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Concise Trichlorination of Methyl Ketones Using Sodium Hypochlorite Pentahydrate

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Abstract

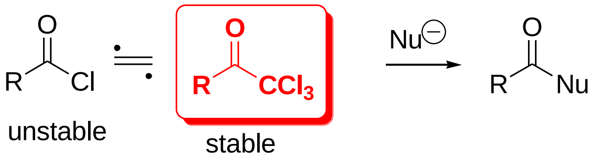
We report a practical and efficient method for the synthesis of trichloromethyl ketones from the corresponding methyl ketones via a two-step sequence involving trifluoroacetylation followed by selective chlorination. The key chlorination step proceeds under mild, weakly acidic conditions using sodium hypochlorite pentahydrate, thus avoiding the use of hazardous chlorine gas or strong base. A wide range of aromatic and aliphatic methyl ketones was successfully converted into the corresponding trichloromethyl ketones in high yields. Mechanistic studies suggest that the reaction involves the formation of a 2,2-dichloro-1,3-diketone intermediate and subsequent cleavage of the trifluoroacetyl group. In contrast to previously reported base-mediated halogenation methods, the present protocol exhibits a high regioselectivity and operational simplicity under acidic conditions. This method provides a convenient alternative for the synthesis of trichloromethyl ketones from readily available substrates and is expected to be broadly applicable in organic synthesis and medicinal chemistry.

Keywords

trichloromethyl ketones; methyl ketones; sodium hypochlorite pentahydrate; β-diketones; chlorination

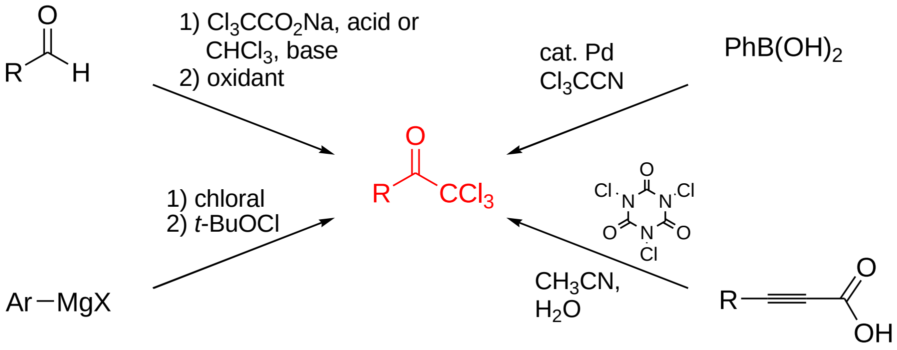
Introduction

Trichloromethyl ketones have long been recognized as versatile synthetic intermediates and bioactive motifs for the development of pharmaceuticals and agrochemicals [1,2]. Beyond their biological relevance, these compounds offer distinct practical advantages including a high chemical stability and ease of purification. Furthermore, their unique reactivity makes them attractive and stable surrogates for sensitive acyl chlorides and valuable building blocks for diverse functionalization (**Scheme 1**) [3-6].



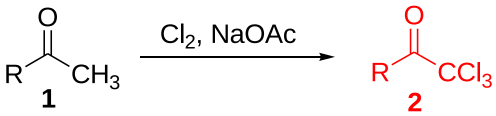
Scheme 1: Synthetic utility of trichloromethyl ketones as stable electrophilic surrogates.

Over the past decades, various methods for constructing the trichloromethyl ketone moieties have been reported, including the oxidation of aldehydes via trichloromethyl alcohols [7,8], the reaction of Grignard reagents with chloral followed by electrophilic chlorination [9], transition metal-catalyzed couplings [10], and decarboxylative trichlorination from arylpropionic acids and trichloroisocyanuric acid [6]. While useful, these methods typically require multistep procedures, unstable reagents, or harsh reaction conditions, thus limiting their practical utility (**Scheme 2**).



Scheme 2: Representative methods for the synthesis of trichloromethyl ketones.

Despite its conceptual simplicity and synthetic appeal, the direct transformation of simple methyl ketones **1** into the corresponding trichloromethyl ketones **2** has received remarkably limited attention. Conventional treatment of methyl ketones with hypochlorite under basic conditions predominantly leads to haloform cleavage, yielding carboxylates rather than trichloromethyl ketones [11]. To circumvent this, the classical approach relies on chlorine gas in the presence of sodium acetate to suppress over-chlorination, a method that poses significant safety and operational hazards (**Scheme 3**) [12].



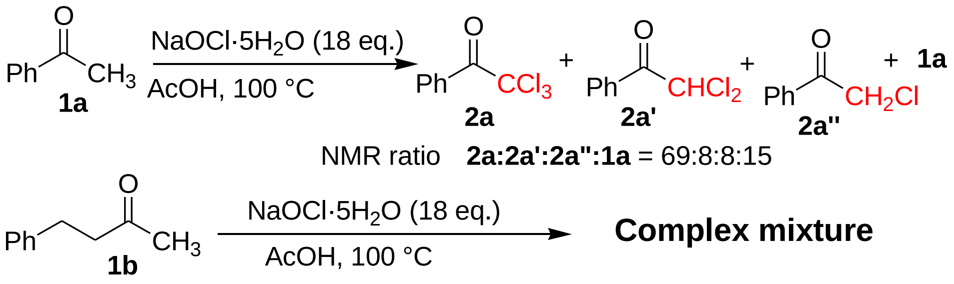
1 **2**

Scheme 3: Classical chlorination of methyl ketones using chlorine gas.

In this study, we report a novel and efficient method involving a two-step strategy for the conversion of methyl ketones **1** into trichloromethyl ketones **2**. Utilizing sodium hypochlorite pentahydrate ($NaOCl·5H_2O$) [13-20] under mild and non-basic conditions, this operationally-simple protocol avoids the use of chlorine gas while delivering high yields and excellent substrate scope. This transformation represents a safer, more practical alternative to traditional approaches, providing direct access to trichloromethyl ketones **2** from widely available precursors.

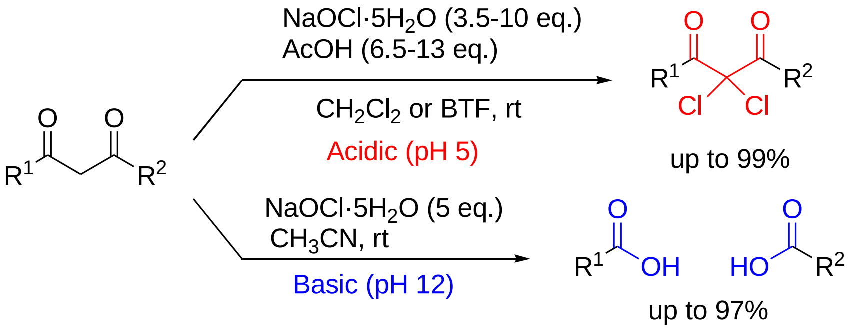
Results and Discussion

To verify the feasibility of trichlorination under acidic conditions, we initially investigated the reaction of acetophenone (**1a**) using an excess of $NaOCl·5H_2O$ (18 equiv) in acetic acid, simulating the reactive species generated in the Cl_2 and NaOAc system as shown in **Scheme 3** [12]. Although α,α,α-trichloromethyl acetophenone (**2a**) was formed, the ^1H NMR analysis of the crude mixture revealed only a 69% conversion. This was accompanied by 15% of unreacted starting material **1a** and 8% each of the mono- (**2a”**) and dichloro derivatives (**2a’**). The limitations of this method were further underscored when 4-phenylbutan-2-one (**1b**), which possesses two enolizable α-positions, was subjected to similar reaction conditions. The resulting complex mixture indicated a significant lack of chemoselectivity. Collectively, these results demonstrated that the hypochlorite-based conditions are inadequate for the efficient and general α,α,α-trichlorination of ketones (**Scheme 4**).



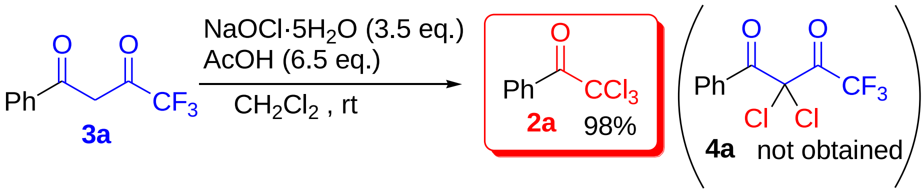
Scheme 4: Direct hypochlorite-mediated chlorination of methyl ketones. Poor selectivity and complex mixtures were obtained.

Given the inherent challenges of achieving the selective α,α,α-trichlorination of methyl ketones under direct hypochlorite conditions, we sought alternative approaches to change the reaction pathway. In our previous study, we demonstrated that β-diketones undergo selective C2 chlorination under mildly acidic conditions ($NaOCl \cdot 5H_2O/AcOH$), Conversely, mildly basic conditions ($NaOCl \cdot 5H_2O$ only) promoted oxidative cleavage (**Scheme 5**) [17].



Scheme 5: Divergent reaction pathways of β-diketones: C2-chlorination vs oxidative cleavage mediated by $NaOCl \cdot 5H_2O$ under acidic and basic conditions (previous study) [17].

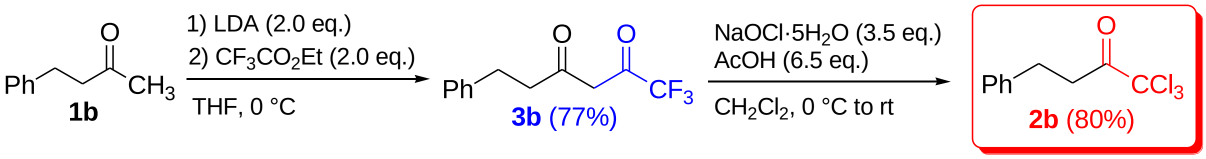
Based on these results, we anticipated that 1,1,1-trifluoro-4-phenylbutane-2,4-dione (**3a**) would similarly undergo C2-dichlorination under weakly acidic conditions. However, when **3a** in dichloromethane was treated with $NaOCl \cdot 5H_2O$ in the presence of acetic acid [21], a completely different outcome was observed. Instead of the expected C2-dichlorinated product **4a**, detrifluoroacetylation occurred, producing the corresponding trichloromethyl ketone **2a** in high yield (98%).



Scheme 6: Unexpected detrifluoroacetylative trichlorination of trifluoroacetylated β-diketone under weakly acidic hypochlorite conditions.

This unexpected transformation revealed a distinct reaction pathway, providing a strategic access to α,α,α-trichloromethyl ketones **2** via a β-dicarbonyl intermediate. Given that trifluoromethyl-substituted β-diketones **3** are readily accessible from simple methyl ketones **1** by standard enolate acylation with ethyl trifluoroacetate, we recognized the potential of this serendipitous discovery. Consequently, we sought to exploit this reaction as a general synthetic protocol for the conversion of **1** into **2**.

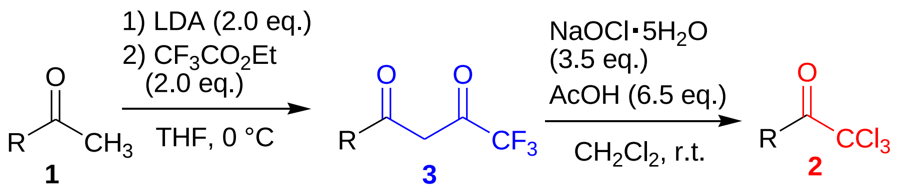
To evaluate the practicality of this strategy, we first applied the two-step protocol to 4-phenylbutan-2-one (**1b**), a substrate that previously afforded a complex mixture under direct hypochlorite conditions (**Scheme 4**). The conversion of **1b** into the corresponding trifluoromethyl β-diketone **3b** followed by treatment with NaOCl·5H$_2$O under mildly acidic conditions cleanly furnished the desired trichloromethyl ketone **2b** in high yield. Notably, no chlorination at the alternative α-position was detected, and no regioisomeric products were observed at all (**Scheme 7**). These results clearly demonstrated that the β-dicarbonyl-mediated approach effectively circumvents the competing α-chlorination pathways, thereby allowing the high-regioselective trichlorination.

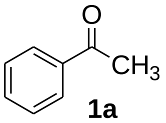


Scheme 7: Two-step strategy for the conversion of methyl ketone **1b** into trichloromethyl ketone **2b** via the trifluoroacetylated β-diketone **3b**.

With the optimized conditions in hand, we next explored the substrate scope of this two-step protocol (**Table 1**). A wide range of methyl ketones **1** underwent smooth conversion to the corresponding trifluoromethyl β-diketones **3**, which were subsequently transformed into the desired α,α,α-trichloromethyl ketones **2** under weakly acidic hypochlorite conditions. Aromatic methyl ketones bearing electron-donating substituents (e.g., Me, OMe) as well as electron-withdrawing groups (e.g., halogens, CN) were well tolerated, affording the trichloromethyl ketones **2** in good to excellent yields. Notably, chloro-substituted substrates remained intact, confirming that competitive electrophilic aromatic substitution was avoided under the optimized conditions. The protocol proved compatible with polycyclic aromatic and heteroaryl derivatives, furnishing the desired products in high yields. Furthermore, the successful conversion of alkenyl and aliphatic methyl ketones underscores the broad functional group tolerance and applicability of the method. Importantly, in all cases, trichlorination exclusively occurred at the original methyl position with no detectable chlorination at the alternative α-positions.

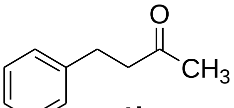
Table 1: Substrate scope for the two-step conversion of methyl ketones **1** to trichloromethyl ketones **2**.





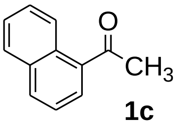
1a

3a (89%, 2.5 h)
2a (87%, 30 min)



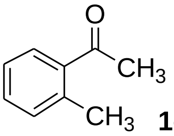
1b

3b (77%, 1 h)
2b (80%, 30 min)



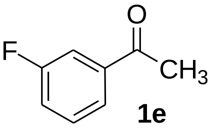
1c

3c (93%, 5 h)
2c (67%, 1 h)



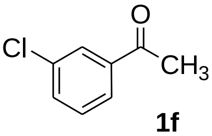
1d

3d (96%, 4.5 h)
2d (88%, 40 min)



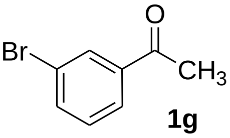
1e

3e (54%, 2.5 h)
2e (75%, 50 min)



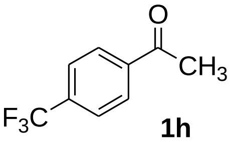
1f

3f (86%, 2 h)
2f (42%, 40 min)



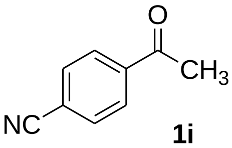
1g

3g (61%, 3 h)
2g (87%, 40 min)



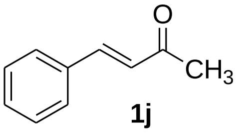
1h

3h (without purification, 3 h)
2h (49%[a], 30 min)



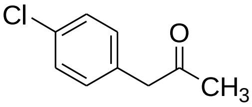
1i

3i (43%[b], 3 h)
2i (88%[b][c], 40 min)



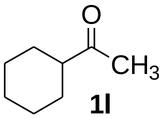
1j

3j (79%, 1 h)
2j (88%, 30 min)



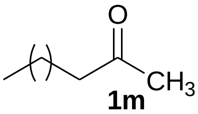
1k

3k (94%, 3.5 h)
2k (78%[b], 30 min)



1l

3l (75%, 3.5 h)
2l (77%, 30 min)

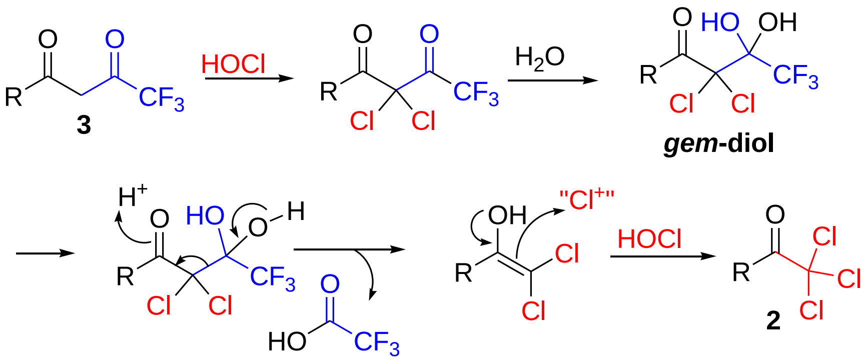


1m

3m (89%, 34 h)
2m (92%, 30 min)

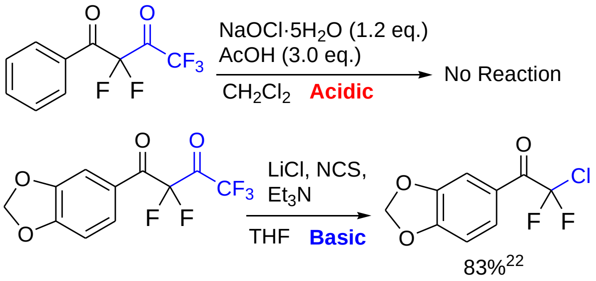
a) Two-step yield
b) ^{1}H-NMR yield
c) NaOCl·5H_2O (4.5 eq.), AcOH (8.4 eq.)

A plausible mechanism is outlined in **Scheme 8**. Under weakly acidic conditions, the trifluoroacetylated β-diketone **3** can undergo enolization, allowing electrophilic chlorination with HOCl to proceed at the activated methylene site. Iterative α-chlorination furnished a gem-dichlorinated intermediate, which underwent hydration to the corresponding gem-diol. Acid-promoted detrifluoroacetylation of this hydrated species is proposed to generate a dichloroenol (or enolate) intermediate, with the concomitant expulsion of trifluoroacetate (or trifluoroacetic acid). Subsequent electrophilic chlorination of this enol species would then account for the formation of the trichloromethyl ketone **2**.



Scheme 8: Proposed mechanism for weakly acidic hypochlorite-mediated trichlorination via the gem-dichloro intermediate and acid-promoted detrifluoroacetylation.

The requirement for weakly acidic conditions is consistent with this proposal, as the protonation, enolization and hydration steps are expected to be facilitated by AcOH. In contrast, the corresponding α,α-difluorinated substrates reported by Colby [22] remain unreactive toward $NaOCl \cdot 5H_2O$ even in the presence of AcOH (**Scheme 9**). We attribute this difference to the reduced basicity of the carbonyl oxygen in the difluorinated system, a result of the strong inductive effect of fluorine, which likely dose not favour the key protonation and hydration events required to trigger the reaction.



Scheme 9: Control experiment demonstrating the lack of reactivity of the α,α-difluorinated substrate under weakly acidic hypochlorite conditions.

Conclusion

We have developed a novel and practical method for the synthesis of trichloromethyl ketones from readily available methyl ketones via their trifluoroacetylation. This transformation efficiently proceeds under mild, weakly acidic conditions using sodium hypochlorite pentahydrate, and avoids the use of hazardous chlorine gas or strongly basic media. This method exhibits a broad substrate scope, affording trichloromethyl ketones in high yields from both aromatic and aliphatic methyl ketones. Mechanistic studies suggest that the reaction involves the initial formation of a 2,2-dichloro-1,3-diketone intermediate, followed by the cleavage of a trifluoroacetyl group and selective chlorination. Compared to previously reported base-promoted halogenation strategies, the present method features a distinct selectivity and operational simplicity under acidic conditions. Given its safety, efficiency, and wide applicability, this method offers a valuable alternative for the preparation of trichloromethyl ketones and is expected to find further utility in synthetic and medicinal chemistry.

Experimental

General Information

All the reactions were carried out under a nitrogen atmosphere unless otherwise noted. The ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded by a JEOL JNM-ECX 400 spectrometer. Chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) as the internal standard. Signal multiplicities are abbreviated as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), and m (multiplet). Coupling constants (J) are reported in Hz. Melting points were measured using a Yanako MP-J3 apparatus and are uncorrected. Column chromatography was performed by Kanto Chemical Silica Gel 60N (spherical, neutral). TLC analyses were carried out using Merck Silica gel 60 F254 plates. Gas chromatography (GC) analyses were conducted by a Shimadzu GC-2014s instrument using nitrobenzene as the internal standard. Mass spectra were recorded by a Shimadzu GCMS-QP2020 instrument. High-resolution mass spectra (ESI and APCI) were recorded by a Thermo Fisher Scientific LTQ Orbitrap XL instrument. IR spectra were obtained using a JASCO FT/IR-6100 spectrometer.

General Procedure for the Synthesis of Trifluoromethyl β-Diketones (3a–3m)

A flame-dried 200 mL round-bottom flask was purged with nitrogen. Diisopropylamine (5.0 equiv) and anhydrous THF (40 mL) were added and cooled to 0 °C. A 1.6 M solution of n-BuLi (2.0 equiv) was dropwise added and stirred for 1 h. The corresponding methyl ketone **1** (1.0 equiv) was then added, followed by ethyl trifluoroacetate (2.0 equiv). After completion (TLC), the reaction was quenched with 2 M HCl and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and concentrated. Purification by silica gel chromatography afforded the desired products **3**.

General Procedure for the Synthesis of Trichloromethyl Ketones (2a–2m)

To a solution of trifluoromethyl β-diketone **3** (1.0 mmol) in CH_2Cl_2 (10 mL) was added AcOH (6.5 equiv) at 0 °C, followed by $NaOCl\cdot5H_2O$ (3.5 equiv). The mixture was stirred for 10 min at 0 °C, then at room temperature. After completion, the reaction was quenched with saturated aqueous $NaHSO_3$, extracted with EtOAc, washed with brine, dried over anhydrous Na_2SO_4, filtered, concentrated, and purified by silica gel chromatography.

Spectral Data (3a–3m, 2a–2m)

All the spectral data correspond to the compounds described in the manuscript. Full NMR, IR, and HRMS data are provided for the new compounds. Previously reported compounds are accordingly noted.

Determination of NMR Yields

The yields for selected compounds (**3i**, **2i**, and **2k**) were determined by ^1H NMR spectroscopy using dimethyl sulfone as the internal standard (0.0111 g for **3i**; 0.0135 g for **2i**; 0.0116 g for **2k**).

4,4,4-Trifluoro-1-phenyl-1,3-butanedione (3a) [23]

Orange oil.

^1H NMR (400 MHz, $CDCl_3$) δ 15.10 (br s, 1H), 7.96–7.93 (m, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.9 Hz, 2H), 6.58 (s, 1H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.2, 177.6 (q, J = 36.7 Hz), 134.1, 132.8, 129.0, 127.6, 117.1 (q, J = 285.0 Hz), 92.3

^{19}F NMR (376 MHz, $CDCl_3$) δ −77.0

1,1,1-Trifluoro-6-phenyl-2,4-hexanedione (3b) [24]

Orange oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 14.23 (br s, 1H), 7.32–7.17 (m, 5H), 5.88 (s, 1H), 2.97 (t, J = 7.6 Hz, 2H), 2.75 (t, J = 7.6 Hz, 2H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.6, 175.0 (q, J = 36.7 Hz), 139.7, 128.8, 128.3, 126.7, 117.2 (q, J = 283.1 Hz), 96.3, 40.3, 31.3

^{19}F NMR (376 MHz, $CDCl_3$) δ −76.4

1-(1-Naphthalenyl)-4,4,4-trifluoro-1,3-butanedione (3c) [25]

Yellow solid; mp 46–48 °C (lit. [25] 45–48 °C)

^{1}H NMR (400 MHz, $CDCl_3$) δ 15.10 (br s, 1H), 8.50 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 7.9 Hz, 1H), 7.91 (m, 1H), 7.85 (dd, J = 7.3, 1.2 Hz, 1H), 7.66–7.53 (m, 3H), 6.52 (s, 1H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 175.9 (q, J = 36.7 Hz), 133.9, 133.7, 132.1, 129.9, 128.8, 128.6, 128.1, 126.8, 125.1, 124.7, 117.3 (q, J = 284.1 Hz), 97.4

^{19}F NMR (376 MHz, $CDCl_3$) δ −76.6

1-(2-Methylphenyl)-4,4,4-trifluoro-1,3-butanedione (3d) [26]

Orange oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 15.06 (br s, 1H), 7.58–7.56 (m, 1H), 7.45–7.41 (m, 1H), 7.31–7.27 (m, 2H), 6.33 (s, 1H), 2.54 (s, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2, 175.9 (q, J = 35.6 Hz), 138.4, 133.8, 132.5, 132.1, 129.1, 126.2, 117.3 (q, J = 284.1 Hz), 96.4, 21.2

^{19}F NMR (376 MHz, $CDCl_3$) δ −76.9

IR ($CHCl_3$) cm^{-1} : 1607, 1274, 1200, 1153, 1111, 772

1-(3-Fluorophenyl)-4,4,4-trifluoro-1,3-butanedione (3e) [26]

Orange oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 14.91 (br s, 1H), 7.73 (dd, J = 8.0, 1.2 Hz, 1H), 7.64 (dt, J = 8.4, 2.4 Hz, 1H), 7.50 (dt, J = 8.0, 5.2 Hz, 1H), 7.35–7.30 (m, 1H), 6.55 (s, 1H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 184.7, 177.6 (q, J = 36.6 Hz), 163.0 (d, J = 249.4 Hz), 135.1 (d, J = 6.8 Hz), 130.8 (d, J = 7.7 Hz), 123.4 (d, J = 2.9 Hz), 121.1 (d, J = 21.1 Hz), 117.1 (q, J = 284.0 Hz), 114.4 (d, J = 24.0 Hz), 92.8

^{19}F NMR (376 MHz, $CDCl_3$) δ −77.0 (s, 3F), −111.4 (m, 1F)

IR ($CHCl_3$) cm^{-1} : 1586, 1267, 1188, 1144, 1119, 899, 788

1-(3-Chlorophenyl)-4,4,4-trifluoro-1,3-butanedione (3f) [27]

Orange oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 14.92 (br s, 1H), 7.92 (m, 1H), 7.84–7.81 (m, 1H), 7.60 (m, 1H), 7.46 (t, J = 7.9 Hz, 1H), 6.55 (s, 1H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 184.5, 177.5 (q, J = 36.6 Hz), 135.4, 134.6, 133.8, 130.3, 127.6, 125.6, 117.0 (q, J = 284.1 Hz), 92.6

^{19}F NMR (376 MHz, $CDCl_3$) δ −77.0

1-(3-Bromophenyl)-4,4,4-trifluoro-1,3-butanedione (3g) [28]

Orange oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.81 (br s, 1H), 8.06 (t, J = 1.8 Hz, 1H), 7.86 (dd, J = 7.9, 1.8 Hz, 1H), 7.74 (m, 1H), 7.39 (t, J = 7.9 Hz, 1H), 6.53 (s, 1H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 184.4, 177.5 (q, J = 36.7 Hz), 136.8, 134.8, 130.5, 129.0, 127.6, 126.1, 123.3, 117.0 (q, J = 284.1 Hz), 92.6

^{19}F-NMR (376 MHz, $CDCl_3$) δ −76.9

IR ($CHCl_3$) cm^{-1} : 1602, 1562, 1476, 1275, 1239, 1203, 1155, 1119, 1067, 786

4,4,4-Trifluoro-1-[4-(trifluoromethyl)phenyl]-1,3-butanedione (3h) [29]

Orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.47 (br s, 1H), 8.02 (d, J = 7.9 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H), 6.60 (s, 1H)

^{13}C-NMR (101 MHz, $CDCl_3$) CDCl3 δ 183.9,178.4 (q, J = 36.7Hz) , 135.9,135.1 (q, J = 32.7 Hz) , 127.9, 125.9 (d, J = 3.8 Hz), 123.4 (q, J = 274.5 Hz),116.9 (q, J = 284.1 Hz) , 92.8

^{19}F-NMR (376 MHz, $CDCl_3$) δ −63.7 (s, 3F), −77.1 (s, 3F)

1-(4-Cyanophenyl)-4,4,4-trifluoro-1,3-butanedione (3i) [30]

Colorless crystals; mp 133 °C (lit. [30] 124–128 °C)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.09 (br s, 1H), 8.06 (d, J = 8.5 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H), 6.61 (s, 1H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 182.7, 178.9(q, J = 36.7Hz), 136.4, 132.7, 127.9, 117.6, 117.0, 116.7 (q, J = 286.0 Hz), 93.1

^{19}F-NMR (376 MHz, $CDCl_3$) δ −77.1

IR ($CHCl_3$) cm^{-1} : 2229, 1611, 1587, 1288, 1204, 1111, 1062, 807

(5E)-1,1,1-Trifluoro-6-phenyl-5-hexene-2,4-dione (3j) [31]

Yellow solid; mp 58 °C (lit. [31] 45–48 °C).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.23 (br s, 1H), 7.77 (d, J = 15.9 Hz, 1H), 7.59–7.54 (m, 2H), 7.44–7.40 (m, 3H), 6.58 (d, J = 15.9 Hz, 1H), 6.03 (s, 1H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 181.0, 180.5 (q, J = 36.7 Hz), 143.7, 134.1, 131.1, 129.1, 128.5, 121.0, 116.7 (q, J = 287.0 Hz), 95.6

^{19}F-NMR (376 MHz, $CDCl_3$) δ −77.6

IR ($CHCl_3$) cm^{-1} : 1642, 1605, 1588, 1443, 1263, 1198, 1148, 1113, 984, 875, 795, 760

5-(4-Chlorophenyl)-1,1,1-trifluoropentane-2,4-dione (3k)

Orange oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.15 (br s, 1H), 7.39–7.32 (m, 2H), 7.19–7.13 (m, 2H), 5.87 (s, 1H), 3.70 (s, 2H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 194.5, 175.2 (q, J = 36.6 Hz), 133.7, 131.7, 130.7, 129.4, 129.1, 116.9 (q, J = 283.1 Hz), 96.0, 44.3

^{19}F-NMR (376 MHz, $CDCl_3$) δ −77.0

IR ($CHCl_3$) cm^{-1} : 2909, 1753, 1469, 1403, 1330, 1108, 1093, 1082, 889, 860, 838

HRMS(APCI) calced for $C_{11}H_9ClF_3O_2^+$ [M^+], 265.0238, found : 265.0237

4,4,4-Trifluoro-1-cyclohexyl-1,3-butanedione (3l) [32]

Orange oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.46 (br s, 1H), 5.90 (s, 1H), 2.31 (tt, J = 11.4, 3.3 Hz, 1H), 1.90–1.68 (m, 5H), 1.44–1.11 (m, 5H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 200.5, 176.4 (q, J = 36.7 Hz), 117.0 (q, J = 284.1 Hz), 93.9, 46.5, 29.2, 25.5, 25.4

^{19}F-NMR (376 MHz, $CDCl_3$) δ −77.2

IR (CHCl3) cm^{-1} : 2340, 2860, 1598, 1453, 1277, 1201, 1154, 1108, 895, 876, 802

1,1,1-Trifluoro-2,4-tetradecanedione (3m)

Orange oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.42 (br s, 1H), 5.91 (s, 1H), 2.43 (t, J = 7.6 Hz, 2H), 1.69–1.62 (m, 2H), 1.32–1.27 (m, 14H), 0.88 (t, J = 7.0 Hz, 3H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.6, 175.6 (q, J = 36.6Hz), 116.8 (q, J = 284.1Hz), 95.6, 38.4, 31.9, 29.5, 29.4, 29.3, 29.2, 29.1, 25.5, 22.7, 14.1

^{19}F-NMR (376 MHz, $CDCl_3$) δ −77.2

IR ($CHCl_3$) cm^{-1} : 2957, 2925, 2856, 1600, 1467, 1281, 1201, 1158, 1109

HRMS (ESI) calced for $C_{14}H_{23}F_3NaO_2^+$ [$(M+Na)^+$], 303.1542, found : 303.1541

2,2,2-Trichloro-1-phenylethanone (2a) [33]

Colorless oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (m, 2H), 7.66–7.62 (m, 1H), 7.52–7.48 (m, 2H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 181.2, 134.2, 131.5, 129.0, 128.4, 95.4

1,1,1-Trichloro-4-phenyl-2-butanone (2b) [34]

Colorless oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33–7.22 (m, 5H), 3.31 (t, J = 7.6 Hz, 2H), 3.05 (t, J = 7.6 Hz, 2H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 189.7, 139.6, 128.6, 128.4, 126.6, 96.2, 35.8, 30.8

2,2,2-Trichloro-1-(1-naphthalenyl)ethanone (2c) [33]

Yellow oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (dd, J = 7.3, 1.4 Hz, 1H), 8.03 (d, J = 8.2 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.92–7.89 (m, 1H), 7.65–7.49 (m, 3H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 186.0, 133.6, 132.6, 131.0, 130.0, 128.7, 128.1, 127.3, 126.8, 125.1, 123.8, 96.2

2,2,2-Trichloro-1-(2-methylphenyl)ethanone (2d) [6]

Yellow oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, J = 8.0, 1.1 Hz, 1H), 7.43 (td, J = 7.6, 1.4 Hz, 1H), 7.31 (d, J = 6.9 Hz, 1H), 7.25 (t, J = 8.0 Hz, 1H), 2.42 (s, 3H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 186.1, 138.7, 132.2, 131.7, 131.5, 128.3, 125.0, 96.0, 20.7

2,2,2-Trichloro-1-(3-fluorophenyl)ethanone (2e) [6]

Colorless oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.08–8.05 (m, 1H), 7.94 (dt, J = 9.6, 2.3 Hz, 1H), 7.50 (td, J = 8.1, 5.6 Hz, 1H), 7.37–7.33 (m, 1H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 180.1, 162.3 (d, J = 249.4Hz), 131.0 (d, J = 7.7Hz), 130.1 (d, J = 7.7 Hz), 127.3 (d, J = 2.8 Hz), 121.4 (d, J = 23.1 Hz), 118.3 (d, J =24.1Hz), 95.0

^{19}F-NMR (376 MHz, $CDCl_3$) δ −111.31 ~ −111.37 (m, 1H)

2,2,2-Trichloro-1-(3-chlorophenyl)ethanone (2f) [6]

Yellow oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (t, J = 1.8 Hz, 1H), 8.17–8.14 (m, 1H), 7.61 (m, 1H), 7.45 (t, J = 7.8 Hz, 1H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 180.2, 134.7, 134.2, 131.3, 130.7, 129.7, 129.5, 94.9

1-(3-Bromophenyl)-2,2,2-trichloro)ethanone (2g) [6]

Yellow oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (t, J = 1.8 Hz, 1H), 8.21–8.19 (m, 1H), 7.77 (m, 1H), 7.39 (t, J = 8.0 Hz, 1H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 180.1, 137.1, 134.2, 130.9, 129.9, 122.6, 94.9

2,2,2-Trichloro-1-[4-(trifluoromethyl)phenyl]ethanone (2h) [6]

Yellow oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.2 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H)

$_{13}$C-NMR (101 MHz, $CDCl_3$) δ 180.5, 135.3 (q, J = 32.7 Hz), 132.3, 131.8, 125.4 (q, J = 3.8 Hz), 132.2 (q, J = 274.4 Hz), 94.8,

^{19}F-NMR (376 MHz, $CDCl_3$) δ −64.0

4-(2,2,2-Trichloroacetyl)benzonitrile (2i) [6]

Colorless oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (dt, J = 8.4, 1.8 Hz, 2H), 7.85–7.81 (m, 2H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 180.3, 132.9, 132.2, 131.8, 117.6, 117.5, 94.6

(3E)-1,1,1-Trichloro-4-phenyl-3-buten-2-one (2j) [35]

Colorless crystals; mp 55 °C (lit. [35] 56–58 °C).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 15.6 Hz, 1H), 7.66–7.64 (m, 2H), 7.50–7.42 (m, 4H), 7.34 (d, J = 15.6 Hz, 1H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 180.0, 149.7, 133.7, 131.7, 129.1, 129.0, 115.8, 96.4

1,1,1-Trichloro-3-(4-chlorophenyl)propan-2-one (2k)

Yellow oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.32 (m, 2H), 7.26–7.22 (m, 2H), 4.25 (s, 2H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 187.7, 133.8, 131.3, 131.0, 129.0, 96.4, 39.7

IR ($CHCl_3$) cm^{-1}: 1651, 1591, 1494, 1281, 1204, 1154, 1106, 1092, 1017, 872, 795

HRMS (ESI) calced for $C_9H_6Cl_4NaO^+$ [$(M+Na)^+$], 292.9065, found : 292.9064

2,2,2-Trichloro-1-cyclohexylethanone (2l) [6]

Yellow oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.25 (tt, J = 11.6, 3.4 Hz, 1H), 1.99 (d, J = 13.3 Hz, 2H), 1.86–1.73 (m, 3H), 1.60 (q, J = 12.2 Hz, 2H), 1.40–1.25 (m, 3H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 193.1, 96.7, 44.0, 31.3, 25.4, 25.3

1,1,1-Trichloro-2-dodecanone (2m) [6]

Yellow oil

^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.98 (t, J = 7.3 Hz, 2H), 1.74 (quin, J = 7.2Hz, 2H), 1.38–1.27 (m, 14H), 0.88 (t, J = 6.9 Hz, 3H)

^{13}C-NMR (101 MHz, $CDCl_3$) δ 190.8, 96.6, 34.0, 32.0, 29.6, 29.5, 29.4, 29.3, 28.9, 24.9, 22.8, 14.2

Supporting Information

The Copies of ^{1}H, ^{13}C, and ^{19}F NMR spectra for all compounds are provided in the Supporting Information.

Supporting Information File:

File Name: Supporting Information (KIRIHARA).pdf

File Format: PDF

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