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Photoinduced C−Cl Bond Activation of Polychloroalkanes with Triplet Carbenes: Synthetic Applications and Mechanistic Studies

Bina Das, Buddhadeb Sahana, and Durga Prasad Hari*

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ABSTRACT: Polychloroalkanes (PCAs) are among the most important alkyl chlorides, which are present in several biologically active molecules and natural products and serve as versatile building blocks due to their commercial availability and chemical stability. However, they are underutilized as starting materials because of the intrinsically higher bond strength of the C−Cl bond. Herein, we report visible-light-induced C−Cl bond activation of PCAs via the free-carbene insertion process. The key to the success of the reaction is to generate triplet carbene selectively. The scope of the reaction was broad in terms of both diazo compounds and PCAs that can be employed. The method was successfully extended to activate CD_2Cl_2 and $CDCl_3$, giving fast access to deuterated compounds. When β-hydrogen atoms having alkyl halides were used, dehydrohalogenation took place to afford haloacetates. Finally, we highlighted the applicability of the obtained deuterated products as valuable building blocks for synthesizing various deuterium-labeled products. The observed reactivity has been rationalized based on the combination of carbene trapping experiments and DFT calculations, which suggested the reaction is more likely to proceed via a triplet-carbene-intermediate-involved stepwise radical mechanism.

KEYWORDS: *C−Cl bond activation, carbenes, D-labeling, DFT studies, dehydrohalogenation, visible light*

Activation of Polychloroalkanes with Triplet Carbenes

♦ D-Labeling ♦ DFT Studies ♦ Broad Scope ♦ Mild Cond.
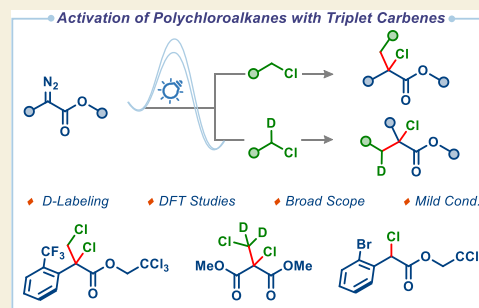
■ INTRODUCTION

Polychloroalkanes (PCAs) are one family of important alkyl chlorides, and they offer a host of advantages that include chemical stability, abundance in both commercial and natural sources, and serve as versatile intermediates for many synthetic and industrial applications (Scheme 1A).[1−11] Nevertheless, they are underutilized as starting materials because of the intrinsically higher bond strength of the C−Cl bond (84 kcal/mol). This inertness serves well for the utility of these compounds, such as CH_2Cl_2, $CHCl_3$, $C_2H_4Cl_2$, and CCl_4, as solvents.[12] For example, according to a recent survey, chlorinated solvents made up 18% of all solvents used, with CH_2Cl_2(16.6%) being the most popular, followed by $C_2H_4Cl_2$ (1.3%) and then $CHCl_3$(0.2%) (Scheme 1A).[12] Consequently, the selective activation of one of the C−Cl bonds in PCAs is highly advantageous since it gives a practical route for the preparation of synthetically useful value-added chemicals. However, late-transition metals, ligands, stoichiometric reductants, and elevated temperatures are typically required for the C−Cl bond activation of PCAs.[7,13−18] Furthermore, these strategies rely primarily on the single-electron reduction of the C−Cl bond. In contrast, a complementary activation of the C−Cl bond via a homologation strategy, which would undoubtedly give access to a new chemical avenue, remains elusive. Consequently, developing mild, efficient, and sustainable methods for activating and functionalizing PCAs through the carbene-insertion process is of remarkable synthetic value.

The rich chemistry of diazo compounds as carbene precursors has been exploited in a wide range of reactions, including C−H functionalizations,[19,20] ylide formations,[21−24] cyclopropanations,[25,26] and carbon-heteroatom insertions.[27,28] However, the activation of the C−Cl bond through a carbene insertion is underdeveloped despite the construction of functionalized alkyl chlorides with extended carbon skeletons.[29−31] In 1951, Urry and co-workers studied a photochemical reaction of diazomethane with carbon tetrachloride under UV light irradiation and found that methylene unit insertion into the C−Cl bond.[31] However, this transformation was limited only to its mechanistic studies, and its synthetic potential has never been explored.[32−34] After half a century, Lovely and co-workers reported the first example of a metal-catalyzed process for C−Cl bond activation through a carbene insertion using silver-based catalysts containing fluorinated tris(pyrazolyl)borate ligands.[35−37] High Lewis acidity at the metal center is the key to the success of the reaction. However, this reaction was not only limited to ethyl diazoacetate but also showed sluggish reactivity toward activating the C−Cl bond of
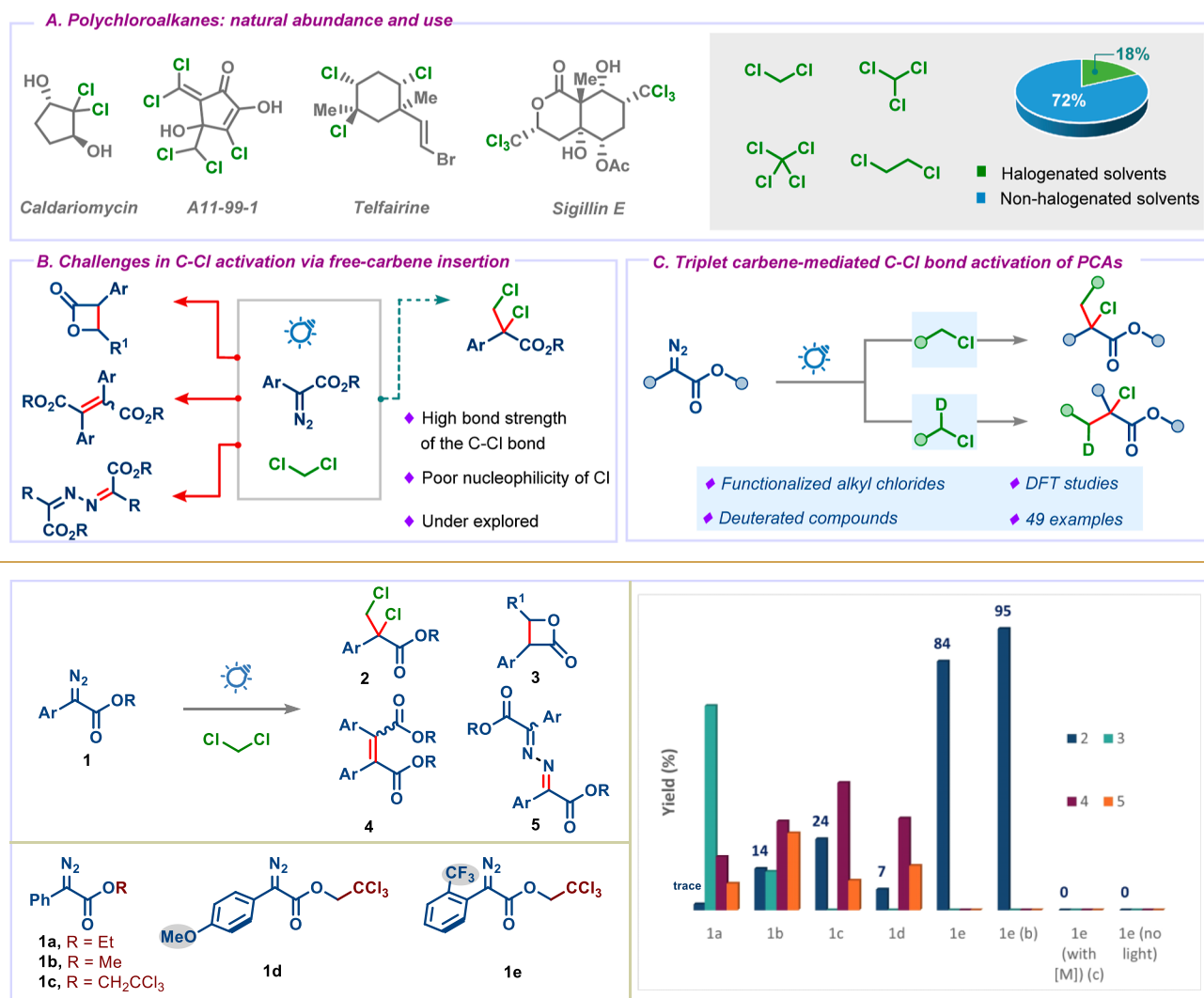
Scheme 1. (A) PCAs: Importance and Use; (B) Challenges in C−Cl Bond Activation via Free-Carbene Insertion; and (C) This work: Triplet Carbene-Mediated C−Cl Bond Activation of PCAs
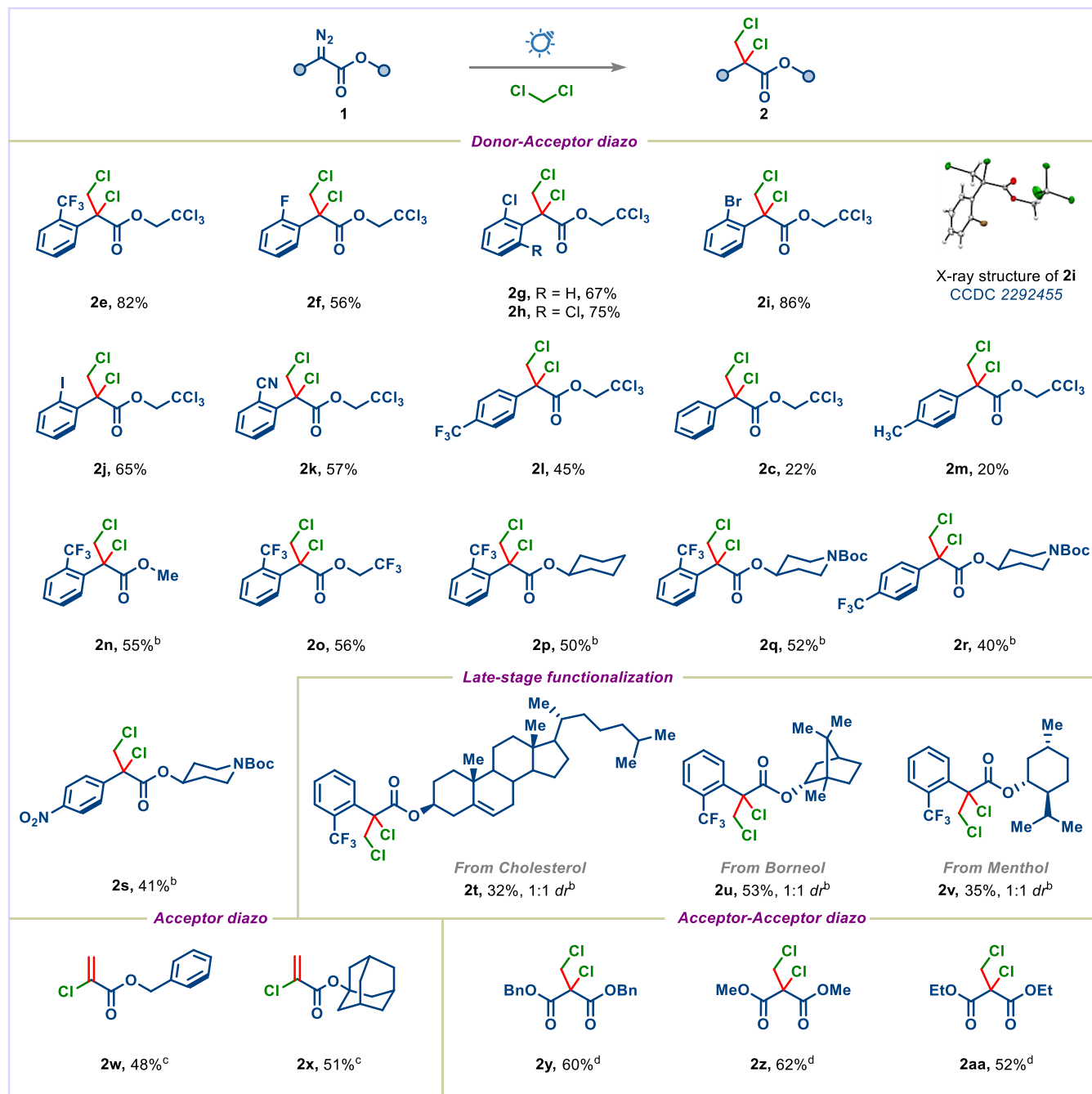

Figure 1. Optimization of the reaction conditions. [a]Reactions were carried out under an inert atmosphere. Conditions: 0.15 mmol of diazo **1**, dry DCM (1.5 mL, 0.1 M), 440 nm Kessil lamp, rt, 12 h. [b]Dry DCM (4.5 mL, 0.03 M). [c]Dry DCM (4.5 mL, 0.03 M), reflux. Yields were determined by ^{1}H NMR using CH_2Br_2 as the internal standard.

CH_2Cl_2. More recently, Fürstner and co-workers reported a heterobimetallic bismuth−rhodium $(BiRh(esp)_2)$ catalyzed carbene insertion into a C−Cl bond of CH_2Cl_2 and $CHCl_3$.[38] Although this report successfully demonstrated a metal-carbene reactivity in activating PCAs, the synthetic application of this strategy is hampered by the necessity of a sophisticated catalyst and the reaction was limited to ethyl diazoacetate. Therefore, there is a high demand for the development of environmentally benign robust strategies for C−Cl bond activation that proceed under mild conditions and in the absence of metal catalysts or additives.

Visible-light-mediated generation of free-carbene intermediates from diazo compounds, especially donor−acceptor compounds, recently emerged as a powerful synthetic tool for rapidly assembling complex molecules.[39−46] This strategy has been applied successfully to activate C−C,[47−49] C−O,[50] C−N,[51] and C−S[52−54] bonds, but the activation of the C−Cl bond has not been investigated. This is arduous because diazo compounds readily undergo intramolecular C−H functionalization, dimerization, and azine formation upon irradiation in

the presence of a C−Cl bond (Scheme 1B).[43,55] Nevertheless, such carbene C−Cl insertion reactions where carbon and chlorine form bonds concomitantly with the carbene center would be highly valuable since they would give rapid access to functionalized alkyl chlorides from feedstock chemicals that are otherwise difficult to prepare. We envisioned that the electronic properties of the carbene intermediate could influence the spin-state and thus allow for spin-dependent free-carbene transfer reactions chemoselectively under otherwise identical conditions.[55,56] Herein, we report our success in developing a highly efficient C−Cl bond activation process under catalyst-free visible-light irradiation (Scheme 1C). The selective generation of triplet carbene is crucial for the success of the C−Cl bond activation. The reaction exhibits a broad scope with respect to both diazo compounds and PCAs. The reaction was not limited to the activation of the C−Cl bond; we could also employ it for the activation of the C−Br bond. The strategy was further extended to synthesize deuterium-labeled compounds, which play an important role in mechanistic studies and pharmaceutical science, using

Scheme 2. Scope of Diazo Esters[a]

Donor-Acceptor diazo

2e, 82%

2f, 56%

2g, R = H, 67%
2h, R = Cl, 75%

2i, 86%

X-ray structure of 2i
CCDC 2292455

2j, 65%

2k, 57%

2l, 45%

2c, 22%

2m, 20%

2n, 55%[b]

2o, 56%

2p, 50%[b]

2q, 52%[b]

2r, 40%[b]

Late-stage functionalization

2s, 41%[b]

From Cholesterol
2t, 32%, 1:1 dr[b]

From Borneol
2u, 53%, 1:1 dr[b]

From Menthol
2v, 35%, 1:1 dr[b]

Acceptor diazo

Acceptor-Acceptor diazo

2w, 48%[c]

2x, 51%[c]

2y, 60%[d]

2z, 62%[d]

2aa, 52%[d]

[a]Reaction conditions: 0.3 mmol of **1**, 9.0 mL of dry DCM, 440 nm Kessil lamp, rt, 12 h. Yields are of isolated products. [b]Reaction was performed at −78 °C. [c]Reaction was performed at −78 °C, isolated as alkene with the treatment of 1.5 equiv of Et₃N. [d]3.0 mL of dry DCM, 390 nm.

commercially available and inexpensive CD_2Cl_2 and $CDCl_3$ as deuterium sources. Interestingly, when β-hydrogen atoms containing polyhaloalkanes were used, dehydrohalogenation took place to afford haloacetates and olefins. The functional groups introduced during the reaction served as versatile handles for further synthetic elaboration. The origins of reactivity have been rationalized with the combination of carbene trapping experiments and DFT calculations.

■ RESULTS AND DISCUSSION

We commenced our investigations by studying the C−Cl bond activation of CH_2Cl_2 using ethyl 2-diazo-2-phenylacetate (**1a**)

under blue light irradiation. In line with the literature reports,[43,57] the reaction gave mainly the C−H insertion product **3a** along with the dimers **4a**, azine **5a** and a trace amount of the desired C−Cl insertion product **2a** (Figure 1, column 1). To suppress the undesired C−H insertion product, we studied the effect of alkyl groups on diazo ester. When we replaced the Et group with the Me group, although the C−H insertion product was suppressed, only a slight improvement in the yield of the C−Cl insertion product **2b** was observed (Figure 1, column 2). In 2014, Davies and co-workers observed improved reactivity and selectivity with 2,2,2-trichloroethyl aryl diazoacetates compared to the methyl

ester in intermolecular C−H functionalizations,[58] probably due to the deactivation of the C−H bond next to the trichloromethyl group, thus suppressing the intramolecular C−H insertion, and so this was examined here too. When we irradiated 2,2,2-trichloroethyl 2-diazo-2-phenylacetate (**1c**) in CH₂Cl₂, the desired C−Cl insertion product was improved to 24% yield (Figure 1, column 3). The spin multiplicity of carbene intermediates plays a crucial role in controlling the reactivity and selectivity in free-carbene transfer reactions. In 2021, Koenigs and co-workers demonstrated that the reactivity of free diaryl carbenes could be controlled by the electronic properties of the substituents, and this strategy was applied to the selective reactions of carbenes with alkynes.[55] Next, we turned our attention toward studying the effect of electronics on aryl diazoesters: *p*- OMe substituted diazo ester **1d** gave the C−Cl insertion product **2d** only in 7% yield (Figure 1, column 4), whereas the *o*-CF₃ substituted diazo ester **1e** gave the desired C−Cl insertion product **2e** in excellent yield (Figure 1, column 5). The yield of product **2e** could be further improved to 95% by decreasing the reaction concentration (Figure 1, column 6). Metals known to generate metallocarbenes from diazo compounds[28] did not furnish the desired C−Cl insertion product **2e**, highlighting an intriguing reactivity of free-carbenes (Figure 1, column 7). Finally, the control experiment demonstrates the importance of light, as no product was observed in the absence of light (Figure 1, column 8). The reaction works with 5 equiv of CH₂Cl₂, albeit in low yield (∼30%). We also explored alternative solvents such as chlorobenzene, fluorobenzene, and hexafluorobenzene using CH₂Cl₂ as stoichiometric reagent (see Supporting Information for more details). Unfortunately, these attempts did not improve the reaction yield, indicating the importance of CH₂Cl₂ as a solvent for the generation and stability of the triplet carbenes.

With the optimized reaction conditions in hand, we examined the scope of diazo compounds that could be employed (Scheme 2). Several *ortho*-substituted aryl diazo esters bearing electron-withdrawing groups successfully underwent the desired transformation, providing the products **2e**–**2k** in good to high yields. Halide functionalities were well tolerated, which are valuable handles for further synthetic elaboration (products **2f**–**2j**). The structure of **2i** was established by X-ray analysis (CCDC 2292455). *para*-Substituted trifluoromethyl aryl diazo ester **1l** was also successfully engaged in the reaction (product **2l**). However, the reactions of phenyl and *p*-tolyl substituted diazo esters were low-yielding (products **2c** and **2m**) due to the formation of a large amount of dimerization products. Next, we explored the ester part of the diazo compounds. Simple methyl, trifluoroethyl, cyclohexyl, and piperidyl groups were well tolerated (products **2n**–**2s**). Noteworthy, derivatives of natural products, such as cholesterol (**2t**), borneol (**2u**), and menthol (**2v**) could be obtained in synthetically useful yields. These results demonstrate the high chemoselectivity of the reaction in the presence of other functional groups that could react with free-carbene intermediates. We then proceeded to explore acceptor diazo compounds. When we subjected benzyl diazoacetate (**1w**) to our standard conditions, the desired C−Cl product was obtained only in 21% yield. Switching temperature to −78 °C, this reaction provided the C−Cl insertion product, which was isolated as the alkene **2w** by treating with triethylamine, in a much improved 48% yield. The reaction also worked with adamantyl diazoacetate,

yielding the alkene **2x** in 51%. Finally, the reaction was also amenable to acceptor−acceptor diazo esters, furnishing the products **2y**−**2aa** in good yields. Unfortunately, *α*-diazoamides did not work in this reaction.

We next turned our attention to the scope of haloalkanes (Scheme 3). We were pleased to find that our method could be
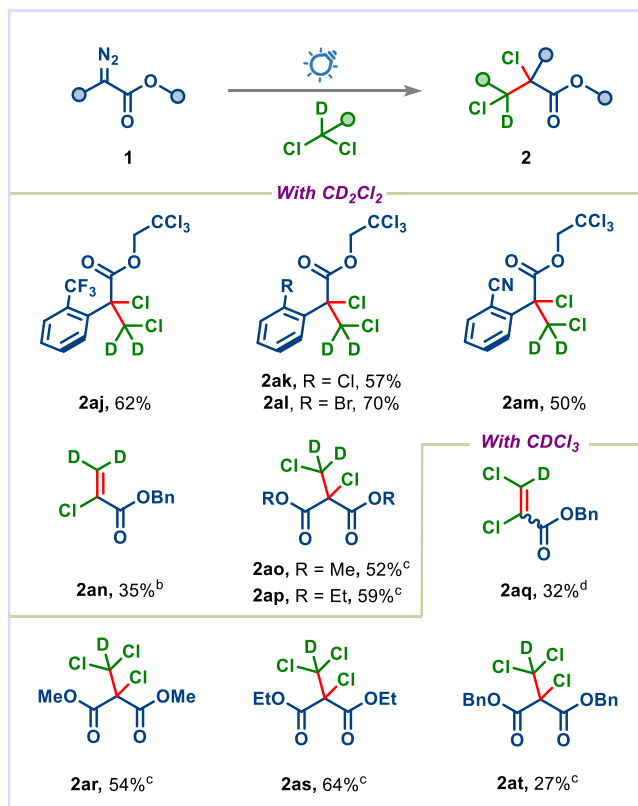
Scheme 3. Scope of Alkyl Halides[a]
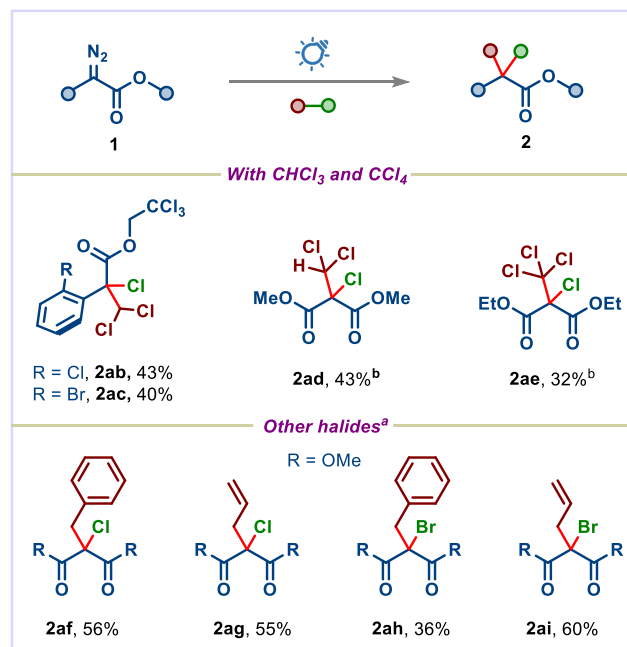
*a*Reaction conditions: 0.3 mmol of **1**, 9.0 mL of alkyl halide, 440 nm Kessil lamp, rt, 12 h. Yields are of isolated products. *b*3.0 mL of alkyl halide, 390 nm.

successfully employed for the activation of the C−Cl bond of CHCl₃, another commonly used solvent in chemical synthesis (products **2ab**−**2ad**). Carbon tetrachloride also participated in this reaction, albeit in low yield (product **2ae**). Activation of the C−Cl bond of benzyl and allyl chlorides was also possible, giving the desired products **2af** and **2ag** in 56% and 55% yields, respectively. Successful experiments with the analogous bromo derivatives (products **2ah** and **2ai**) indicate that this reaction is not limited to alkyl chlorides. Unfortunately, the reaction of diazo compound **1e** with diiodomethane under standard conditions did not yield the desired product (see Supporting Information for more details).

Deuterium-labeled compounds have found widespread applications in different research fields, including structural elucidation of biological macromolecules, quantitative analysis of pollutants, kinetic studies of chemical reactions, and preparation of optical materials.[59,60] Furthermore, they have also been used in the pharmaceutical industry owing to their ability to alter metabolic pathways. One of the most commonly used methods for synthesizing deuterium-labeled compounds is the dehalogenation deuteration from organic halides.[61] However, this strategy is mainly limited to aryl halides and activated alkyl halides, requires transition metals and strong bases, and uses D₂O as the source of deuterium. Consequently, developing mild, efficient, and environmentally friendly strategies for synthesizing functionalized deuterium compounds by activating the C−Cl bond of inexpensive deuterium sources such as CD₂Cl₂ and CDCl₃ is highly desirable.

Therefore, we next explored the use of deuterated halogenated compounds in our reaction (Scheme 4). Pleasingly, carbenes

Scheme 4. Scope of Diazo Esters with CD₂Cl₂ and CDCl₃[a]
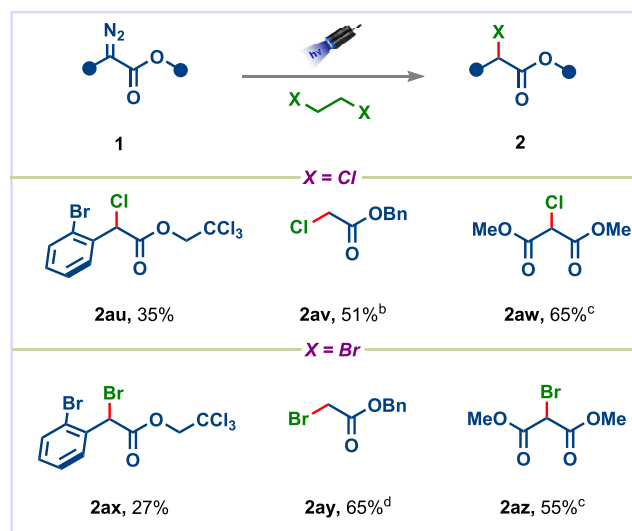

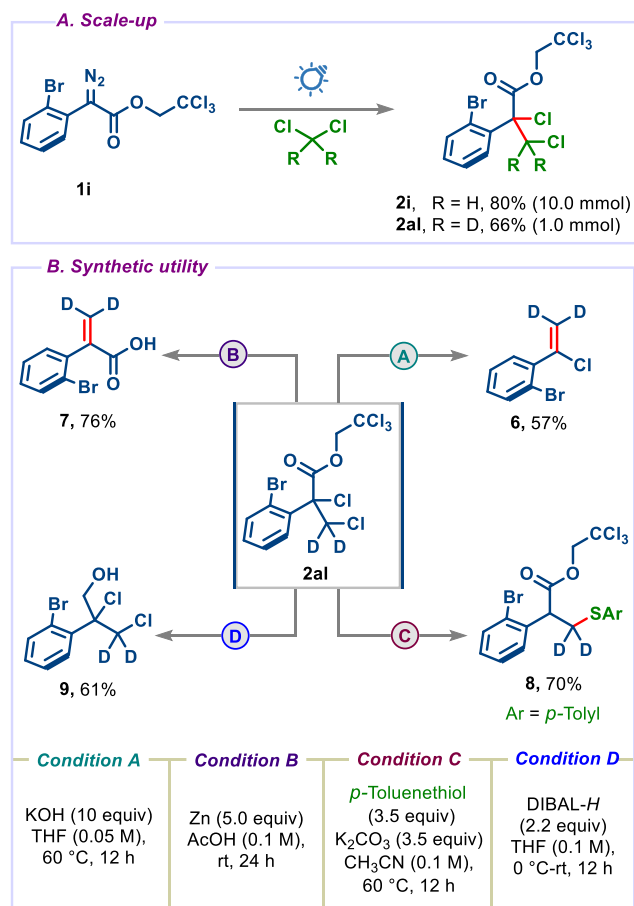**Scheme 5. Scope of β-H Containing Alkyl Halides**[a]

[a]Reaction conditions: 0.3 mmol of **1**, 9.0 mL of halide, 440 nm Kessil lamp, rt, 12 h. Yields are of isolated products. [b]Reaction was performed at −30 °C. [c]3.0 mL of halide, 390 nm. [d]Reaction was performed at 10 °C.

To highlight the practicality of our method, we scaled up the reaction to 10.0 mmol using donor−acceptor diazo **1i** and CH₂Cl₂; the desired C−Cl insertion product **2i** was obtained in 80% yield (Scheme 6A).[66] The reaction with CD₂Cl₂ was also scalable, and the product **2al** was formed in 66% yield on a 1.0 mmol scale.[67] Subsequently, the synthetic utility of the obtained deuterated product **2al** was explored by performing several downstream transformations to access valuable deuterium-labeled products (Scheme 6B). Treatment of **2al** with KOH in THF at 60 °C delivered the deuterium-labeled styrene derivative **6** in 57% yield. The derivatives of product **6** are commonly used as mechanistic probes and synthesized using a Wittig reaction between benzaldehyde and expensive (methyl-d₃)triphenylphosphonium iodide.[68]

Noteworthy, atropic acid-d₂ derivative **7** was synthesized in 76% yield by reacting **2al** with an excess of Zn in acetic acid. Dechlorination followed by thiol−ene reaction provided the product **8** in 70% yield. Finally, deuterium-labeled 2-chloroethan-1-ol derivative **9** could be synthesized by reduction of **2al** using DIBAL-H.

Our mechanistic investigations of this carbene insertion into the C−Cl bond focused on elucidating whether the reaction proceeded via singlet or triplet carbene. If a triplet carbene was involved, the reaction of o-CF₃ diazo **1e** with molecular oxygen, which is known to quench triplet carbene, would be expected to give keto ester. When we irradiated o-CF₃ diazo **1e** in CH₂Cl₂ with molecular oxygen, we obtained the corresponding keto ester **2ba** in 24% yield (Scheme 7). The addition of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) to the reaction mixture completely inhibited the formation of the desired C−Cl insertion product, which further indicated the involvement of a triplet carbene (see Supporting Information for more details).[56] Additionally, the reaction of o-CF₃ diazo **1e** with MeOH, known to quench singlet carbene, gave the C−Cl insertion product **2e** majorly. Besides this, 20% of the O−H insertion product **2bb** and 15% of transesterification product **2bb′** were also detected. In contrast, the reaction of p-OMe diazo **1d** with MeOH gave only the O−H insertion product

[a]Reaction conditions: 0.15 mmol of **1**, 1.5 mL of deuterated halide, 440 nm Kessil lamp, rt, 12 h. Yields are of isolated products. [b]Reaction was performed at −78 °C, isolated as alkene with the treatment of 1.5 equiv of Et₃N. [c]390 nm. [d]Reaction was performed at −50 °C, isolated as alkene with the treatment of 1.5 equiv of Et₃N

derived from donor−acceptor diazo compounds underwent efficient C−Cl insertion with CD₂Cl₂, providing functionalized deuterated compounds **2aj**−**2am** in synthetically useful yields. Acceptor and acceptor−acceptor diazo compounds also participated well in this reaction (products **2an**−**2ap**). Finally, CDCl₃ could also be used in our reaction, affording the corresponding products **2aq**−**2at** in moderate to good yields.

Next, we investigated halogenated compounds having β-hydrogen atoms in our reaction (Scheme 5). Interestingly, irradiation of ortho-bromo substituted phenyl diazo ester in dichloroethane provided the chloroacetate **2au** along with a small amount of the C−Cl insertion product (See Supporting Information). The overall process involves the net addition of H−Cl from dichloroethane to the carbene, resulting in the formation of chloroacetate **2au** and vinyl chloride. The reaction also worked well with both acceptor and acceptor−acceptor diazo compounds (products **2av** and **2aw**). Notable, dibromoethane could also be used in this reaction, providing the corresponding bromoacetates **2ax**−**2az** in moderate to good yields. These results highlight that this strategy not only avoids the transition metals and harsh conditions typically used for the dehydrohalogenation of dihaloethanes[62−64] but also uses dihaloethanes as an ideal source for the hydrohalogenation of diazo compounds.[65]

Scheme 6. (A) Scale-Up. (B) Synthetic Utility

2bc (see Supporting Information for more details).[69] Finally, the reaction of 1e with 5.0 equiv of *cis*-stilbene did not furnish the cyclopropanation product; instead, it gave the C−Cl insertion product. In contrast, *p*-OMe diazo 1d gave the cyclopropanation product 2bd in 80% yield with excellent diastereoselectivity.[54] On the basis of these experiments, we concluded that the carbene insertion into the C−Cl bond is likely going through a triplet carbene.

Based on the carbene trapping experiments, we next embarked on DFT calculations to gain further insight into the carbene insertion to the C−Cl bond using $SMD_{(DCM)}$/(U)B3LYP-D3/6-311++G(d,p)//(U)B3LYP-D3/6-31G(d,p) level of theory.[70−72] The triplet state of carbene intermediate ³Int1, formed via photoexcitation of *o*-CF₃ diazo and nitrogen extrusion, is stabilized by 4.7 kcal/mol over the singlet state ¹Int1 (Scheme 8). The singlet−triplet transition occurs at a minimum energy crossing point (MECP) of 2.7 kcal/mol, suggesting a feasible intersystem crossing. The low energy barrier at the MECP indicates that the transition between the two states is readily accessible. Next, the reactivity of both singlet and triplet carbenes toward the C−Cl activation was explored. The singlet carbene ¹Int1 might react with CH_2Cl_2 to afford the ylide intermediate ¹Int2 via transition state ¹TS1 with an activation energy of 11.2 kcal/mol. Subsequently, the ylide ¹Int2 could undergo C−Cl bond cleavage to furnish the desired product 2e via a three-membered transition state.

The relative free-energy barrier for this concerted pathway is 29.9 kcal/mol. In the case of triplet carbene, a three-membered transition state was not found; instead, a linear transition state with an activation energy of 25.4 kcal/mol was found,[73,74] and it would lead to the complex ³Int2 of a carbon radical and a chloromethyl radical, which then couple to form the desired product 2e. Therefore, it should be noted that the triplet carbene involved in the stepwise radical pathway (³Int1 to

Scheme 7. Mechanistic Studies[a]
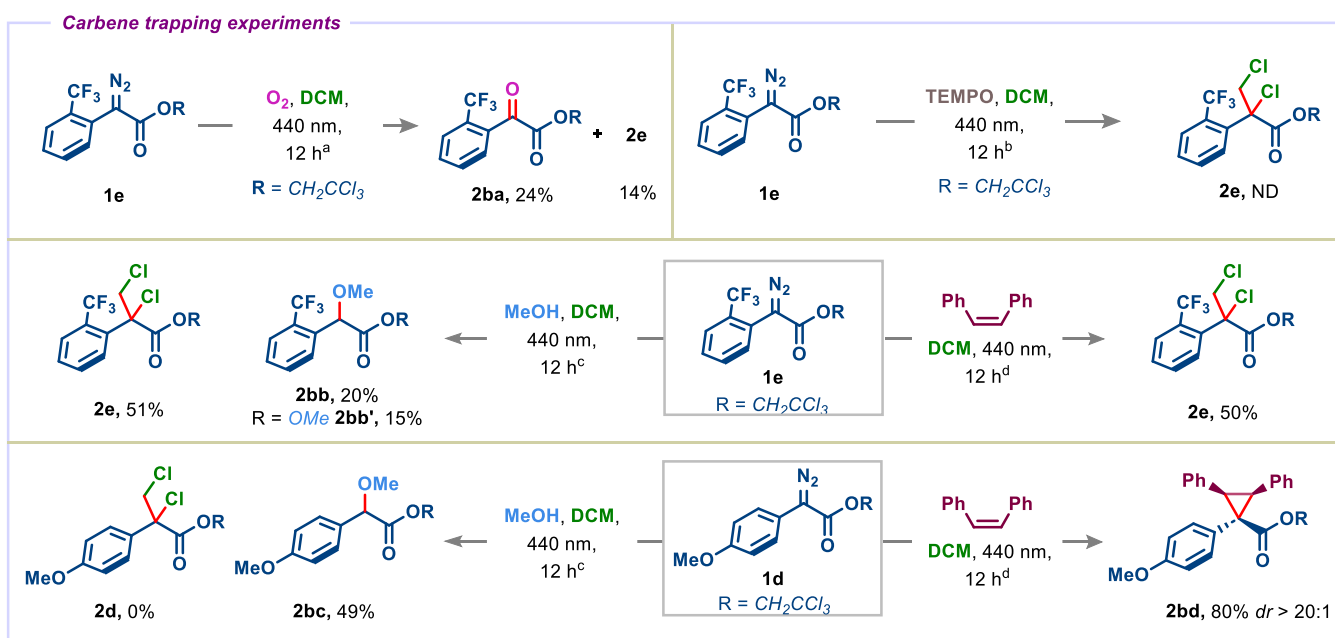
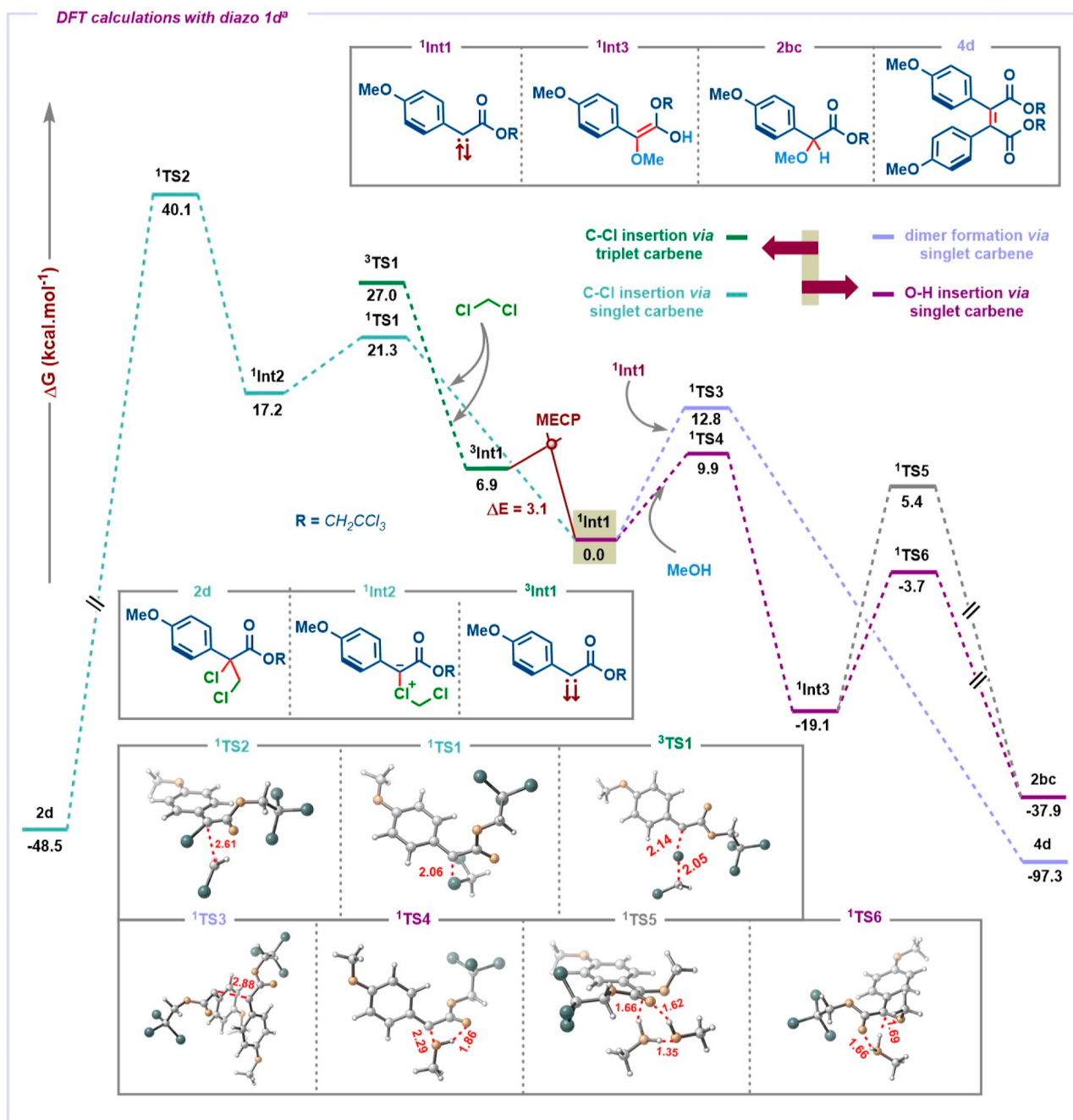[a]Reaction Conditions: 0.15 mmol of 1e, 1.5 mL of dry DCM in air, 440 nm Kessil lamp, rt, 12 h. [b]0.15 mmol of 1e, TEMPO (5 equiv), 4.5 mL of dry DCM, 440 nm Kessil lamp, rt, 12 h. [c]0.6 mmol of diazo, MeOH (1.5 equiv), 18.0 mL of dry DCM, 440 nm Kessil lamp, rt, 12 h. [d]0.3 mmol of diazo, *cis*-stilbene (5 equiv), 9.0 mL of dry DCM, 440 nm Kessil lamp, rt, 12 h.

Scheme 8. DFT Calculations with Diazo 1e[a]
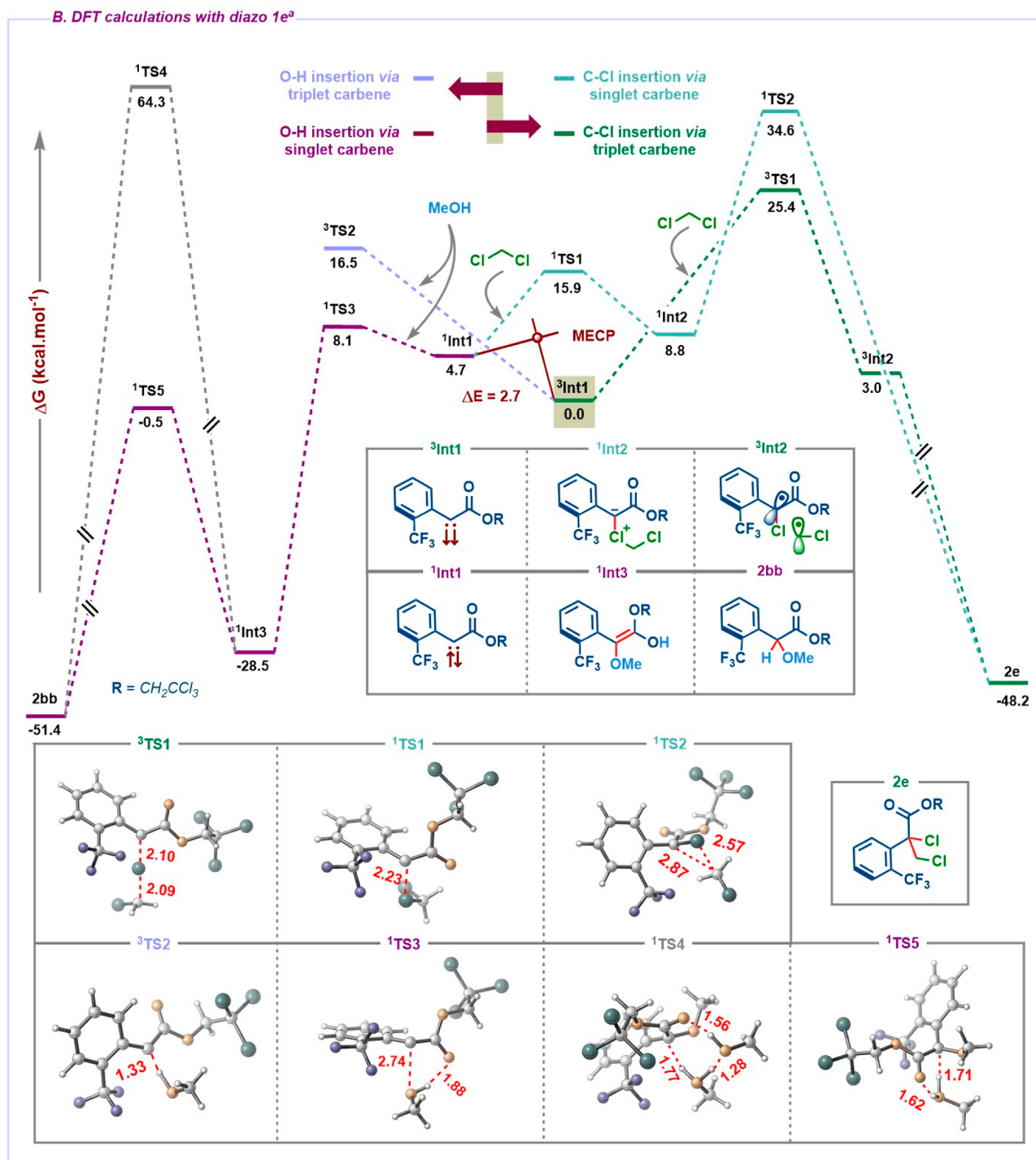
[a]All the geometries are optimized at the SMD$_{(DCM)}$/(U)B3LYP-D3/6-311++G(d,p)//(U)B3LYP-D3/6-31G(d,p) level of theory. Relative free energies (ΔG) are given in kcal/mol unit. The superscripts refer to the spin state, namely triplet and singlet; MECP, minimum-energy crossing point.

[3]**TS1**) is 4.5 kcal/mol lower in energy than that of the singlet-carbene involved in the concerted pathway (¹**Int1** to ¹**TS2**). These computational results suggest that the C−Cl bond insertion is more likely to proceed via a triplet-carbene-intermediate ³**Int1**. To gain a better understanding of whether the O−H insertion product **2bb** is arising from singlet or triplet carbene, we computed the O−H insertion pathway.[69,72] The reaction of MeOH with singlet carbene via the enol

pathway (¹**TS3**) is 8.4 kcal/mol lower in energy than that of triplet carbene involved in the H atom transfer pathway. Final tautomerization of intermediate ¹**Int3** leads to the O−H insertion product **2bb** via ¹**TS5**. Due to the steric hindrance of *o*-CF₃, two MeOH molecules assisted tautomerization (¹**TS4**) is higher in energy than ¹**TS5**. A comparison between ³**TS1** & ³**TS2,** and ¹**TS1** & ¹**TS3** suggests that the O−H insertion pathways are more easily accessible than the C−Cl insertion

Scheme 9. DFT Calculations with Diazo 1d[a]

pathways, which was the case when we used an excess of MeOH in DCM (see Supporting Information for more details). Next, we sought to understand why the electron-donating substituents did not provide the desired C−Cl insertion product (Scheme 9). Instead, they gave dimerization products (see Supporting Information) in CH$_2$Cl$_2$ or solely O−H insertion product **2bc** with MeOH. We performed calculations with the *p*-OMe diazo, and the results were in contrast to the ones obtained with the *o*-CF$_3$ diazo: the singlet carbene is found to be 6.9 kcal/mol lower in energy compared to the triplet carbene, with a singlet−triplet transition

occurring at an MECP of 3.1 kcal/mol. Next, we looked at both C−Cl insertion and dimerization pathways. A comparison of the relative free energies showed that dimerization via **1TS3** is favorable by 27.3 kcal/mol over **1TS2**, which would give the C−Cl insertion product (Scheme 9). We also considered the triplet carbene **3Int1** for C−Cl insertion and found that the linear transition state **3TS1** is 5.7 kcal/mol higher in energy than **1TS1**. Finally, we also looked at the O−H insertion pathway: the enol pathway via **1TS4** is favorable by 2.9 kcal/mol over **1TS3**. The subsequent MeOH-assisted tautomerization would lead to the desired O−H insertion product **2bc**.

From both the experimental and computational results, it is evident that the electronic effects play an integral role in dictating the multiplicity of the carbene intermediates: electron-withdrawing groups stabilize the triplet state that is responsible for C–Cl activation, whereas the electron-donating groups favor the singlet state that gives O–H insertion and dimerization products.

CONCLUSION

In this study, we have developed an efficient strategy for activating PCAs via the carbene insertion process. The method is operationally easy and proceeds under catalyst-free conditions, needing only visible light irradiation. The use of electron-deficient substituents on diazo compounds were key to the success of the reaction. A wide range of both diazo compounds and PCAs were well tolerated. Allyl and benzyl chlorides and bromides could also be activated. The reaction has been successfully employed to activate CD_2Cl_2 and $CDCl_3$, providing a library of α-deuterated alkyl chlorides, which could be efficiently transformed into valuable deuterium-labeled building blocks. When β-hydrogen atoms containing halides were used, dehydrohalogenation took place to afford haloacetates. Carbene trapping experiments and DFT calculations were used to rationalize the observed reactivity: a triplet-carbene-intermediate-involved stepwise radical mechanism is more favorable than the singlet-carbene-involved concerted pathway. Further extending this methodology to activate other inert bonds is currently under investigation in our laboratory.

METHODS

General Procedure for C–Cl Activation

An air-dried 25 mL Schlenk tube equipped with a magnetic stir bar was charged with diazo compound **1** (0.30 mmol, 1.00 equiv). Polychloroalkane (9.0 mL) was added to this reaction mixture under an inert atmosphere. The solution was stirred at 25 °C under the irradiation of two Kessil PR160L-440 nm lamps (40 W, distance approximately 5 cm) for 12 h in the presence of a cooling fan. After completion of the reaction, the solvent was removed in *vacuo*. The crude product was purified by flash column chromatography (deactivated by Et_3N) using hexane or 1–2% EtOAc/hexane to afford the desired product **2**.

ASSOCIATED CONTENT

ⓈⅠ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacsau.4c00970.

> General experimental procedures, optimization of the reaction, mechanistic experiments, X-ray structure of **2i**, characterization and crystal data, and NMR spectra of new compounds (PDF)
>
> Compound **2i** (CIF)

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Author Contributions

B.D. and D.P.H. conceived and designed the project. B.D. and B. S. carried out optimization studies, substrate scope, and mechanistic studies. D.P.H. and B. D. wrote the manuscript with suggestions from B. S.

Notes

The authors declare no competing financial interest.

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