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Graphical Abstract

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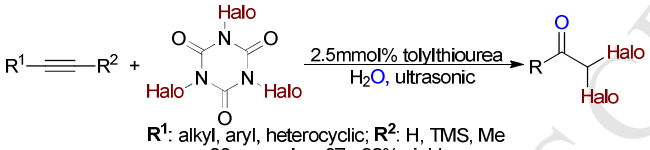

R1: alkyl, aryl, heterocyclic; **R2**: H, TMS, Me
28 examples, 37 - 92% yield

Tetrahedron
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Ultrasound-assisted tandem reaction of alkynes and trihaloisocyanuric acids by thiourea as catalyst in water

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ABSTRACT

With water as the sole solvent, a green and efficient method has been developed for the synthesis of various α,α-dihaloketones *via* ultrasound assisted *p*-tolylthiourea catalyzed tandem reaction of alkynes with trihaloisocyanuric acids. This synthetic route could effectively avoid the use of toxic organic solvents and transition metal catalysts, and the products could be obtained in a very short time at room temperature with good to excellent yields.

1. Introduction

α,α-Dihaloketones are important structural motifs and intermediates for pharmaceuticals, agrochemicals and natural products, and their high reactivity makes them react with a large number of nucleophiles to provide a variety of useful compounds.[1] Consequently, the development of general and efficient methods for synthesis of α,α-dihaloketone is an active research topic in modern organic synthesis and medicinal chemistry. Traditionally, α,α-dihaloketones have been synthesized through halogenation of α-methylketones,[2] acylation of arenes[3] and oxyhalogenation of alkynes[4]. Although these methods are favorable, there are still some limitations as follows: (i) these methods are usually restricted to synthesis of α,α-dichloroketones and α,α-dibromoketones; (ii) the non-methyl phenylketone and internal alkyne substrates show low selectivity; and (iii) hazardous or toxic reagents and solvents, metallic or acidic catalyst, and high reaction temperatures for long reaction times are required. Novel methods of halogenation with high selectivity that satisfy the requirements of green chemistry are still desirable.

Trihaloisocyanuric acids (TXCA) are stable and inexpensive solids, easily available in pool supplies and frequently used as swimming-pool disinfectant and bleaching agent. In contrast to common halogenating reagents, TXCA has no irritating odor and is able to transfer most part of their mass to the substrates. Furthermore, in these reactions, cyanuric acid precipitates as a by-product, which can be recovered by filtration and reused to prepare trihaloisocyanuric acid.[5]

Ultrasound-assisted organic synthesis has proved as a clean and advantageous ~~mothed~~ method in organic synthesis. When ultrasonic waves are passed through a solvent medium, vibrational motions are induced. As the cycle exceeds the compression cycle, it breaks through the intermolecular forces of attraction maintaining the cohesion of the medium causing a sudden drop in pressure, resulting in the production of micro oscillating cavitation bubbles of gaseous substances. The bubbles then enlarge to an unstable size with each succession of applied ultrasonic energy causing instantaneous asymmetric violent implosion of the bubbles in less than a microsecond at the interface, resulting in the formation of high pressure micro-jets and high energetic shockwaves that aid in triggering the solid catalyst, causing the interfacial boundary to destruct and thereby intensifying adequate contact by means of efficient turbulent mixing and acoustic streaming. As a result of this, the rate of the reaction increases by many times as the rate of mass transfer across the

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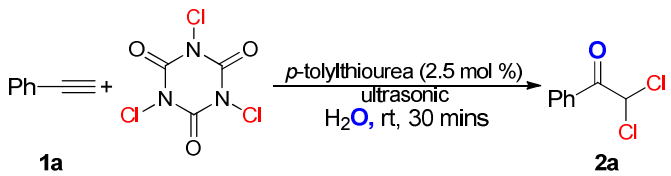
interfacial surface increases.[6] The ultrasonic effect induces very high local pressure and temperatures inside the bubbles and enhances mass transfer and turbulent flow in the liquid. This unique property of ultrasonic decisively affects the chemical reactivity through dissipation of energy. Compared with the traditional heating, ultrasound irradiation has some significant advantages: ultrasonification largely enhances the reaction rate, improves yields, minimizes side-product formation by providing the activation energy in micro environment. It offers environmentally friendly and sustainable synthetic processes by means of using small amounts of solvents, mild reaction condition, and easier manipulation.[7] To the best of our knowledge, there is no report in the literature on the preparation of α,α-dihaloketone from alkynes and trihaloisocyanuric acids using ultrasound irradiation in water. We purpose in this work an improved synthesis of α,α-dihaloketone using an catalytic amount of *p*-tolylthiourea in water under ultrasound irradiation. This method allows for high yields in a short time at room temperature.

2. Results and Discussion

We initiated our investigations with phenylacetylene **1a** as the model substrate. After scrupulous evaluation of all of the reaction parameters, we found that a cocktail consisting of trichloroisocyanuric acid[8] (**TCCA**, 1.0 equiv.) and *p*-tolylthiourea (2.5 mol %) as the catalyst in water (1.5 ml) was sonicated at 60 W power for 30 min delivered α,α-dichloroketone **2a** in 94% GC yield (Table 1, entry 1). It is worth noting that α-monochloro ketone was not detected in the crude mixtures. As expected, the nature of the catalyst played a critical role on the reaction outcome; while otherwise related thioureas provided inferior results (entries 2 - 4). A complicated reaction mixture of chlorination products (**2a**, 2-chloroacetophenone **3a** and 1,2-dichloro-vinyl)-benzene **4a**) was detected in the absence of thioureas (entry 5). Decreasing the amount of TCCA from 1.0 equiv. to 0.5 equiv. resulted in the formation of product **2a** with only a 74% GC yield (entry 6). In order to verify the effect of ultrasound irradiation, we performed the halogenation reaction of **1a** by stirring at 50℃ and 100℃ for 12 hours in the absence of ultrasonic wave. The yields of **2a** were 34% and 59% (entries 7 and 8), respectively, which were less than that obtained via ultrasonic-assisted synthesis. Encouraged by these results, various ultrasonic powers were screened to optimize the reaction conditions. Decreasing the ultrasonic powers resulted in slightly lower yields (entry 9). No benefit was obtained by increasing the ultrasonic power (entry 10). Thus, it was clear from the data that ultrasound can accelerate the halogenation reaction affording higher yield than thermal conditions and significantly reducing the reaction time and temperature.

Table 1. Optimization Studies [a]



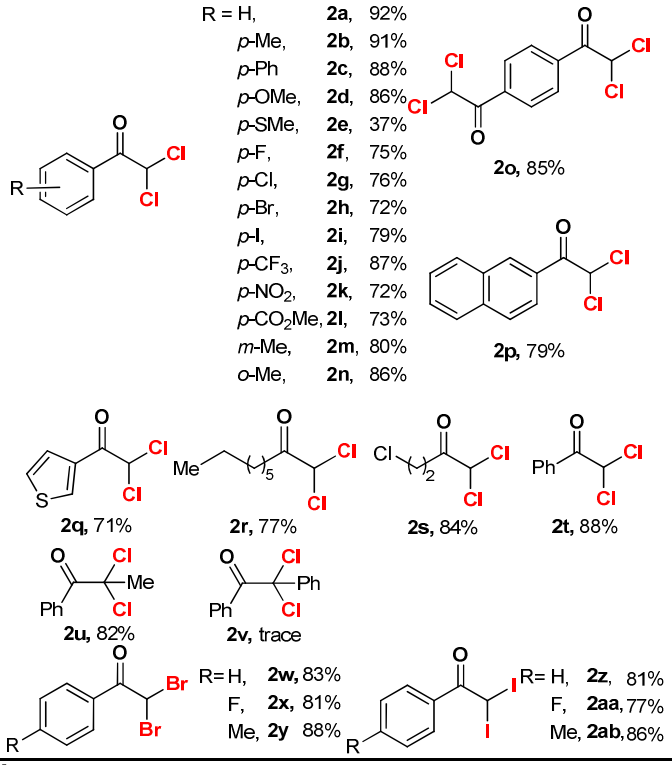
1a **2a**

Entry	Variation from standard conditions above	Time	Yield[b]
1	None	30 min	94%
2	Thioure instead of *p*-tolylthiourea	30 min	81%
3	*N*-Methylthiourea instead of *p*-tolylthiourea	30 min	84%
4	*N,N'*-Diphenylthiourea instead of *p*-	30 min	89%
5	Without *p*-tolylthiourea	30 min	53%
6	TCCA (0.5 equiv.) instead of (1.0 equiv.)	30 min	74%
7	Stirring at 50℃ instead of ultrasonic	12 h	34%
8	Stirring at 100℃ instead of ultrasonic	12 h	59%
9	sonicated at 40 W power instead of 60 W	50 min	85%
10	sonicated at 100 W power instead of 60 W	30 min	94%

[a] Reaction conditions: **1a** (0.1 mmol), TCCA (1.0 equiv.) *p*-tolylthioure (2.5 mmol %), water (1.5 ml) in vial was sonicated at 60 W power.
[b] Determined by GC-MS using ethylbenzene as the internal standard.

With the optimal reaction conditions in hand, we investigated various alkynes so as to gauge the scope of this ultrasound-assisted tandem reaction. As shown in Table 2, phenylacetylenes bearing both electron-donating groups and electron-withdrawing groups at the *para-*, *meta-*, and *ortho*-positions of the phenyl ring could furnish the desired α,α-dihaloketones in high yields (**2a** – **2n**). These results indicated that neither electronic effect nor steric hindrance of phenylacetylenes significantly influences the efficiency of this method. Thioether group (**2e**), which may not be used in oxyhalogenation of alkynes is compatible. Halogen substituents such as F, Cl, Br and I were all well tolerated (**2f** – **2i**), which made this methodology more useful for further transformations. Diethylnylbenzene proceeded smoothly to give the double chlorination product **2o** in 85 % yield. Polycyclic and heteroaromatic substituted acetylenes could also be transformed into the corresponding products in good yields (**2p** and **2q**). In addition, aliphatic terminal alkynes were good substrates (**2r** – **2s**). Notably, the reaction could be extended to thermodynamically more stable internal alkynes. Subjecting the substrate trimethyl(phenylethynyl)silane **1t** to the standard reaction conditions could successfully afford the **2t** in 88% yield, allowing access to phenylacetylene via deprotection of the TMS group. Phenylpropyne was good for the reaction to deliver product **2u**. However, the diphenylacetylene substrate only provided a trace amount of the desired product **2v** in the present catalytic system. Gratifyingly, the present ultrasound promoted halogenation reaction was also successfully applied to produce α,α-dibromoketones (**2w** – **2y**) and α,α-diiodoketones (**2z** – **2ab**) and afford the corresponding products in good yields.

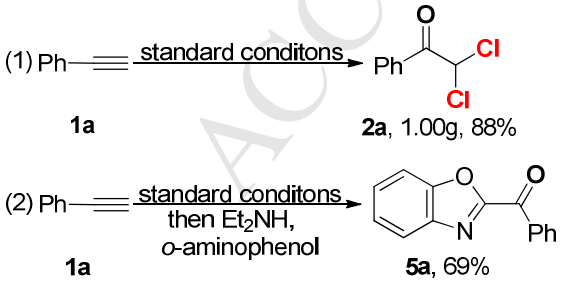
Table 2. Reaction Scopes [a,b]



[a] Reaction conditions: 1 (0.3 mmol), TCCA (0.3 mmol) *p*-tolylthioure (2.5 mmol %), water (1.5 ml) in vial was sonicated at 60 W power. [b] isolated yield.

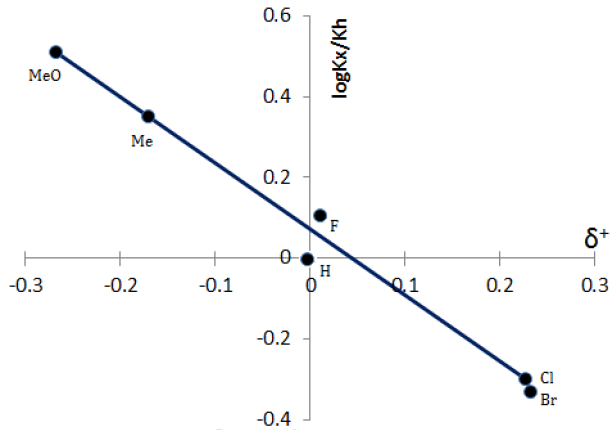
Further, the scalability of our catalytic system was examined. Phenylacetylene **1a** with TCCA could be performed on the 6 mmol scale. After 30 min, an insoluble gum-like substance of a yellowish colour formed in water. The reaction mixture was extracted with ether and then crude **2a** could be purified simply by recrystallization from hexanes and ether to give the desired product **2a** in 88% yield (Scheme 1a). Notably, the developed process avoids using column chromatography. Finally, a one-pot, sequential reaction followed by Et_2NH mediated cyclization to provide **5a** has been demonstrated (see Scheme 1b)[1e]. Although moderate yields are obtained, the one-pot methodology is expected to be of high synthetic utility.

Scheme 1 Gram scale synthesis and Application



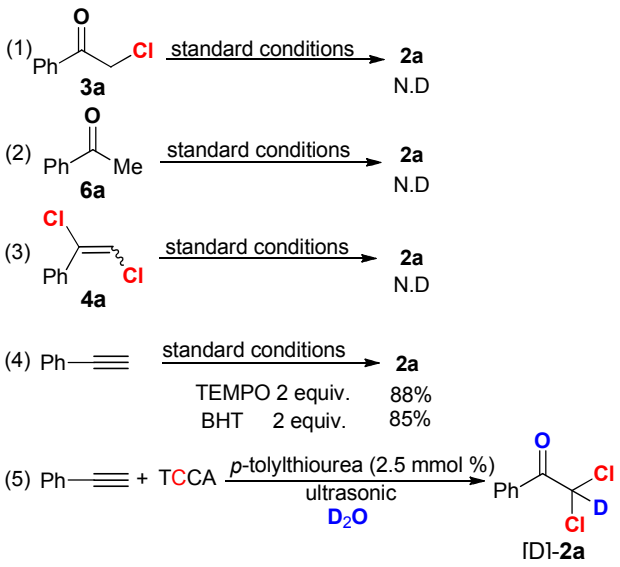
Given this departure from our initial expectation, a Hammett plot was constructed for the migration of *para*-substituted phenylacetylene **1**. In this way, we hoped to gain an understanding of the type of intermediates that were involved in the reaction. Figure 1 shows a reasonable linearity between the log(k_X/k_H) and Brown–Okamoto constant (δ^+) value of the respective substituents. This negative slope (Hammett ρ^+ value: -1.35.) suggests that the reaction process involved a build-up of positive charge in the transition state, with the positive charge on the α-carbon atom adjacent to the phenyl ring, that is, a chloronium ion.[9]

Figure 1. Hammett Equation



To further verify the tandem reaction mechanism, several control experiments were performed and the results were shown in Scheme 2. α-Chloroacetophenone **3a**,[10] 1-phenylethanone **6a** and (1,2-dichlorovinyl)benzene **4a**,[11] which could be generated from alkyne **1a**, failed to afford **2a** under the present conditions (Scheme 2, eqn. 1-3). These results ruled out the possibility of **3a**, **4a** and **6a** as intermediates of the transformation. Subsequently, the reaction **1a** with TCCA in the presence of 2,6-di-tertbutyl-4-methylphenol (BHT) or 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as a radical scavenger gave the corresponding products in good yields, thus suggesting that a radical mechanism or single-electron-transfer (SET) might not be involved in these reaction processes (Scheme 2, eqn. 4). Furthermore, deuterium labeling experiment was performed (Scheme 2, eqn.5). Treating **1a** with TCCA in the presence of *p*-tolylthiourea (2.5 mmol%) in D_2O (0.5 mL), deuterated products [D]-**2a** could be formed, implying that the α-hydrogen atom of **2a** originated from water .

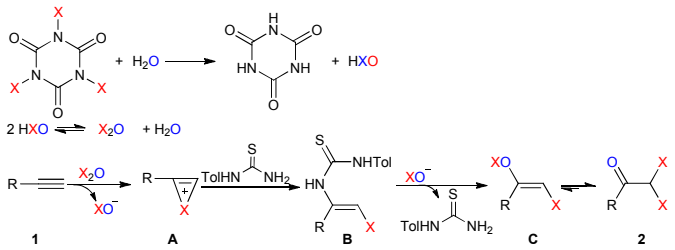
Scheme 2. Control Experiments



On the basis of all these results and previous reports[12], a possible reaction pathway was proposed as depicted in Scheme 3. ~~First, a dihalo monoxide (X_2O) is *in situ*~~

~~generated from TXCA and water with simultaneous production of tricyanic acid.~~ Initially, TXCA reacts with water to give the HXO[12a, 13] and release tricyanic acid. Then, hypohalous acid converts into dihalo monoxide (X_2O)[12b] and reacts with alkyne **1** to yield the halonium ion intermediate **A**. Then, **A** is trapped by *p*-tolylthiourea to afford the key intermediate haloenamine **B**, followed by intermolecular nucleophilic attack with XO^- to form the intermediate **C**, which converts to more stable product **2** via enol keto tautomerism.

Scheme 3. Plausible Mechanism



3. Conclusion

In conclusion, we have developed an ultrasound assisted one-pot three-component procedure for the preparation of α,α-dihaloketone starting with commercially available alkynes, green halogenating reagent and water using common and cheap *p*-tolylthiourea as a catalyst. Utilizing ultrasonic irradiation techniques provided dramatic improvements in terms of higher yields and shorter reaction times compared with conventional heating method. The advantages of this ultrasonic promoted approach involve the mild reaction conditions, low catalyst loading, ease of operation, the simplicity of separation, no requirement for any matel salt and oxidant, excellent chemoselectivity, and good functional-group tolerance. To the best of our knowledge, this method is the first example of synthesis of α,α-dihaloketone through ultrasonic irradiation utilizing *p*-tolylthiourea as a catalyst.

4. Experimental Section

4.1. General methods and materials

All organic solvents were purchased from commercial sources and used as received unless otherwise stated. All other chemicals were purchased from 9dingchem and used without further purification. Reactions were monitored by thin-layer chromatography (TLC) using silicycle pre-coated silica gel plates. Chromatographic purifications were carried out on a Biotage Isolera instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on 400 MHz NMR plus spectrometer using residue solvent peaks as internal standards. Infrared spectra were recorded with IR spectrometer and are reported in reciprocal centimeter (cm^{-1}). High resolution mass spectra were obtained using GCT-TOF instrument with EI or ESI source. Sonication was performed by K1000E-type sonicator (with a frequency of 40 kHz and ultrasonic peak max. 100 W).

4.2.1 General Procedure for the Synthesis of 2

Procedure for 2: To a solution of alkyne (0.3 mmol) in water (1.5 mL) in sealed tube was added TXCA (0.3 mmol) and *p*-tolylthiourea (0.075 mmol, 12 mg), the reaction mixture was ultrasonic at room temperature under and the reaction was monitored by TLC. The reaction typically took 20 mins. Upon completion, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: hexanes/ethyl acetate) to afford **2a** – **2aa**.

4.3. Characterization of the compounds

4.3.1. 2,2-dichloro-1-phenylethanone ***(2a)***[4e]: Yellow oil (52.1 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.69 (s, 1 H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.66 (t, *J* = 7.6 Hz, 1 H), 8.09 (d, *J* = 7.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.81, 128.98, 129.80, 131.32, 134.63, 185.95.

4.3.2. 2,2-dichloro-1-(p-tolyl)ethanone ***(2b)***[2c]: Colorless oil (55.4 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3 H), 6.61 (s, 1 H), 7.22 (d, *J* = 8 Hz, 2H), 7.88 (t, *J* = 8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.91, 67.68, 128.74, 129.72, 129.88, 145.97, 185.62.

4.3.3. 1-([1,1'-biphenyl]-4-yl)-2,2-dichloroethanone ***(2c)***[2c]: Colorless solid (69.9 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ =6.71 (s, 1 H), 7.46 (m, *J* = 8.4 Hz, 3H), 7.64 (d, *J* = 8.4 Hz, 2 H), 7.74 (d, *J* = 8.4 Hz, 2 H), 8.17 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.91, 127.38, 127.54, 128.74, 129.13, 129.89, 130.45, 139.39, 147.33, 185.59.

4.3.4. 2,2-dichloro-1-(4-methoxyphenyl)ethanone ***(2d)***[2c]: Yellow solid (56.4 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ =3.89 (s, 3 H), 6.64 (s, 1H), 6.97 (t, *J* = 8.4 Hz, 2 H), 8.06 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.71, 67.91, 114.24, 123.91, 132.32, 164.67, 184.65.

4.3.5. 2,2-dichloro-1-(4-(methylthio)phenyl)ethanone (2e)[2b]: Colorless oil (26.1 mg, 37%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 3H), 6.68 (s, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 8.01 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 14.62, 39.13, 124.91,126.57, 130.03, 148.32, 184.97.

4.3.6 2,2-dichloro-1-(4-fluorophenyl)ethanone ***(2f)***[2b]: Colorless oil (46.6 mg, 75%).^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.60 (s, 1 H), 7.20 (t, *J* = 8.4 Hz, 2H), 8.16 (dd, *J* = 8.4, 5.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.84, 116.18, 116.40, 127.51, 132.84, 167.76, 184.60.

4.3.6. 2,2-dichloro-1-(4-chlorophenyl)ethanone ***(2g)***[2b]: Colorless solid (50.9 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ =6.60 (s, 1 H), 7.50 (t, *J* = 8.4 Hz, 2 H), 8.05 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.80, 128.94, 129.34, 131.09, 131.28, 141.29, 184.97.

4.3.7. 1-(4-bromophenyl)-2,2-dichloroethanone ***(2h)***[2b]: Colorless solid (57.9 mg, 72%).^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.59 (s, 1 H), 7.67(d, *J* = 8.4 Hz, 2H), 7.96 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.77, 129.89, 130.13, 131.30, 132.34, 185.19.

4.3.8. 2,2-dichloro-1-(4-iodophenyl)ethanone ***(2i)***[2c]: Colorless solid (69.6 mg, 79%).^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.60 (s, 1 H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2 H), 7.88 (d, *J* = 8.0 Hz, 2 H), 8.04 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.82, 103.22, 129.35, 129.49, 130.46, 131.03, 138.33, 141.27, 184.51.

*4.3.9. 2,2-dichloro-1-(4-(trifluoromethyl)phenyl)ethanone****(2j)***[2c]: Colorless oil (67.1 mg, 87%).^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.62 (s, 1 H), 7.79 (d, *J* = 8.4 Hz, 2H), 8.23 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.81, 125.94, 125.98, 128.36, 128.62, 133.99, 135.48, 185.15.

4.3.10. 2,2-dichloro-1-(4-nitrophenyl)ethanone ***(2k)***[2c]: Yellow oil (50.6 mg, 72%).^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.59 (s, 1 H), 7.50 (d, *J* = 8.4 Hz, 2H), 8.05 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.80, 129.34, 131.27, 141.29, 147.81, 185.05.

4.3.11. methyl 4-(2,2-dichloroacetyl)benzoate ***(2l)*** [2c]: Colorless oil (54.1 mg , 73%).^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.94 (s, 3 H), 6.69 (s, 1 H), 8.13 (s, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.71, 67.83, 129.74, 129.97, 134.60, 135.05, 165.82, 185.51.

4.3.12. 2,2-dichloro-1-(m-tolyl)ethanone ***(2m)***[14]: Colorless oil (48.8 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 6.72 (s, 1 H), 7.42 (m, *J* = 7.6 Hz, 2H), 7.87 (t, *J* = 3.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.42, 67.81, 126.89, 128.83, 130.18, 131.41, 135.50, 139.01, 186.10.

4.3.13. 2,2-dichloro-1-(o-tolyl)ethanone ***(2n)***[14]: Colorless oil (52.3 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 3 H), 6.66 (s, 1 H), 7.32 (m, *J* = 8.4 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 1 H) 7.73 (d, *J* = 7.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.36, 68.97, 125.81, 128.56, 132.33, 132.47, 132.93, 140.75, 188.43.

4.3.14. 1,1'-(1,4-phenylene)bis(2,2-dichloroethanone) ***(2o)***[14]: White solid (65.0 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.62 (s, 2 H), 8.24 (s, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.81, 130.18, 135.44, 185.24.

4.3.15. 2,2-dichloro-1-(naphthalen-2-yl)ethanone ***(2p)***[15]: White solid (56.7 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (s, 1 H), 7.35 (m, 3 H), 7.68 (m, 1 H), 7.95 (m, 1 H), 8.10 (m, 1 H), 8.63 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 53.49, 125.89, 126.36, 127.16, 127.28, 128.39, 128.93, 131.07, 132.38, 135.91, 197.64.

4.3.16. 2,2-dichloro-1-(thiophen-3-yl)ethanone ***(2q)***[16]: Colorless oil (41.7 mg, 71%) . ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.42 (s, 1 H), 7.39 (m, *J* = 4 Hz, 1H), 7.67 (d, *J* = 4.8 Hz, 1 H), 8.39 (d, *J* = 4.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 68.24, 126.77, 126.80, 135.56, 180.71

4.3.17. 1,1-dichlorooctan-2-one ***(2r)***[4e]: Colorless oil (32.7 mg, 77%) . ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 0.91 (t, *J* = 6.8 Hz, 3H), 1.35 (m, 6H), 1.69 (t, *J* = 11.2 Hz, 2H), 2.94 (t, *J* = 7.5 Hz, 2H), 5.81 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 14.07, 22.50, 24.34, 28.61, 31.49, 34.94, 43.03, 197.16.

4.3.18. 1,1,5-trichloropentan-2-one ***(2s)***: Colorless oil (40.8 mg, 84%). IR (neat): 3088.2, 2962.2, 1443.4, 1311.0, 1295.7, 1071.2, 906.2, 800.4, 731.1 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.05 (t, *J* = 7.2 Hz, 2 H), 2.70 (t, *J* = 7.2 Hz, 2 H), 3.56 (t, *J* = 6.4 Hz, 2 H), 6.21 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.39, 30.71, 43.52, 115.05, 134.68. HRMS (EI): *m/z* $[M]^+$ calcd for $C_5H_7Cl_3O$: 187.9589, found: 187.9588.

4.3.19. 2,2-dichloro-1-phenylpropan-1-one ***(2u)***[2c]: Yellow solid (50.1 mg, 82%) . ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 3 H), 7.49 (t, *J* = 8.4 Hz, 2H), 7.60 (t, *J* = 8.4 Hz, 1H), 8.32 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.32, 82.72, 128.18, 131.25, 133.69, 188.13.

4.3.20. 2,2-dibromo-1-phenylethanone ***(2w)***[4e]: Colorless oil (69.3 mg, 83%) . ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 6.65 (s, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.57 (t, *J* = 7.8 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 39.74, 129.00, 129.76, 130.85, 134.53, 186.01.

4.3.21. 2,2-dibromo-1-(4-fluorophenyl)ethanone ***(2x)***[4e]: Yellow oil (72.0 mg, 81%) . ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 6.56 (s, 1H), 7.12 (t, *J* = 7.8 Hz, 2H), 8.08 (m, *J* = 7.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 0.02, 38.37, 115.12, 115.34, 126.01, 126.05, 131.63, 131.73, 166.59, 183.55.

4.3.22. 2,2-dibromo-1-p-tolylethanone **(2y)**[4e]: yellow solid (77.1 mg, 88%). δ = 2.37 (s, 3 H), 6.63 (s, 1 H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.90 (t, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.90, 39.94, 128.20, 129.72, 129.87, 145.81, 185.69.

4.3.23. 2,2-diiodo-1-phenylethanone **(2z)**[4e]: yellow solid (90.3 mg, 81%).^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.53 (s, 1 H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 7.6 Hz, 1 H), 8.01 (d, *J* = 7.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 126.59, 127.07, 131.67, 132.23, 186.34.

4.3.24. 1-(4-fluorophenyl)-2,2-diiodoethanone **(2aa)**: yellow solid (90.0 mg, 77%). IR (neat): 3461, 1693, 1599, 1508, 1410.5, 1264, 836, 768, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.45 (s, 1 H), 7.15 (t, *J* = 7.6 Hz, 2H), 8.08 (m, *J* = 4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 115.18, 115.27, 115.40, 131.35, 131.45, 166.40, 185.82. HRMS (EI): *m/z* $[M]^+$ calcd for $C_8H_5FI_2O$: 389.8362, found: 389.8358.

4.3.25. 2,2-diiodo-1-p-tolylethanone **(2ab)**[4e]: Yellow solid (99.6 mg, 86%).^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 2.34 (s, 3H), 6.61 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.88 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 22.51, 68.48, 129.34, 130.32, 130.48, 146.57, 186.22.

4.3.26. benzo[d]oxazol-2-yl(phenyl)methanone **(5a)**[1e]: Colorless solid (99.6 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.48 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.2 Hz, 3H), 7.69 (m, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 7.6 Hz, 1H), 8.54 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 111.82, 122.34, 125.69, 128.41, 128.58, 130.94, 134.28, 134.94, 140.68, 150.36, 157.03, 180.53.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http:// .

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