Trichloromethyl Carbanion in Aqueous Micelles: Mechanistic Insights and Access to Carboxylic Acids from (Hetero)aryl Halides

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ABSTRACT: While suppressing the decomposition of trichloromethyl carbanions (generated from $CHCl_3$ using LiOH base) to carbon monoxide and their participation in transmetallation and reductive elimination steps of cross-coupling's catalytic cycle, a micelle-enabled catalytic carboxylation of (hetero)aryl halides is developed. The aqueous micelles play a crucial role in stabilizing both the highly reactive trichloromethyl carbanion and the single metal atom catalyst to facilitate the desired reaction pathway efficiently. Comprehensive mechanistic analyses including kinetic studies in presence of trichloromethyl carbanion or carbon monoxide, H/D exchange via trichloromethyl anion, and mass spectrometric analysis of reaction intermediates, support a carbanion pathway. Simultaneously, the scope of this method was demonstrated over 40 substrates signifying broad functional and protecting group tolerance. This methodology was applied to the synthesis of isotopically enriched carboxylic acids using simple $^{18}OH_2$ and/or $^{13}CHCl_3$ labeled precursors.

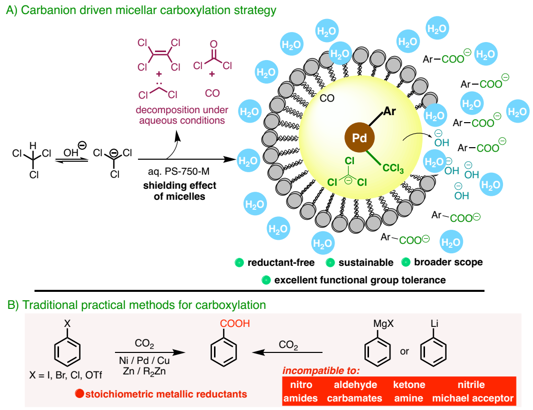
KEYWORDS. micellar catalysis, carbanion, cross-couplings, carboxylic acids, organometallic catalysis, chemistry in water

Introduction. Using water as a reaction media presents a number of environmental benefits compared to traditional organic solvents.[1-4] Over the last ten years, great strides have been made using designer surfactants to generate aqueous micelles where a myriad of organic transformations efficiently occur.[5-7] But perhaps even more exciting chemistry includes the novel and sometimes complimentary reactivity offered inside of these self-assembled micelles. We have been particularly interested in exploiting the unique environment found within micelles to stabilize otherwise highly reactive species to harness their use in transition metal catalysis.[8-10] Due to the possibility of stabilization of extremely sensitive intermediates under the protecting environment of micelles,[11-13] we studied trichloromethyl carbanion and its inhibition to carbon monoxide formation. Simultanously we employ trichloromethyl carbanion as C1 source for palladium-catalyzed carboxylations of aryl halides. Such an approach could provide an orthogonal method for carboxylation compatibly with the demands of late-stage functionalization of complex molecules.

In micellar catalysis, the catalysis happens either in the lipophilic micellar core or at the polar-nonpolar interface.[5] We expected that the presence of reaction sites away from water and the micelle's protective effect should enhance the trichloromethyl carbanion's stability. The resulting carbanion could transmetallate to a palladium(II)-aryl species, leading to a carboxylation product after hydrolysis of trichloromethyl(hetero)aryl species under basic conditions. Due to the higher solubility in water, the end product, a carboxylate salt of a (hetero)aryl carboxylic acid extrudes from the reaction site into water. These events facilitate that the reaction sites are available after the end of each catalytic cycle (Scheme 1A). After the reaction, the desired carboxylic acid can be isolated by adjusting the pH from basic or neutral to slightly acidic, avoiding the need for organic solvents throughout the process. Hence, a sustainable solution to carboxylation of (hetero)aryl compounds could help synthetic chemists meet the sustainability challenges.[14]

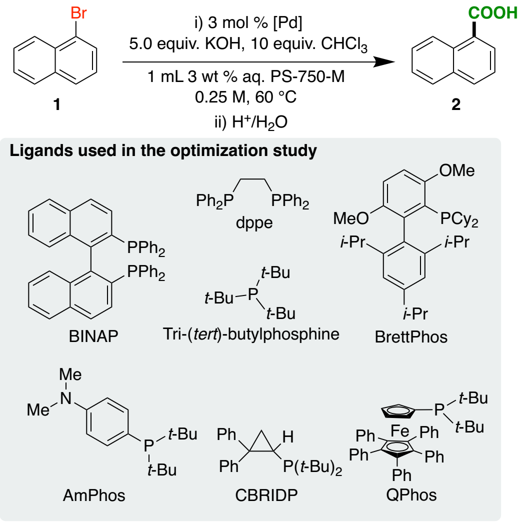
(Hetero)aryl carboxylic acid scaffolds have significance across biology and the chemical industry, including in pharmaceuticals.[15-19] The carboxylate functional group plays a crucial role in determining the hydrophilicity,[15,17] bioavailability,[15,18] and host-guest interactions of various drug molecules.[15,16] This unit also serves as a valuable handle for the diversification of bioactive compounds for the structure-activity relationship analysis. Traditional synthetic methods involve the oxidation of aldehydes and alcohols using strong oxidants or toxic reagents.[20-24] Recently, carboxylation employing readily available CO_2 or CO as the C1 source has emerged as a powerful technique.[25-29] Alternatively, strong organometallic reagents, such as Grignard or organolithiums, are required for the desired carboxylation.[30-32] Even though this strategy affords benzoic acid derivatives in high yields, its implementation in the late-stage diversification of densely functionalized molecules remains limited due to the unavoidable side reactions (Scheme 1B).

Scheme 1. Carboxylation chemistry. (A) Catalytic carboxylation in water via proposed carbanion route. (B) Traditional practical methods of carboxylation with limited scope



Results and Discussions. To address the abovementioned issues, we propose a novel catalytic cross-coupling strategy for installing a carboxylic acid group onto (hetero)aromatic rings through aqueous micellar carbanion chemistry while understanding the mechanism. We outlined the Pd-catalyzed cross-coupling of (hetero)aryl halide and trichloromethyl carbanion derived from chloroform. The resulting trichloromethyl (hetero)arene product obtained after reductive elimination is unstable and undergoes hydrolysis to afford the corresponding carboxylate ion under basic aqueous conditions. Notably, the lifetime of the trichloromethyl carbanion is exceptionally short due to its thermodynamically driven decomposition to dihalocarbene and other derivatives.[33] Therefore, suppression of these unwanted reaction pathways is critical for successfully executing the proposed reaction over a broad range of substrates with excellent functional group tolerance. The prolongation of the lifetime of trichloromethyl carbanion the protective environment of micelles and the presence of a catalyst system compatible with the desired catalytic cycle under an aqueous micellar medium are the critical factors in obtaining the desired outcome. This way, the decomposition of trichloromethyl carbanion to carbon monoxide is controlled to avoid the catalyst's deactivation, enabling a broad scope of potential coupling partners.

Table 1. Ligand screening[a]

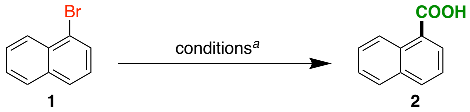


entry	[ligated Pd catalyst][a]	**2** (%)[b]
1	BINAP-Pd(crotyl)Cl	traces
2	(dppe)$PdCl_2$	traces
3	BrettPhosPd(allyl)OTf	traces
4	AmPhosPd(crotyl)Cl	traces
5	$(t\text{-}Bu_3P)_2Pd$	26
6	cBRIDP-Pd(crotyl)Cl	29[c]
7	QPhosPd(crotyl)Cl	61
8	*t*-BuXPhosPd(crotyl)Cl	traces

[a] **Conditions**: **1** (0.25 mmol), [Pd] (3 mol %), KOH (1.25 mmol), $CHCl_3$ (2.5 mmol), 1.0 mL 3 wt % aq. PS-750-M, 60 °C, 16 h; [b] isolated yield; [c] LiOH was used instead of KOH.

We began our study under aqueous micellar conditions by using 1-bromonapthalene **1** as a benchmark substrate, KOH as the base (5 equiv.), chloroform as the C1 source (10 equiv.), and typical bidentate ligands, such as BINAP or dppe, which gave only trace product (Table 1, entries 1 and 2). We next explored the much more electron-rich BrettPhos ligand, anticipating that it would facilitate reductive elimination of electron-deficient trichloromethyl and naphthyl groups, however, only traces of desired acid **2** were observed (entry 3). Rationalizing that perhaps a bidentate ligand was not required, we switched our search to a monodentate electron-rich ligand, i.e., AmPhos. Once again, only traces of **2** were obtained (entry 4). Although AmPhos is considered an electron-rich monodentate ligand, it can still potentially form dinuclear Pd species through the assistance of the NMe_2 group, which could adversely affect the reaction outcome. Therefore, we decided to explore other electron-rich, truly monodentate phosphine ligands. To our delight, tri-(*tert*)-butyl phosphine ($t\text{-}Bu_3P$) ligand afforded **2** in 26% isolated yield (entry 5). Although its Pd-complex is an L2 type, most likely, it changes into L1-Pd species in the catalytic cycle. Likewise, Pd ligated with cBRIDP provided a slightly better yield (29%, entry 6). Notably, the ferrocene-based electron-rich bulky ligand, QPhos, afforded **2** in 61% isolated yield and indicated that electron-rich monodentate phosphine ligands are critical for the optimal activity (entry 7).[34,35] *t*-BuXPhos, another bulky ligand, was ineffective for this transformation (entry 8).

Table 2. Optimization studies[a]

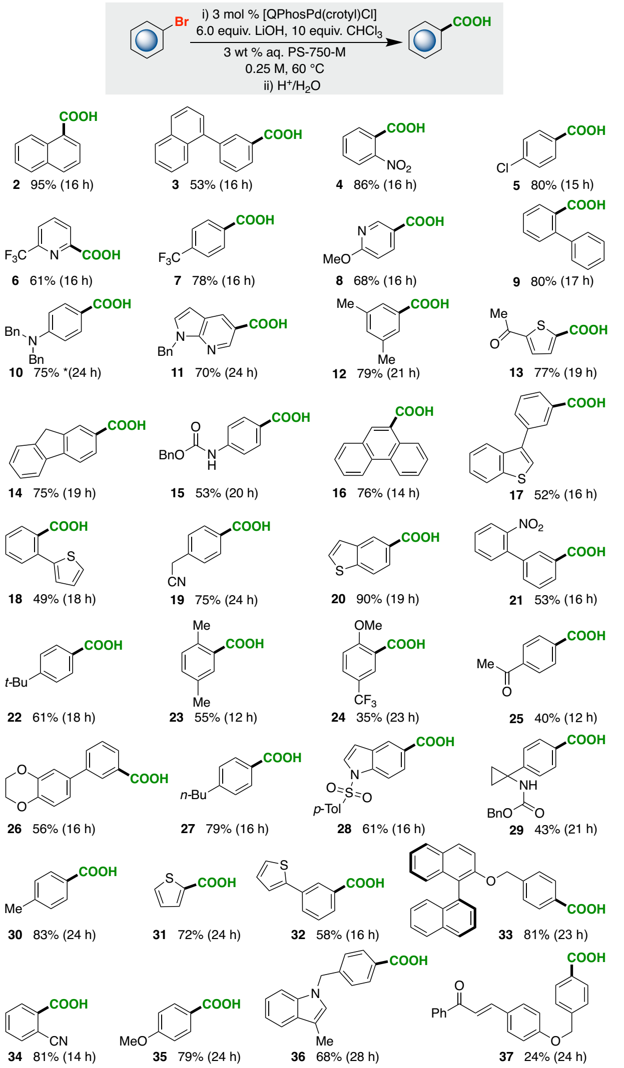


entry	[Pd] and deviation from general conditions	**2** (%)[b]
1	QPhosPd(crotyl)Cl	95
2	No ligand (Pd(crotyl)Cl)	n.d.
3	KOH[c] instead of LiOH	73
4	Et_3N[c] instead of LiOH	n.d.
5	2 equiv. LiOH instead of 6 equiv.	40
6	H_2O instead of PS-750-M	21
7	TPGS-750-M instead of PS-750-M	72
8	Tween 20 instead of PS-750-M	89
9	Pluronic instead of PS-750-M	n.d.
10	$CHCl_3$ instead of PS-750-M	traces
11	THF or DMF instead of PS-750-M	n.d.

[a] **Conditions**: (i) **1** (0.25 mmol), [Pd] (3 mol %), LiOH (1.5 mmol), $CHCl_3$ (2.5 mmol), 1.0 mL 3 wt % aq. PS-750-M, 60 °C, 16 h, (ii) H^+/H_2O; [b] isolated yield; [c] 5.0 equivalents instead of 6.0.

We further optimized the reaction conditions ultimately defining QPhosPd(crotyl)Cl as the catalyst. 6.0 equivalent lithium hydroxides as the base, 10 equivalent chloroform as the C1 source, 3 mol % QPhosPd(crotyl)Cl as the catalyst, 3 wt % aq. PS-750-M as the reaction medium and 0.25 global concentration as optimal, affording the desired product 1-naphthoic acid **2** in 95% isolated yield (Table 2, entry 1). The role of each reagent was validated through extensive optimization studies (see Supporting information, Tables S1-S7; pages S2-S5). In the absence of ligand, no desired product **2** was observed (entry 2).

Table 3. Substrate scope – carboxylation of aryl bromides[a]

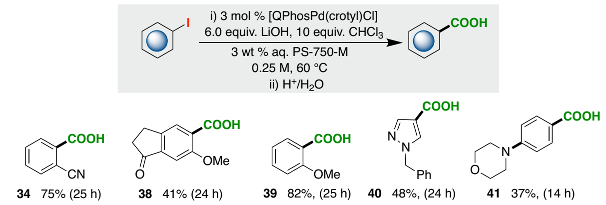


[a]**Conditions**: Aryl bromide (0.25 mmol, 1.0 equiv.), QPhosPd(crotyl)Cl (3 mol %), LiOH (1.5 mmol, 6.0 equiv.), CHCl$_3$ (2.5 mmol, 10 equiv.), 1.0 mL 3 wt % aq. PS-750-M, 60 °C. *In-process yield (isolated yield was 11%). All reported yields are isolated yields.

As we determined that the ligand QPhos played a crucial role in the catalytic activity compared to other monodentate electron-rich bulky ligands (cBRIDP and *t*-Bu$_3$P), we decided to explore further why QPhos is more effective than cBRIDP and *t*-Bu$_3$P. In our previous studies, we found that the cBRIDP-Pd species forms nanoaggregates under basic conditions or in the presence of charcoal.[36] The formation of nanoaggregates may be responsible for the inferior catalytic activity. However, as evidenced by HRTEM (high-resolution transmission electron microscopy) and EDAX (energy-dispersive X-ray spectroscopy) analysis of reaction mixture containing QPhosPd(crotyl)Cl in aq. PS-750-M, the catalyst remained in the molecular form and most likely acts as a single metal atom catalyst (for details, see Supporting information, pages S17, S18). When LiOH was replaced with KOH, 73% of **2** was obtained (entry 3), whereas the use of Et$_3$N base does not afford any desired product (entry 4). This indicates that a strong inorganic base is required to facilitate both the carbanion generation and the hydrolysis of the resulting trichloro(hetero)aryl intermediate. The optimal loading of LiOH was 6.0 equivalents. 2.0 equivalents of LiOH only afford 40% carboxylic acid **2** (entry 5). Using neat water as a reaction medium was ineffective, and only 21% of the desired carboxylic acid **2** was obtained (entry 6). This is most likely due to the instability of the carbanion intermediate in neat water, leading to its decomposition to CO. This implies that the micelle's effect is vital in enabling the desired reaction. The role of other state-of-the-art amphiphiles was also investigated. Replacing PS-750-M with TPGS-750-M only affords 72% of desired acid **2** (entry 7). Tween 20 was better than TPGS-750-M but not as effective as PS-750-M (entry 8). The aqueous micelles of Pluronic were ineffective for this catalytic pathway, and no desired product was observed when it was used as a reaction medium (entry 9). Likewise, in neat chloroform, only traces of product were observed (entry 10). THF or DMF solvents were also ineffective (entry 11), highlighting the novel reactivity offered in aqueous surfactant media.

The substrate scope was explored with these optimized conditions to assess the functional and protecting group tolerance. To our surprise, this procedure is remarkably general for a broad range of substrates with mostly moderate-to-excellent yields (Table 3, **2**-**37**). Compounds bearing nitro (**4**, **21**) or ketone (**13**, **25**) functionalities can easily be carboxylated under these conditions without undesired side reactions. Notably, the carboxylation of such compounds under traditional conditions is extremely difficult, as the reduction of nitro and ketone functional groups is hard to avoid with organometallic reagents (such as alkyllithiums and Grignard reagent). Aryl bromides bearing active methyl (**13**, **25**) or methylene (**14**, **19**) groups afford the corresponding acids without unwanted *α*-arylated byproducts. Substrates containing other important functional groups, such as nitriles (**19**, **34**), ethers (**8**, **24**, **26**, **33**, **35**, **37**), trifluoromethyl (**6**, **7**, **24**), *tert*-amine (**10**), and carbamate (**15**) exhibited good reactivity. Although the reaction based on the conversion as determined by in-process NMR analysis was good-to-excellent, the isolated yield of the substrate containing dibenzyl amine (**10**) was poor. This is likely due to the product isolation from water, as the desired product acts as a zwitterion at neutral pH and ammonium salt at acidic pH. However, the in-process yield of **10** was 75% (for details, see Supplementary Materials, pages S39-S40). A chloro group (**5**) remained intact under these conditions, which can act as a functional handle for further chemical transformations. Heteroaromatics, such as thiophenes (**13**, **18**, 31, **32**), benzothiophenes (**17**, **20**), indoles (**28**, **36**), pyridines (**6**, **8**), and 1*H*-pyrrolo[2,3-*b*]pyridine (**11**) were all compatible with this method. All these substrates provide the corresponding acids in moderate-to-excellent yields. Interestingly, the highly constrained cyclopropyl ring bearing benzyl carbamate exhibited moderate reactivity without ring-opening or Cbz cleavage (**29**). Other protecting groups, such as *N*-benzyl (**10**, **11**, **36**), *O*-benzyls (**33**, **37**), benzyl carbamates (**15**, **29**), and *N*-sulfonyl (**28**), were very well tolerated under these conditions. Notably, carboxylation of the substrate containing chalcone (**37**) can also be achieved, although a lesser yield was obtained in this case. The highly reactive chalcone double bond did not undergo any side reactions.[37,38] Although the reaction yield was low, the remaining unreacted starting material was recovered.

Table 4. Substrate scope – carboxylation of aryl iodides[a]



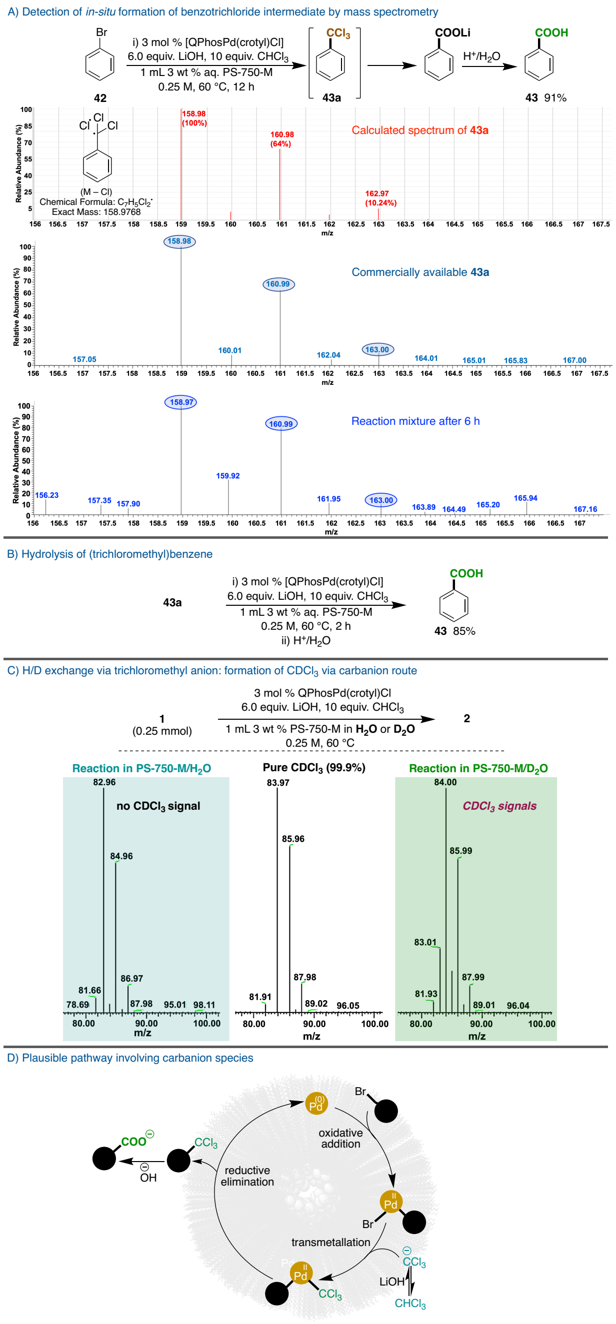
[a]**Conditions**: Aryl iodide (0.25 mmol, 1.0 equiv.), QPhosPd(crotyl)Cl (3 mol %), LiOH (1.5 mmol, 6.0 equiv.), $CHCl_3$ (2.5 mmol, 10 equiv.), 1.0 mL 3 wt % aq. PS-750-M, 60 °C. All reported yields are isolated yields.

Using the conditions optimized for carboxylation of aryl bromides, the substrate scope was extended to (hetero)aryl iodides (Table 4). Good-to-excellent reactivity was observed in these examples (**34**, **38**-**41**). A substrate bearing ketone and active methylene group (**38**) provides moderate yield, while good-to-excellent yields were observed in substrates containing nitrile (**34**) or ether (**39**) groups. Heterocycles, such as pyrazole (**40**) and morpholine (**41**) were tolerated under these aqueous reaction conditions. However, moderate yields were obtained, and the unreacted substrates were recovered.

In considering the mechanistic pathway for this transformation, we envisioned two discreet possibilities: (1) a carbanion pathway, where the trichloromethyl carbanion transmetallates, then reductively eliminates to form a trichloromethylarene intermediate, which is subsequently hydrolyzed to the corresponding carboxylate. (2) A hydroxycarbonylation pathway where the trichloromethyl carbanion is hydrolyzed first under basic conditions to form carbon monoxide, which then participates in catalysis in an analogous fashion to other previously reported hydroxycarbonylations using carbon monoxide (CO). Based on our initial screening results, where C1 sources that were more easily hydrolyzed to CO were completely ineffective for this transformation (for details see supporting information, Table S5, page S4), we expected the carbanion pathway to be more likely operative. Thus, we set out to perform additional mechanistic studies to further support this hypothesis.

To gain evidence that a (trichloromethyl)arene intermediate is present in the reaction pathway, we chose a control carboxylation reaction of bromobenzene (**42**), leading to the formation of (trichloromethyl)benzene (**43a**) intermediate that quickly hydrolyzes under aqueous basic conditions forming desired acid **43** (Scheme 2A). This substrate was chosen because **43a** is commercially available to be used as a marker in the control experiment. The reaction mixture from the standard reaction depicted in Scheme 2A was analyzed by mass spectrometry every 3-hour intervals to track the formation of transient **43a** (For details, see Supporting information, pages S19-S22). The mass spectrum of the marker of **43a** shows a signal at 158.98 amu that corresponds to M – Cl. The isotope pattern and mass ratios of the marker were in agreement with the calculated spectrum. Likewise, the reaction mixture at 3, 6, and 9 h also shows a M – Cl peak with the desired isotope pattern that supports the formation of **43a** via reductive elimination of phenyl and trichloromethyl anion (for details, also see Supporting information, pages S19-S21). This study confirms that hydrolysis of the trichloromethyl group occurs after the catalytic C-C bond forming event, and not before, effectively ruling out the hydroxycarbonylation mechanism as the dominant reaction pathway.

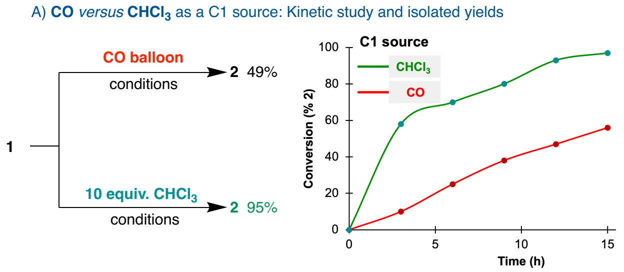
Scheme 2. Experimental evidence of carbanion intermediate



To confirm the facile hydrolysis of trichloromethyl arene during reaction conditions, a hydrolysis study of commercially available **43a** was performed under the reaction conditions (see Supplementary Materials, pages S21-S22). The hydrolysis reaction was fast under standard reaction conditions, and **43a** was hydrolyzed entirely in 2 hours to afford an 85% isolated yield of **43** (Scheme 2B). Notably, this hydrolysis even proceeds without a catalyst as well as on water, indicating the extreme instability of such species under aqueous basic conditions.

The formation of trichloromethyl anion under aqueous reaction conditions was further confirmed by performing the standard carboxylation reaction of **1** using $CHCl_3$ as a C1 source in aqueous PS-750-M in D_2O (Scheme 2C; also see Supplementary Materials, pages S23-S24). This reaction revealed the formation of $CDCl_3$ via carbanion-mediated H/D exchange; the formation of $CDCl_3$ was confirmed by mass spectrometry. The mass spectra of neat $CDCl_3$ and reaction mixture were consistent with each other revealing the H/D exchange. Therefore, all the control experiments support the formation and participation of carbanion species, corroborating the possible reaction pathway depicted in Scheme 2D.

Scheme 3. Hydroxycarbonylation *versus* trichloromethylation


A) **CO** *versus* **$CHCl_3$** as a C1 source: Kinetic study and isolated yields

conditions: i) 0.25 mmol **1**, 3 mol % [QPhosPd(crotyl)Cl], 6.0 equiv. LiOH, 2.5 mmol $CHCl_3$ or CO, 1 mL 3 wt % aq. PS-750-M, 0.25 M, 60 °C. ii) H^+/H_2O

B) C1 (carbanion) source and reaction outcome

$$\mathbf{1} \xrightarrow{\text{conditions}} \mathbf{2}$$

C1 source	2 (%)
$CHCl_3$	95%
$CHBr_3$	traces (<1%)
CHI_3	traces (<1%)
$CHBrCl_2$	traces (<1%)

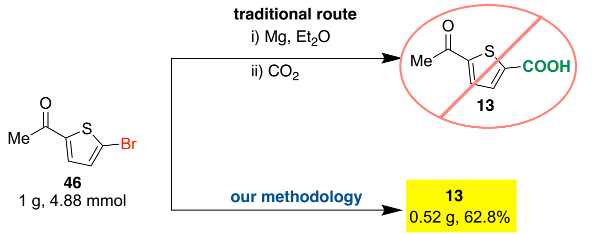
conditions: i) 3 mol % [QPhosPd(crotyl)Cl], 6.0 equiv. LiOH, **C1 source,** 1 mL 3 wt % aq. PS-750-M, 0.25 M, 60 °C. ii) H^+/H_2O

To determine whether the hydroxycarbonylation pathway is feasible under the aqueous reaction conditions, reaction kinetics were compared under CO (1 atm) as a sole C1 source versus $CHCl_3$ as a carbanion source (Scheme 3A; for details, see Supplementary Materials, pages S29–S39). Under CO atmosphere as the sole C1 source, only *ca.* 10% product was formed in 3 h, while using $CHCl_3$ as the C1 source, *ca.* 60% product was formed. In 15 h, only 56% conversion to **2** (49% isolated) was obtained under CO atmosphere, while using $CHCl_3$ as a C1 source, *ca.* 98% conversion (95% isolated) to the desired product was obtained, illustrating the enhanced kinetics/reactivity of the carbanion pathway under these conditions (Scheme 3A).

Compared to $CHCl_3$, other haloforms, such as $CHBr_3$, $CHBrCl_2$, and CHI_3, readily decompose to CO under aqueous basic conditions. If the hydroxycarbonylation is the dominant pathway, the reaction would be expected to proceed more efficiently with other haloforms compared to the one involving $CHCl_3$ as a C1 or carbanion source. Therefore, control experiments were performed using $CHCl_3$, $CHBr_3$, $CHBrCl_2$, and CHI_3 as C1 sources (Scheme 3B; see Supplementary Materials, pages S4, S34). Only $CHCl_3$ provided the desired product in 95% isolated yield, while the other three C1 sources ($CHBr_3$, $CHBrCl_2$, and CHI_3) were completely ineffective, and only traces of desired product were observed. The trace product formation under these conditions compared to the 49% product shown in Scheme 3A is due to the equivalents of CO available to the reaction. In the haloform study, only 10 equivalents of C1 source were used, while in reaction conducted under a CO atmosphere, a large excess of CO was used. This suggests that even if the hydroxycarbonylation route is possible under a CO atmosphere, the transformation is not competitive kinetically under these conditions due to the requirement for large excesses of CO. In summary, our mechanistic studies support that while both pathways may be in operation, the carbanion pathway is much more dominant.

Next, the scalability of this methodology was showcased on a gram-scale carboxylation of 2-acetyl-5-bromothiophene (**13**) under standard conditions (for details, see Supplementary Materials, page S9). The desired carboxylic acid **13** was obtained in moderate yield (62.8%). Notably, the formation of **13** is challenging under the traditional route involving Grignard or organolithium reagents, as compound **46** possesses both an active CH_3 and a sensitive carbonyl functional group (Scheme 4).

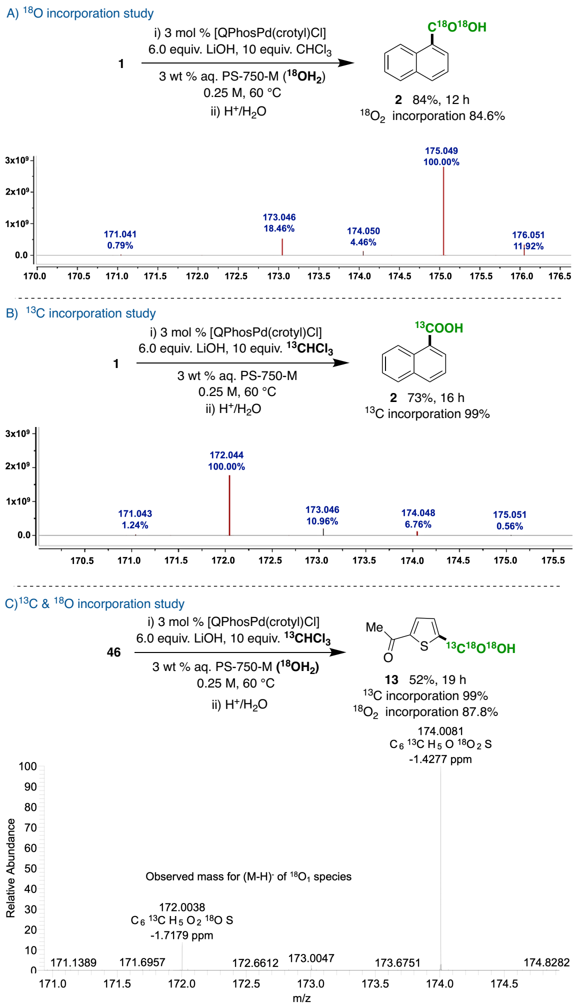
Scheme 4. Scalability test



conditions
i) 3.5 mol % [QPhosPd(crotyl)Cl], 6.0 equiv. LiOH, 11.5 equiv. $CHCl_3$
19.5 mL 3 wt % aq. PS-750-M, 0.25 M, 60 °C. ii) H^+/H_2O

From a synthetic applications perspective, this approach can be extended to the synthesis of various isotope-enriched carboxylic acids, providing an excellent opportunity to access isotopic labelling of multiple atoms in the –COOH group (Scheme 5). The ^{13}C and ^{18}O labeled carboxylic acids were synthesized respectively using readily available isotope sources; $^{13}CHCl_3$ as the C1 source, and $^{18}OH_2$ as the ^{18}O source. The proposed strategy was demonstrated by synthesizing ^{18}O enriched naphthoic acid **2** (Scheme 5A). The desired product was obtained in 84% isolated yields with the incorporation of 84.6% of two ^{18}O in acid **2**. Notably, isotopically enriched LiOH is not required. Likewise, ^{13}C enriched acid **2** was achieved in a 73% isolated yield with 99% incorporation of ^{13}C in the acid functionality (Scheme 5B). The strength of this methodology was further demonstrated by incorporating two isotopically labeled atoms (^{18}O and ^{13}C) into the carboxylic acid functionality. This was showcased in the synthesis of 5-acetyl thiophene-2-carboxylic acid **13** with isotopically enriched ^{18}O and ^{13}C in the acid group (Scheme 5C; for details, see Supplementary Materials, pages S10-S14). Such multi-atom labeling in acid functionality is challenging due to the limited availability of isotopically labeled C1 precursors. In this case, 52% of the desired acid was isolated with 99% ^{13}C and 87.8% of double ^{18}O incorporation.

Scheme 5. Isotope incorporation studies



Conclusions. In summary, we have developed the first micelle-enabled trichloromethyl carbanion-mediated carboxylation using (hetero)aryl halides and CHCl$_3$ as the C1 source. This pathway is most likely operative due to the effect of the micelle stabilizing the trichloromethyl carbanion and partitioning the resulting carboxylate precursor. The catalyst under our reaction conditions likely remains monometallic and does not form any aggregates. The generality of this approach is established over 40 substrates with broad functional and protecting group tolerance. This methodology provides a unique platform to access one or more (^{18}O or ^{13}C) isotope-labeled carboxylic acids, which is extremely challenging with the traditional approaches. Control experiments reveal the significance of amphiphile PS-750-M on the reaction outcome. From a mechanistic perspective, this reaction predominantly proceeds through a carbanion pathway. This route completely circumvents the use of harsh reductants or strong organometallic reagents for carboxylation; hence the functional and protecting group compatibility can be harnessed to strengthen the scope and compatibility for late-stage functionalization of complex molecules.

ASSOCIATED CONTENT

, spectroscopic data are included in this document

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Notes

Any additional relevant notes should be placed here.

SUPPORTING INFORMATION

The Supporting Information is available free of charge on the ACS Publications website. It contains experimental procedures, compound characterization, and analytical data.

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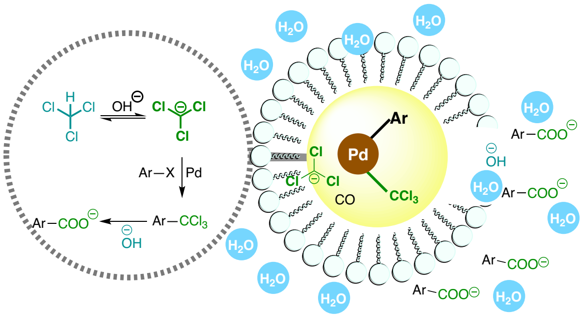

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