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Dichlorination of olefins with diphenyl sulfoxide/oxalyl chloride

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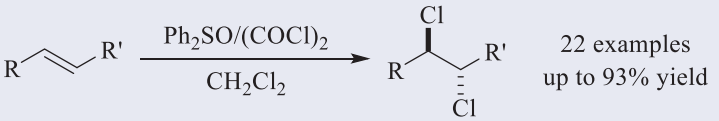
ABSTRACT

The combination of diphenyl sulfoxide and oxalyl chloride was used to accomplish the dichlorination of olefins, in which chlorodiphenylsulfonium salt generated in situ was proposed to be the real active species as a chloronium ion source.

GRAPHICAL ABSTRACT



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KEYWORDS
Chlorodiphenylsulfonium salt; dichlorination; diphenyl sulfoxide; Olefins; oxalyl chloride

Introduction

Dichlorination of olefins is a very versatile tool for organic chemists since organochlorines are a class of valuable intermediates and building blocks of many bioactive compounds. The research interest in chlorination methods of olefins has been increasing continuously in recent years and a lot of new developed chlorination reagents emerged in the literature. In addition to the traditional reagent molecular chlorine, the relatively early developed alternatives include selenium reagents,[1] (dichloroiodo)benzene,[2] various Mn mediated combined reagents,[3] tetraethylammonium trichloride,[4] HCl/H_2O_2,[5] and hexachloroethane.[6] During the last decade, more and more novel reagents have been developed, such as Bu_4NI/dichloroethane,[7] trichloroisocyanuric acid,[8] NCS/Ph_3P,[9] oxone/chloride,[10] SO_2Cl_2/Ph_3PO,[11] bisacetoxyiodobenzene/pyridine hydrochloride,[12] transition metal Pd or V based combined reagents,[13] and 1-chloro-1,2-benziodoxol-3-(1H)-one.[14] Lin's group reported two electrocatalytic approaches to accomplish the dichlorination of alkenes recently.[15] Some of these reagents were applied successfully to the total syntheses of chlorosulpholipid cytotoxins[16] or stereoselective dichlorination using catalysts with chiral ligands.[17] A variety of available chlorination methods provide a convenient platform for the development of organochlorines with important bioactivities.

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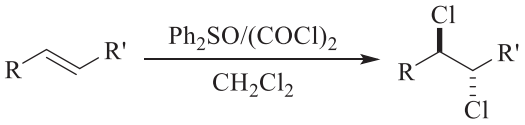


Scheme 1. Dichlorination of alkenes with $Ph_2SO/(COCl)_2$.

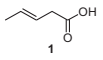
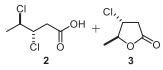
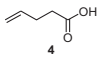
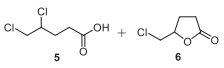
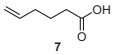
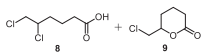
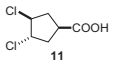
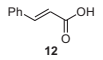
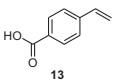
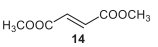
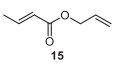
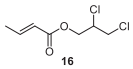
A straightforward method of sulfenyllactonization of olefin acids has been developed using the combination of dimethyl sulfoxide and oxalyl chloride in our previous work, in which a series of lactones containing a methylthio group can be obtained.[18] However, when diphenyl sulfoxide, in analogy with dimethyl sulfoxide, was combined with oxalyl chloride to react with olefin acids, chlorolactones or dichlorocarboxylic acids were produced instead of corresponding lactones with a phenylthio group.[19] The formation of dichlorocarboxylic acids prompted us to investigate generality of $Ph_2SO/(COCl)_2$ as chlorination reagent for alkenes. Herein, we report a new dichlorination method for various double bonds by using $Ph_2SO/(COCl)_2$ (Scheme 1).

Results and discussion

Dichlorination of olefin acids with $Ph_2SO/(COCl)_2$

The results of several typical types of olefin acids are shown in Table 1 (entries 1–6, Table 1). The first three substrates were examined in our previous work about chlorolactonization of olefin acids, which gave dichlorides mainly in the absence of K_2CO_3.[19] *trans*-3-Pentenoic acid **1** was treated with $Ph_2SO/(COCl)_2$ to afford *anti*-3,4-dichloropentanoic acid **2** in 70% yield with small amount of chlorolactone **3** (28% yield) (entry 1, Table 1). 4-Pentenoic acid **4** gave the dichloride **5** and the chlorolactone **6** in a ratio of about 1:1 (entry 2, Table 1). The reaction of 5-hexenoic acid **7** produced the dichloride **8** in 87% yield and the chlorolactone **9** in 11% yield (entry 3, Table 1). Fortunately, the dichlorocarboxylic acids and chlorolactones were easy to separate by routine work-up, such as adjusting pH values and extraction. In contrast, the addition of K_2CO_3 could avoid the production of dichlorides to give an α,β-unsaturated lactone (for *trans*-3-pentenoic acid **1**) or chlorolactones (for 4-pentenoic acid **4** and 5-hexenoic acid **7**) as we discussed in our previous work.[19] In all the reactions, a cyclic chloronium ion intermediate was formed first, which was then attacked by a nucleophile, chloride ion or carboxyl group. For these substrates, the acidic condition favored the attack of chloride ion against carboxyl group to give dichlorides mainly, whereas the reaction of carboxyl group predominated under the basic condition. In addition to these three olefin acids, three more unsaturated acids were investigated. 3-Cyclopenten-1-carboxylic acid afforded the dichloride **11** in 85% yield without the chlorolactone by-product (entry 4, Table 1). For two conjugated olefin acids **12** and **13**, no dichloride was obtained with most of the starting materials recovered (entries 5 and 6, Table 1). Moreover, two conjugated esters were also explored. No reaction occurred to dimethyl fumarate **14** (entry 7, Table 1). Allyl *trans*-3-butenoate **14** was converted to 2,3-dichloropropyl *trans*-3-butenoate **15** in 80% yield (entry 8, Table 1), in which the double bond conjugated to carbonyl group was unreactive.

Table 1. Dichlorination of olefin acids with $Ph_2SO/(COCl)_2$.[a]

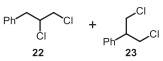
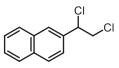
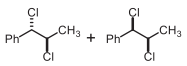
Entry	Substrate	Product	Yield (%)[b]
1			72 (**2**)/ 28 (**3**)
2			49 (**5**)/47 (**6**)
3			87 (**8**)/ 11 (**9**)
4			85
5		-	NR[c]
6		-	NR[c]
7		-	NR[c]
8			80

[a]All reactions were carried out in CH_2Cl_2 at −78 °C to room temperature using alkene (1 equiv.), Ph_2SO (1.2 equiv.) and $(COCl)_2$ (1.2 equiv.).
[b]Isolated yield after column chromatographic purification.
[c]NR: no reaction.

Dichlorination of simple olefins

Dichlorination of a series of olefins was also carried out using $Ph_2SO/(COCl)_2$ under the similar conditions (Table 2). Cyclohexene **17** was converted to *trans*-1,2-dichlorohexane **18** in 83% yield (entry 1, Table 2). The reaction of 1-decene **19** afforded 1,2-dichlorodecane **20** in 92% yield (entry 2, Table 2). When allylbenzene **21** was treated with $Ph_2SO/(COCl)_2$, a mixture of two isomers **22** and **23** with a ratio of 4: 1 was obtained in 93% yield (entry 3, Table 2). The formation of the minor product **23** should be due to the 1,2-shift of phenyl group of the intermediate during the reaction. Styrene **24** reacted with $Ph_2SO/(COCl)_2$ to give a mixture of the dichloride **25** and monochloro-substituted styrene with a ratio of 3.3: 1 (entry 4, Table 2). The yield of the dichloride **25** was 71% after column chromatographic purification. Similarly, the reaction of 2-vinylnaphthalene **26** produced the dichloride **27** in 73% yield, but also with a small amount of monochloro-substituted 2-vinylnaphthalene (ca. 17% by GC) (entry 5, Table 2). The reactions of both *cis*- and *trans*-1-phenyl-1-propenes (**28** and **32**) generated a mixture of *anti*- and *syn*-dichlorides (**29** and **30**) in 75% and 82% yields respectively (entries 6 and 7, Table 2). *cis*-1-Phenyl-1-propene **28** gave a 2.5: 1 *anti*: *syn* ratio, whereas reactant **32** with the *trans*-configuration gave a 4.3: 1 *anti*: *syn* ratio. As in the

Table 2. Dichlorination of olefins with $Ph_2SO/(COCl)_2$.[a]

Entry	Substrate	Product	Yield (%)
1	 17	 18	83
2	 R = n-C8H17 19	 R = *n*-C_8H_{17} 20	92
3	 21	 22 23	93[b,c]
4	 24	 25	71
5	 26	 27	73
6	 28	 29 30	75[b,d]
7	 32		82[b,e]

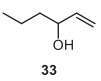
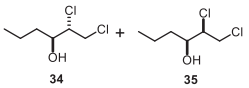
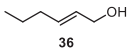
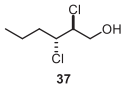
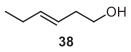
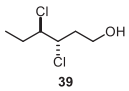
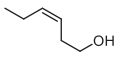
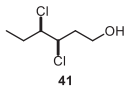
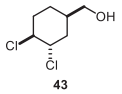
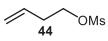
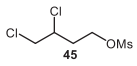
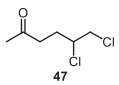
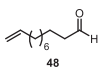
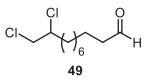
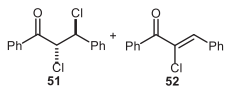
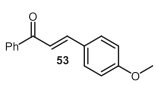
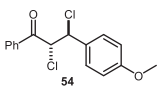
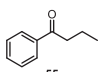
[a]Isolated yield.
[b]Combined isolated yield.
[c]The ratio of two isomers was 4:1.
[d]2.5:1 *anti*:*syn* dichloride was obtained.
[e]4.3: 1 *anti*: *syn* dichloride was obtained.

case of styrene **24**, a monochloro-substituted by-product (*E*)-1-phenyl-2-chloro-1-propene **31** was also produced in about 10% yield.

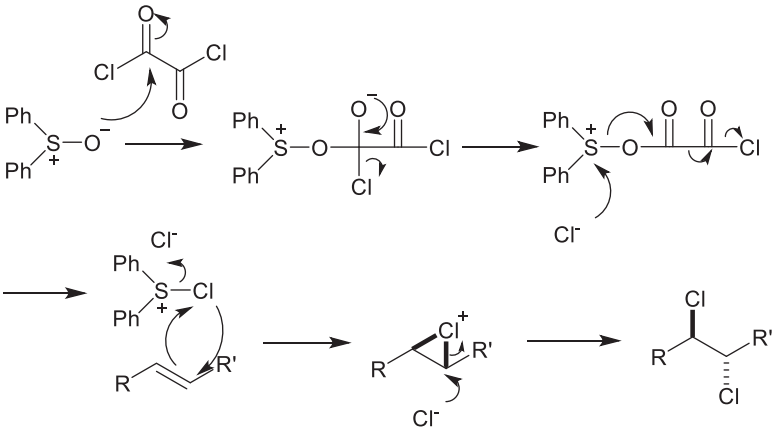
Dichlorination of olefins with other functional groups

A series of unsaturated alcohols were treated with $Ph_2SO/(COCl)_2$ to produce the corresponding dichlorides with hydroxyl group intact (entries 1–5, Table 3). The reaction of 1-hexen-3-ol **33** with $Ph_2SO/(COCl)_2$ gave a mixture of *anti*- and *syn*-1,2-dichloro-3-hexanols **34** and **35** with a ratio of 1: 2.2 in a combined yield of 85% (entry 1, Table 3). *trans*-2-Hexen-1-ol **36** was converted to *anti*-2,3-dichloro-1-hexanol **37** in 89% yield (entry 2, Table 3). The reactions of both *trans*- and *cis*-3-hexen-1-ols **38** and **40** produced the corresponding dichlorides, but with different relative configuration (entries 3 and 4, Table 3). *trans*-3-Hexen-1-ol **38** gave *anti*-3,4-dichloro-1-hexanol **39** in 93% yield (entry 3, Table 3), whereas *cis*-3-hexen-1-ol **40** afforded *syn*-3,4-dichloro-1-hexanol **41** in 91% yield (entry 4, Table 3). 3-Cyclohexene-1-methanol **42** reacted with $Ph_2SO/(COCl)_2$ to produce (1 *R**,3*S**,4*S**)-3,4-dichlorocyclohexylmethanol **43** in 90% yield (entry 5, Table 3). Moreover, but-3-enyl mesylate **44** was also converted to the corresponding dichloride (±)-**45** in 90% yield with the mesyloxy group unchanged (entry 6, Table 3).

Table 3. Dichlorination of olefins containing hydroxyl or carbonyl groups with $Ph_2SO/(COCl)_2$.

Entry	Substrate	Product	Yield (%)
1	 33	 34 + 35	85[a,b]
2	 36	 37	89
3	 38	 39	93
4	 40	 41	91
5	 42	 43	90
6	 44	 45	90
7	 46	 47	87
8	 48	 49	93
9	 50	 51 + 52	55 (**51**) 27 (**52**)
10	 53	 54	81
11	 55		NR[c]

[a]Combined isolated yield.
[b]1:2.2 *anti*:*syn* dichloride was obtained.
[c]NR: no reaction.

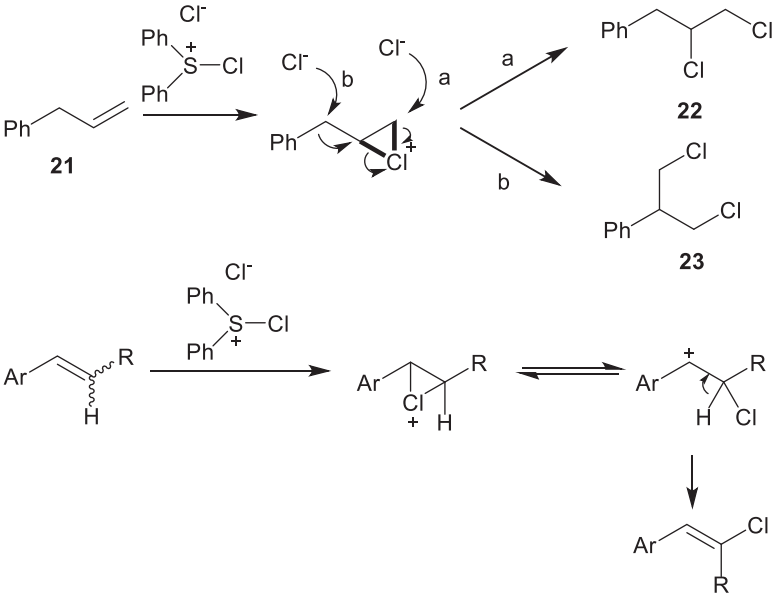


Scheme 2. The mechanism of dichlorination of the double bonds with $Ph_2SO/(COCl)_2$.

In addition, four unsaturated carbonyl compounds were also investigated by treatment with $Ph_2SO/(COCl)_2$. 5-Hexen-2-one **46** was transformed into 5,6-dichloro-2-hexanone (±)-**47** in 87% yield (entry 7, Table 3). Likewise, the reaction of 10-undecenal **48** produced 10,11-dichloroundecanal (±)-**49** in 93% yield (entry 8, Table 3). For these two substrates **46** and **48**, no α chlorination of carbonyl groups occurred under the investigated conditions. When chalcone **50** reacted with $Ph_2SO/(COCl)_2$, a mixture of *anti*-2,3-dichloro-1,3-diphenylpropan-1-one **51** and (*Z*)-2-chloro-1,3-diphenylprop-2-en-1-one **52** was formed with a ratio of 2: 1, which were separated by column chromatography in 55% and 27% yields respectively (entry 9, Table 3). For 4-methoxychalcone **53**, *anti*-2,3-dichloro-1-phenyl-3-*p*-methoxyphenylpropan-1-one **54** was obtained in 81% yield also with a small amount of by-product monochloro-substituted 4-methoxychalcone (ca. 11% determined by GC) (entry 10, Table 3). In the case of a simple ketone, butyrophenone **55**, no α chlorinated product was observed when it was treated with $Ph_2SO/(COCl)_2$ (entry 11, Table 3).

Proposed mechanism for dichlorination of double bonds

The mechanism of dichlorination of double bonds with $Ph_2SO/(COCl)_2$ was proposed to be as follows (Scheme 2). First, Ph_2SO reacted with $(COCl)_2$ to generate the active intermediate chlorodiphenylsulfonium salt, which acted as a source of chloronium ion. Then the chlorodiphenylsulfonium salt underwent electrophilic addition to a double bond to produce a cyclic chloronium ion. The chloride ion attacked the cyclic chloronium ion to afford the corresponding dichloride. Several substrates were observed to give single isomers stereoselectively, such as *trans*-3-pentenoic acid **1** (entry 1, Table 1), 3-cyclopentene-1-carboxylic acid **10** (entry 4, Table 1), cyclohexene **17** (entry 1, Table 2), *trans*-2-hexen-1-ol **36**, *trans*- and *cis*-3-hexen-1-ols **38** and **40**, and 3-cyclohexene-1-methanol **42**, chalcone **50** and 4-methoxychalcone **53** (entries 2∼5, 9 and 10, Table 3), which indicated the involvement of cyclic chloronium ions as intermediates. It was a powerful evidence for the presence of cyclic chloronium ions as intermediates that the reactions of *trans*- and *cis*-3-hexen-1-ols **38** and **40** afforded the products with the relative configurations that can only be predicted via this mechanism (entries 3 and 4, Table 3). Meanwhile, the fact that the



Scheme 3. The effect of phenyl groups adjacent or attached to the double bonds on dichlorination.

double bonds of two conjugated olefin acids **12** and **13**, dimethyl fumarate **14** (entries 5–7, Table 1), as well as the double bond conjugated to the carbonyl group of allyl *trans*-2-butenoate **15** (entry 8, Table 1), didn't react with $Ph_2SO/(COCl)_2$, indicated that this dichlorination is an electrophilic addition to the double bond.

The reaction of allylbenzene **21** produced a mixture of two isomeric dichlorides **22** and **23** (entry 3, Table 2), which was different from that of 1-dencene **19** with a single dichloride product. Obviously, the isomer **23** was a rearrangement product, which should be attributed to the 1,2-shifting propensity of phenyl group in the cyclic chloronium ion intermediate (Scheme 3). All the substrates with double bonds conjugated to phenyl groups, including substrate **24**, **26**, **28**, **32** (entries 4–7, Table 2), and two chalcones **50** and **53** (entries 9 and 10, Table 3), produced certain amounts of monochloro-substituted products. Moreover, both *cis*- and *trans*-1-phenyl-1-propenes **28** and **32** gave *anti*- and *syn*-dichlorides **29** and **30** with poor stereoselectivity (entries 6 and 7, Table 2). These results could be explained by the involvement of carbocations stabilized by the conjugated phenyl groups. The carbocations were able to undertake fragmentation to produce momochloro substituted products (Scheme 3).

It is noteworthy that the substrates containing hydroxyl group gave the corresponding dichlorides with hydroxyl group unchanged (entries 1–5, Table 3). Even relatively reactive hydroxyl groups attached to allyl groups didn't participate the reaction, although it was reported that allyl alcohols could be converted to the corresponding halides with halodimethylsulfonium salts generated in situ from $(CH_3)_2S/Br_2$[20] or $(CH_3)_2S$/NBS (NCS).[21] Our results demonstrated that the combination of $Ph_2SO/(COCl)_2$ has excellent chemoselectivity toward a double bond and hydroxyl group, which might be a problem for some chlorination reagents, such as chlorine, or NCS/Ph_3P.[9] It was found that unsaturated alcohols were easy to be converted to the corresponding cyclic ethers with a methylthio group with DMSO/$(COCl)_2$ in our previous work.[22] However, no

cyclization product was obtained, which indicated that no intramolecular nucleophilic attack of the hydroxyl group on the intermediate cyclic chloronium ion occurred. Moreover, the presence of active mesyloxy group in the substrate can be tolerated in the dichlorination (entry 6, Table 3).

In addition, for the substrates **46** and **48** containing a double bond and unconjugated carbonyl group, the combination of $Ph_2SO/(COCl)_2$ also presented chemoselectivity toward the double bond. No α chlorinated product was generated as a by-product (entries 7 and 8, Table 3). Butyrophenone **55** was not able to be converted to the corresponding α chlorinated product (entry 11, Table 3). These results demonstrated that this method possesses unique chemoselectivity for a double bond against a carbonyl group, which is also a common problem for some chlorination reagents.[4,8,13] It was a little surprised that chalcone **50** and 4-methoxychalcone **53** also underwent dichlorination although the double bond here is conjugated with a carbonyl group (entries 9 and 10, Table 3), which seems to conflict with the results of those unsaturated acids and esters (entries 5–8, Table 1). More substrates with α,β-unsaturated carbonyl groups may need to be explored further.

It was interesting to find that combination of $DMSO/(COCl)_2$ didn't undergo dichlorination of double bonds, which should imply that chlorodimethylsulfonium salt is unable to act as an active chloronium ion source toward a double bond. The chlorodimethylsulfonium salt and chlorodiphenylsulfonium salt demonstrate different reactivity. On the other hand, we did find that both $DMSO/(COBr)_2$ and $Ph_2SO/(COBr)_2$ can act as a bromonium ion source to accomplish various bromination of double bonds, triple bonds, or carbonyl compounds in our previous work.[23] These results might give us some insights about the reactivity of halodialkylsulfonium and halodiarylsulfonium salts.

Conclusion

In summary, the combination of $Ph_2SO/(COCl)_2$ has been demonstrated to be an efficient reagent for dichlorination of olefins, which presents excellent chemoselectivity for the double bonds of the substrates containing hydroxyl, mesyloxy or unconjugated carbonyl groups. It has several remarkable advantages, such as short reaction time, easy availability of the reagents, and functionality tolerance. This method provides us an attractive alternative for the chlorination of olefins.

Experimental

NMR spectra were obtained on a Bruker AV 300 spectrometer (^1H NMR at 300 MHz, ^{13}C NMR at 75 MHz) in $CDCl_3$ using TMS as an internal standard. Chemical shifts (δ) were given in ppm and coupling constants (*J*) in Hz. HRMS data were obtained on a Micromass GCT Mass Spectrometer or Bruker Solarix XR FTMS. TLC was performed with precoated TLC plates, silica gel 60 F-254, layer thickness 0.25 mm. Flash chromatography separations were performed on 100–200 mesh silica gel. Reagents and solvents are commercial grade and were used as supplied. Substrates are commercially available and were purchased from Innochem.

General procedures for dichlorination of olefin acids using Ph_2SO and $(COCl)_2$

To a solution of oxalyl chloride (0.51 mL, 6.0 mmol, 1.2 equiv.) in CH_2Cl_2 (10 mL) cooled at −78 °C was added dropwise a solution of diphenyl sulfoxide (1.21 g, 6.0 mmol, 1.2 equiv.) in CH_2Cl_2 (10 mL) under the atmosphere of nitrogen. After 10 min, a solution of alkenoic acid (5 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) was added. The mixture was then allowed to warm up to room temperature and stirred for 1 h. The mixture was carefully basified with saturated $NaHCO_3$ (aq.) at 0 °C. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 20 mL). The aqueous layer was acidified with 2 M HCl solution and extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with brine, dried (Na_2SO_4), filtered, and concentrated in vacuum to afford the corresponding dichloro acids (**2**, **5**, **8**, **11**).

Trans-3,4-dichlorocyclopentanecarboxylic acid (11)

White solid, 778 mg, 85% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.43–4.40 (m, 1 H, H-C-3 or H-C-4), 4.37–4.32 (m, 1 H, H-C-4 or H-C-3), 3.39–3.24 (m, 1 H, H-C-1), 2.92–2.76 (m, 2 H, H-C-2 and H-C-5), 2.48–2.28 (m, 2 H, H′-C-2 and H′-C-5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 180.60 (COOH), 65.39, 64.17 (C-3 and C-4), 40.21 (C-1), 36.49, 36.39 (C-2 and C-5). HRMS (ESI), *m/z* $[M-H]^-$ calcd for $C_6H_7Cl_2O_2$: 180.9828; found: 180.9826.

General procedure for dichlorination of olefins or olefins with hydroxy or carbonyl group using Ph_2SO and $(COCl)_2$

To a solution of oxalyl chloride (0.51 mL, 6.0 mmol, 1.2 equiv.) in CH_2Cl_2 (10 mL) cooled at −78 °C was added dropwise a solution of diphenyl sulfoxide (1.21 g, 6.0 mmol, 1.2 equiv.) in CH_2Cl_2 (10 mL) under the atmosphere of nitrogen. After 10 min, a solution of substrate (5 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) was added. The mixture was then allowed to warm up to the temperature and stirred until TLC showed the reaction completed. Distilled water (30 mL) was added dropwise at 0 °C. After stirring for 10 min, the organic layer was separated and successively washed with brine. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuum. For **16**, **34**, **35**, and **37**, the residue was purified by flash chromatography (silica gel, petroleum ether/ethyl acetate = 30:1 for **16**, and 10:1 for **34**, **35** and **37**). For **17**, **19**, **21**, **24**, **26**, **28** and **32**, the corresponding dichloroalkanes and the byproduct diphenyl sulfide cannot be separated by chromatography due to the similar polarity. The problem can be solved by oxidizing diphenyl sulfide to diphenyl sulfoxide to differentiate the polarity. The residue was dissolved in CH_3CN (20 mL), then aqueous 30% H_2O_2 (1.5 mL, 15 mmol, 3.0 equiv.) and TMSCl (0.96 mL, 7.5 mmol, 1.5 equiv.) were added. The mixture was stirred at room temperature for 30 min. After the disappearance of diphenyl sulfide, the reaction mixture was quenched by adding water (20 mL), extracted with CH_2Cl_2 (3 × 20 mL), and the extract washed with brine, dried (Na_2SO_4), filtered, and concentrated in vacuum. Purification by flash chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) afforded the corresponding dichloroalkanes.

(1R,3S*,4S*)-3,4-dichlorocyclohexylmethanol (43)*

Colorless oil, 823 mg, 90% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.40 (m, 1 H, H-C-2), 4.34 (q, J = 3.0 Hz, 1 H, H-C-1), 3.53 (d, J = 5.7 Hz, 2 H, H-CH_2OH), 2.35 (dddd, J = 15,3, 12.3, 4.2, 3.0 Hz, 1 H, H′-C-6), 2.00–2.14 (m, 2 H, H′-C-3 and H-C-4), 1.84–1.98 (m, 2 H, H-C-3 and H-C-6), 1.50–1.70 (m, 2 H, H-C-5), 1.45 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 66.93 (C-CH$_2$OH), 59.81 (C-1), 59.74 (C-2), 33.33 (C-4), 30.63 (C-3), 27.16 (C-6), 22.33 (C-5). HRMS (EI), m/z [M – H_2O]$^+$ calcd for $C_7H_{10}Cl_2$: 164.0154; found: 164.0152.

1-Mesyloxy-3,4-dichlorobutane (45)

Colorless oil, 994 mg, 90% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.41 (m, 2 H, H-C-1), 4.23 (m, 1 H, H-C-3), 3.82 (dd, J = 11.7, 5.1 Hz, 1 H, H-C-4), 3.70 (dd, J = 11.7, 6.9 Hz, 1 H, H′-C-4), 3.03 (s, 3 H, CH_3 (MsO)), 2.48 (m, 1 H, H-C-2), 2.05 (1 H, H′-C-2). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 66.10 (C-1), 56.46 (C-3), 47.96 (C-4), 37.25 (CH_3 (MsO)), 34,53 (C-2). HRMS (ESI), m/z [M + Na]$^+$ calcd for $C_5H_{10}Cl_2NaO_3S$: 242.9620; found: 242.9621.

5,6-Dichloro-2-hexanone (47)

Light yellow oil, 835 mg, 87% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.12 (dddd, J = 9.9, 7.2, 5.1, 3.0 Hz, 1 H, H-C-5), 3.78 (dd, J = 11.4, 5.1 Hz, 1 H, H′-C-6), 3.66 (dd, J = 11.4, 7.2 Hz, 1 H, H-C-6), 2.61–2.80 (m, 2 H, H-C-3), 2.30–2.42 (m, 1 H, H′-C-4), 2.19 (s, 3 H, H-C-1), 1.83–1.97 (m, 1 H, H-C-4). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 207.04 (C-2), 60.30 (C-5), 48.20 (C-6), 39.58 (C-3), 29.99 (C-1), 29.01 (C-4). HRMS (ESI), m/z [M + Na]$^+$ calcd for $C_6H_{10}Cl_2NaO$: 191.0001; found: 191.0005.

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