



Title	Electrochemical C(sp ³)-H Functionalization Using Acetic Acid as a Hydrogen Atom Transfer Reagent
Author(s)	Morii, Yuma; Watanabe, Taito; Saga, Yutaka et al.
Citation	ChemElectroChem. 2024, 11, p. e202400061
Version Type	VoR
URL	https://hdl.handle.net/11094/97092
rights	This article is licensed under a Creative Commons Attribution 4.0 International License.
Note	

The University of Osaka Institutional Knowledge Archive : OUKA

<https://ir.library.osaka-u.ac.jp/>

The University of Osaka

Electrochemical C(sp³)–H Functionalization Using Acetic Acid as a Hydrogen Atom Transfer Reagent

Yuma Morii,^[a] Taito Watanabe,^[a] Yutaka Saga,^{*[a, b]} Tetsuya Kambe,^[a, b] Mio Kondo,^[a, c, d] and Shigeyuki Masaoka^{*[a, b]}

In this study, we developed a novel electrochemical protocol that enables the functionalization of inherently inert C(sp³)–H bonds. In this protocol, one-electron oxidation of acetic acid was used to successfully generate methyl radical, which cleaves the benzylic C(sp³)–H bonds of the substrates via a hydrogen atom transfer (HAT) process, and further reaction with the formed species yields the targeted C(sp³)–H functionalized

products. To the best of our knowledge, this is the first example of the use of acetic acid in a HAT process. Notably the reaction has environment-friendly and fine atom economy nature: the reaction is driven by the electrochemical conditions in the absence of expensive or hazardous reagents, producing only gaseous small molecules, hydrogen, carbon dioxide, and methane, as side products.

Introduction

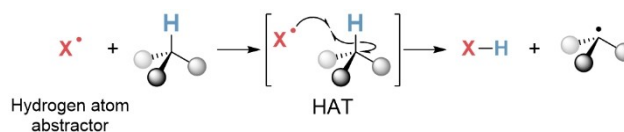
The development of a methodology for the functionalization of unreactive C(sp³)–H bonds, which are ubiquitous in many organic compounds, is an important research topic.^[1–4] Owing to their mild and selective nature, such transformations have a wide range of applications, e.g., in the synthesis of pharmaceuticals, natural products, and polymers.^[5–9] Traditional approaches to the functionalization of C(sp³)–H bonds require the pre-functionalization of substrates via costly chemical reactions.^[10] Therefore, many researchers have targeted the direct transformation of C(sp³)–H bonds without pre-functionalization to improve both step and atom economy.^[11,12]

Over the past few decades, transition metal catalysis has emerged as a powerful tool for direct C(sp³)–H

functionalization,^[13,14] with high efficiency and regioselectivity. However, this catalysis process faces several critical challenges, including (1) the use of expensive precious metals (Pd, Ru, or Ir), (2) the use of stoichiometric amounts of strong and hazardous oxidants or reductants, and (3) the requirement for high temperatures.^[13]

In recent years, the hydrogen atom transfer (HAT) process has gained significant attention as a promising strategy for the functionalization of C(sp³)–H bonds (Scheme 1).^[15–18] In contrast to traditional transition metal catalysis, HAT enables the activation of inherently inert C(sp³)–H bonds using photochemical or electrochemical energy as the driving force.^[19–22] Additionally, recent studies have revealed that HAT processes enable the construction of metal-free systems for C(sp³)–H functionalization.^[23–26] Therefore, this reaction can be performed successfully in the absence of (1) transition metals and (2) chemical oxidants or reductants, (3) under mild conditions.

The HAT process involves the abstraction of a hydrogen atom from a substrate using a hydrogen atom abstractor, which is typically a radical species.^[27] The choice of a hydrogen atom abstractor has a definitive influence on the efficiency and selectivity of the process.^[28–30] Thus, the development of a novel hydrogen atom abstractor could provide a dramatic expansion in synthetic organic chemistry. Methyl radical can function as a new class of hydrogen atom abstractor suitable for C(sp³)–H functionalization because of its exceptionally high bond dissociation energy (BDE = 105 kcal/mol)^[31] and unique nucleophilic nature.^[32] Despite attractive properties, the generation of methyl radical, an sp³-hybridized carbon-centered radical,^[33–35] is



Scheme 1. Schematic representation of the activation of a C(sp³)–H bond via HAT.

[a] Y. Morii, T. Watanabe, Dr. Y. Saga, Prof. Dr. T. Kambe, Prof. Dr. M. Kondo, Prof. Dr. S. Masaoka
Division of Applied Chemistry, Graduate School of Engineering
Osaka University
2-1 Yamadaoka, Suita, Osaka 565-0871, Japan
E-mail: ysaga@chem.eng.osaka-u.ac.jp
masaoka@chem.eng.osaka-u.ac.jp

[b] Dr. Y. Saga, Prof. Dr. T. Kambe, Prof. Dr. S. Masaoka
Innovative Catalysis Science Division
Institute for Open and Transdisciplinary Research Initiatives (ICS-OTRI),
Osaka University
2-1 Yamadaoka, Suita, Osaka 565-0871, Japan

[c] Prof. Dr. M. Kondo
Department of Chemistry, School of Science
Tokyo Institute of Technology
2-12-1 Ookayama, Meguro-ku, Tokyo 152-8551, Japan

[d] Prof. Dr. M. Kondo
PRESTO, Japan Science and Technology Agency (JST)
4-1-4 Honcho, Kawaguchi, Saitama 332-0012, Japan

Supporting information for this article is available on the WWW under <https://doi.org/10.1002/celec.202400061>

© 2024 The Authors. ChemElectroChem published by Wiley-VCH GmbH. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

quite challenging; therefore, there have been very few reports on the use of methyl radical for the functionalization of C(sp³)–H bonds. In 2002, the Tomioka group was the first to demonstrate the use of methyl radical as a hydrogen atom abstractor for C(sp³)–H functionalization.^[36] In their study, the α -hydrogen of ether was successfully abstracted by using methyl radical generated from (CH₃)₂Zn and atmospheric oxygen (Scheme 2a, top) to add ethers to imines. In 2021, Doyle's group achieved benzylic C(sp³)–H functionalization via a photochemical HAT-ORPC (oxidative radical-polar crossover) mechanism using methyl radical as the hydrogen atom abstractor (Scheme 2a, bottom).^[37] They employed *N*-acyloxyphthalimide as a precursor to produce methyl radical via one-electron oxidation by an iridium-based photocatalyst. Despite these outstanding achievements, there are several challenges in this field, including poor atom economy of the reaction and use of hazardous or expensive metal reagents for the generation of methyl radical. These facts indicate that although the use of methyl radical is expected to open a new avenue in the field of C(sp³)–H functionalization, a method for utilizing the radical in a sustainable fashion is still lacking. In other words, there is significant demand for developing a metal-free methodology for C(sp³)–H functionalization using methyl radical as a hydrogen atom abstractor with high atom economy.

In this study, electrochemical HAT-driven C(sp³)–H functionalization was achieved using acetic acid (AcOH) as a readily available and inexpensive HAT reagent for the methyl radical generation (Scheme 2b). The generation of methyl radical occurs under environment-friendly conditions upon simple

anode oxidation of AcOH, which does not require any hazardous or expensive reagents. Furthermore, the side products of the reaction were limited to small gaseous molecules, hydrogen (H₂), carbon dioxide (CO₂), and methane (CH₄), throughout the entire system, overcoming the poor atom economy encountered in previous studies. This is the first example of using methyl radical for HAT process in an electrochemical manner.

Results and Discussion

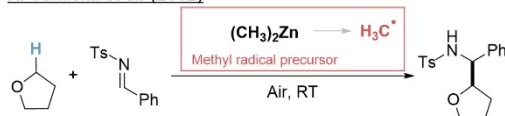
Investigation of HAT Reagents for Electrochemical C(sp³)–H Functionalization

In this study, to enable the functionalization of inherently inert C(sp³)–H bonds, we employed electrochemical approaches known for their advantages in organic transformations of inactive substrates.^[38–40] More specifically, if methyl radical is generated electrochemically from its precursor (a HAT reagent), active species for hydrogen atom abstraction generates without using reducing or oxidizing reagents. Therefore, we initially focused on anodic oxidation, i.e., the decarboxylation of an acetate anion to form methyl radical under electrochemical conditions. This process is known as the Kolbe electrolysis, which is the earliest reported synthetic electro-organic transformation that can produce alkyl radical species from carboxylic acids.^[41–44] We hypothesized that methyl radical formed by the Kolbe electrolysis undergoes a HAT process with a substrate to cleave the C(sp³)–H bond, whereby further reaction of the formed species yields a C(sp³)–H-functionalized product.

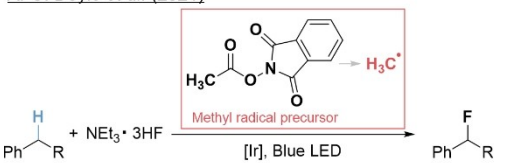
Based on the above-mentioned hypothesis, electrosynthesis was performed in the presence of an acetate source using diphenylmethane (**1**) as a model substrate and methanol (MeOH) as a model nucleophile^[45] in acetonitrile (MeCN) containing tetra-*n*-butylammonium perchlorate (TBAP) as the electrolyte. The reactions were conducted in an undivided cell using a reticulated vitreous carbon (RVC) anode and a glassy carbon plate (GC) cathode at a constant voltage of 4 V in an argon (Ar) atmosphere (see Experimental Section). The desired methoxylated product (**2**) was not obtained using an organic acetate source, tetra-*n*-butylammonium acetate (TBAA) (Table 1, entry 1). In contrast, the desired product (**2**) was obtained in 4% yield using sodium acetate (NaOAc) as the acetate source (entry 2). Subsequently, transition metal acetate sources were found to afford the desired methoxylated product (entries 3–7), and the highest yield (24%) was obtained using copper acetate (Cu(OAc)₂) (entry 7). More significantly, **2** was produced even when AcOH was used as the acetate source (13%, entry 8). Finally, the reaction was performed in the absence of acetate sources, forming a negligible amount of the desired product (entry 9), which indicates that an acetate source is essential in our system. Note that the direct oxidation of the substrate does not trigger the formation of the product because the reaction does not proceed in the absence of acetic acid. Based on these results, AcOH was used as an acetate source for subsequent studies because it is an inexpensive, abundant, and non-toxic

(a) Previous works using methyl radical as a hydrogen atom abstractor

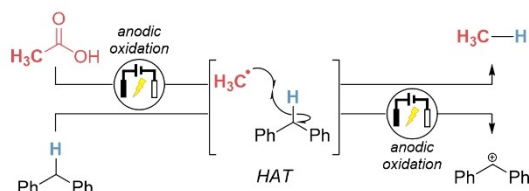
K. Tomioka *et al.* (2002)



A. G. Doyle *et al.* (2021)



(b) Electrochemical HAT with AcOH (**This work**)



- ✓ Atom-economical, readily available, and cheap HAT reagent
- ✓ Methyl radical generation in electrochemical strategy

Scheme 2. (a) Previous studies on HAT-driven C(sp³)–H functionalization using methyl radical as a hydrogen atom abstractor (b) Summary of this work.

Table 1. Initial investigation of benzylic C(sp³)-H functionalization.^[a]

Entry	Acetate source	Yields of 2 (%) ^[b]
1	tetra- <i>n</i> -butyl ammonium acetate (TBAA)	0
2	NaOAc	4
3	Mn(OAc) ₂	8
4	Fe(OAc) ₂	5
5	Co(OAc) ₂	6
6	Zn(OAc) ₂	3
7	Cu(OAc) ₂	24
8	AcOH	13
9	–	1

^[a] Reaction conditions: **1** (0.40 mmol), MeOH (1.2 mmol), acetate source (0.80 mmol) 0.1 M TBAP in MeCN (4.0 mL), RVC (anode), GC (cathode), 4 V, Ar atmosphere, room temperature. ^[b] Yields were determined by crude ¹H NMR analysis using 1,1,2,2-tetrachloroethane as the internal standard.

acetate source with the highest atom economy among the examined acetate sources.

Evaluation of AcOH as a HAT Reagent

To clarify the role of AcOH in our system, the following measurements were performed: First, linear sweep voltammetry (LSV) measurements of AcOH and **1** were conducted in MeCN with TBAP as the electrolyte (Figure 1, Figures S1–S4). The oxidation wave of AcOH was not observed in MeCN (Figure 1a, blue line), indicating that the oxidation of AcOH cannot proceed within the potential window of an MeCN solution with TBAP. Subsequently, the LSV measurement of AcOH was conducted in the presence of 1 equiv. of tetra-*n*-butylammonium hydroxide (TBAOH) as a base. As a result, the oxidation wave started from 0.9 V vs. Fc/Fc⁺ was observed (Figure 1a, red line). Considering the low pK_a of AcOH in MeCN,^[46] the peak observed in the presence of TBAOH can be attributed to the oxidation of the acetate anion (AcO⁻). We also conducted LSV measurements of **1**, thereby observing the oxidation wave of **1** at 1.6 V vs. Fc/Fc⁺ (Figure 1b, green line). Moreover, the LSV curve of a solution containing **1**, AcOH and TBAOH was quite similar to that in the absence of **1** in the potential region of 0.5–1.5 V, indicating that the oxidation potential of **1** does not shift even in the presence of AcO⁻ (Figure S3). Collectively, the difference in the oxidation potentials of AcOH and **1** (0.7 V) indicates that AcO⁻ is more easily oxidized than **1** during electrolysis. The low oxidation potential of acetate anion (AcO⁻) suggests that the target reaction can proceed under mild reaction conditions.

Second, the gaseous products produced during electrolysis were analyzed. Electrochemical synthesis was performed under the conditions of entry 8 in Table 1, and the gas phase of the

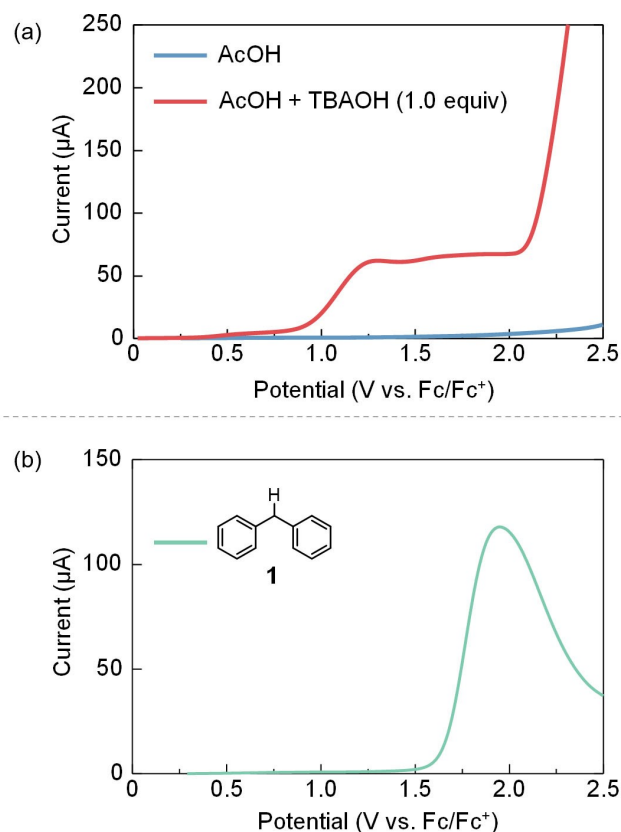


Figure 1. Linear sweep voltammetry curves of (a) AcOH with/without TBAOH (1 equiv) as base and (b) **1** in acetonitrile (MeCN) with TBAP (0.1 M) under Ar. [Working electrode: glassy carbon (GC), counter electrode: Pt wire, scan rate: 10 mV s⁻¹, c(AcOH) = c(**1**) = 10 mM].

reaction vessel was analyzed. As a result, the formation of several gaseous products, CH₄, CO₂, H₂ and C₂H₆, was detected by gas chromatography (for details, see Supporting Information (SI) (Figure S5–S6)). In the mass spectra of the gas phase, the peak at m/z = 16 was detected (Figure 2a), confirming the generation of CH₄. To acquire further insight into the formation process of CH₄, the reaction using the deuterium-labeled acetic acid (CD₃COOD) was performed. In this case, a peak at m/z = 19 (CHD₃), along with other peaks, was observed (Figure 2b), indicating that CD₃COOD transforms into CHD₃ via the formation of deuterated methyl radical ([•]CD₃) under electrochemical conditions. The detection of C₂H₆ by gas chromatography indicates that the coupling between two methyl radicals proceeds as a side reaction, which supports the formation of methyl radical during electrolysis. Next, analysis of the gas phases after the reaction using deuterium-labeled substrate **1-d** yielded the peak at m/z = 17 (CH₃D, Figure 2c). This result indicates that methyl radical cleaves the benzylic C(sp³)-H bond of **1-d**, converting to CH₃D. Collectively, it was demonstrated that AcOH electrochemically produces methyl radical (methyl radical formation process), and the resulting methyl radical promotes hydrogen atom abstraction from the benzylic C(sp³)-H bond of **1** (HAT process). In other words, AcOH can serve as a HAT reagent for C(sp³)-H functionalization under electrochemical conditions. This is the first reported example of

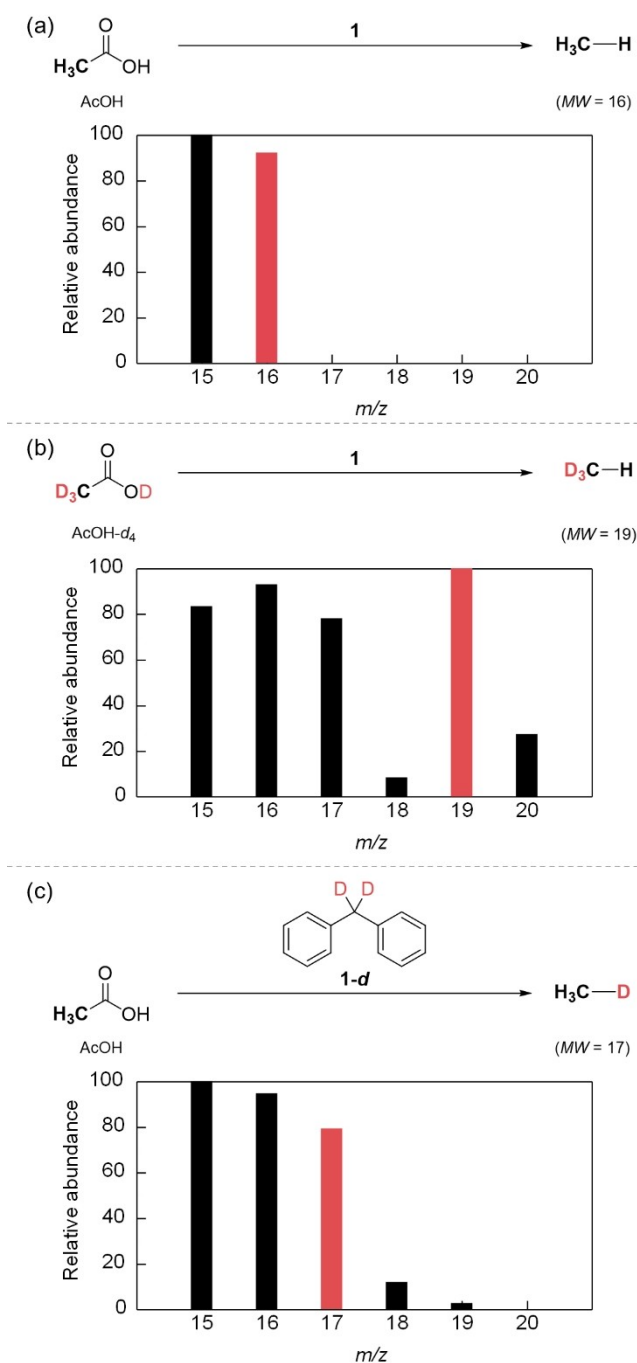


Figure 2. Results of deuterium isotope labeling experiments [Reaction conditions: 1/1-d (0.40 mmol), MeOH (1.2 mmol), AcOH/AcOH-d₄ (4.0 mmol), 0.1 M TBAP in MeCN (4.0 mL), RVC (anode), GC (cathode), 4 V, Ar atmosphere, room temperature, 1 h].

AcOH, a readily available and inexpensive reagent, facilitating the HAT process. Furthermore, it provides a powerful strategy for methyl radical formation, overcoming poor atom economy, which is a serious drawback of conventional systems.

Reaction Optimization

Encouraged by the aforementioned results, indicating that AcOH can work as a HAT reagent under electrochemical conditions, we optimized the reaction conditions for the benzylic C(sp³)-H functionalization of 1 (Table 2, Tables S1–S4). The use of 10 equiv. AcOH increased the yield of 2 to 27% (entry 1). Subsequent investigations revealed that TBAP was the optimal electrolyte for this reaction (entries 1–4). The use of tetra-*n*-butylammonium tetrafluoroborate (TBABF₄) slightly decreased the yield of 2 (entry 2). In addition, the redox-active electrolytes tetra-*n*-butylammonium iodide (TBAI) and tetra-*n*-butylammonium bromide (TBABr) were incompatible with our system (entries 3–4).

Next, the materials for the anode and cathode were investigated. Changing either the anode material to GC and platinum (Pt) or the cathode material to RVC, copper (Cu), or titanium (Ti) slightly decreased the yield of 2 (entries 5–9). Note that there is a possibility that reactions proceeding at a cathode change depending on cathode materials, and the cathodic reaction can affect the yield of the target compound. Notably, our electrochemical protocol did not require precious metals such as Pt electrodes, which are generally used in the Kolbe electrolysis (entry 6).^[47–49] Electrosynthesis conducted for two and three hours afforded 2 in 40% and 49% yields, respectively (entries 10 and 11). We also tried the reactions with increased amount of methanol (10 eq.) at various reaction time (for

Table 2. Screening of the reaction conditions.^[a]

Entry	Anode	Cathode	Electrolyte	Time (h)	Yields of 2 (%) ^[b]
1	RVC	GC	0.1 M TBAP	1	27
2	RVC	GC	0.1 M TBABF ₄	1	18
3	RVC	GC	0.1 M TBAI	1	0
4	RVC	GC	0.1 M TBABr	1	0
5	GC	GC	0.1 M TBAP	1	18
6	Pt	GC	0.1 M TBAP	1	25
7	RVC	RVC	0.1 M TBAP	1	16
8	RVC	Cu	0.1 M TBAP	1	26
9	RVC	Ti	0.1 M TBAP	1	25
10	RVC	GC	0.1 M TBAP	2	40
11	RVC	GC	0.1 M TBAP	3	49
12 ^[c]	RVC	GC	0.1 M TBAP	3	55 (56) ^[d]

^[a] Reaction conditions: 1 (0.40 mmol), MeOH (1.2 mmol), AcOH (4.0 mmol), an electrolyte in MeCN (4.0 mL), RVC (anode), GC (cathode), 4 V, Ar atmosphere, room temperature. ^[b] Yields were determined by crude ¹H NMR analysis. ^[c] 10 equiv. of MeOH. ^[d] Isolated yield is shown in the parenthesis.

details, see P.S14 of the SI), and found the optimal conditions. Under optimized conditions (i.e., in the presence of 10 equiv. of AcOH and 10 equiv. of MeOH in MeCN containing TBAP (0.1 M) at a constant voltage of 4 V in an undivided cell with an RVC anode and GC cathode in an Ar atmosphere at room temperature), the yield of **2** was 55%. We detected several other byproducts which are also derived from the HAT process, dimethoxylation product, acyloxylation product,^[50] and hydroxylation product (Scheme S3). The total conversion yield derived from the HAT process exceeds 70%, providing proof-of-concept results to demonstrate that acetic acid can function as a HAT reagent under electrochemical conditions.

Effect of Functional Groups

Next, we studied the effect of the functional groups on our reaction system under optimized conditions (Table 3). The reaction of diphenylmethanes bearing electron-donating groups, such as methyl (**3**), proceeded. In addition, our electrochemical system successfully produced methoxylated products

Table 3. Substrate scope. ^[a]	
	<p>Reaction conditions: 1 (0.40 mmol), MeOH (4.0 mmol), AcOH (4.0 mmol), 0.1 M TBAP in MeCN (4.0 mL), RVC (anode), GC (cathode), 4 V, Ar atmosphere, room temperature, 3 h. Isolate yields are shown.</p>
<p>2, 56%</p>	<p>3, 26%</p>
<p>4, 30%</p>	<p>5, 50%</p>
<p>6, 27%</p>	

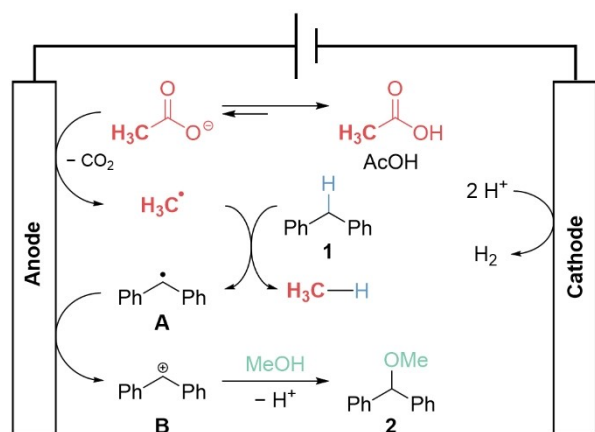


Figure 3. Proposed reaction mechanism.

with substrates bearing halogenated groups, including fluoro (**4**) and chloro (**5**) groups. The substrate with an extended aromatic moiety also afforded the desired product (**6**). In contrast, other substrates bearing benzylic C(sp³)–H bonds and alkane cannot undergo the target reaction under the conditions optimized for diphenylmethane (Table S7), indicating that further optimizations of reaction conditions are required for these substrates. Collectively, this reaction is applicable to several kinds of diphenylmethane derivatives, although the yields were affected by substituents in some cases.

Proposed Reaction Mechanism

Finally, based on the experimental results, a plausible reaction mechanism was proposed for our system, as shown in Figure 3. The reaction is initiated by the anodic one-electron oxidation of the acetate anion (AcO[−]), which exists as an equilibrium state of AcOH, as evidenced by LSV measurements. Subsequent decarboxylation generates methyl radical (•CH₃), as confirmed by the detection of CO₂ using gas chromatography (Figure S6). The radical quenching experiments using 2,2,6,6-tetramethyl-1-piperidinyloxy radical (TEMPO) as the radical trapping reagent (Scheme S5) indicate that the radical process is involved in the reaction. The thus-formed methyl radical then abstracts the hydrogen atom from the benzylic C(sp³)–H bond of **1** to generate radical **A**. For the formation of radical **A**, the mechanism in which the oxygen-centered radical functions as a hydrogen atom abstractor instead of methyl radical should be considered.^[51–53] Therefore, we performed the reaction using a catalytic amount (20 mol%) of acetic acid and found that the yield of the product (**2**) drastically decreased to 5% (see the SI (P. S13) for details). Moreover, the result that the reaction yield significantly decreased to 14% when using benzoic acid, which can produce an oxygen-centered radical, also indicated that methyl radical derived from acetic acid mainly functions as a hydrogen atom abstractor in our system. (Scheme S2). This hypothesis was also supported by the detection of methane using gas chromatography (Figure S6) and mass spectroscopy (Figure 2a), as well as the results of deuterium labeling experiments (Figures 2b and 2c). The KIE study using **1** and **1-d** as substrates (Table S8 and Figure S8) demonstrates that the cleavage of the benzylic C(sp³)–H bond is involved in the rate-determining step. The radical species **A** is further oxidized at the anode, affording cationic intermediate **B**. Finally, the nucleophilic addition of MeOH to **B** and deprotonation yield the desired product **2**. Meanwhile, the reduction of protons on the cathode produces hydrogen gas, as demonstrated by the results of the gas chromatography analysis (Figure S6).

Conclusions

In conclusion, we have developed a new method for the functionalization of benzylic C(sp³)–H bonds under mild conditions. The key to its success was employing AcOH as an atom-economical and inexpensive HAT reagent for the generation of

methyl radical via electrochemical one-electron oxidation, which can overcome the limitation of methyl radical generation in conventional systems with poor atom economy. The electrochemical reaction proceeded under environment-friendly conditions, without using additives other than the HAT reagent. Electrochemical analysis and deuterium labeling experiments supported the oxidative formation of methyl radical from AcOH and the activation of C(sp³)–H bonds by methyl radical. Collectively, this study demonstrates the use of acetic acid as an inexpensive and readily available HAT reagent for realizing C(sp³)–H functionalization, thus expanding the possibility of electrochemical methods available for organic synthesis.

Experimental section

General Procedure for Electrosynthesis

Prior to electrolysis, the reaction vessel, electrodes (RVC, 36 mm × 6 mm × 5 mm; GC, 50 mm × 8 mm × 2 mm), and stirrer were evacuated for 20 min. Then, diphenylmethane **1** (0.40 mmol, 66.9 μL), AcOH (4.0 mmol, 228.8 μL), and MeOH (4.0 mmol, 162.3 μL) were added to 4.0 mL of MeCN solution containing 0.1 M TBAP in the vessel containing the stirrer. Ar gas was bubbled at about 25 mL/min for 20 min. Subsequently, constant-voltage electrolysis (4 V) was performed for 3 h. After electrolysis, the reaction mixture was quenched with 5 mL of water, extracted by ethyl acetate (3 × 10 mL) and dried over Na₂SO₄, and filtered. After evaporation of the solvent, the yield was determined by ¹H NMR spectroscopic analysis. The crude mixture was purified using flash silica gel column chromatography to obtain the corresponding product **2** as a colorless oil (44.4 mg, 56%).

Supporting Information

The authors have cited additional references in Supporting Information.^[54–58]

Acknowledgements

This work was supported by the Japan Society for the Promotion of Science KAKENHI [Grant Nos. 22K19048, 22K21348 and 23H04903 (Green Catalysis Science) (S.M.); 20H02754, 22K19086, and 23H04628 (M.K.); 20K15955 and 22K06525 (Y.S.); 22H04507 and 23H02043 (T.K.); and 23KJ1511 (T.W.)], Japan Science and Technology Agency (JST) PRESTO [Grant No. JPMJPR20A4 (M.K.)], JST CREST [Grant No. JPMJCR20B6 (S.M.)], and JST FOREST [Grant No. JPMJFR223I (T.K.)]. Funding was also received from the Iwatani Naoji Foundation (M.K.), Mazda Foundation (M.K.), and Yazaki Memorial Foundation for Science and Technology (M.K.).

Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Hydrogen atom transfer · C(sp³)–H functionalization · Electrochemistry · Acetic acid · Kolbe electrolysis

- [1] Q. Lu, F. Glorius, *Angew. Chem. Int. Ed.* **2017**, *56*, 49–51.
- [2] G. Laudadio, Y. Deng, K. van der Wal, D. Ravelli, M. Nuño, M. Fagnoni, D. Guthrie, Y. Sun, T. Noël, *Science* **2020**, *369*, 92–96.
- [3] H.-H. Li, X. Chen, S. Kramer, *Chem. Sci.* **2023**, *14*, 13278–13289.
- [4] K. P. Bryliakov, *ACS Catal.* **2023**, *13*, 10770–10795.
- [5] J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960–9009.
- [6] P. B. Brady, V. Bhat, *Eur. J. Org. Chem.* **2017**, *35*, 5179–5190.
- [7] J. J. Topczewski, P. J. Cabrera, N. I. Saper, M. S. Sanford, *Nature* **2016**, *531*, 220–224.
- [8] E. E. Stache, V. Kottisch, B. P. Fors, *J. Am. Chem. Soc.* **2020**, *142*, 4581–4585.
- [9] I. Maksoo, R. C. Samanta, Y. Zhan, K. Zhang, S. Warratz, L. Ackermann, *Chem. Sci.* **2023**, *14*, 8109–8118.
- [10] H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417–424.
- [11] B. M. Trost, *Science* **1991**, *254*, 1471–1477.
- [12] P. A. Wender, V. A. Verma, T. J. Paxton, T. H. Pillow, *Acc. Chem. Res.* **2008**, *41*, 40–49.
- [13] J. Das, S. Guin, D. Maiti, *Chem. Sci.* **2020**, *11*, 10887–10909.
- [14] B. Liu, A. M. Romine, C. Z. Rubel, K. M. Engle, B.-F. Shi, *Chem. Rev.* **2021**, *121*, 14957–15074.
- [15] J. C. K. Chu, T. Rovis, *Angew. Chem. Int. Ed.* **2018**, *57*, 62–101.
- [16] L. M. Stateman, K. M. Nakafuku, D. A. Nagib, *Synthesis* **2018**, *50*, 1569–1586.
- [17] L. Capaldo, L. L. Quadri, D. Ravelli, *Green Chem.* **2020**, *22*, 3376–3396.
- [18] D. L. Golden, S.-E. Suh, S. S. Stahl, *Nat. Chem. Rev.* **2022**, *6*, 405–427.
- [19] L. Capaldo, D. Ravelli, M. Fagnoni, *Chem. Rev.* **2022**, *122*, 1875–1924.
- [20] S. Zhang, M. Findlater, *ACS Catal.* **2023**, *13*, 8731–8751.
- [21] Y. Li, M. Lei, L. Gong, *Nat. Catal.* **2019**, *2*, 1016–1026.
- [22] N. Li, J. Li, M. Qin, J. Li, J. Han, C. Zhu, W. Li, J. Xie, *Nat. Commun.* **2022**, *13*, 4224.
- [23] Q.-Y. Meng, T. E. Schirmer, A. L. Berger, K. Donabauer, B. König, *J. Am. Chem. Soc.* **2019**, *141*, 11393–11397.
- [24] C. Shu, A. Noble, V. Aggarwal, *Nature* **2020**, *586*, 714–719.
- [25] J. Grover, G. Prakash, C. Teja, G. K. Lahiri, D. Maiti, *Green Chem.* **2023**, *25*, 3431–3436.
- [26] J. Sim, B. Ryou, M. Choi, C. Lee, C.-M. Park, *Org. Lett.* **2022**, *24*, 4264–4269.
- [27] F. S. Meger, J. A. Murphy, *Molecules* **2023**, *28*, 6127.
- [28] J. P. Roth, J. C. Yoder, T.-J. Won, J. M. Mayer, *Science* **2001**, *294*, 2524–2526.
- [29] M. Galeotti, M. Salamone, M. Bietti, *Chem. Soc. Rev.* **2022**, *51*, 2171–2223.
- [30] Y. Liang, X. Zhan, F. Li, H. Bi, W. Fan, S. Zhang, M.-B. Li, *Chem Catal.* **2023**, *3*, 100582.
- [31] X.-S. Xue, P. Ji, B. Zhou, J.-P. Cheng, *Chem. Rev.* **2017**, *117*, 8622–8648.
- [32] L. Chang, S. Wang, Q. An, L. Liu, H. Wang, Y. Li, K. Feng, Z. Zuo, *Chem. Sci.* **2023**, *14*, 6841–6859.
- [33] S. Sarkar, K. P. S. Cheung, V. Gevorgyan, *Chem. Sci.* **2020**, *11*, 12974–12993.
- [34] C.-Y. Huang, J. Li, C.-J. Li, *Chem. Sci.* **2022**, *13*, 5465–5504.
- [35] S. Yang, H. Hu, J.-H. Li, M. Chen, *ACS Catal.* **2023**, *13*, 15652–15662.
- [36] K.-I. Yamada, H. Fujihara, Y. Yamamoto, Y. Miwa, T. Taga, K. Tomioka, *Org. Lett.* **2002**, *4*, 3509–3511.
- [37] I. N.-M. Leibler, M. A. Tekle-Smith, A. G. Doyle, *Nat. Commun.* **2021**, *12*, 6950.
- [38] A. Shatskiy, H. Lundberg, M. D. Kärkäs, *ChemElectroChem* **2019**, *6*, 4067–4092.
- [39] C. Kingston, M. D. Palkowitz, Y. Takahira, J. C. Vantourout, B. K. Peters, Y. Kawamata, P. S. Baran, *Acc. Chem. Res.* **2020**, *53*, 72–83.
- [40] L. F. T. Novaes, J. Liu, Y. Shen, L. Lu, J. M. Meinhardt, S. Lin, *Chem. Soc. Rev.* **2021**, *50*, 7941–8002.

- [41] H. von Kolbe, *Annalen der chemie und pharmacie*, DOI 10.1002/jlac.18490690302.
- [42] M. Yan, Y. Kawamata, P. S. Baran, *Chem. Rev.* **2017**, *117*, 13230–13319.
- [43] M. C. Leech, K. Lam, *Acc. Chem. Res.* **2020**, *53*, 121–134.
- [44] Y. Hioki, M. Costantini, J. Griffin, K. C. Harper, M. P. Merini, B. Nissl, Y. Kawamata, P. S. Baran, *Science* **2023**, *380*, 81–87.
- [45] P. Xiong, H.-B. Zhao, X.-T. Fan, L.-H. Jie, H. Long, P. Xu, Z.-J. Liu, J. Cheng, H.-C. Xu, *Nat. Commun.* **2020**, *11*, 2706.
- [46] K. Sarmini, E. Kenndler, *J. Biochem. Biophys. Methods* **1999**, *38*, 123–137.
- [47] J. Meyers, N. Kurig, C. Gohlke, M. Valeske, S. Panitz, F. J. Holzhäuser, R. Palkovits, *ChemElectroChem* **2020**, *7*, 4873–4878.
- [48] L. Iang, Y. Li, J. C.-H. Lam, Y. Ding, X. Yin, C. Wu, *Sustain. Energy Fuels* **2022**, *6*, 2797–2804.
- [49] N. Teetz, D. Holtmann, F. Harnisch, M. Stöckl, *Angew. Chem. Int. Ed.* **2022**, *61*, e202210596.
- [50] A. P. Atkins, A. C. Rowett, D. M. Heard, J. A. Tate, A. J. J. Lennox, *Org. Lett.* **2022**, *24*, 5105–5108.
- [51] S. Mukherjee, B. Maji, A. Tlahuext-Aca, F. Glorius, *J. Am. Chem. Soc.* **2016**, *138*, 16200–16203.
- [52] S. Mukherjee, R. A. Garza-Sanchez, A. Tlahuext-Aca, F. Glorius, *Angew. Chem. Int. Ed.* **2017**, *56*, 14723–14726.
- [53] S. Mukherjee, T. Patra, F. Glorius, *ACS Catal.* **2018**, *8*, 5842–5846.
- [54] T. Kurita, K. Hattori, S. Seki, T. Mizumoto, F. Aoki, Y. Yamada, K. Ikawa, T. Maegawa, Y. Monguchi, H. Sajiki, *Chem. Eur. J.* **2008**, *14*, 664–673.
- [55] Y. Hu, L. Liang, W.-T. Wei, X. Sun, X.-J. Zhang, M. Yan, *Tetrahedron* **2015**, *71*, 1425–1430.
- [56] K. M. Arendt, A. G. Doyle, *Angew. Chem. Int. Ed.* **2015**, *54*, 9876–9880.
- [57] D. E. Laycock, H. Alper, *J. Org. Chem.* **1981**, *46*, 289–293.
- [58] Y. Masui, T. Hattori, M. Onaka, *J. Am. Chem. Soc.* **2017**, *139*, 8612–8620.

Manuscript received: January 22, 2024

Revised manuscript received: March 2, 2024

Version of record online: April 15, 2024