Note

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Trichloromethanesulfonyl chloride: a chlorinating reagent for aldehydes

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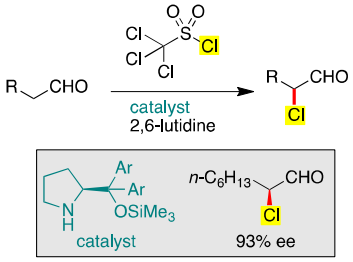
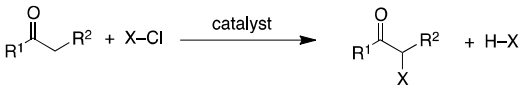


Abstract. Trichloromethanesulfonyl chloride (CCl_3SO_2Cl), a commercially available reagent, has been found to perform efficiently in the α-chlorination of aldehydes, including its catalytic asymmetric version, under very mild reaction conditions. Under our reaction conditions, this compound outperforms typical chlorinating reagents for organic synthesis, facilitates work-up and purification of the product, and minimizes the formation of toxic, chlorinated organic waste.

α-Chlorinated aldehydes are very useful building blocks for synthesis of a of pharmaceutically important compounds.[1] They can be prepared via a variety of reactions, among them, the direct catalytic α-chlorination of ketones and aldehydes is the most established procedure (Scheme 1). The catalysts used for this transformation are metal derivatives and secondary amines. By using chiral secondary amine catalysts, enantioselective α-chlorinations of aldehydes and ketones have been reported.



Scheme 1. General representation of the α-chlorination of ketone and aldehydes.

The selection of the chlorinating agent is also a key element of the process since it determines the nature of the by-products. It also strongly influences the mechanism of the chlorination reaction and therefore the yield as well as the level of enantioselectivity of the process.[2] Numerous different chlorinating reagents have been used, ranging from inorganic compounds to polychlorinated organic molecules. Molecular chlorine may be considered the most atom economical, but its high reactivity and the difficulties associated with handling of this gas make it often impractical. No asymmetric version is known using gaseous chlorine, but a clever approach using lithium chloride combined with a strong oxidant like sodium persulfate and copper(II) salts has been described.[5] Enantioselective catalytic chlorination are typically run with a chlorinated organic compound such as *N*-chlorosuccinimide (NCS) and a metal-[6-10] or an organocatalyst.[11-18] Other useful reagents include hypervalent iodine compounds,[19] *N*-chlorophthalimide,[20] 2,2,6,6-tetrachlorocyclohexanone,[21] hexachlorocyclohexadienone,[22-25] and trichloroquinolinone,[26] They have been widely used in combination with organocatalysts or metal catalysts. In any case, organic waste in the form of succinimide, phthalimide, chlorocyclohexanones and chlorophenols are generated requiring a careful purification of the products. Sulfuryl chloride[27] and *p*-toluenesulfonyl chloride (TsCl)[28] have also been employed with some success. Trichloromethylsulfonyl chloride had been also used as a chlorinating reagent of preformed silyl enol ethers in a ruthenium-catalyzed process.[29] Interestingly, trifluoromethanesulfonyl fluoride (CF_3SO_2F) have been used in both non-catalyzed[30] and asymmetric metal-catalyzed fluorination reactions.[31]

Recently, we described how the commercially available trichloromethanesulfonyl chloride, was an extremely efficient reagent for radical carbochlorination reactions.[32,33] When trying to extend this reaction to the carbochlorination of enamines with trichloromethylsulfonyl chloride, we discovered that instead of the desired reaction, an electrophilic chlorination was taking place. Based on this initial observation, we report here a fast and clean method for the α-monochlorinations of aldehydes using pyrrolidine-type catalysts and trichloromethanesulfonyl chloride.[34-38] This reagent proved to behave also very well in an enantioselective version of this reaction outperforming other well-established chlorinating

agents.

The reaction conditions were optimized for the chlorination of 3-phenylpropanal (**1a**) using pyrrolidine as a catalyst in different solvents in the presence and in the absence of a base and water (eq. 1). Results are summarized in Table 1. Reaction in dry CH_2Cl_2 without base was disappointing, the conversion just reached only 31% and a mixture of mono- (**2a**) and dichlorinated (**2a'**) aldehydes was obtained (entry 1, Table 1). In 1,2-dimethoxyethane (DME), the conversion was even lower (entry 2, Table 1). Gratifyingly, when two equivalents of a base, 2,6-lutidine, was added, the conversion reached 98% but 1:1 mixture of mono- and dichlorinated products were obtained. When three equivalents H_2O was added in the absence of a base, only the monochlorinated aldehyde **2a** was detected, but the reaction was very slow (entry 4, Table 1). The combination of 2,6-lutidine (2 equivalents) and H_2O (3 equivalents) gave the best results (Table 1, entry 5). After reduction of the crude chlorinated aldehyde **2a** with $NaBH_4$, the stable 2-chloroalcohol **3a** was obtained in 95% yield (entry 5, Table 1). The use of dichloromethane in the presence of 2,6-lutidine and H_2O led to full conversion but lower chemoselectivity (Table 1, entry 6), which, after reductive work up, led to alcohol **3a** in lower yield.

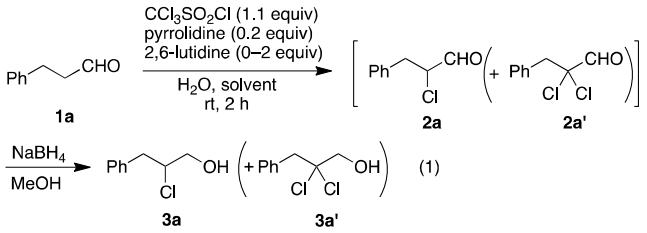


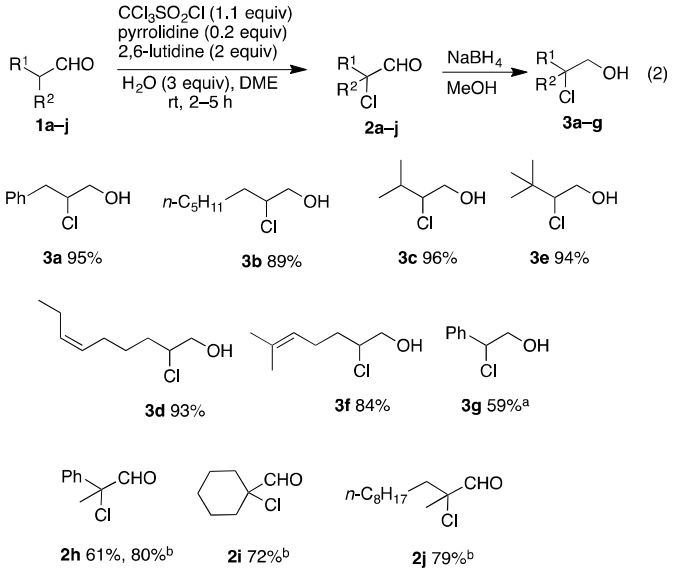
Table 1. Optimization of the chlorination reaction of **1a** according to Equation 1.

Entry	Solvent	2,6-Lutidine	H_2O	Conversion[a]	2a/2a'	Yield 3a[b]
1	CH_2Cl_2	-	-	31	1:1	-
2	DME	-	-	<20	1:1	-
3	DME	2 equiv	-	>98	1:1	-
4	DME	-	3 equiv	49	>99:1	-
5	DME	2 equiv	3 equiv	>99	>99:1	95%

6	CH_2Cl_2	2 equiv	3 equiv	>99[c]	4:1	74%

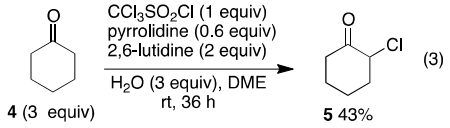
[a] Determined by ^{1}H-NMR on the crude mixture. [b] Isolated yield after flash chromatography.

The scope and limitation of the method was then examined with a range of aliphatic aldehydes (Scheme 2). Unsubstituted aldehydes **1a**–**1d** provided the desired β-chloro alcohols **3a**–**3d** in ≥89% yield. Substrates containing double bonds such as **1d** and **1f** reacted smoothly too. Phenylacetaldehyde **1g** provided the desired product **3g** in moderate yield together with some dichlorinated product. This result may be explained by the increased acidity of this system that favors a rapid isomerization of the α-chloroiminium ion to the chloroenamine competing with the hydrolysis step. Then, sterically more demanding α-substituted aldehydes were tested. Reaction of 2-phenylpropanal **1h** was slower, and the amount of CCl_3SO_2Cl had to be increased to 1.4 equivalents and the temperature to 60 °C. Under these conditions, the desired aldehyde was isolated in 61% yield. In the course of the reaction, a white precipitate appeared that we identified as the result of reaction of 2,6-lutidine with CCl_3SO_2Cl. The structure of this precipitate could not be characterized but it showed a complex oligomeric nature. We rationalized that the rate of enamine formation from aldehydes and pyrrolidine decreased with α-substitution of the aldehydes and therefore the reaction between the base and the trichloromethylsulfonyl chloride can proceed, thus reducing the efficacy of the process. To avoid this competing reaction, the bulkier 2,6-di-*tert*-butylpyridine was used as a base and the yield increased to 80% after 5 hours. This procedure was then applied with success to other α-disubstituted aldehydes such as **1i** and **1j**.



Scheme 2. α-Chlorination of aldehydes with CCl_3SO_2Cl and pyrrolidine as a catalyst. [a]) 2,2-Dichloro-2-phenyl-ethan-1-ol (16%) is also formed. [b]) Using 2,6-di-*tert*-butylpyridine instead of 2,6-lutidine and 1.3 equivalents of CCl_3SO_2Cl.

Next, the chlorination of cyclohexanone **4** was examined (eq. 3). When 1.1 equivalents of CCl_3SO_2Cl were used under the optimized conditions developed for aldehydes (see above), the major product was the dichlorinated cyclohexanone. However, when using cyclohexanone in excess and longer reaction time (36 h), the desired α-chlorocyclohexanone **5** was obtained in a modest 43% yield together with some polychlorinated products. All attempts to improve this yield by using bases such as 2,6-di-tert-butylpyridine were unsuccessful (Scheme 3).



Scheme 3. α-Chlorination of cyclohexanone.

The efficient pyrrolidine catalyzed α-chlorination of aldehydes using CCl_3SO_2Cl as an electrophilic source of chlorine atom offers the possibility of developing an organocatalytic asymmetric version of this reaction. The α-chlorination of 3-phenylpropanal **1a** and *n*-octanal **1b** was investigated (equation 4, Table 2). 2,6-Lutidine was used as a base and DME as a

solvent.[2] A rapid initial screening of commercial asymmetric organocatalysts showed that the simple diarylprolinol silyl ether **6** is a suitable catalyst for this reaction.[39,40] Surprisingly, this commercially available and general catalyst has not been used in chlorination reaction at the exception of the mechanistic work of Blackmond.[2] The addition of a small amount of water (3 equiv.) was essential for the reaction to proceed efficiently.[41,42] To avoid racemization, the chlorinated aldehydes (*S*)-**2a** and (*S*)-**2b** were not isolated but directly reduced with sodium borohydride to the corresponding alcohol (*S*)-**3a** and (*S*)-**3b**. The alcohol (*S*)-**3a** was obtained in 74% yield and 81% ee (Table 2, entry 1). Aldehyde **1b** was converted to (*S*)-**3b** in 98% yield and 93% ee under the same reaction conditions (Table 2, entry 5). The absolute configuration of (*S*)-**3a** and (*S*)-**3b** were attributed based on comparison of measured optical rotations with literature values (See SI).[5] Both yields and ee's compare well with the results described in the literature.[5,14,17,24] Higher ee's were only reported by Jorgensen[14] (2 × 95% ee) and MacMillan[24] (92% and 52% ee) for the chlorination of aldehydes **1a** and **1b**, respectively. The ee's and yields obtained under our conditions are noticeably higher than the one obtained by Blackmond with the same catalyst and NCS for the chlorination of 3-methylpropanal.[2] For comparison purposes, the chlorination of **1a** with NCS was performed with and without 2,6-lutidine. Both reaction conditions afforded low enantioselectivities and low to moderate yields (Table 2, entries 2 and 3). Other chlorinating agents were also tested under our reaction conditions: hexachlorocyclohexadienone and trifluoromethanesulfonyl chloride gave with both substrates lower yields and enantioselectivities, (Table 2, entries 4, 6 and 7) but always the same absolute configuration of product.

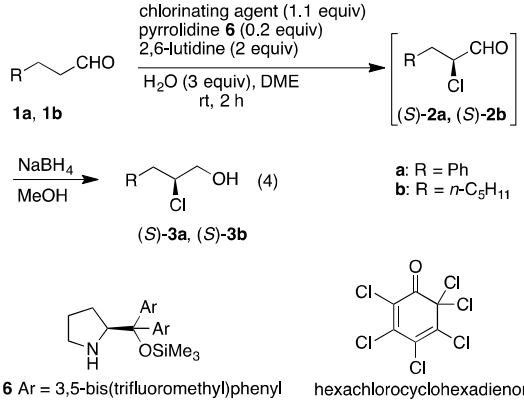
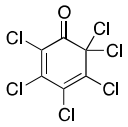
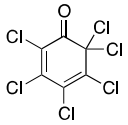


Table 2. Enantioselective chlorination of aldehydes according to equation 4.

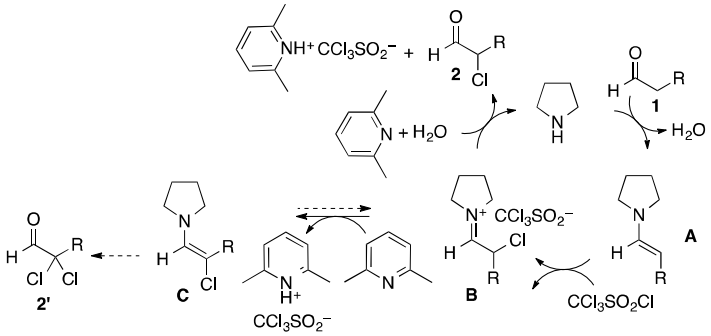
Entry	Aldehyde **1**	Reagent	Yield (*S*)-**3a/3b**[b]	Ee's (*S*)-**3a/3b**[c]

1	**1a** (R = Ph)	CCl_3SO_2Cl	74%	81% ee
2	**1a** (R = Ph)	NCS	<10%	26% ee
3[a]	**1a** (R = Ph) [a]	NCS [a]	50% [a]	6% ee[a]
4	**1a** (R = Ph)		76%	69% ee
5	**1b** (R = *n*-C_5H_{11})	CCl_3SO_2Cl	95%	93% ee
6	**1b** (R = *n*-C_5H_{11})		66%	82% ee
7	**1b** (R = *n*-C_5H_{11})	CF_3SO_2Cl	57%	84% ee

[a]) Without 2,6-lutidine according to Blackmond's conditions.[2] [b]) Isolated yield after flash chromatography. [c]) Determined by HPLC or GC on chiral stationary phases.

Trichloromethanesulfonic chloride is a very potent source of electrophilic chlorine atom. Its reactivity may be rationalized by the acidity of the trichloromethanesulfinic acid (pKa 2.19) that lies very close to trifluoromethanesulfinic acid (pKa 2.09). Trichloromethanesulfinic acid is several orders of magnitude more acidic that pentachlorophenol (pKa 4.68) and succinimide (pKa 9.62), the conjugated acids of the anion generated when hexachlorocyclohexadienone and *N*-chlorosuccinimide are used as source of electrophilic chlorine atom. Concerning the mechanism of this process, we believe that the reaction involves a conventional enamine formation, chlorination, and hydrolysis pathway (Scheme 4). In contrast to the work of Jorgensen[13] and Blackmond,[2] no formation of an adduct between the iminium ion **B** and the trichloromethylsulfinate could be detected by ^{1}H-NMR. Either such an adduct decomposes rapidly in the presence of 2,6-lutidine or it is not formed. Indeed, it seems reasonable to have a direct and possibly reversible conversion of the iminium **B** to the chloroenamine **C** in presence of 2,6-lutidine. A second chlorination of chloroenamine **C** rationalize the formation of the 2,2-dichloroaldehyde **2'** side product. In the asymmetric version of the reaction, the stereocontrol is set either during the chlorination of enamine **A** or during the protonation of enamine **C**. If, as expected based on minimization of dipole–dipole interactions, enamine **C** exists preferentially in a *E* geometry, both reactions should lead to the same enantiomer of **2**. However, if a fast reversible formation of enamine

C from iminium **B** is reached, the situation becomes more complex and the rate of hydrolysis of the diastereomeric forms of iminium ion **B** may also influence the stereochemical outcome of the reaction. The *N*-chlorination–sigmatropic rearrangement mechanism proposed by Jorgensen[13] cannot be ruled out but it is inconsistent with the observed influence of the chlorinating agent on the level of enantioselectivity.



Scheme 4. Proposed mechanism for the chlorination reaction

In conclusion, an efficient procedure for the α-chlorination of aldehydes using trichloromethylsulfonyl chloride as source of electrophilic chlorine atom has been developed. The reaction takes place in the presence of 2,6-lutidine to neutralize the trichloromethanesulfonic acid generated during the reaction. Due to the ionic nature of the 2,6-lutidinium trichloromethanesulfonate by-product , the pure β-chloroalcohols are easily obtained after acid washing and flash chromatography through silica gel.

Experimental Section

General. Commercially available solvents and reagents were used as received. Reactions were performed in standard laboratory glassware under atmospheric conditions, without any special caution. Silica gel 60 Å (40-63 µm) was used for flash column chromatography (FC). ^{1}H and ^{13}C NMR spectra were recorded on a spectrometer operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C at 22 °C unless otherwise stated. Chemical shift data are reported in units of δ (ppm) using residual $CHCl_3$ as the internal standard (δ = 7.26 for ^{1}H NMR spectra and δ = 77.0 for ^{13}C NMR spectra). Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad) for ^{1}H spectra. Coupling constants, *J*, are reported in Hz. GC-MS were obtained with gas chromatograph coupled to a single quadrupole mass spectrometry detector (EI, 70 ev). HRMS were measured on a double-focusing magnetic

sector mass spectrometer in EI mode at 45 eV. Determination of enantiomeric excesses by HPLC analyses were performed on a Chiralcel IA column, with a 90:10 mixture of hexanes/isopropanol at 0.9 mL/min flow. Determination of enantioselective excess by GC analyses were performed on a Chiraldex Tau column, at 90 °C isothermal.

Experimental procedures for the α-chlorination of aldehydes:

General Procedure A: Pyrrolidine catalyzed chlorination. A 10 mL two-necked flask was charged with the aldehyde (1.0 mmol), DME (2 mL), pyrrolidine (16 µL, 0.2 mmol), 2,6-lutidine (230 µL, 2.0 mmol) and H_2O (54 µl, 3.0 mmol). Cl_3CSO_2Cl (240 mg, 1.1 mmol) was added to this mixture and the solution was stirred at rt for 2 to 4 h. After the aldehyde was completely consumed (NMR monitoring), the reaction mixture was diluted with MeOH (4 mL), cooled to 0 ^{o}C and $NaBH_4$ (150 mg, 4.0 mmol) was added. After 25 min, the reaction mixture was warmed to room temperature for 5 min and CH_2Cl_2, was added followed by saturated NH_4Cl (10 mL). The solution was extracted with CH_2Cl_2, the organic phases were washed with diluted HCl and brine successively, dried over anhydrous Na_2SO_4, filtered and finally concentrated *in vacuo*. Purification of the resulting oil by FC with pentane/TBME afforded the desired 2-chloroalcohol.

General Procedure B: Pyrrolidine catalyzed chlorination. A 10 mL two-necked flask was charged with aldehyde (1.0 mmol), DME (2 mL), pyrrolidine (16 µL, 0.2 mmol), 2,6-*tert*-butyl-pyridine (450 µL, 2.0 mmol) and H_2O (54 µL, 3.0 mmol). Cl_3CSO_2Cl (305 mg, 1.4 mmol) was added and the reaction mixture was stirred at 60 ^{o}C for 5 h. After the aldehyde was completely consumed (NMR monitoring), CH_2Cl_2 and saturated NH_4Cl (10 mL) were added. The solution was extracted with CH_2Cl_2, the combined organic phases were washed with diluted HCl and brine, dried (Na_2SO_4), filtered and then concentrated *in vacuo*. Purification of the resulting oil by FC with pentane/TBME afforded the desired α-chloroaldehyde or α-chloroketone.

General Procedure C: Enantioselective Chlorination. The chlorinating reagent (0.55 mmol) was dissolved in DME (1 mL) and then the aldehyde (0.5 mmol) and 2,6-lutidine (117 µl, 1 mmol) were successively added followed by the chiral amine **6** (60 mg, 0.1 mmol) and by water (27 µl, 1.5 mmol). The mixture was stirred at rt for 2 h and then treated with H_2O, acidified with 0.2 M HCl and extracted with Et_2O. The combined organic layers were washed with 0.5 M HCl (2 ×), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was dissolved in MeOH (2 mL) and $NaBH_4$ (83 mg, 2.2 mmol) was added at 0 °C. After 30 min, the reaction was treated with sat. aq. NH_4Cl and extracted with CH_2Cl_2. The product was

purified by FC eluting with mixture of pentane/TBME of increasing polarity.

2-Chloro-3-phenyl-propan-1-ol 3a. Prepared according to the General Procedure A from 3-phenylpropanal **1a** (130 µL, 1 mmol), 2 h reaction time. Colorless oil, 162 mg (95% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.26 (m, 5H), 4.31-4.23 (m, 1H), 3.88-3.81 (m, 1H), 3.77-3.69 (m, 1H), 3.14 (qd, *J* = 7.2, 14.1 Hz, 2H), 2.10 (t, *J* = 7.2 Hz, 1H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 137.1, 129.4, 128.6, 127.0, 65.9, 64.9, 40.8 ppm. In accordance to reported literature data.[5]

2-Chloro-octan-1-ol 3b. Prepared according to the General Procedure A from 1-octanal (160 µL, 1 mmol), 2 h reaction time. Colorless oil, 147 mg (89% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.06-3.98 (m, 1H), 3.82-3.74 (m, 1H), 3.70-3.61 (m, 1H), 2.12 (dd, *J* = 5.7, 7.8 Hz, 1H), 1.83-1.64 (m, 2H), 1.57-1.28 (m, 8H), 0.88 (t, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 67.1, 65.4, 34.3, 31.6, 28.8, 26.3, 22.6, 14.0 ppm. In accordance to reported literature data.[5]

2-Chloro-3-methyl-butan-1-ol 3c. Prepared according to the General Procedure A from isovaleraldehyde (107 µL, 1 mmol), 4 h reaction time. Colorless oil, 118 mg (96% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.95-3.89 (m, 1H), 3.85-3.69 (m, 2H), 2.11-2.03 (m, 1H), 2.00-1.93 (m, 1H), 1.03 (d, *J* = 6.0 Hz, 3H), 1.01 (d, *J* = 6.0 Hz, 3H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 71.9, 65.5, 31.5, 20.0, 18.2 ppm. In accordance to reported literature data.[43,44]

(*Z*)-2-Chloro-non-6-en-1-ol 3d. Prepared according to the General Procedure A from *cis*-6-nonenal (170 µL, 1 mmol), 2 h reaction time. Colorless oil, 164 mg (93% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.45-5.25 (m, 2H), 4.06-3.98 (m, 1H), 3.83-3.75 (m, 1H), 3.70-3.62 (m, 1H), 2.13-1.98 (m, 5H), 1.83-1.42 (m, 4H), 0.96 (t, *J* = 7.5 Hz, 3H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 132.5, 128.1, 67.0, 65.2, 33.8, 26.5, 26.4, 20.6, 14.3 ppm. EI-MS: *m/z* (rel. intensity) 176 (M^+, 0.7), 140 (7), 123 (11), 109 (16), 93 (22), 81 (42), 67 (96), 41 (100). EI-HRMS cacld. for M^+ ($C_9H_{17}ClO$): 176.0969, found 176.0968. In accordance to reported literature data.[5]

2-Chloro-3,3-dimethyl-butan-1-ol 3e. Prepared according to the General Procedure A from 3,3-dimethylbutanal (125 µL, 1 mmol), 4 h reaction time. Colorless oil, 128 mg (94% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.03-3.86 (m, 2H), 3.69-3.61 (m, 1H), 2.05-2.01 (m, 1H), 1.04 (s, 9H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 76.9, 64.0, 34.9, 27.0 ppm. In accordance to reported literature data.[14]

2-Chloro-3,7-dimethyloct-6-en-1-ol 3f. Prepared according to the General Procedure A from *rac*-citronellal (180 µL, 1 mmol), 4 h reaction time. Colorless oil, 160 mg (84% yield). Mixture of diastereomers (The ratio is about 55:45). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.07 (m, 1H), 4.07 (m, 0.55 H, diast. A), 3.97 (m, 0.45 H, diast. B), 3.86-3.69 (m, 2H), 2.11-1.84 (m, 4H), 1.68 (s,

3H), 1.60 (s, 3H), 1.47 (m, 1H), 1.32 (m, 1H), 1.02 (d, *J* = 6.9 Hz, 1.4H, diast. B), 0.95 (d, *J* = 6.9 Hz, 1.6H, diast. A) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, diast. A and B) δ 132.1(A), 132.0(B), 123.9(A), 123.8(B), 71.1(A), 70.1(B), 65.8(B), 64.9(A), 36.4(A), 35.3(B), 34.3(B), 32.8(A), 25.7(A and B), 25.3(A and B), 17.7(A and B), 16.3(A), 14.6(B) ppm. EI-MS: *m/z* (rel. intensity) 190 (M^+, 1), 172 (2), 137 (8), 121 (12), 95 (15), 82 (28), 69 (100), 55 (65), 41 (75). EI-HRMS cacld. for M^+ ($C_{10}H_{19}ClO$): 190.1126, found 190.1124. In accordance to reported literature data.[45]

2-Chloro-2-phenyl-ethan-1-ol 3g. Prepared according to the General Procedure A from phenylacetaldehyde (115 µL, 1 mmol), 2 h reaction time. Colorless oil, 92 mg (59% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.00 (dd, *J* = 5.7, 7.2 Hz, 1H), 3.96-3.92 (m, 2H), 2.17 (br, 1H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 137.9, 128.9, 128.8, 127.5, 67.9, 64.9 ppm. In accordance to reported literature data.[46]

2-Chloro-2-phenyl-propan-1-al 2h. Prepared according to the General Procedure B from 2-phenylpropionaldehyde (134 µL, 1 mmol). Colorless oil, 135 mg (80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.45 (s, 1H), 7.49-7.36 (m, 5H), 1.98 (s, 3H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 191.7, 129.0, 128.9, 126.7, 77.0, 25.5 ppm. In accordance to reported literature data.[47]

1-Chloro-cyclohexanecarbaldehyde 2i. Prepared according to General Procedure B from cyclohexanecarboxaldehyde (105 µL, 1 mmol). Colorless oil, 106 mg (72% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.40 (s, 1H), 1.93-1.89 (m, 4H), 1.86-1.71 (m, 2H), 1.64-1.58 (m, 3H), 1.40-1.29 (m, 1H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 195.3, 74.4, 33.6, 24.9, 21.7 ppm. In accordance to reported literature data.[48]

2-Chloro-2-methyl-undecan-1-al 2j. Prepared according to the General Procedure B from 2-methylundecanal (220 µL, 1 mmol). Colorless oil, 173 mg (79% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.43 (s, 1H), 1.98-1.78 (m, 2H), 1.58 (s, 3H), 1.43-1.26 (m, 14H), 0.88 (t, *J* = 6.6 Hz, 3H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 195.9, 73.6, 38.7, 31.9, 29.6, 29.5, 29.4, 29.3, 24.2, 23.6, 22.7, 14.1 ppm. EI-MS: *m/z* (rel. intensity) 218 (M^+, 0.5), 142 (3), 111 (18), 97 (53), 92 (52), 83 (39), 69 (61), 55 (100), 43 (53).[49]

(*S*)-2-Chloro-3-phenyl-propan-1-ol (*S*)-3a. Prepared according to General Procedure C from trichloromethane sulfonyl chloride (120 mg, 0.55 mmol) and 3-phenylpropanal **1a** (65 µL, 0.5 mmol). (*S*)-**3a** was isolated as a colorless oil, 58 mg (74% yield). Chiral HPLC analysis of the *p*-nitrobenzoate derivative afforded 81% ee. $[\alpha]_D^{25}$ = –18.2 (c=1.0, CH_2Cl_2). Lit. $[\alpha]_D^{25}$ = –21.67 (c=1.0, $CHCl_3$, 95% ee).[5]

(*S*)-2-Chloro-octan-1-ol (*S*)-3b. Prepared according to General Procedure C from

trichloromethane sulfonyl chloride (120 mg, 0.55 mmol) and 1-octanal **1b** (80 µL, 0.5 mmol). (*S*)-**3b** was isolated as a colorless oil, 79 mg (95% yield), Chiral GC analysis of (*S*)-**3b** afforded 93% ee. $[\alpha]_D^{25}$ = –36.7 (c = 1.4, CH_2Cl_2). Lit. $[\alpha]_D^{25}$ = –25.30 (c=1.0, $CHCl_3$, 96% ee).[5]

Associated Content

Supporting Information

The supporting information is available free of charge on the ACS Publications website at DOI:

Determination of ee's of compounds **3a** and **3b**. ^{1}H- and ^{13}C- NMR spectra of all chlorinated products.

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Notes

The authors declare no competing financial interest.

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