 mg, 99% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.53 (m, 1H), 7.40 (m, 2H), 7.34 (m, 1H), 6.69 (d, *J* = 0.8 Hz, 1H), 6.36 (d, *J* = 0.9 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 192.1, 164.3, 142.2, 137.9, 134.9, 132.4, 130.4, 130.3, 127.0, 121.1, 61.5, 13.9.

Ethyl 2-(4-(trifluoromethyl)benzoyl)acrylate (**1i**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1i** as a yellow oil (1115 mg, 82% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.95 (m, 2H), 7.73 (m, 2H), 6.74 (m, 1H), 6.15 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 192.3, 164.1, 141.2, 139.3, 134.9 (q, *J* = 32.8 Hz), 132.7, 129.7, 125.8 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 272.8 Hz), 61.9, 14.1.

Ethyl 2-(4-methoxybenzoyl)acrylate (**1j**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1j** as an orange oil (854 mg, 73% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.88 (m, 2H), 6.96 (m, 2H), 6.68 (m, 1H), 6.02 (m, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 192.0, 164.6, 164.2, 141.7, 132.1, 130.6, 129.3, 114.0, 61.6, 55.7, 14.2.

Ethyl 2-(3-methoxybenzoyl)acrylate (**1k**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1k** as a colorless oil (1123 mg, 96% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.39 (m, 3H), 7.13 (m, 1H), 6.68 (m, 1H), 6.05 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 193.2, 164.5, 159.9, 141.6, 137.7, 131.4, 129.7, 122.6, 120.5, 113.2, 61.7, 55.6, 14.1.

Ethyl 2-(4-methylbenzoyl)acrylate (**1l**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1l** as a yellow oil (1079 mg, 99% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.76 (m, 2H), 7.26 (m, 2H), 6.66 (m, 1H), 6.02 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 192.3, 164.6, 144.7, 141.7, 133.9, 131.1, 129.8, 129.0, 61.6, 21.9, 14.1.

Ethyl 2-(2-naphthoyl)acrylate (**1m**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1m** as a yellow oil (914 mg, 72% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.61 (m, 1H), 8.91 (m, 1H), 7.90 (m, 1H), 7.74 (m, 1H), 7.62 (m, 1H), 7.56 (m, 1H), 7.48 (m, 1H), 6.69 (m, 1H), 6.21 (m, 1H), 4.71 (q, *J* = 7.2 Hz, 2H), 1.08 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 194.9, 164.9, 143.5, 134.6, 134.0, 133.4, 132.8, 130.8, 129.8, 128.6, 128.3, 126.8, 125.8, 124.3, 61.6, 14.0.

Ethyl 2-(furan-2-carbonyl)acrylate (**1n**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1n** as a green oil (960 mg, 99% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.64 (dd, *J* = 1.7 Hz; *J* = 0.8 Hz, 1H), 7.19 (dd, *J* = 3.6 Hz; *J* = 0.8 Hz, 1H), 6.65 (m, 1H), 6.57 (dd, *J* = 3.6 Hz; *J* = 1.7 Hz, 1H), 6.19 (m, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 180.0, 164.2, 152.1, 147.7, 140.7, 132.0, 120.3, 112.7, 61.7, 14.2.

Ethyl 2-methylene-3-oxohexanoate (**1o**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1n** as a colorless oil (510 mg, 60% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 6.40 (d, *J* = 1.0 Hz, 1H), 6.32 (d, *J* = 1.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.73 (t, *J* = 7.3 Hz, 2H), 1.65 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 199.9, 165.0, 142.4, 132.2, 61.5, 43.2, 17.5, 14.2, 13.8.

Ethyl (E)-2-methylene-3-oxo-5-phenylpent-4-enoate (**1p**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1n** as a yellow oil (1138 mg, 99% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.61 (m, 1H), 7.57 (m, 2H), 7.41 (m, 3H), 6.61 (d, *J* = 0.9 Hz, 1H), 6.33 (d, *J* = 0.9 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 190.2, 164.8, 145.6, 141.8, 134.6, 132.7, 131.0, 129.1, 128.7, 124.7, 61.7, 14.3.

Ethyl 2-(4-bromobenzo[d][1,3]dioxole-5-carbonyl)acrylate (**1q**): The reaction was purified through liquid-liquid extraction with ethyl ether to afford product **1q** as a yellow oil (1553 mg, 95% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.02 (s, 1H), 7.00 (s, 1H), 6.67 (m, 1H), 6.30 (m, 1H), 6.05 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 191.8, 164.3, 150.9, 147.5, 142.1, 133.0, 113.7, 113.3, 110.4, 102.6, 61.6, 14.3.

General Procedure for the synthesis of products 2a-q and 3: In a 2.0 mL vial flask, 0.2 mmol of the previously prepared substrates **1a-q** were added, followed by addition of 0.4 mL of anhydrous dimethylsulfoxide (DMSO). For products **2a-q**, this mixture was heated (until 40 or 50 °C) and kept under magnetic stirring; for product **3**, the reaction was kept under magnetic stirring at room temperature. Next, the trichloroacetate salt (0.4 mmol, 2 equiv.) were added to the solution and the reaction kept under magnetic stirring and constant temperature for 30 minutes. Next, the crude reaction mixture was diluted in dichloromethane

10.1002/chem.201904149

(30.0 mL) and a liquid-liquid extraction employing distilled water (four aliquots of 20.0 mL) carried out to remove KCl and DMSO. The organic phase was then dried under reduced pressure and further purification by flash column chromatography (silica gel) using isocratic eluent 1:1 dichloromethane/hexane was carried out.

Ethyl 1-benzoyl-2,2-dichlorocyclopropane-1-carboxylate (**2a**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2a** as a colorless oil (46 mg, 81% yield). IR (ATR, cm^{-1}): 2925, 1739, 1686, 762. ^1H NMR (500 MHz, $CDCl_3$) δ: 8.05 (m, 2H), 7.64 (m, 1H), 7.54 (m, 1H), 4.11 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.11 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 2.52 (d, *J* = 7.6 Hz, 1H), 2.46 (d, *J* = 7.6 Hz, 1H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 189.4, 165.3, 135.8, 133.9, 129.9, 128.6, 62.8, 59.8, 45.9, 30.4, 13.9. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{12}Cl_2NaO_3$ 309.0061, found 309.0054.

Ethyl 2,2-dichloro-1-(4-fluorobenzoyl)cyclopropane-1-carboxylate (**2b**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2b** as a colorless oil (45 mg, 75% yield). IR (ATR, cm^{-1}): 2982, 1733, 1682, 848. ^1H NMR (500 MHz, $CDCl_3$) δ: 8.08 (m, 2H), 7.22 (m, 2H), 4.22 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.13 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 2.54 (d, *J* = 7.8 Hz, 1H), 2.44 (d, *J* = 7.8 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 187.9, 167.3, 165.2 (d, *J* = 16.7 Hz), 132.7 (d, *J* = 9.5 Hz), 132.3 (d, *J* = 3.2 Hz), 115.8 (d, *J* = 22.0 Hz), 62.9, 59.7, 46.0, 30.3, 13.9. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{11}Cl_2FNaO_3$ 326.9967, found 326.9962.

Ethyl 2,2-dichloro-1-(2-fluorobenzoyl)cyclopropane-1-carboxylate (**2c**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2c** as a colorless oil (48 mg, 80% yield). IR (ATR, cm^{-1}): 2922, 1745, 1683, 763. ^1H NMR (500 MHz, $CDCl_3$) δ: 8.04 (m, 1H), 7.61 (m, 1H), 7.28 (m, 1H), 7.19 (m, 1H), 4.25 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.09 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 2.53 (d, *J* = 7.6 Hz, 1H), 2.43 (d, *J* = 7.6 Hz, 1H), 1.07 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 185.9, 165.3 (d, *J* = 2.1 Hz), 162.4 (d, *J* = 257.1 Hz), 135.7 (d, *J* = 9.5 Hz), 131.1 (d, *J* = 2.1 Hz), 124.7 (d, *J* = 10.5 Hz), 124.5 (d, *J* = 3.5 Hz), 116.6 (d, *J* = 23.6 Hz), 62.4, 47.8 (d, *J* = 2.1 Hz), 30.5, 13.7. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{11}Cl_2FNaO_3$ 326.9967, found 326.9967.

Ethyl 1-(4-bromobenzoyl)-2,2-dichlorocyclopropane-1-carboxylate (**2d**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2d** as a yellow oil (71 mg, 99% yield). IR (ATR, cm^{-1}): 2983, 1739, 1686, 841. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.88 (m, 2H), 7.67 (m, 2H), 4.19 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.11 (dq, *J* = 10.8 Hz; 7.1 Hz, 1H), 2.51 (d, *J* = 7.7 Hz, 1H), 2.42 (d, *J* = 7.7 Hz, 1H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 188.6, 165.0, 134.6, 132.0, 131.4, 63.0, 59.7, 45.9, 30.3, 14.0. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{11}BrCl_2NaO_3$ 386.9166, found 386.9151.

Ethyl 1-(2-bromobenzoyl)-2,2-dichlorocyclopropane-1-carboxylate (**2e**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2e** as a yellow oil (53 mg, 74% yield). IR (ATR, cm^{-1}): 2923, 1736, 1698, 759. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.67 (m, 2H), 7.44 (m, 2H), 7.36 (m, 1H), 4.10 (m, 2H), 2.60 (d, *J* = 7.7 Hz, 1H), 2.50 (d, *J* = 7.7 Hz, 1H), 1.04 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 189.9, 164.6, 138.5, 134.0, 132.4, 130.2, 127.2, 120.5, 62.7, 61.4, 48.3, 30.4, 13.6. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{11}BrCl_2NaO_3$ 386.9166, found 386.9161.

Ethyl 2,2-dichloro-1-(4-chlorobenzoyl)cyclopropane-1-carboxylate (**2f**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2f** as a colorless oil (52 mg, 83% yield). IR (ATR, cm^{-1}): 2983, 1735, 1685, 842. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.96 (m, 2H), 7.50 (m, 2H), 4.19 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.11 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 2.51 (d, *J* = 7.6 Hz, 1H), 2.42 (d, *J* = 7.6 Hz, 1H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 188.3, 165.0, 140.4, 134.2, 131.3, 129.0, 62.9, 59.7, 45.9, 30.3, 14.0. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{11}Cl_3NaO_3$ 342.9672, found 342.9660.

Ethyl 2,2-dichloro-1-(3-chlorobenzoyl)cyclopropane-1-carboxylate (**2g**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2g** as a colorless oil (52 mg, 83% yield). IR (ATR, cm^{-1}): 2982, 1738, 1688, 768. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.99 (m, 1H), 7.89 (m, 1H), 7.59 (m, 1H), 7.47 (m, 1H), 4.21 (dq, *J* = 10.8 Hz; *J* = 7.2 Hz, 1H), 4.10 (dq, *J* = 10.8 Hz; *J* = 7.2 Hz, 1H), 2.52 (d, *J* = 7.7 Hz, 1H), 2.44 (d, *J* = 7.7 Hz, 1H), 1.09 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 188.3, 165.0, 137.4, 134.9, 133.8, 129.9, 129.6, 128.2, 63.0, 59.7, 45.9, 30.4, 13.9. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{11}Cl_3NaO_3$ 342.9672, found 342.9666.

Ethyl 2,2-dichloro-1-(2-chlorobenzoyl)cyclopropane-1-carboxylate (**2h**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2h** as a colorless oil (55 mg, 87% yield). IR (ATR, cm^{-1}): 2983, 1735, 1698, 764. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.77 (m, 1H), 7.46 (m, 1H), 7.40 (m, 1H), 4.12 (m, 2H), 2.59 (d, *J* = 7.6 Hz, 1H), 2.48 (d, *J* = 7.6 Hz, 1H), 1.05 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 189.2, 165.0, 136.4, 133.0, 132.9, 130.9, 130.8, 62.8, 61.6, 48.4, 30.6, 13.7. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{11}Cl_3NaO_3$ 342.9672, found 342.9664.

Ethyl 2,2-dichloro-1-(4-(trifluoromethyl)benzoyl)cyclopropane-1-carboxylate (**2i**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2i** as a colorless oil (44 mg, 63% yield). IR (ATR, cm^{-1}): 2922, 1738, 1693, 776. ^1H NMR (500 MHz, $CDCl_3$) δ: 8.14 (m, 2H), 7.80 (m, 2H), 4.19 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.12 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 2.55 (d, *J* = 7.5 Hz, 1H), 2.47 (d, *J* = 7.5 Hz, 1H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 188.6, 164.7, 134.9 (q, *J* = 32.7 Hz), 130.0, 125.5 (q, *J* = 3.7 Hz), 123.5 (q, *J* = 272.6 Hz), 62.9, 59.6, 45.8, 30.1, 13.8. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{11}Cl_2F_3NaO_3$ 376.9935, found 376.9919.

Ethyl 2,2-dichloro-1-(4-methoxybenzoyl)cyclopropane-1-carboxylate (**2j**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford

product **2j** as a colorless oil (58 mg, 92% yield). IR (ATR, cm^{-1}): 2976, 1733, 1676, 841. ^1H NMR (500 MHz, $CDCl_3$) δ: 8.01 (m, 2H), 6.99 (m, 2H), 4.19 (dq, *J* = 10.8 Hz; *J* = 7.2 Hz, 1H), 4.11 (dq, *J* = 10.8 Hz; *J* = 7.2 Hz, 1H), 3.90 (s, 3H), 2.48 (d, *J* = 7.6 Hz, 1H), 2.38 (d, *J* = 7.6 Hz, 1H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 187.6, 165.3, 164.1, 132.3, 128.6, 113.7, 62.6, 59.7, 55.6, 45.9, 30.2, 13.9. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{14}Cl_2NaO_4$ 339.0167, found 339.0157.

Ethyl 2,2-dichloro-1-(3-methoxybenzoyl)cyclopropane-1-carboxylate (**2k**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2k** as a colorless oil (62 mg, 99% yield). IR (ATR, cm^{-1}): 2974, 1736, 1686, 769. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.60 (m, 1H), 7.55 (m, 1H), 7.42 (m, 1H), 7.17 (m, 1H), 4.20 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.10 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 3.88 (s, 3H), 2.49 (d, *J* = 7.6 Hz, 1H), 2.43 (d, *J* = 7.6 Hz, 1H), 1.08 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 189.0, 165.2, 159.6, 136.9, 129.5, 122.6, 120.5, 113.4, 62.6, 59.7, 55.5, 45.7, 30.4, 13.8. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{14}Cl_2NaO_4$ 339.0167, found 339.0164.

Ethyl 2,2-dichloro-1-(4-methylbenzoyl)cyclopropane-1-carboxylate (**2l**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2l** as a colorless oil (59 mg, 99% yield). IR (ATR, cm^{-1}): 2977, 1736, 1682, 771. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.92 (m, 2H), 7.31 (m, 2H), 4.19 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.10 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 2.48 (d, *J* = 7.6 Hz, 1H), 2.44 (s, 3H), 2.41 (d, *J* = 7.7 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 188.7, 165.3, 144.9, 133.2, 129.9, 62.6, 59.7, 45.8, 30.2, 21.8, 14.0. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{14}Cl_2NaO_3$ 323.0218, found 323.0208.

Ethyl 1-(2-naphthoyl)-2,2-dichlorocyclopropane-1-carboxylate (**2m**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2m** as a colorless oil (52 mg, 78% yield). IR (ATR, cm^{-1}): 2983, 1732, 1679, 776. ^1H NMR (500 MHz, $CDCl_3$) δ**:** 8.81 (m, 1H), 8.14 (m, 1H), 8.08 (m, 1H), 7.91 (m, 1H), 7.60 (m, 3H), 4.07 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 3.99 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 2.64 (d, *J* = 7.5 Hz, 1H), 2.49 (d, *J* = 7.5 Hz, 1H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 190.5, 165.6, 134.2, 134.1, 132.7, 131.1, 128.7, 128.7, 126.7, 125.8, 124.4, 62.6, 60.7, 48.0, 30.5, 13.7. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{17}H_{14}Cl_2NaO_3$ 359.0218, found 359.0215.

Ethyl 2,2-dichloro-1-(furan-2-carbonyl)cyclopropane-1-carboxylate (**2n**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2n** as a yellow oil (44 mg, 80% yield). IR (ATR, cm^{-1}): 2983, 1736, 1675, 764. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.69 (dd, *J* = 1.7 Hz; *J* = 0.8 Hz, 1H), 7.39 (dd, *J* = 3.6 Hz; *J* = 0.8 Hz, 1H), 6.62 (dd, *J* = 3.6 Hz; *J* = 1.7 Hz, 1H), 4.25 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 4.14 (dq, *J* = 10.8 Hz; *J* = 7.1 Hz, 1H), 2.45 (d, *J* = 7.6 Hz, 1H), 2.38 (d, *J* = 7.6 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 177.5, 164.8, 152.0, 147.2, 119.8, 112.7, 62.7, 59.4, 45.6, 30.0, 13.9. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{11}H_{10}Cl_2NaO_4$ 298.9854, found 298.9853.

Ethyl 1-butyryl-2,2-dichlorocyclopropane-1-carboxylate (**2o**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2o** as a colorless oil (32 mg, 65% yield). IR (ATR, cm^{-1}): 2963, 1736, 1716, 758. ^1H NMR (500 MHz, $CDCl_3$) δ: 4.29 (q, *J* = 7.1 Hz, 2H), 3.04 (m, 1H), 2.86 (m, 1H), 2.40 (d, *J* = 7.7 Hz, 1H), 2.27 (d, *J* = 7.7 Hz, 1H), 1.68 (m, 2H), 1.33 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 198.3, 164.9, 62.9, 49.7, 44.8, 30.5, 29.0, 17.3, 14.2, 13.8. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{10}H_{14}Cl_2NaO_3$ 275.0218, found 275.0209.

Ethyl 2,2-dichloro-1-cinnamoylcyclopropane-1-carboxylate (**2p**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2p** as a yellow oil (9 mg, 15% yield). IR (ATR, cm^{-1}): 2923, 1733, 1685, 748. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.72 (d, *J* = 15.9 Hz, 1H), 7.64 (m, 2H), 7.43 (m, 3H), 7.37 (d, *J* = 15.9 Hz, 1H), 4.29 (m, 2H), 2.42 (d, *J* = 7.7 Hz, 1H), 2.40 (d, *J* = 7.7 Hz, 1H), 1.30 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 187.6, 164.9, 145.1, 134.5, 131.2, 129.2, 128.9, 124.7, 62.9, 59.5, 48.9, 28.9, 14.2. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{15}H_{14}Cl_2NaO_3$ 335.0218, found 335.0216.

Ethyl 1-(4-bromobenzo[d][1,3]dioxole-5-carbonyl)-2,2-dichlorocyclopropane-1-carboxylate (**2q**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **2q** as a colorless oil (70 mg, 87% yield). IR (ATR, cm^{-1}): 2910, 1733, 1693, 748. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.23 (s, 1H), 7.10 (s, 1H), 6.09 (s, 1H), 4.16 (m, 2H), 2.52 (d, *J* = 7.6 Hz, 1H), 2.48 (d, *J* = 7.6 Hz, 1H), 1.14 (t, *J* = 7.2 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 188.1, 164.8, 151.1, 147.3, 131.0, 114.3, 114.2, 110.7, 102.7, 62.7, 61.3, 47.8, 30.6, 13.8. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{11}BrCl_2NaO_5$ 430.9065, found 430.9065.

Ethyl 2-benzoyl-4,4,4-trichlorobutanoate (**3**): The reaction was purified through column chromatography on silica gel (elution: hexanes/DCM 1:1) to afford product **3** as a yellow oil (41 mg, 64% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.08 (m, 2H), 7.62 (m, 1H), 7.51 (m, 2H), 4.90 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.67 (dd, *J* = 15.4 Hz, 5.8 Hz, 1H), 3.57 (dd, *J* = 15.3 Hz, 5.0 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ: 193.2, 167.9, 135.9, 134.1, 129.3, 129.0, 98.0, 62.5, 53.1, 51.9, 14.0. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{13}Cl_3NaO_3$ 344.9828, found 344.9818.

General Procedure for the preparation of product 4: To a 2.0 mL vial flask containing 0.20 mmol of product **2a**, 0.4 mL of dichloromethane was added, followed by 0.08 mmol of aluminum chloride (0.4 equiv.). The reaction mixture was kept at 50 °C under magnetic stirring for 3 hours. The crude reaction mixture was then washed twice with distilled water, dried with sodium sulphate and the solvent removed under reduced pressure. Flash column chromatography (silica gel) using the isocratic eluent 1:1 dichloromethane/hexane was then carried out.

Ethyl 4-chloro-1-hydroxy-2-naphthoate (**4**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **4** as a white solid (24 mg, 48% yield). Melting point: 84.3 – 85.2°C. IR (NaCl, cm^{-1}): 3693, 2991, 1651, 763. ^1H NMR (500 MHz, $CDCl_3$) δ: 12.02 (s, 1H), 8.46 (m,

1H), 8,19 (m, 1H), 7.88 (s, 1H), 7.47 (m, 1H), 7.60 (m, 1H), 4.47 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ: 170.3, 160.1, 134.3, 130.5, 126.1, 126.0, 124.6, 124.5, 124.0, 121.7, 106.0, 62.0, 14.4. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{11}ClNaO_3$ 273.0294, found 273.0311.

General Procedure for the preparation of product 5: To a 2.0 mL vial flask containing 0.2 mmol of product **2a**, 0.4 mL of ethanol was added, followed by 0.6 mmol of sodium borohydride (3.0 equiv.). The reaction was kept under magnetic stirring at room temperature (20 °C) for 6 hours. Next, the solvent was removed under reduced pressure, and the crude reaction mixture submitted to a liquid-liquid extraction employing dichloromethane and water. Next, the organic phase was dried with sodium sulphate and the solvent removed under reduced pressure. Flash column chromatography (silica gel) using the isocratic eluent 1:1 dichloromethane/hexane was then carried out.

Ethyl 2,2-dichloro-1-(hydroxy(phenyl)methyl)cyclopropane-1-carboxylate (**5**): The reaction was purified through column chromatography on silica gel (elution: hexane/DCM 1:1) to afford product **5** as a yellow oil (51 mg, 89% yield, d.r. > 19:1). IR (NaCl,cm^{-1}): 3500, 2981, 1733, 798. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.35 (m, 5H), 4.70 (d, *J* = 10.3 Hz, 1H), 4.26 (d, *J* = 10.3 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 2.47 (d, *J* = 7.8 Hz, 1H), 1.89 (d, *J* = 7.8 Hz, 1H), 1.12 (t, *J* = 7.2 Hz, 3H).^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ: 167.9, 140.8, 128.7, 128.1, 125.5, 76.3, 62.5, 61.2, 44.4, 30.6, 14.0. HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{14}Cl_2NaO_3$ 311.0218, found 311.0208.

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Keywords: *gem*-dichlorocyclopropane • Michael Initiated Ring Closure • dihalocyclopropanation • density functional theory

[1] K. W. Quasdorf, L. E. Overman, *Nature* **2014**, *516*, 181–191.

[2] I. F. S. Marra, A. M. de Almeida, L. P. Silva, P. P. de Castro, C. C. Corrêa, G. W. Amarante, *J. Org. Chem.* **2018**, *83*, 15144–15154.

[3] N. D. C. Tappin, W. Michalska, S. Rohrbach, P. Renaud, *Angew. Chem. Int. Ed.* **2019**, DOI 10.1002/anie.201907962.

[4] N. D. C. Tappin, W. Michalska, S. Rohrbach, P. Renaud, *Angew. Chem.* **2019**, ange.201907962.

[5] T. Chidley, I. Jameel, S. Rizwan, P. Peixoto, L. Pouységu, S. Quideau, W. S. Hopkins, G. K. Murphy, *Angew. Chem. Int. Ed.* **2019**, DOI 10.1002/anie.201908994.

[6] T. Chidley, I. Jameel, S. Rizwan, P. Peixoto, L. Pouységu, S. Quideau, W. S. Hopkins, G. K. Murphy, *Angew. Chem.* **2019**, ange.201908994.

[7] Z. Shao, *Angew. Chem. Int. Ed.* **2019**, DOI 10.1002/anie.201909596.

[8] Z. Shao, *Angew. Chem.* **2019**, ange.201909596.

[9] C. Ebner, E. M. Carreira, *Chem. Rev.* **2017**, *117*, 11651–11679.

[10] W. Wu, Z. Lin, H. Jiang, *Org. Biomol. Chem.* **2018**, *16*, 7315–7329.

[11] D. Y.-K. Chen, R. H. Pouwer, J.-A. Richard, *Chem. Soc. Rev.* **2012**, *41*, 4631.

[12] A. P. Thankachan, K. S. Sindhu, K. K. Krishnan, G. Anilkumar, *Org. Biomol. Chem.* **2015**, *13*, 8780–8802.

[13] I. D. Jurberg, *Chem. Eur. J.* **2017**, *23*, 9716–9720.

[14] R. A. Moss, *J. Org. Chem.* **2010**, *75*, 5773–5783.

[15] D. S. Lee, M. J. Durán-Peña, L. Burroughs, S. Woodward, *Chem. Eur. J.* **2016**, *22*, 7609–7616.

[16] E. P. Ávila, I. F. de Souza, A. V. B. Oliveira, V. Kartnaller, J. Cajaiba, R. O. M. A. de Souza, C. C. Corrêa, G. W. Amarante, *RSC Adv.* **2016**, *6*, 108530–108537.

[17] G. C. Q. da Silva, T. M. Cardozo, G. W. Amarante, C. R. A. Abreu, B. A. C. Horta, *Phys. Chem. Chem. Phys.* **2018**, *20*, 21988–21998.

[18] P. S. Baran, Y.-L. Zhong, *J. Am. Chem. Soc.* **2001**, *123*, 3183–3185.

[19] M. S. Santos, F. Coelho, *RSC Adv.* **2012**, *2*, 3237.

[20] N. J. Lawrence, J. P. Crump, A. T. McGown, J. A. Hadfield, *Tetrahedron Lett.* **2001**, *42*, 3939–3941.

[21] Y. He, J. Tang, M. Luo, X. Zeng, *Org. Lett.* **2018**, *20*, 4159–4163.

[22] L. He, L. Zhang, X. Liu, X. Li, M. Zheng, H. Li, K. Yu, K. Chen, X. Shen, H. Jiang, et al., *J. Med. Chem.* **2009**, *52*, 2465–2481.

[23] Z. He, A. P. Pulis, D. J. Procter, *Angew. Chemie Int. Ed.* **2019**, *58*, 7813–7817.

[24] G. E. S. M. J. Frisch, G. W. Trucks, H. B. Schlegel, B. M. M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, H. P. H. G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, M. H. A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, T. N. M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, J. Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, E. B. J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, J. N. K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. T. K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. B. C. M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, et al., Gaussian 09, Revision A.01. Gaussian, Inc., Wallingford CT, **2009**.

[25] Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215–241.

[26] H. B. Schlegel, *J. Comput. Chem.* **1982**, *3*, 214–218.

[27] S. Maeda, Y. Harabuchi, Y. Ono, T. Taketsugu, K. Morokuma, *Int. J. Quantum Chem.* **2015**, *115*, 258–269.

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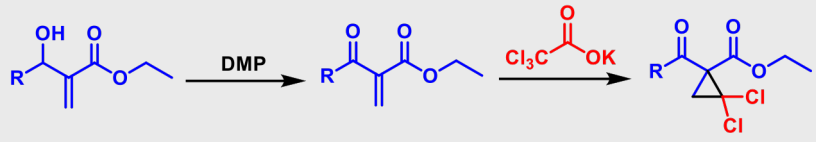

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- Michael initiated ring closure process

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Page No. – Page No.

gem-Dichlorocyclopropanation of Dicarbonyl Derivatives

A simple protocol for the 1,1-dichlorocyclopropanation of dicarbonyl conjugated olefins through a Michael initiated ring closure process. A wide variety of the respective *gem*-dichlorocyclopropane structures have been obtained with high functional group tolerance. Reaction scale-up, as well as novel applications for these derivatives, were also reported.