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# One-Pot Synthesis of Trichloromethyl Carbinols from Primary Alcohols

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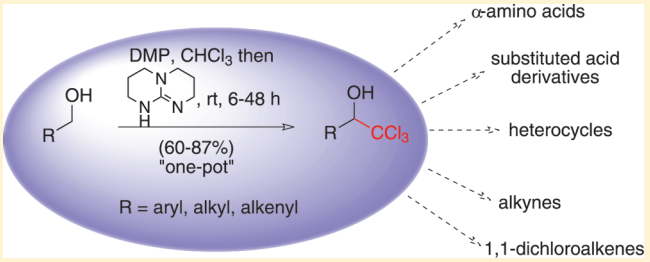
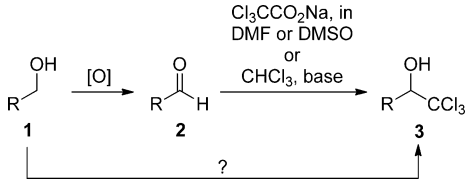
Supporting Information

**ABSTRACT:** Versatile trichloromethyl carbinols can be prepared in one pot from primary alcohols by treatment with Dess–Martin periodinane (DMP) in $CHCl_3$ followed by introduction of commercially available 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD). A modification of the method was used to convert chiral primary alcohol (*R*)-(−)-2,2-dimethyl-1,3-dioxolane-4-methanol to the corresponding trichloromethyl carbinol with complete stereochemical fidelity, despite the reactant proceeding through a base-sensitive aldehyde intermediate.




Trichloromethyl carbinols (**3**) are useful precursors to α-amino acids,[1] α-substituted carboxylic acids,[2] substituted enoic acids,[3] heterocycles,[4] terminal alkynes,[5] and 1,1-dichloroalkenes,[6] to name just a few compound classes.[7] The carbinols (**3**) are typically prepared by addition of weakly nucleophilic trichloromethide to aldehydes (**2**). Trichloromethide is formed by decarboxylation of sodium trichloroacetate in DMF[8] or DMSO[9] or by treatment of chloroform with a base (Scheme 1).[1c,10] The latter method is generally restricted to additions to hindered or nonenolizable aldehydes because of the potential for side reactions resulting from enolate formation.

**Scheme 1. Preparation of Trichloromethyl Carbinols from Primary Alcohols**




The instability of many aldehydes coupled with the attractive potential of primary alcohols serving as direct precursors to trichloromethyl carbinols led us to consider means of converting **1** to **3** without isolating the intermediate aldehydes **2** (Scheme 1). Because many aldehydes used to prepare trichloromethyl carbinols are formed by oxidation of the corresponding alcohols, a convenient one-pot preparation of **3** from **1** would enhance step economy in the many applications involving **3**. The combination of oxidation and in situ trichloromethylation would also obviate the need for isolation and purification of aldehydes **2**, many of which are difficult to isolate or store without some decomposition.

We considered two possibilities for conversion of **1** to **3** without isolation of **2** based upon the requirements for trichloromethide formation and its addition to aldehydes. The most significant factor is the solvent, in the case of decarboxylation of sodium trichloroacetate, and the choice of base, in the case of trichloromethide formation from chloroform. Pairing reliable oxidation methods with these requirements for trichloromethide formation would provide an opportunity to bypass isolation of **2** in the preparation of **3**. Modifications of activated dimethyl sulfoxide-mediated[11] or Dess–Martin periodinane-based[12] oxidations were appealing options for evaluation of potential one-pot oxidation–trichloromethylation reactions because of the generality of the oxidation methods, and because both feature reaction conditions that appeared amenable to modification for in situ trichloromethylation of the aldehyde formed by the alcohol oxidation process.

We began our investigation by exploring modifications of the Swern,[13] Parikh–Doering,[14] Albright–Goldberg,[15] and related oxidations.[11] The employment of DMSO in these approaches suggested that introduction of sodium trichloroacetate during, or after completion of, the alcohol oxidation step might allow for trichloromethide formation and subsequent addition to the incipient aldehyde in a one-pot operation. However, systematic changes to the amount of DMSO included, the DMSO activator, the base used in the oxidation, and the amount of time allowed for addition of sodium trichloroacetate did not lead to satisfactory formation of **3** in a one-pot process. In most cases, the oxidation step proceeded as expected; however, trichloromethide formation or its addition to **2** was incomplete under all conditions screened even after more than 48 h.

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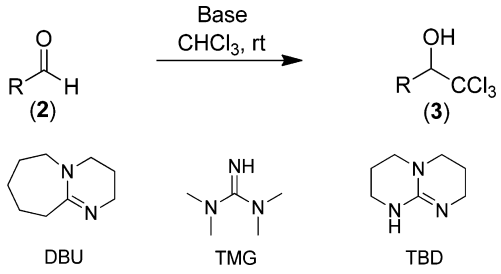
Hence, only modest yields of **3** with isolation of unreacted **2** were encountered in even the best cases.

Because of limited success in modifications of activated DMSO-mediated oxidations, we shifted our attention to modifying the Dess–Martin periodinane (DMP)-based oxidation of **1** to develop a one-pot approach to **3**. We reasoned that substituting chloroform for the dichloromethane typically employed as the solvent in DMP oxidations and then adding a base capable of deprotonating chloroform to form trichloromethide should promote the formation of **3** from **1**. The key to this approach was identifying a base capable of deprotonating weakly acidic chloroform ($pK_a$ = 13.6),[16] thereby potentially allowing the poorly nucleophilic trichloromethide to add to the intermediate aldehyde.

Several commercially available bases were screened for their ability to form trichloromethide from chloroform and to promote addition to benzaldehyde and to less electrophilic 4-methoxybenzaldehyde (Table 1). As expected, triethylamine was insufficiently basic to form useful quantities of trichloromethide (Table 1, entry 1), and 1,1,3,3-tetramethylguanidine (TMG) gave inferior results (Table 1, entries 4–5). Aggarwal and co-workers reported that DBU may be used to deprotonate $CHCl_3$ in a convenient procedure for the trichloromethylation of aldehydes. They also reported one example of 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene serving a comparable function.[10b] In comparing the trichloromethylation yields and reaction times between DBU and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD), we noted that the reaction with the latter was faster than with DBU, although both bases ultimately proved effective in highly concentrated solutions of substrate (2.5 M) (Table 1, entries 3 and 7). Dess–Martin periodinane shows incomplete solubility in $CH_2Cl_2$ and $CHCl_3$ at 2.5 M concentration, but it is fully soluble at a 0.67 M substrate concentration. When we screened DBU and TBD at 0.67 M aldehyde concentrations, we found that DBU was markedly less effective under the more dilute reaction conditions needed to allow for efficient DMP oxidation of a primary alcohol (Table 1, entry 8). However, TBD proved highly capable at both 2.5 and 0.67 M substrate concentrations (Table 1, entries 7 and 9), thereby making it attractive for use in our desired one-pot oxidation-trichloromethyl reactions. The cyclic guanidine even permitted effective trichloromethylation of 4-methoxybenzaldehyde after 24 h (Table 1, entry 11), whereas DBU showed poor conversion (Table 1, entry 10).

**Table 1. Screening of Bases for Trichloromethylation of Benzaldehydes in Chloroform**




| entry | R | [2][a] (M) | base | time (h) | 3:2 (%)[b] |
|---|---|---|---|---|---|
| 1 | Ph | 2.5 | $Et_3N$ | 24 | <5:95 |
| 2 | Ph | 2.5 | DBU | 1 | 82:18 |
| 3 | Ph | 2.5 | DBU | 16 | >98:2 |
| 4 | Ph | 2.5 | TMG | 1 | 23:77 |
| 5 | Ph | 2.5 | TMG | 24 | 86:14 |
| 6 | Ph | 2.5 | TBD | 1 | 90:10 |
| 7 | Ph | 2.5 | TBD | 3 | >98:2 |
| 8 | Ph | 0.67 | DBU | 24 | 45:55 |
| 9 | Ph | 0.67 | TBD | 3 | >98:2 |
| 10 | 4-$CH_3O$Ph | 0.67 | DBU | 24 | 26:74 |
| 11 | 4-$CH_3O$Ph | 0.67 | TBD | 24 | 87:13 |

[a]Reactions were conducted by treating **2** (0.50 mmol) with the corresponding base (0.60 mmol) in $CHCl_3$. [b]Relative percentages of **3** and **2** were determined by $^1H$ NMR analyses of crude reaction mixtures.

With TBD identified as the optimal base, we evaluated its ability to promote trichloromethylation of a series of aldehyde intermediates generated by initial DMP oxidation of the corresponding primary alcohols in $CHCl_3$ (Table 2). The alcohol oxidations did not proceed in high yields when DMP and TBD were combined with the alcohol substrates in $CHCl_3$, perhaps because of the guanidine competing with the primary alcohol for coordination to the acetoxyperiodinane intermediates.[17] However, by combining the oxidant and the alcohol in $CHCl_3$ and then adding 3.3 equiv of TBD when the oxidation was judged complete by TLC analysis (4–8 h), the desired trichloromethyl carbinols were afforded in yields comparable to those resulting from separate alcohol oxidation and aldehyde trichloromethylation reactions (vide infra). The method necessitates the use of at least 3 equiv of base, since 2 equiv of acetic acid are generated from DMP during the oxidation step. Addition of 2 equiv of NaOH to neutralize the generated acetic acid and 1.3 equiv of TBD to promote the trichloromethylation after the alcohol oxidation did not afford the desired trichloromethyl carbinols. Also, replacement of TBD with commercially available 1,5,7-triazabicyclo[4.4.0]dec-5-ene bound to polystyrene afforded products **3** in very low yields (5–15%), even after reaction times of greater than 48 h.

The one-pot oxidation–trichloromethylation strategy worked well with both electron-rich and electron-poor functionalized benzyl alcohols (**1a–1d**) and with 2-naphthalenemethanol (**1e**). It also provided yields of 70% with 2-furylmethanol (**1j**) and 61% with 2-thienylmethanol (**1k**), compounds which form sensitive aldehydes that are difficult to oxidize, isolate, and trichloromethylate in high yields. Similarly, allylic alcohols **1l** and **1m** were trichloromethylated in good yields. Substrates proceeding through enolizable aldehydes (**1f–1i**) were trichloromethylated in yields ranging from 60 to 75%, although these compounds generally required longer reaction times than most of the nonenolizable substrates for the trichloromethylations to reach completion. Propargylic alcohols **1n** and **1o** were not compatible substrates, since several byproduct were formed upon addition of base to the intermediate ynals.

We compared the traditional two step oxidation–trichloromethylation strategy to the one-pot sequential procedure outlined herein with four varied primary alcohols (Table 3). Notably, the one-pot process offered yields comparable or superior to the two-step approach with substrates **1b** and **1k**, although the overall yields were slightly lower using the one-pot approach with cinnamyl alcohol (**1l**) and hydrocinnamyl alcohol (**1f**). However, even with the latter compounds, the new procedure obviates the need for isolation and purification of the intermediate aldehydes and, hence, offers advantages in terms of total materials costs and overall preparation time.

Next we examined the ability to oxidize–trichloromethylate a primary alcohol (**1p**) possessing an $\alpha$-stereocenter that is prone


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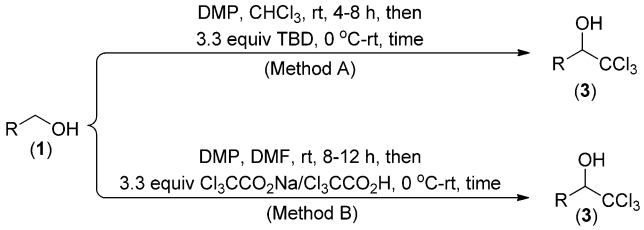
**Table 2. One-Pot Oxidation−Trichloromethylation of Primary Alcohols**




| entry | Compd[a] | R | Method[b,c] | time (h) | product | yield (%)[d] |
|---|---|---|---|---|---|---|
| 1 | **1a** | 4-$CH_3OPh$ | A | 24 | **3a** | 83 |
| 2 | **1b** | Ph | A | 8 | **3b** | 87 |
| 3 | **1c** | 4-$NO_2Ph$ | A | 6 | **3c** | 85 |
| 4 | **1d** | 4-$CF_3Ph$ | A | 8 | **3d** | 86 |
| 5 | **1e** | 2-naphthyl | A | 16 | **3e** | 84 |
| 6 | **1f** | $PhCH_2CH_2$ | A | 30 | **3f** | 71 |
| 7 | **1f** | $PhCH_2CH_2$ | B | 36 | **3f** | 61 |
| 8 | **1g** | $CH_3(CH_2)_8$ | A | 30 | **3g** | 60 |
| 9 | **1g** | $CH_3(CH_2)_8$ | B | 16 | **3g** | 34 |
| 10 | **1h** | $TBSO(CH_2)_4$ | A | 25 | **3h** | 62 |
| 11 | **1i** | Cy | A | 14 | **3i** | 73 |
| 12 | **1j** | 2-furyl | A | 18 | **3j** | 70 |
| 13 | **1k** | thiophen-2-yl | A | 48 | **3k** | 61 |
| 14 | **1k** | thiophen-2-yl | B | 48 | **3k** | 34 |
| 15 | **1l** | *E*-PhCH=CH | A | 18 | **3l** | 62 |
| 16 | **1l** | *E*-PhCH=CH | B | 20 | **3l** | 55 |
| 17 | **1m** | $(CH_3)_2C=CH$ | A | 18 | **3m** | 80 |
| 18 | **1n** | Ph—≡ | A | 10 | **3n** | 34 |
| 19 | **1n** | Ph—≡ | B | 16 | **3n** | 27 |
| 20 | **1o** | $CH_3(CH_2)_4$—≡ | A | 12 | **3o** | <10 |
| 21 | **1o** | $CH_3(CH_2)_4$—≡ | B | 16 | **3o** | 18 |

[a]All reactions were conducted on a 1 mmol scale. [b]Method A: 1.2 equiv of DMP, $CHCl_3$, 4−8 h, and then 3.3 equiv of TBD, 0 °C to rt, 6−48 h. [c]Method B: 1.2 equiv of DMP, DMF, 4−8 h, and then 3.3 equiv of $Cl_3CCO_2Na$, 3.3 equiv of $Cl_3CCO_2H$, 0 °C to rt, 16−48 h. [d]Yield of purified product.

to racemization upon oxidation (Scheme 2). Treatment of (*R*)-(−)-2,2-dimethyl-1,3-dioxolane-4-methanol **1p** with DMP in $CHCl_3$ followed by introduction of 3.3 equiv of TBD after the alcohol was consumed afforded a complex mixture of polar materials. We altered the reaction conditions to test an approach that might allow for sequential oxidation−trichloromethylation of **1p** without decomposition or racemization of the intermediate aldehyde. Conducting the reaction with DMP in DMF followed by addition of 3.3 equiv of both sodium trichloroacetate and trichloroacetic acid[8] afforded a 63:37 mixture of diastereomers (*S*,*S*)-**3p**, and (*S*,*R*)-**3p** in 72% combined yield. Notably, the combined yield of (*S*,*S*)-**3p** and (*S*,*R*)-**3p** was slightly higher using the one-pot method under the buffered conditions than that reported for the trichloromethylation of (*S*)-isopropylideneglyceraldehyde alone (68%).[2d] Conversion of the diastereomeric mixture to Mosher ester derivatives[18] confirmed that each was a single stereoisomer.[19] Hence, no racemization of the stereogenic center occurred in the intermediate aldehyde under the modified buffered conditions. Despite the successful employment of the buffered conditions in the oxidation−trichloromethylation of **1p**, this procedure did not improve the yields of **3f**, **3g**, **3k**, **3l**, or **3n** relative to the use of TBD in $CHCl_3$, although the buffered system did allow for generation of **3o**, albeit in poor yield, where TBD failed (Table 2). These results suggest that the basicity of TBD is not solely responsible for the moderate yields of these products in the reactions involving the guanidine base.

The introduction of a sequential oxidation−trichloromethylation of primary alcohols now makes it possible to convert such alcohols to one-carbon homologated carboxylic acids in two operational steps. Combining the outlined approach with our previously reported homologation−functionalization procedure,[2f] representative alcohols **1e**, **1f**, **1j**, and **1m** were homologated to carboxylic acids **4**−**7** in 65−79% overall yields in two steps (Scheme 3). A similar strategy may be employed to prepare any member of the vast array of products derived from trichloromethyl carbinols[1−7] in just two operational steps starting from primary alcohols.

In summary, we devised a conversion of primary alcohols to trichloromethyl carbinols in a convenient one-pot operation. The approach obviates the isolation and purification of sensitive aldehydes and is compatible with a wide range of primary alcohol substrates. Functionalized aryl and heteroaryl methanols and hindered aliphatic alcohols are particularly suitable for the outlined method. The approach can be combined with any of the several one-pot transformations of trichloromethyl carbinols[1−7] to rapidly elaborate primary alcohols in a step-economical fashion.

## EXPERIMENTAL SECTION

**General Information.** The $^1H$ spectra were recorded at 500 or 360 MHz as indicated. The $^{13}C$ NMR spectra were recorded at 125 MHz. High-resolution mass spectra were recorded on an EBE sector instrument using electron ionization (EI) at 70 eV. Dess−Martin periodinane was prepared by the method of Boeckman et al.[20]

**General Procedure for the Preparation of Trichloromethyl Carbinols from Primary Alcohols.** *Method A.* To a solution of primary alcohol (1.0 mmol) in anhydrous $CHCl_3$ (1.5 mL) was added Dess−Martin periodinane (509 mg, 1.2 mmol) at 0 °C under an argon atmosphere. The reaction mixture was brought to room temperature and allowed to stir until starting alcohol was consumed, as determined by TLC analysis. TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene) (446 mg, 3.2 mmol) was added in 3 portions and stirred very rapidly at 0 °C. After 6−8 h, the mixture was monitored by TLC. If corresponding aldehyde remained, 1 equiv of TBD was added with vigorous stirring. Once the reaction was judged complete, the mixture was diluted with aqueous $NaHCO_3$ (5 mL) and $CH_2Cl_2$ (5 mL). The precipitated solids were filtered through a bed of diatomaceous earth, the filter cake was rinsed with $CH_2Cl_2$, and the biphasic filtrate was separated. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 10 mL), and then the combined organic layers were dried ($Na_2SO_4$), and the solvent was evaporated. The resulting residue was eluted through a plug of silica gel with indicated ratios of EtOAc/hexanes to afford the corresponding trichloromethyl carbinols.


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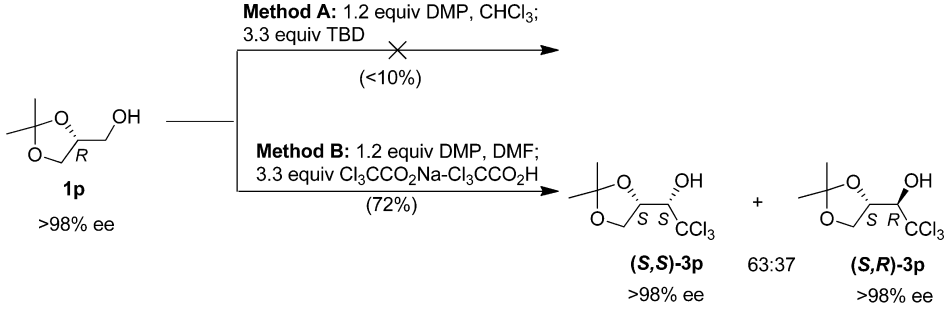
**Table 3. Comparative Study of Conventional Two-Step vs Outlined One-Pot Preparations of Trichloromethyl Carbinols from Varied Primary Alcohols**

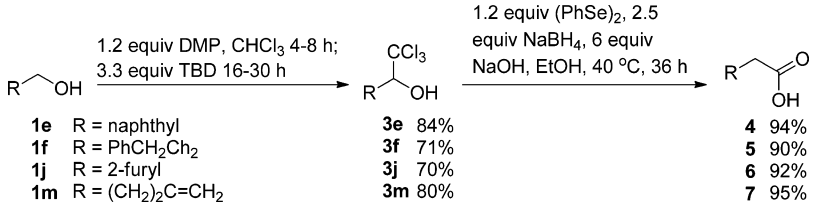
| | | | DMP oxidation[a] | | trichloromethylation[b] | | | |
|---|---|---|---|---|---|---|---|---|
| entry | compd | R | time (h) | yield (%) | time (h) | yield (%) | product | combined yield[c]/ one-pot yield (%) |
| 1 | **1b** | Ph | 6 | 96 | 18 | 93 | **3b** | 89/87 |
| 2 | **1f** | $PhCH_2CH_2$ | 8 | 94 | 24 | 87 | **3f** | 82/71 |
| 3 | **1k** | thiophen-2-yl | 4 | 72 | 48 | 78 | **3k** | 56/61 |
| 4 | **1l** | *E*-PhCH=CH | 4 | 81 | 12 | 84 | **3l** | 68/62 |

[a]1.2 equiv of DMP, $CH_2Cl_2$, 4−8 h, followed by flash chromatography purification. [b]1.5 equiv of $Cl_3CCO_2Na$, DMF, 0 °C to rt, 12−48 h, followed by flash chromatography purification. [c]Reactions were conducted on a 1.0 mmol scale.

**Scheme 2. One-Pot Trichloromethylation−Oxidation of a Chiral Alcohol (1p)**




**Scheme 3. Two-Step One-Carbon Homologation−Functionalization of Primary Alcohols**




*Method B.* To a solution of primary alcohol (1.0 mmol) in anhydrous DMF (1.5 mL) was added Dess−Martin periodinane (509 mg, 1.2 mmol) at 0 °C under an atmosphere of argon. The reaction mixture was brought to room temperature and allowed to stir until starting primary alcohol was consumed, as determined by TLC analysis. The reaction was cooled to 0 °C, then trichloroacetic acid (539 mg, 3.3 mmol) and sodium trichloroacetate (604 mg, 3.3 mmol) were quickly added. The reaction was allowed to warm to room temperature and stir until the corresponding aldehyde was consumed (12−48 h). After the reaction was judged complete, the mixture was diluted with aqueous $NaHCO_3$ (5 mL) and ethyl acetate (10 mL), and the precipitated solids were filtered through a bed of diatomaceous earth. The filter cake was rinsed with EtOAc, and the biphasic filtrate was separated. The aqueous layer was extracted with EtOAc (3 × 10 mL), and then the combined organic layers were dried ($Na_2SO_4$), and the solvent was evaporated. The resulting residue was eluted through a plug of silica gel with indicated ratios of EtOAc/hexanes to afford the corresponding trichloromethyl carbinols.

*2,2,2-Trichloro-1-(4-methoxyphenyl)ethanol (**3a**).*[2f] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 9:1 hexane/EtOAc as the eluant. The indicated compound was obtained as a white solid in 83% yield (212 mg): mp 44−45 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.53 (d, $J$ = 8.8 Hz, 2H), 6.92 (d, $J$ = 8.8 Hz, 2H), 5.14 (d, $J$ = 4.1 Hz, 1H), 3.82 (s, 3H), 3.61 (d, $J$ = 4.1 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 160.2, 130.3, 127.0, 113.1, 103.3, 84.0, 55.2; HRMS $m/z$ calcd for $C_9H_9O_2Cl_3$, 253.9668; found 253.9665.

*2,2,2-Trichloro-1-phenylethanol (**3b**).*[2f,21] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 9:1 hexane/EtOAc as the eluant. The indicated compound was obtained as a colorless oil in 87% yield (196 mg): $^1$H NMR ($CDCl_3$, 360 MHz) $\delta$ 7.71−7.53 (m, 2H), 7.50−7.34 (m, 3H), 5.22 (s, 1H), 3.28 (s, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 134.8, 129.4, 129.2, 127.8, 103.0, 84.4; HRMS $m/z$ calcd for $C_8H_7Cl_3O$, 223.9562; found 223.9563.

*2,2,2-Trichloro-1-(4-nitrophenyl)-ethanol (**3c**).*[2f] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 8:2 hexane/EtOAc as the eluant. The indicated compound was obtained as an off-white solid in 85% yield (230 mg): mp 107−108 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.23 (d, $J$ = 8.8 Hz, 2H), 7.83 (d, $J$ = 8.8 Hz, 2H), 5.34 (d, $J$ = 3.5 Hz, 1H), 3.64 (d, $J$ = 3.5 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 148.4, 141.5, 130.4, 122.8, 102.0, 83.4; HRMS $m/z$ calcd for $C_8H_6Cl_3NO_3$, 268.9413; found 268.9406.

*2,2,2-Trichloro-1-(4-(trifluoromethyl)phenyl)ethanol (**3d**).*[22] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as a white solid in 86% yield (253 mg): mp 34−35 °C; $^1$H NMR ($CDCl_3$, 360 MHz) $\delta$ 7.76 (d, $J$ = 8.2 Hz, 2H), 7.66 (d, $J$ = 8.2 Hz, 2H), 5.28 (d, $J$ = 3.8 Hz, 1H), 3.38 (d, $J$ = 3.8 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 138.4, 131.4 (q, $J$ = 35.8 Hz), 129.7, 124.7 (q, $J$ = 3.7 Hz), 122.8 (q, $J$ = 270.4 Hz), 102.5, 83.8; $^{19}$F NMR ($CDCl_3$, 360 MHz) $\delta$ −62.7; HRMS $m/z$ calcd for $C_8H_6F_3O$, 175.0371; found 175.0373, which corresponds to $[M - CCl3]^+$.

*2,2,2-Trichloro-1-napthalen-2-yl-ethanol (**3e**).*[2f] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 9:1 hexane/EtOAc as the eluant. The indicated compound was obtained as an off-white solid in 84% yield (232 mg): mp 93−94 °C; $^1$H NMR ($CDCl_3$, 360 MHz) $\delta$ 8.09 (s, 1H), 7.94−7.83 (m, 3H), 7.74 (dd, $J$ = 8.6, 1.8 Hz, 1H), 7.58−7.49 (m, 2H), 5.40 (d, $J$ = 3.9 Hz, 1H), 3.37 (d, $J$ = 3.9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Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 133.6, 132.4, 132.2, 129.2, 128.3, 127.6, 127.3, 126.8, 126.3, 126.0, 103.1, 84.5; HRMS $m/z$ calcd for $C_{12}H_9OCl_3$, 273.9712; found 273.9713.

*1,1,1-Trichloro-4-phenylbutan-2-ol (**3f**).*[2f] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 9:1 hexane/EtOAc as the eluant. The indicated compound was obtained as a colorless oil in 71% yield (180 mg): $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.41−7.12 (m, 5H), 3.98 (ddd, $J$ = 10.0, 5.5, 1.8 Hz, 1H), 2.99 (ddd, $J$ = 13.8, 9.1, 4.7 Hz, 1H), 2.86−2.71 (m, 2H), 2.47−2.31 (m, 1H), 2.04−1.91 (m, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 140.7, 128.6, 128.5, 126.3, 104.1, 82.0, 32.9, 31.9; HRMS $m/z$ calcd for $C_{10}H_{11}Cl_3O$, 251.9875; found 251.9885.

*1,1,1-Trichloroundecan-2-ol (**3g**).* The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as a colorless oil in 60% yield (165 mg): IR (film) 3431, 2926, 2856, 1461, 1266 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 360 MHz) $\delta$ 4.00 (ddd, $J$ = 9.4, 5.6, 1.9 Hz, 1H), 2.65 (dd, $J$ = 5.6, 1.5 Hz, 1H), 2.11−1.98 (m, 1H), 1.74−1.56 (m, 2H), 1.50−1.41 (m, 1H), 1.37−1.21 (m, 12H), 0.88 (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 104.4, 83.0, 31.9, 31.5, 29.5, 29.4, 29.3, 29.2, 26.1, 22.7, 14.1; HRMS $m/z$ calcd for $C_{10}H_{21}O$, 157.1592; found 157.1586, which corresponds to [M − CCl3]$^+$.

*6-[(tert-Butyldimethylsilyl)oxy]-1,1,1-trichlorohexan-2-ol (**3h**).*[2f] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as a colorless oil in 62% yield (208 mg): $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 4.01 (ddd, $J$ = 9.0, 5.6, 1.8 Hz, 1H), 3.69−3.63 (m, 2H), 2.89 (s, 1H), 2.14−2.04 (m, 1H), 1.78−1.48 (m, 5H), 0.90 (s, 9H), 0.06 (s, 6H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 104.3, 83.1, 63.0, 32.2, 31.2, 22.8, 19.2, 18.4, −5.3; HRMS $m/z$ calcd for $C_8H_{16}Cl_3SiO_2$ [M − C4H9]$^+$, 276.9985; found 276.9977.

*2,2,2-Trichloro-1-cyclohexylethanol (**3i**).*[2f] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as a colorless oil in 73% yield (169 mg): $^1$H NMR ($CDCl_3$, 360 MHz) $\delta$ 3.86 (d, $J$ = 2.2 Hz, 1H), 2.78 (d, $J$ = 6.0 Hz, 1H), 2.15−1.96 (m, 2H), 1.82−1.64 (m, 4H), 1.48−1.14 (m, 5H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 104.2, 86.4, 39.9, 32.9, 26.7, 26.5, 26.0, 25.9; HRMS $m/z$ calcd for $C_7H_{13}O$ [M − $CCl_3$]$^+$, 113.0966; found 113.0965.

*2,2,2-Trichloro-1-furan-2-yl-ethanol (**3j**).*[2f] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as a white solid in 70% yield (151 mg): mp 34−35 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.47 (d, $J$ = 1.7 Hz, 1H), 6.61 (d, $J$ = 3.3 Hz, 1H), 6.44 (dd, $J$ = 3.3, 1.7 Hz, 1H), 5.24 (d, $J$ = 7.3 Hz, 1H), 3.34 (d, $J$ = 7.3 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) 148.4, 143.1, 110.9, 110.7, 101.2, 79.3; HRMS $m/z$ calcd for $C_6H_5Cl_3O_2$, 213.9355; found 213.9352.

*2,2,2-Trichloro-1-thiophen-2-ylethanol (**3k**).*[2f] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as an off-white solid in 61% yield (140 mg): mp 29−30 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.41 (dd, $J$ = 5.1, 1.2 Hz, 1H), 7.33−7.31 (m, 1H), 7.05 (dd, $J$ = 5.1, 3.6 Hz, 1H), 5.48 (d, $J$ = 4.7 Hz, 1H), 3.30 (d, $J$ = 4.7 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 137.3, 129.1, 127.1, 126.3, 102.5, 81.6; HRMS $m/z$ calcd for $C_6H_5Cl_3SO$, 229.9127; found 229.9122.

*(E)-1,1,1-Trichloro-4-phenylbut-3-en-2-ol (**3l**).*[24] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as an off-white solid in 62% yield (156 mg): mp 62−63 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.45 (d, $J$ = 7.2 Hz, 2H), 7.29−7.38 (m, 3H), 6.91 (d, $J$ = 15.9 Hz, 1H), 6.38 (dd, $J$ = 15.9, 5.9 Hz, 1H), 4.78 (t, $J$ = 5.9 Hz, 1H), 2.98 (d, $J$ = 5.9 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 136.8, 135.6, 128.7, 128.6, 126.9, 122.6, 102.8, 83.4; HRMS $m/z$ calcd for $C_{10}H_9Cl_3O$, 249.9719; found 249.9729.

*1,1,1-Trichloro-4-methylpent-3-en-2-ol (**3m**).*[2f,25] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as a white solid in 80% yield (163 mg): mp 85−86 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 5.36 (dd, $J$ = 8.3, 1.2 Hz, 1H), 4.78 (dd, $J$ = 8.3, 6.0 Hz, 1H), 2.67 (d, $J$ = 6.0 Hz, 1H), 1.83 (s, 3H), 1.81 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 142.5, 119.5, 103.6, 79.5, 26.1, 19.2; HRMS $m/z$ calcd for $C_5H_9O$, 85.0653; found 85.0650, which corresponds to [M − CCl3]$^+$.

*1,1,1-Trichloro-4-phenylbut-3-yn-2-ol (**3n**).*[23] The crude material (prepared following Method A) was purified by flash chromatography through a plug of silica gel using 95:5 hexane/EtOAc as the eluant. The indicated compound was obtained as a colorless oil in 34% yield (85 mg): $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.54−7.47 (m, 2H), 7.42−7.29 (m, 3H), 5.04 (d, $J$ = 9.0 Hz, 1H), 3.10 (d, $J$ = 9.0 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 132.0, 129.4, 128.4, 121.2, 101.1, 88.1, 83.0, 75.8; HRMS $m/z$ calcd for $C_{10}H_7Cl_3O$, 247.9562; found 247.9559.

*1,1,1-Trichloronon-3-yn-2-ol (**3o**).* The crude material (prepared following Method B) was purified by flash chromatography through a plug of silica gel using 98:2 hexane/EtOAc as the eluant. The indicated compound was obtained as a colorless oil in 18% yield (45 mg): IR (film) 3387, 2932, 2860, 1621, 1379 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.78 (dt, $J$ = 8.8, 1.9 Hz, 1H), 2.95 (d, $J$ = 8.8 Hz, 1H), 2.26 (td, $J$ = 7.1, 1.9 Hz, 2H), 1.60−1.49 (m, 2H), 1.43−1.26 (m, 4H), 0.90 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 101.6, 89.8, 75.4, 74.6, 30.9, 27.7, 22.1, 18.6, 13.9; HRMS $m/z$ calcd for $C_8H_{13}O$ [M − $CCl_3$]$^+$, 125.0966; found 125.0968.

*(S)-(−)-2,2,2-Trichloro-1-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-ethanol ((S,S)-**3p**).* The crude material (prepared following Method B) was purified by flash chromatography through a plug of 1% pyridine-saturated silica gel using 95:5 hexane/EtOAc as the eluant. A 67:33 mixture of diastereomers ((***S,S***)-**3p**) and ((***S,R***)-**3p**), respectively, was afforded in combined 72% yield (178 mg). Pure ((***S,S***)-**3p**) was obtained as a white crystal. No racemization was indicated in the NMR spectra of the Mosher ester derivative; see theSupporting Information for details: mp 80−82 °C; $[\alpha]_D^{20}$ −21.3 ($c$ 3.8, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 4.59 (ddd, $J$ = 3.0, 6.5, 6.5 Hz, 1H), 4.36 (dd, $J$ = 4.0, 3.5 Hz, 1H), 4.27 (dd, $J$ = 6.5, 9.0 Hz, 1H), 4.10 (dd, $J$ = 6.5, 9.0 Hz, 1H), 3.06 (d, $J$ = 4.0 Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 109.2, 100.6, 82.4, 75.1, 64.7, 26.3, 25.3; HRMS $m/z$ calcd for $C_6H_{11}O_3$, 131.0708; found 131.0711, which corresponds to [M − CCl3]$^+$.

*(R)-(−)-2,2,2-Trichloro-1-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-ethanol ((S,R)-**3p**).* The crude material (prepared following Method B) was purified by flash chromatography through a plug of 1% pyridine-saturated silica gel using 95:5 hexane/EtOAc as the eluant. A 67:33 mixture of diastereomers ((***S,S***)-**3p**) and ((***S,R***)-**3p**), respectively, was afforded in 72% combined yield (178 mg). Pure ((***S,R***)-**3p**) was obtained as a colorless oil. No racemization was indicated in the NMR spectra of the Mosher ester derivative; see the Supporting Information for details: $[\alpha]_D^{20}$ −10.5 ($c$ 2.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 4.57 (ddd, $J$ = 2.5, 6.5, 6.5 Hz, 1H), 4.25 (dd, $J$ = 6.5, 8.5 Hz, 1H), 3.98 (dd, $J$ = 2.5, 8.5 Hz, 1H), 3.91 (dd, $J$ = 7, 8.5 Hz, 1H), 3.72 (d, $J$ = 8.5 Hz, 1H), 1.49 (s, 3H), 1.44 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 110.9, 101.3, 81.1, 73.2, 68.4, 26.1, 25.7; HRMS $m/z$ calcd for $C_7H_{11}O_3Cl_3$, 246.9696; found 246.9701.

**General Procedure for the Preparation of One-Carbon Homologated Carboxylic Acids from Trichloromethyl Carbinols.** Diphenyl diselenide (374 mg, 1.2 mmol) was added under a blanket of argon to a dry round-bottom flask equipped with a stir bar. Absolute ethanol (4 mL) was added, the system was cooled to 0 °C, and the solution was deoxygenated by passing argon through a needle submersed in the EtOH. After 30 min, $NaBH_4$ (95 mg, 2.5 mmol) was added rapidly in one portion. Once the yellow solution became colorless (<5 min), the ice bath was removed, and the solution was stirred for an additional 30 min. Neat trichloromethyl carbinol (1.0 mmol) was quickly added, followed by powdered NaOH (240 mg, 6.0 mmol). The solution purge needle was removed, and the reaction was


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heated to 40 °C under argon and allowed to mix for 24−36 h while being monitored for consumption of starting material by TLC. (Note: diphenyl diselenide rapidly reforms if oxygen is introduced into the system. Leaving the argon purge needle submersed in the EtOH until all components are added can improve product yields.) After completion, the ethanol was removed by rotary evaporation, and the amorphous solids were dissolved in 5 mL of ethyl acetate and 5 mL of $H_2O$. The resulting solution was cooled to 0 °C and adjusted to pH 1 with 1 N HCl. The product was extracted with ethyl acetate (5 × 10 mL), dried ($Na_2SO_4$), and then concentrated by rotary evaporation. The crude material was purified by flash chromatography through a small plug of silica using the specified eluants, affording the pure carboxylic acid.

*Naphthalen-2-ylacetic Acid (**4**).*[27] The crude material was purified by flash chromatography through a plug of silica gel using hexane to remove diphenyldiselenide and then 8:2 hexane/EtOAc as the eluant. The indicated compound was obtained as a white solid in 94% yield (175 mg): mp 142−143 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 11.00 (brs, 1H), 7.84−7.79 (m, 3H), 7.74 (s, 1H), 7.49−7.45 (m, 2H), 7.41 (dd, 1H, $J$ = 4.5 Hz, 13.5 Hz), 3.82 (s, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 177.4, 133.4, 132.6, 130.7, 128.3, 128.2, 127.7, 127.7, 127.3, 126.2, 125.9, 41.1; HRMS $m/z$ calcd for $C_{12}H_{10}O_2$, 186.0681; found 186.0683.

*4-Phenylbutanoic Acid (**5**).*[26] The crude material was purified by flash chromatography through a plug of silica gel using hexane to remove diphenyldiselenide and then 85:15 hexane/EtOAc as the eluant. The indicated compound was obtained as a colorless crystal in 90% yield (148 mg): mp 50−51 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 10.70 (brs, 1H), 7.29 (dd, 2H, $J$ = 7.5, 7.5 Hz), 7.22−7.17 (m, 3H), 2.68 (t, 2H, $J$ = 7.5 Hz), 2.39 (t, 2H, $J$ = 7.5 Hz), 2.01−1.95 (m, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 179.5, 141.2, 128.5, 128.4, 126.0, 35.0, 33.3, 26.2; HRMS $m/z$ calcd for $C_{10}H_{12}O_2$, 164.0842; found 164.0837.

*2-(Furan-2-yl)acetic Acid (**6**).*[2f,28] The crude material was purified by flash chromatography through a plug of silica gel using hexane to remove diphenyldiselenide and then 85:15 hexane/EtOAc as the eluant. The indicated compound was obtained as a white solid in 92% yield (116 mg): mp 60−61 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 10.96 (brs, 1H), 7.38 (dd, 1H, $J$ = 1.8, 0.7 Hz), 6.37 (dd, 1H, $J$ = 3.2, 1.8 Hz), 6.28 (dd, 1H, $J$ = 3.2, 0.7 Hz), 3.77 (s, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 173.7, 146.9, 142.3, 110.6, 108.4, 33.5; HRMS $m/z$ calcd for $C_6H_6O_3$, 126.0321; found 126.0317.

*4-Methylpent-3-enoic Acid (**7**).*[2f,29] The crude material was purified by flash chromatography through a plug of silica gel using hexane to remove diphenyldiselenide and then 9:1 hexane/EtOAc as the eluant. The indicated compound was obtained as a yellow oil in 95% yield (108 mg): $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 5.31−5.29 (m, 1H), 3.07 (d, 2H, $J$ = 7 Hz), 1.75 (s, 3H), 1.64 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 178.7, 136.3, 115.0, 33.5, 25.6, 17.9; HRMS $m/z$ calcd for $C_6H_{10}O_2$, 114.0681; found 114.0678.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

NMR spectra ($^1$H and $^{13}$C) of all products, $^{19}$F spectra of **3d**, and Mosher ester derivatives of **3p**. This material is available free of charge via the Internet at http://pubs.acs.org

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### Notes

The authors declare no competing financial interest.

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