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Graphical Abstract

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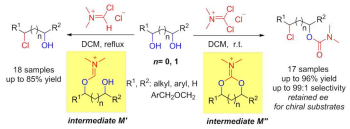
Liqun Yang [a], Xiaotong Li [a], Yu Wang [a], Chengyang Li [a], Xiaoyu Wu [a], Zhaoguo Zhang [a,b], and Xiaomin Xie [a,*]

School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, China



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Liqun Yang [a], Xiaotong Li [a], Yu Wang [a], Chengyang Li [a], Xiaoyu Wu [a], Zhaoguo Zhang [a,b], and Xiaomin Xie[a,] *

[a] *School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, China*
[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Fenglin Road, Shanghai 200032, China*

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ABSTRACT

Chlorinated iminium chlorides have been identified to promote the highly efficient and selective mono-chlorination of unsymmetrical vicinal diols. Vilsmeier reagent, namely, (chloromethylene)dimethyliminium chloride, enables highly reactive and regioselective chlorination of 1,2- and 1,3-diols featured one secondary benzylic hydroxy group and one primary aliphatic hydroxy group to give the corresponding 1,2- and 1,3-chlorohydrins. Viehe's salts (α,α-dichloro iminium salts) exhibit excellent reactivity and good selectivity for vicinal diols to give the corresponding chlorohydrin carbamates via a cyclic intermediate in situ. The chlorination protocols tolerate diverse functional groups, including halogens, naphthalene rings, nitro, and cyano. Moreover, the optical purity of chiral diols could be retained during this chlorination reaction.

* Corresponding author. Tel.: +86-021-5474-8925; fax: +86-021-5474-8925; e-mail: xiaominxie@sjtu.edu.cn

1. Introduction

Chlorohydrins are an class of versatile synthons for natural products, pharmaceuticals, pesticides and organic functional materials.[1] Among the multiple accesses to chlorohydrins, selective chlorination of polyhydroxy compounds might be one of the most efficient owing to the richness and ready availability of polyhydroxy compounds.[2] Numerous chlorination reagents or recipes have been developed to the conversion of mono alcohols to corresponding chlorides, such as hydrogen chloride[3], thionyl chloride[4], phosphorus halides[5], PPh_3/various chlorinated reagents [6], chloro iminium salts[2a,7], aromatic chloro carbocations[8], and chlorohydrosilanes[9]. More recently, catalytic Appel reactions and formamides catalyzed chlorination have been reported.[10] However, the selective chlorination of unsymmetrical polyhydroxy molecules remains challenging, especially for vicinal diols wherein the existence of two adjacent -OH groups usually induces more side reactions like etherification and rearrangement, let alone the regioselectivity.[11] To realize selective chlorination of the designated hydroxyl group in the presence of other hydroxyl groups, the use of protecting groups was generally required.[12] Vicinal diols were often firstly converted to form cyclic intermediates to achieve selective chlorination such as ketal acids[13], sulfates and sulfites[14], and orthoesters[15]. Nevertheless, these cyclic intermediates must be preformed and isolated before subjection to chlorination, which debate themselves for practical applications by rather laborious and uneconomic steps.

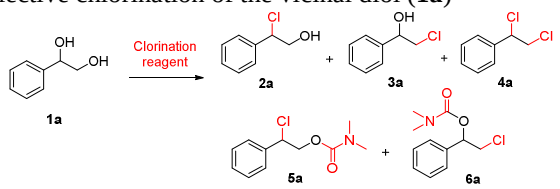
In terms of the direct and selective chlorination of unsymmetrical polyhydroxy molecules, effective chlorination reagents or reaction systems were still much sought after until recently. NCS/Me_2S duet selectively chlorinated allylic or benzylic alcohols over other primary alkyl alcohols at low temperature.[16] Bulky chloroenamines or triphosgene/Et_3N combination allowed the selective chlorination of the primary over tertiary hydroxy within diols.[17] Yasuda et al. reported the use of $HSiMe_2Cl$/Benzil/$InCl_3$ for the selective chlorination of tertiary alcohols in the presence of a primary alcohols.[9b] These chlorination systems, however, were impotent for the discrimination between primary and secondary hydroxyls in diols.[9b,17] Only sporadic reports researched the selective chlorination of unsymmetric vicinal diols. Taneja's group achieved a regioselective monochlorination of various unsymmetrical vicinal diol scaffolds via Mitsunobu reaction with TMSCl as the chlorination reagent.[18] Primary hydroxyl in carbohydrates and other sterically hindered non-saccharide polyols were preferentially chlorinated, while the chlorination predominantly occurred at the secondary alcohols with selectivity ranging from 3:1 to 4:1 for other 1,2- and 1,3-diols.[18] Canela and coworkers used carboxylic acids in the selective chlorination of 1,3-butanediols by TMSCl.[19] The in situ formed deoxygenated ring undergoes nucleophilic ring opening during the chlorination process. The regioselectivity of the chlorination, which could be optimized up to 3/1, depends on the pKa value of the carboxylic acids.[19b] Accordingly, the development of a highly efficient and regioselective monochlorination of unsymmetrical vicinal diols is very attractive and challenging. From the precedents, chlorinated iminium salts may provide a solution for monochlorination of unsymmetrical vicinal diols. Viehe's salt ((dichloromethylene)dimethylammonium chloride) was reported to show high selectivity for chlorination in carbohydrates and symmetric diols by formation *in situ* of cyclic intermediates.[20] We speculated that chlorinated iminium salts may be reacted with vicinal diols to generate a cyclic intermediate (M) which may avoid side reactions such as etherification and rearrangement and the adjustable reactivity of the chlorinated iminium salts by altering the substituent at *a* position may take advantage to discriminate the different hydroxyl groups. Herein, we presented the details of a study about the direct and selective chlorination of unsymmetrical vicinal diols with chlorinated iminium salts.

2. Results and Discussion

1-Phenylethane-1,2-diol (**1a**) was chosen as the model substrate to explore the direct and selective chlorination of unsymmetrical vicinal diols (Table 1). We firstly tested the chlorination of the vicinal diol **1a** with Viehe's salts ((dichloromethylene)di-methylammonium chloride) which may form cyclic intermediates **M** with diols. To our delight, in the reaction of **1a** with 1.2 molar equivalent of Viehe's salts in dichloromethane (DCM) at room temperature, the chlorination of benzyl alcohol, the more acidic alcohol, was dominated to give mono-chlorinated carbamates in 85% yield and the selectivity of 97:3 (**5a**:**6a**) (entry 1). Comparing with classical chlorinating reagents, the reaction of **1a** with $SOCl_2$ or $POCl_3$ only resulted in trace amount of chlorinated products either at room temperature or the refluxing temperature, and mixtures of ethers were observed as the main products (Table 1, entries 2-5). In case of PPh_3/CCl_4 as the chlorinating reagent, the reaction proceeded with poor selectivity to give the monochlorination product **2a** in 37% yield and dichlorination product **4a** in 4% yield (entry 6). The results were consistent with the reports.[11b,11c] Definitely, the chlorinated iminium salt performed good selectivity and reactivity for the monochlorination of **1a**.

In order to improve the selectivity of the monochlorination of **1a**, Vilsmeier reagent ((chloromethylene)dimethyl-ammonium chloride) was then explored which may display less electrophilicity than Viehe's salts caused by one chloro substituent at α position of iminium salt. The reaction of the diol **1a** with 1.2 molar equivalent of Vilsmeier reagent at room temperature showed excellent regioselectivity for the monochlorination to produce monochlorinated alcohol **2a** in 79% yield, together with 5% yield of monochlorinated ester (**7a**, 2-chloro-2-phenylethyl formate) and the mixed ethers as main byproducts. Remarkably, no chlorinated isomer **3a** or dichlorination product **4a** was observed (entry 7). Then, tetramethyl-*a*-chloro-enamine with less electrophilicity and more hindrance than Vilsmeier reagent was tested. A lower reactivity was observed. A monochlorinated ester (**7a'**, 2-chloro-2-phenylethyl isobutyrate) was observed in 36% yield, and 52% of **1a** was converted to 2-hydroxy-2-phenylethyl isobutyrate (entry 8). In some cases, Vilsmeier reagent could be replaced with TCT (2,4,6-trichloro[1,3,5]triazine)/DMF or pivaloyl chloride/DMF which may form the α-chloro iminium chloride in situ.[7d,7e] Using pivaloyl chloride/DMF as the chlorination reagent gave selectively the monochlorinated product **2a** in 45% yield (entry 9). In the case of TCT/DMF, the reaction gave monochlorination product **2a** in only 8% yield with trace amount of dichlorination product **4a**, and the monochlorinated ester **7a** was observed as the main product in 49% yield (entry 10). Formamide-catalyzed chlorination with TCT as an efficient chlorination system was also be examined[10d]. The monochlorinated alcohol **2a** was selectively obtained in 54% yield and the mixed ethers was observed as byproducts (entry 11). These results demonstrated that Vilsmeier reagent (isolated α-chloro iminium salts) showed better selectivity for the chlorination of the diol **1a** than the in situ formed α-chloro iminium salts.

Table 1. The optimization of reaction conditions for the selective chlorination of the vicinal diol (**1a**)[a]



Entry	Chlorination reagent	Solvent	Temp. □	Conv. %	Yield % 2a	3a	4a
1	Viehe's salts	DCM	rt	93	85 (**5a**)	3(**6a**)	-
2	$SOCl_2$	DCM	rt	76	trace	-	-
3	$SOCl_2$	DCM	40	99	6	-	trace
4	$POCl_3$	DCM	rt	98	trace	-	-
5	$POCl_3$	DCM	40	99	trace	-	trace
6	PPh_3/CCl_4[b]	DCM	rt	88	37	-	4
7	Vilsmeier reagent	DCM	rt	99	79 + 5 (**7a**)	-	-
8	*a*-chloroenamine	DCM	rt	88	36 (**7a'**)	-	-
9	Pivaloyl chloride/DMF	DCM	rt	92	45	-	-
10	TCT/DMF	DCM	rt	99	8 + 49 (**7a**)	-	trace
11	TCT/DMF[c]	DCM	40	99	54	-	-
12	Vilsmeier[d] reagent	DCM	rt	76	57 + 6 (**7a**)	-	-
13	Vilsmeier reagent	DCM	40	99	93	-	-
14	Vilsmeier reagent	Toluene	40	99	80 + trace (**7a**)	-	-
15	Vilsmeier reagent	DCE	40	99	60	-	trace
16	Vilsmeier reagent	Et_2O	40	99	53	-	5
17	Vilsmeier reagent	THF	40	99	48	trace	trace
18	Vilsmeier reagent	MeCN	40	99	35 + trace(**7a**)	-	trace
19	Vilsmeier reagent	DMF	40	99	46	trace	-
20	Viehe's salts	DCM	40	93	78 (**5a**)	trace	-

[a] Reaction conditions: **1a** (1.0 mmol), chlorination reagent (1.2 mmol), DCM (4.0 mL), 12 h; conversions and yields are determined by GC (internal standard: 1,2,4,5-tetramethylbenzene).

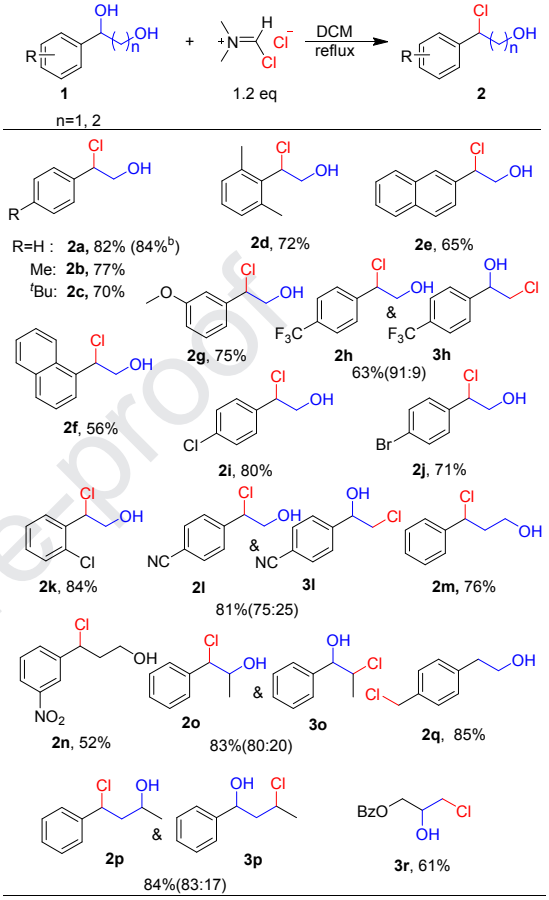
[b] PPh_3 (1.2 mmol), CCl_4 (1.0 mL).

[c] TCT (0.4 mmol), DMF (0.4 mmol).

[d] Vilsmeier reagent (1.0 mmol).

Then we explored the effect on the chlorination of the vicinal diol from the stoichiometry of chlorination reagent, reaction temperature and solvents. Reducing Vilsmeier reagent to 1.0 equivalent resulted in lower conversion of **1a** (entry 12). Raising the reaction temperature to the reflux temperature of DCM, the yield of the monochlorination product **2a** was increased to 93% (Table 1, entry 13). In the nonpolar solvents such as toluene, Vilsmeier reagent retained good selectivity (entry 14). The chlorination in DCE generated desired product **2a** in 60% yield (entry 15). Using the ether solvents or polar solvents led to a decreased selectivity (entries 16-19). In DMF, the reaction generated **2a** in 46% yield, and the mixed ethers were observed as the main byproducts (entry 19). The observation was in accord with that of pivaloyl chloride/DMF or TCT/DMF as the chlorination reagent wherein the excess DMF may decrease the selectivity of the reagent. In case of Viehe's salts as the chlorination reagent, the chlorination of **1a** in refluxing DCM gave the monochlorination products (**5a** and **6a**) in a slightly decreased yield (entry 20). Therefore, the optimized reaction conditions for the selective chlorination of the unsymmetrical vicinal diol was 1.2 molar equivalent of Vilsmeier reagent in refluxing DCM, or 1.2 molar equivalent of Viehe's salts in DCM at room temperature.

Table 2. The selective chlorination of the unsymmetrical vicinal diols with vilsmeier reagent [a]



[a] Reaction conditions: vicinal diol (1.0 mmol), Vilsmeier reagent (153.6 mg, 1.2 mmol), DCM (4.0 mL), 40 °C, 12 h; isolated yields; the ratio of isomers was detected by ^{1}H NMR of the regioisomers mixture.

[b] **1a** (1.4 g, 10 mmol) was reacted.

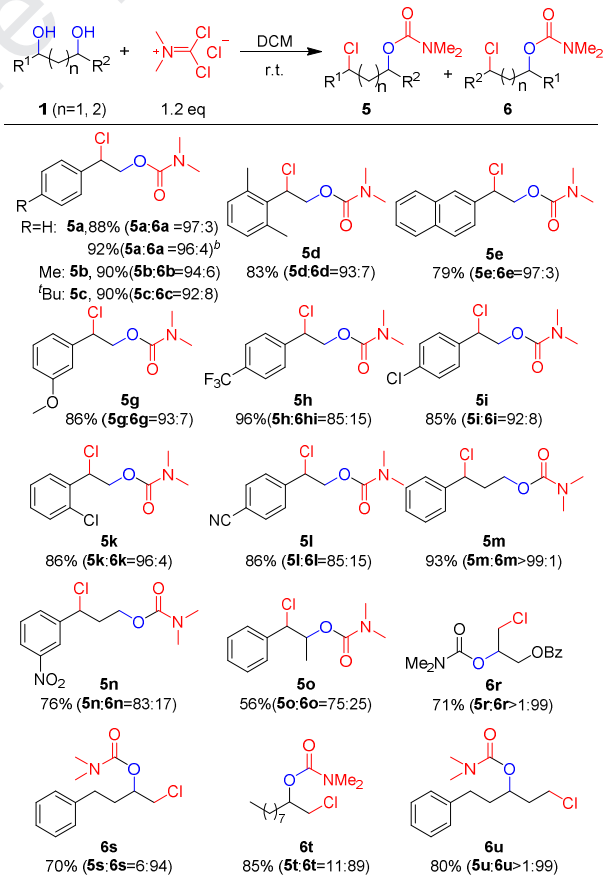
The scope of the selective chlorination of vicinal diols with Vilsmeier reagent was then examined under the optimized reaction conditions. As shown in Table 2, Vilsmeier reagent exhibited good activity and selectivity in the chlorination of 1,2-diols that feature one benzylic secondary alcohol together with an aliphatic primary alcohol. For all the diols, the benzylic second alcohols, the more acidic alcohols, were selectively chlorinated in good to moderate isolated yields. The chlorination of alkyl substituted 1-arylethane-1,2-diol (**1a-1f**) selectively gave the corresponding chlorination products (**2a-2f**) in the yields ranging from 56% to 82%, and no other chlorinated products were observed. The sterically hindered 1-(2,6-dimethylphenyl)ethane-1,2-diol (**1d**) was also reacted smoothly to give the chlorination product **2d** in 72% yield. This protocol showed good tolerance for functional groups. 2-Chloro-2-phenylethan-1-ol with *m*-methoxy group (**2g**) or *p*-bromo (**2j**) was selective obtained in 75% and 71% yield, respectively. Even the chlorination of 1-*o*-chlorophenylethane-1,2-diol (**1k**) could give the

corresponding product **2k** in 84% yield. However, an electron-withdrawing group on the aromatic group decreased the regioselectivity for chlorination. The reaction of 1-(4-cyanophenyl)ethane-1,2-diol (**1l**) afforded the monochlorinated products (**2l** and **3l**) in 81% yield with a ratio of 75 : 25, and no hydrolysis of the cyano group was observed. Moreover, Vilsmeier reagent is also amenable to the selective chlorination of 1,3-diols. The chlorination of 1-phenylpropane-1,3-diol (**1m**) proceeded efficiently to the corresponding mono-chlorinated product **2m** in 76% yield. Similarly, the chlorination of 1,3-diol **1n** with *m*-nitro group gave the monochlorinated product **2n** in 52% yield and dichlorinated product **4n** in 21% yield. Changing the aliphatic primary alcohol of 1,2- and 1,3-diols to aliphatic secondary alcohol, benzyl alcohols were also chlorinated preferentially, but the regioselectivity was lower. The reaction of 1-phenylpropane-1,2-diol (**1o**) gave a mixture of 1-chloro-1-phenylpropan-2-ol (**2o**) and 2-chloro-1-phenylpropan-1-ol (**3o**) in a ratio of 80: 20. 1-Phenylbutane-1,3-diol (**1p**) could also be chlorinated to give the monochlorination products of **2p** and **3p** in a 83:17 ratio. In the case of the diol **1q** that featured a primary benzylic and an aliphatic primary alcohol, the benzylic alcohol also could be selectively chlorinated to give the corresponding product **2q** in 85% yield. Regretfully, the reaction of 1-phenylbutane-1,4-diol generated the corresponding cyclic ether as the main product. *p*-Methoxy substituted 1-phenylethane-1,2-diol was not suitable for the chlorination, and the rearranged product, 2-(4-methoxyphenyl)acetaldehyde, was observed as the main product.[11f]

Gratifyingly, the standard conditions were also suitable for the monochlorination of 1-*o*-benzylglycerol (**1r**), the mono-protected glycerol, Nevertheless, in the case of the diol with the similar acidic hydroxyl groups, the less sterically hindered primary alcohol was selectively chlorinated to afford the corresponding product **3r** in 61% yield without the formation of any other chlorinated products. To evaluate the scalability of this facile procedure, 10 mmol of **1a** was subjected to the optimized conditions and monochlorinated product **2a** was isolated in 84% yield.

Viehe's salts also exhibited good selectivity for the monochlorination of the model unsymmetrical diol **1a**, and the mono-chlorinated carbamate **5a** was generated as the main product which is appropriate for further manipulations of the chloride. Therefore, the scope of the selective chlorination of the unsymmetrical vicinal diols with Viehe's salts was also examined under the optimized reaction conditions. As shown in Table 3, Viehe's salts performed excellent reactivity and good selectivity in the chlorination of 1-arylethane-1,2-diols (**1a-1l**). Although the regioselectivity was slightly lower than Vilsmeier reagent, the yield of the monochlorination products improved significantly. The secondary benzylic alcohols with more acidity were also selectively chlorinated to give 2-chloro-2-arylethyl carbamates with the diverse substituents (**5a-5l**) in the yields ranging from 79% to 96% and the selectivity was up to 97:3. The selective chlorination of sterically hindered (2,6-dimethylphenyl)ethane-1,2-diol (**1d**) generated the monochlorinated carbamates in 83% yield with the 93 : 7 regioselectivity. Similarly, the presence of an electron-withdrawing group at the aromatic group decreased the regioselectivity for chlorination. The chlorination of (4-trifluoromethylphenyl)ethane-1,2-diol (**1h**) with Viehe's salts gave the mono chlorination products in 96% yield and 85 : 15 regioselectivity. 1-Phenylpropane-1,3-diols (**1m**) also underwent regioselective chlorination to give the monochlorinated carbamate **5m** in high yields and excellent selectivity. The chlorination of 1,3-diol **1n** with *m*-nitro group offered the corresponding mono-chlorinated carbamates (**5n** and **6n**) in 76% yield and the ratio of 83 : 17. While, in cases of 1,2-diols featured a benzylic and one aliphatic secondary alcohol, the regioselectivity was also reduced. The reaction of 1-phenylpropane-1,2-diol (**1o**) gave the monochlorinated mixture with ratio of 75 : 25. Moreover, in the chlorination of the unsymmetrical diols (**1r-1u**) with two similar acidic hydroxyl groups, the primary alcohol, less sterically hindered alcohol, was selectively chlorinated. The chlorination of the mono-protected glycerol (**1r**) with Viehe's salts gave the monochlorinated carbamate **6r** in 71% yield and >99% selectivity. Even, in the chlorination of the unsymmetrical diols (**1s**, **1t** and **1u**) that features aliphatic primary and secondary alcohols, successful discrimination between the aliphatic primary and secondary alcohols was achieved. The chlorination occurred selectively at the primary alcohol to give the products in the yields ranging from 70 to 85%. 5-Phenylpentane-1,3-diol (**1u**) is chlorinated to obtain the mono-chlorinated carbamates **6u** in 80% yield with the selectivity of 99:1. The reaction conditions also scale effectively; selective chlorination of 1-phenylethane-1,2-diol (**1a**) with Viehe's salts afforded a 92% isolated yield of the monochlorinated carbamate **5a** with the 94:6 selectivity when performed on a 10 mmol scale.

Table 3. The selective chlorination of the unsymmetrical vicinal diols with Viehe's Salt [a]

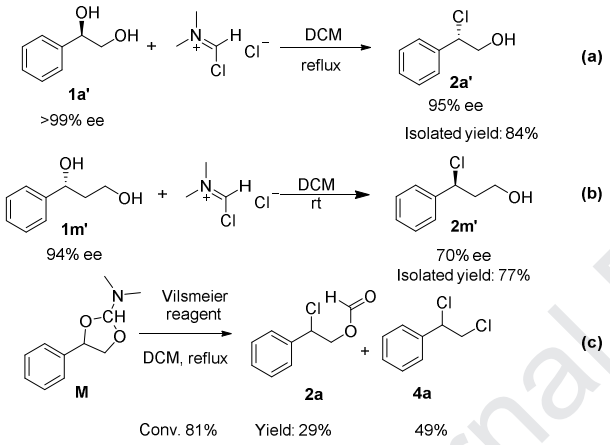


[a] Reaction conditions: vicinal diol (1.0 mmol), Viehe's salt (197.0 mg, 1.2 mmol), DCM (4.0 mL), 25 □, 12 h; isolated yields; the ratio of isomers was detected by ^{1}H NMR of the crude products.

[b] **1a** (1.4 g, 10 mmol) was reacted.

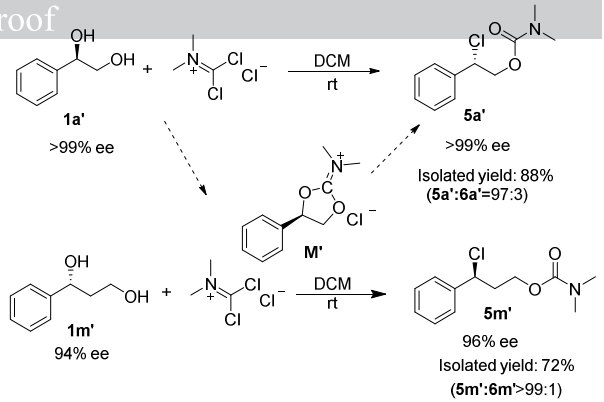
To probe into the pathway of selective monochlorination of unsymmetrical vicinal diols with chloro-iminium salts, we

carried out several control experiments (Schemes 1 & 2). We firstly treated (R)-1-phenylethane-1,2-diol (**1a'**, >99% ee) with Vilsmeier reagent under standard conditions, the monochlorinated product **2a'** was obtained in 84% isolated yield and in 95% ee with the inverted configuration (Scheme 1a). The observations indicated that the chlorination of vicinal diols with Vilsmeier reagent may occur mainly through S_N2 process rather than S_N1 by using TMSCl under SFRC[9d]. Therefore, in the chlorination of (R)-1-phenylpropane-1,3-diol (**1m'**, 94% ee), the product 2m' with the inverted configuration should be dominated, although the reduced enantiopure was observed (Scheme 1b). Furthermore, the cyclic intermediate M preformed by the reaction of *N*,*N*-dimethylformamide dimethyl acetal and the diol was reacted with Vilsmeier reagent. Only 81% conversion was observed and the mono- and dichlorination product(**2a** and **4a**)were obtained a ratio of 1:1.69 (Schemes 1c). Therefore, the monochlorination of vicinal diols with Vilsmeier reagent may not involve the cyclic intermediate M. The good regioselectivity may arise from the discrimination of Vilsmeier reagent between the alcohols with the different acidity or steric hindrance under the optimized conditions.



Scheme 1. The selective chlorination of (*R*)-vicinal diols and probably intermediate M with Vilsmeier reagent

In the cases of chlorination with Viehe's salt, the mono-chlorinated carbamates (**5** or **6**) were obtained as the main products in excellent to moderate yields, and the generation of the mixed ethers as byproducts was depressed greatly. When (R)-1-phenylethane-1,2-diol (**1a'**) and (R)-1-phenylpropane-1,3-diol (**1m'**) were subjected to the reaction conditions, the enantiopure of the products (**5a'** and **5m'**) maintained entirely. These observations demonstrated that there was no nucleophilic attack of free hydroxy groups to the activated alcohols or the formation of carbocation. Thus, the chlorination of diols with Viehe's salts underwent the cyclic intermediate M' and the substitution of chlorination occurred by S_N2 pathway. The configuration of **5a'** and **5m'** should be inverted to *S*-type. The two chlorides at α-position of iminium salt may account for the high activity of Viehe's salts to form the cyclic intermediate M' with vicinal diols and the high selective chlorination of aliphatic diols.



Scheme 2. The selective chlorination of (R)-vicinal diols with Viehe's Salt

3. Conclusion

In summary, we developed a mild and useful chlorination method for the selective chlorination of unsymmetrical vicinal diols by using iminium salts (Vilsmeier reagent and Viehe's salt) as the reagents. The unsymmetrical vicinal diols with different acidic hydroxyl groups were selectively chlorinated at the more acidic alcohol to give the corresponding mono-chlorohydrins or chlorohydrin carbamates in moderate to good yields. For the diols with similar electronic nature of alcohols, less sterically hindered alcohol was selectively chlorination. The chlorination protocol showed a good tolerance of halogens, naphthalene rings, nitro, and cyano groups. The optical purity of chiral diols may also be maintained during this chlorination.

4. Experimental Section

Unless otherwise noted, all reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques. Materials were purchased from commercial suppliers and used without further purification. The preparation of Vilsmeier reagent and Viehe's salt was based on the reports[7c,21]. Anhydrous DCM, DCE, Toluene, Et_2O, THF, DMF and CH_3CN were freshly distilled from calcium hydride or sodium. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on 400 MHz or 500 MHz spectrometers, and tetramethylsilane (TMS) was used as a reference. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.16). HRMS were obtained on ESI-TOF mass spectrometer. Flash column chromatography was performed on silica gel (300-400 mesh).

4.1. A typical procedure for the selective chlorination of unsymmetrical vicinal diols with Vilsmeier reagent

A 25 mL oven-dried reaction Schlenk tube was added with the vicinal diol **1** (1.0 mmol,1.0 equiv) and DCM (4.0 mL). Vilsmeier reagent (153.6 mg, 1.2 mmol,1.2 equiv) was added to the solution under nitrogen. The resulting solution was stirred at 40 ^{o}C for 12 h. After cooling to room temperature, the reaction mixture was added to aqueous $NaHCO_3$ (5%, 10 mL), aqueous phase was extracted with DCM (5 mL× 3). The combined organic phase was washed with brine, and then dried over anhydrous Na_2SO_4. After the solvent was removed under vacuum and the residue was purified by column chromatography to give the corresponding products.

2-Chloro-2-phenylethan-1-ol (2a):[22] Yellow liquid, 128.5 mg, 82 % yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.47 – 7.31 (m,

5H), 5.00 (dd, *J* = 7.5, 5.0 Hz, 1H), 3.99 – 3.86 (m, 2H), 2.17 (brs, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.9, 129.0, 128.9, 127.6, 68.0, 65.0. **(*S*)-2-Chloro-2-phenylethan-1-ol (2a')**:[23] Yellow liquid, 131.6 mg, 84 % yield. HPLC: Chiralcel AD-H column, hexane/*i*-PrOH=99/1, 0.8 ml/min, 230 nm, t_1=26.1 min, t_2=29.6 min. $[\alpha]_D^{25}$ = + 111.0 (*c* =0.10 in $CHCl_3$) for (*S*)-enantiomer with 95.2% ee. (Lit. $^{23}[\alpha]_D^{20}$ = +52.7 (*c* =1.0 in $CHCl_3$) for (S)-enantiomer with 44% ee).

2-Chloro-2-(*p*-tolyl)ethan-1-ol (2b):[24] Light yellow liquid, 131.1 mg, 77 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.26 (m, 2H), 7.21 – 7.14 (m, 2H), 4.95 (t, *J* = 5.6 Hz, 1H), 3.99 – 3.79 (m, 2H), 2.35 (s, 3H), 2.23 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 135.0, 129.6, 127.5, 67.9, 64.9, 21.3.

2-(4-(tert-Butyl)phenyl)-2-chloroethan-1-ol (2c): White solid, 149.0 mg, 70 % yield. M.P.:67.1-68.5 □. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.37 (m, 2H), 7.37 – 7.29 (m, 2H), 4.99 (dd, *J* = 7.6, 5.6 Hz, 1H), 4.01 – 3.86 (m, 2H), 2.15 – 2.02 (m, 1H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 134.9, 127.3, 125.9, 68.0, 65.0, 34.8, 31.4. HRMS-EI (m/z): Calculated for $C_{12}H_{17}{}^{35}ClO$ $(M)^+$: 212.0968, Found: 212.0970.

2-Chloro-2-(2,6-dimethylphenyl)ethan-1-ol (2d): Colorless liquid, 133.1 mg, 72 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.08 – 6.94 (m, 3H), 4.92 (dd, *J* = 8.0, 5.6 Hz, 1H), 3.98 – 3.85 (m, 2H), 2.33 (s, 6H), 2.13 (brs, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.6, 137.7, 130.7, 125.3, 67.9, 65.1, 21.4. HRMS-EI (m/z): Calculated for $C_{10}H_{13}{}^{35}ClO$ $(M)^+$: 184.0655, Found: 184.0660.

2-Chloro-2-(naphthalen-2-yl)ethan-1-ol (2e):[24] White solid, 134.0 mg, 65 % yield. M.P.:59.8-61.6 □. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97 – 7.80 (m, 4H), 7.61 – 7.42 (m, 3H), 5.17 (dd, *J* = 7.2, 5.2 Hz, 1H), 4.13 – 3.96 (m, 2H), 2.11 (brs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.2, 133.5, 133.1, 129.0, 128.2, 127.9, 127.1, 126.8, 126.8, 124.8, 67.9, 65.1.

2-Chloro-2-(naphthalen-1-yl)ethan-1-ol (2f):[24] Light yellow liquid, 115.0 mg, 56 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (d, *J* = 8.4 Hz, 1H), 7.93 – 7.84 (m, 2H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.62 – 7.47 (m, 3H), 5.86 (t, *J* = 6.4 Hz, 1H), 4.22 – 4.12 (m, 2H), 2.43 (brs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.9, 133.3, 130.7, 129.6, 129.2, 126.9, 126.1, 125.4, 125.4, 122.7, 67.3, 61.4. HRMS-EI (m/z): Calculated for $C_{12}H_{11}{}^{35}ClO$ $(M)^+$: 206.0498, Found: 206.0497.

2-Chloro-2-(3-methoxyphenyl)ethan-1-ol (2g): Light yellow liquid, 140.0 mg, 75 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 1H), 7.01 – 6.94 (m, 2H), 6.91 – 6.86 (m, 1H), 4.96 (dd, *J* = 6.8, 6.0 Hz, 1H), 3.96 – 3.90 (m, 2H), 3.82 (s, 3H), 2.09 (dd, *J* =8.0, 6.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 139.4, 129.9, 119.8, 114.3, 113.3, 67.9, 64.6, 55.4. HRMS-EI (m/z): Calculated for $C_9H_{11}{}^{35}ClO_2$ $(M)^+$: 186.0448, Found: 186.0446.

2-Chloro-2-(4-(trifluoromethyl)phenyl)ethan-1-ol (2h): Yellow liquid, 141.5 mg, 63% yield (**2h**:**3h**=91:9). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.64 (m, 2H), 7.61 – 7.54 (m, 2H), 5.05 (t, *J* = 6.0 Hz, 1H), 4.12 – 3.89 (m, 2H), 2.22 (brs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 131.2(q, *J* = 32.8 Hz), 128.1, 125.9(q, *J* = 3.7 Hz), 123.9(q, *J* =273.3 Hz), 67.8, 63.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.76. HRMS-EI (m/z): Calculated for $C_9H_8{}^{35}ClF_3O$ $(M)^+$: 224.0216, Found: 224.0219.

2-Chloro-2-(4-chlorophenyl)ethan-1-ol (2i):[24] Light yellow liquid, 152.9 mg, 80 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.29 (m, 4H), 5.03 – 4.88 (m, 1H), 3.96 – 3.82 (m, 2H), 2.38 (brs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.5, 134.8, 129.1, 129.0, 67.8, 63.9.

2-(4-Bromophenyl)-2-chloroethan-1-ol (2j):[24] Yellow liquid, 167.2 mg, 71 % liquid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 – 7.47 (m, 2H), 7.33 – 7.27 (m, 2H), 4.94 (t, *J* = 6.4 Hz, 1H), 3.97 – 3.85 (m, 2H), 2.11 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.1, 132.1, 129.3, 123.0, 67.9, 64.0.

2-Chloro-2-(2-chlorophenyl)ethan-1-ol (2k): Yellow liquid, 161.0 mg, 84 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 – 7.54 (m, 1H), 7.45 – 7.22 (m, 3H), 5.56 (dd, *J* = 7.6, 4.0 Hz, 1H), 4.07 – 3.83 (m, 2H), 2.32 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.3, 133.0, 129.9, 129.8, 129.2, 127.5, 66.9, 61.1. HRMS-ESI (m/z): Calculated for $C_8H_8{}^{35}Cl_2ONa$ $(M + Na)^+$: 212.9844, Found: 212.9848.

4-(1-Chloro-2-hydroxyethyl)benzonitrile (2l): Yellow liquid, 111.0 mg, 61 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 – 7.65 (m, 2H), 7.59 – 7.50 (m, 2H), 5.00 (t, *J* = 6.0 Hz, 1H), 3.94 (t, *J* = 6.4 Hz, 2H), 2.21 (t, *J* = 6.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 132.7, 128.5, 118.4, 112.8, 67.6, 63.3. HRMS-ESI (m/z): Calculated for $C_9H_8{}^{35}ClNO$ $(M)^+$:181.0294, Found: 181.0293.

4-(2-Chloro-1-hydroxyethyl)benzonitrile (3l): Yellow liquid, 21.8 mg, 12 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 5.02 – 4.94 (m, 1H), 3.76 (dd, *J* = 11.2, 3.6 Hz, 1H), 3.62 (dd, *J* = 11.6, 8.4 Hz, 1H), 2.81 (d, *J* = 3.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.1, 132.6, 127.0, 118.6, 112.4, 73.3, 50.5. HRMS-ESI (m/z): Calculated for $C_9H_8{}^{35}ClNO$ $(M)^+$:181.0294, Found: 181.0294.

3-Chloro-3-phenylpropan-1-ol (2m):[18] Yellow liquid, 129.4 mg, 76 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.28 (m, 5H), 5.21 – 5.07 (m, 1H), 3.94 – 3.82 (m, 1H), 3.79 – 3.68 (m, 1H), 2.42 – 2.19 (m, 2H), 1.79 (brs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.6, 128.8, 128.5, 127.1, 60.4, 59.9, 42.3. **(S)-3-Chloro-3-phenylpropan-1-ol (2m')**:[25] HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 99/1, 1.0 mL/min, 250 nm): t_1 = 24.2 min, t_2 = 29.2 min. $[\alpha]_D^{25}$ = – 72.0 (*c* = 0.10 in $CHCl_3$) for (*S*)-enantiomer with 69.4% ee.

3-Chloro-3-(3-nitrophenyl)propan-1-ol (2n) : Yellow liquid, 112.0 mg, 52 % yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 – 8.24 (m, 1H), 8.19 – 8.11 (m, 1H), 7.76 – 7.68 (m, 1H), 7.60 – 7.51 (m, 1H), 5.11 (dd, *J* = 8.8, 4.0 Hz, 1H), 3.86 – 3.75 (m, 1H), 3.65 – 3.56 (m, 1H), 2.32 – 2.06 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.7, 146.2, 132.0, 129.8, 122.9, 120.9, 70.4, 41.6, 41.4. HRMS-ESI (m/z): Calculated for $C_9H_{10}{}^{35}ClNO_3$ $(M)^+$:215.0349, Found: 215.0350.

1-Chloro-1-phenylpropan-2-ol (2o):[26] Yellow liquid, 143.3 mg, 84% yield (**2o**:**3o**=80:20). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.35 (m, 5H), 4.75 (d, *J* = 7.6 Hz, 1H), 4.22 – 4.09 (m, 1H), 2.63 (d, *J* = 3.6 Hz, 1H), 1.12 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 128.8, 128.8, 127.8, 72.1, 71.2, 19.5.

4-Chloro-4-phenylbutan-2-ol (2p): Yellow liquid, 152.8 mg, 83% yield(**2p**:**3p**=83:17). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.28 (m, 5H), 5.08 (t, *J* = 7.2 Hz, 1H), 3.75 – 3.62 (m, 1H), 2.41 – 2.30 (m, 1H), 2.23 – 2.11 (m, 1H), 1.64 (s, 1H), 1.21 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.2, 128.8, 128.6, 127.3, 65.9, 60.8, 49.0, 23.9. HRMS-ESI (m/z): Calculated for $C_{10}H_{13}{}^{35}ClO$ $(M - H_2O)^+$:166.0549, Found: 166.0551.

2-(4-(Chloromethyl)phenyl)ethan-1-ol (2q): White solid, 145.0 mg, 85% yield. M.P.:61.8-64.9 □. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.31 (m, 2H), 7.25 – 7.19 (m, 2H), 4.57 (s, 2H), 3.83 (t, *J* = 6.5 Hz, 2H), 2.85 (t, *J* = 6.5 Hz, 2H), 1.78 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.1, 135.7, 129.5, 128.9,

63.5, 46.2, 38.9. HRMS-ESI (m/z): Calculated for $C_9H_{11}{}^{35}ClONa$ $(M + Na)^+$: 193.0391, Found: 193.0396.

1-(Benzyloxy)-3-chloropropan-2-ol (3r):[18] Yellow liquid, 122.5 mg, 61% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.28 (m, 5H), 4.57 (s, 2H), 4.01 (t, *J* = 5.6 Hz, 1H), 3.70 – 3.54 (m, 4H), 2.60 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 128.6, 128.1, 127.9, 73.7, 70.9, 70.4, 46.2.

4.2. A typical procedure for the selective chlorination of unsymmetrical vicinal diols with Viehe's salt

A 25 mL oven-dried reaction Schlenk tube was added with the vicinal diol **1** (1.0 mmol,1.0 equiv) and DCM (4.0 mL). Viehe's salt (197.0 mg, 1.2 mmol,1.2 equiv) was added to the solution under N_2. The resulting solution was stirred at room temperature for 12 h. The reaction mixture was added to aqueous $NaHCO_3$ (5%, 10 mL), aqueous phase was extracted with DCM (5 mL × 3). The combined organic phase was washed with brine, and then dried over anhydrous Na_2SO_4. After the solvent was removed under vacuum and the residue was purified by column chromatography to give the corresponding products.

2-Chloro-2-phenylethyl dimethylcarbamate (5a): Yellow liquid, 196.2 mg, 86% yield (**5a**:**6a** = 97:3). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.30 (m, 5H), 5.10 (dd, *J* = 7.6, 6.0 Hz, 1H), 4.48 – 4.38 (m, 2H), 2.91 (brs, 3H), 2.86 (brs, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 138.0, 128.9, 128.8, 127.6, 69.0, 60.4, 36.6, 36.0. HRMS-ESI (m/z): Calculated for $C_{11}H_{14}{}^{35}ClNO_2$ Na (M + Na) $^+$:250.0605, Found: 250.0623. **(*R*)-2-Chloro-2-phenylethyl dimethylcarbamate (5a'):** Yellow liquid, 200.4 mg, 88% yield (**5a**:**6a** = 97:3). HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 254 nm): t_1 = 9.4 min, t_2 = 9.8 min. $[\alpha]_D^{25}$ = +73.8 (*c* = 0.10 in $CHCl_3$) for (*S*)-enantiomer with 99.9% ee.

2-Chloro-2-(*p*-tolyl)ethyl dimethylcarbamate (5b): Yellow liquid, 217.6 mg, 90% yield (**5b**:**6b** = 94:6). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 2H), 7.20 – 7.14 (m, 2H), 5.07 (t, *J* = 7.2 Hz, 1H), 4.45 – 4.37 (m, 2H), 2.91 (brs, 3H), 2.87 (brs, 3H)., 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 138.8, 135.1, 129.5, 127.4, 68.9, 60.4, 36.6, 36.0, 21.3. HRMS-ESI (m/z): Calculated for $C_{12}H_{16}{}^{35}ClNO_2Na$ (M + Na) $^+$: 264.0762, Found: 264.0776.

2-(4-(*tert*-Butyl)phenyl)-2-chloroethyl dimethylcarbamate (5c): White solid, 255.0 mg, 90% yield (**6c**:**7c** = 92:8). 63.5-65.0 □. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.32 (m, 4H), 5.09 (dd, *J* = 7.6, 5.2 Hz, 1H), 4.48 – 4.36 (m, 2H), 2.91 (brs, 3H), 2.89 (brs, 3H)., 1.32 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0, 152.0, 134.9, 127.2, 125.7, 69.0, 60.5, 36.6, 36.0, 34.8, 31.4. HRMS-ESI (m/z): Calculated for $C_{15}H_{22}{}^{35}ClNO_2Na$ (M + Na)$^+$: 306.1231, Found: 306.1247.

2-Chloro-2-(2,6-dimethylphenyl)ethyl dimethylcarbamate (5d): Yellow liquid, 212.4 mg, 83% yield (**5d**:**6d** = 93:7). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.02 (s, 2H), 6.96 (s, 1H), 5.03 (dd, *J* = 8.0, 5.6 Hz, 1H), 4.46 – 4.33 (m, 2H), 2.92 (brs, 3H), 2.89 (brs, 3H), 2.32 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0, 138.4, 137.8, 130.6, 125.3, 69.1, 60.8, 36.6, 36.0, 21.4. HRMS-ESI (m/z): Calculated for $C_{13}H_{18}{}^{35}ClNO_2Na$ (M + Na) $^+$: 278.0918, Found: 278.0930.

2-Chloro-2-(naphthalen-2-yl)ethyl dimethylcarbamate (5e): White solid, 180.2 mg, 79% yield (**5e**:**6e** = 97:3). M.P.: 88.9-90.1 □. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.92 – 7.78 (m, 4H), 7.57 – 7.42 (m, 3H), 5.27 (t, *J* = 6.8 Hz, 1H), 4.52 (d, *J* = 6.8 Hz, 2H), 2.89 (brs, 3H), 2.82 (brs, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 135.3, 133.4, 133.1, 128.8, 128.2, 127.8, 126.9, 126.7, 126.6, 124.8, 68.8, 60.6, 36.6, 36.0. HRMS-ESI (m/z): Calculated for $C_{15}H_{16}{}^{35}ClNO_2Na$ (M + Na) $^+$: 300.0762, Found: 300.0774.

2-Chloro-2-(3-methoxyphenyl)ethyl dimethylcarbamate (5g): Yellow liquid , 222.0 mg, 86% yield (**5g**:**6g** = 93:7). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.24 (m, 1H), 7.02 – 6.94 (m, 2H), 6.91 –6.84 (m, 1H), 5.16 – 4.99 (m, 1H), 4.47 – 4.36 (m, 2H), 3.82 (s, 3H), 2.91 (brs, 3H), 2.87 (brs, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9, 155.9, 139.5, 129.8, 119.8, 114.5, 113.1, 69.0, 60.4, 55.4, 36.6, 36.0. HRMS-ESI (m/z): Calculated for $C_{12}H_{16}{}^{35}ClNO_3Na$ (M + Na) $^+$: 280.0711, Found: 280.0720.

2-Chloro-2-(4-(trifluoromethyl)phenyl)ethyl dimethylcarbam-ate (5h): Yellow liquid, 266.0 mg, 96% yield (**5h**:**6h** = 85:15). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.68 – 7.61 (m, 2H), 7.58 – 7.53 (m, 2H), 5.14 (t, *J* = 6.8 Hz, 1H), 4.43 (d, *J* = 6.8 Hz, 2H), 2.91 (brs, 3H), 2.85 (brs, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.7, 142.0,131.1(q, *J* = 32.6 Hz), 128.0, 127.0,125.8(q, *J* = 4.0 Hz), 123.9(q, *J* = 272.8 Hz),68.6, 59.2, 36.6, 35.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.7. HRMS-ESI (m/z): Calculated for $C_{12}H_{13}{}^{35}ClF_3NO_2Na$ (M + Na) $^+$: 318.0479, Found: 318.0446.

2-Chloro-2-(4-chlorophenyl)ethyl dimethylcarbamate (5i) : Yellow liquid, 221.0 mg, 85% yield (**5i**:**6i** = 92:8). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.33 (m, 4H), 5.07 (t, *J* =7.2 Hz, 1H), 4.42 – 4.37 (m, 2H), 2.91 (brs, 3H), 2.85 (brs, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 136.6, 134.8, 129.0, 129.0, 68.7, 59.4, 36.6, 36.0. HRMS-ESI (m/z): Calculated for $C_{11}H_{13}{}^{35}Cl_2NO_2Na$ (M + Na) $^+$: 284.0216, Found: 284.0229.

2-Chloro-2-(2-chlorophenyl)ethyl dimethylcarbamate (5k) : Yellow liquid, 224.6 mg, 86 % yield (**5k**:**6k** = 96:4). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.66 – 7.60 (m, 1H), 7.41 – 7.24 (m, 4H), 5.64 (dd, *J* = 7.2, 5.6 Hz, 1H), 4.50 – 4.38 (m, 2H), 2.91 (brs, 3H), 2.87 (brs, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 135.6, 133.2, 130.0, 129.7, 129.2, 127.5, 67.9, 56.1, 36.6, 36.0. HRMS-ESI (m/z): Calculated for $C_{11}H_{13}{}^{35}Cl_2NO_2Na$ (M + Na) $^+$: 284.0216, Found: 284.0222.

2-Chloro-2-(4-cyanophenyl)ethyl dimethylcarbamate (5l): Yellow liquid, 217.3 mg, 86% yield (**5l**:**6l** = 85:15). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.70 – 7.61 (m, 2H), 7.57 – 7.50 (m, 2H), 5.10 (t, *J* = 6.8 Hz, 1H), 4.39 (d, *J* = 6.8 Hz, 2H), 2.88 (brs, 3H), 2.81 (brs, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 143.1, 128.4, 118.3, 112.7, 68.3, 58.8, 36.6, 35.9. HRMS-ESI (m/z): Calculated for $C_{12}H_{14}{}^{35}ClN_2O_2$ (M + H) $^+$: 253.0738., Found: 253.0723.

3-Chloro-3-phenylpropyl dimethylcarbamate (5m): Yellow liquid, 224.2 mg, 93% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.28 (m, 5H), 5.00 (dd, *J* = 8.5, 6.0 Hz, 1H), 4.29 – 4.10 (m, 2H), 2.90 (brs, 3H), 2.87 (brs, 3H), 2.49 – 2.33 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4, 141.2, 128.9, 128.6, 127.0, 62.5, 60.3, 39.4, 36.6, 36.0. HRMS-ESI (m/z): Calculated for $C_{12}H_{16}{}^{35}ClNO_2Na$ (M + Na) $^+$: 264.0762, Found: 264.0772. **(S)-3-Chloro-3-phenylpropyl dimethylcarbamate (5m'):** Yellow liquid, 217.0 mg, 90% yield. HPLC (Chiralcel AS-H column, hexane/*i*-PrOH = 99/1, 0.8 mL/min, 230 nm): t_1 =14.5 min, t_2 = 18.7 min. $[\alpha]_D^{23}$ = 56.0 (*c* = 0.10 in $CHCl_3$) for (*R*)-enantiomer with 95.8% ee.

3-Chloro-3-(3-nitrophenyl)propyl dimethylcarbamate (5n): Yellow liquid, 217.3 mg, 76% yield (**5n**:**6n** = 83:17). ^1H NMR (500 MHz, Chloroform-*d*) δ 8.26 (t, *J* = 2.0 Hz, 1H), 8.21 – 8.15 (m, 1H), 7.77 – 7.72 (m, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 5.07 (dd, *J* = 8.5, 6.0 Hz, 1H), 4.32 – 4.13 (m, 2H), 2.90 (brs, 3H), 2.87 (brs,

3H), 2.51 – 2.36 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2, 148.5, 143.4, 133.2, 130.0, 123.5, 122.2, 76.9, 62.1, 58.6, 39.3, 36.6, 36.0. HRMS-ESI (m/z): Calculated for $C_{12}H_{16}{}^{35}ClN_2O_4$ (M + H) $^+$: 287.0793, Found: 287.0788.

3-Chloro-1-(3-nitrophenyl)propyl dimethylcarbamate (6n): Yellow liquid, 22.9 mg, 8% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 (t, *J* = 2.0 Hz, 1H), 8.19 – 8.13 (m, 1H), 7.70 – 7.67 (m, 1H), 7.58 – 7.51 (m, 1H), 5.93 (dd, *J* = 9.0, 5.0 Hz, 1H), 3.69 – 3.46 (m, 2H), 3.02 (s, 3H), 2.90 (s, 3H), 2.48 – 2.35 (m, 1H), 2.25 – 2.17 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.4, 148.7, 143.0, 132.7, 129.8, 123.2, 121.0, 73.2, 40.5, 39.6, 36.7, 36.1. HRMS-ESI (m/z): Calculated for $C_{12}H_{16}{}^{35}ClN_2O_4$ (M + H) $^+$: 287.0793, Found: 287.0796.

1-Chloro-1-phenylpropan-2-yl dimethylcarbamate (5o) : Yellow liquid, 200.2 mg, 83% yield. (**5o**:**6o** = 75:25). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.29 (m, 7H), 5.26 – 5.16 (m, 1H), 4.89 (d, *J* = 6.8 Hz, 1H), 2.93 (s, 6H). HRMS-ESI (m/z): Calculated for $C_{12}H_{16}{}^{35}ClNO_2Na$ (M + Na) $^+$: 264.0762, Found: 264.0764.

1-(Benzyloxy)-3-chloropropane-2-yl dimethylcarbamate (6r): Yellow liquid, 192.9 mg, 71% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.27 (m, 5H), 5.13 – 5.03 (m, 1H), 4.61 – 4.52 (m, 2H), 3.84 – 3.62 (m, 4H), 2.90 (brs, 3H), 2.84 (brs, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 138.0, 128.6, 127.9, 127.8, 73.5, 72.5, 68.6, 43.7, 36.6, 36.1. HRMS-ESI (m/z): Calculated for $C_{13}H_{18}{}^{35}ClNO_3Na$ (M + Na) $^+$:294.0867, Found: 294.0872.

1-Chloro-4-phenylbutan-2-yl dimethylcarbamate (6s): Yellow liquid, 179.0 mg, 70% yield (**5s**:**6s** = 6:94). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.31 – 7.27 (m, 2H), 7.22 – 7.17 (m, 3H), 5.01 – 4.94 (m, 1H), 3.74 – 3.59 (m, 2H), 2.93 (s, 3H), 2.90 (s, 3H), 2.77 – 2.63 (m, 2H), 2.16 – 1.93 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 141.3, 128.6, 128.4, 126.2, 73.3, 46.4, 36.6, 35.9, 33.5, 31.6. HRMS-ESI (m/z): Calculated for $C_{13}H_{19}{}^{35}ClNO_2$ (M + H) $^+$: 256.1099, Found: 256.1085.

1-Chlorodecan-2-yl dimethylcarbamate (6t): Yellow liquid, 223.4 mg, 85% yield (**5t**:**6t** = 11:89). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.95 – 4.85 (m, 1H), 3.71 – 3.55 (m, 2H), 2.92 (s, 6H), 1.74 – 1.63 (m, 2H), 1.40 – 1.18 (m, 12H), 0.88 (t, *J* = 6.8, 6.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 73.8, 46.4, 36.5, 35.9, 31.9, 31.7, 29.5, 29.3, 25.2, 22.8, 14.2. HRMS-ESI (m/z): Calculated for $C_{13}H_{27}{}^{35}ClNO_2$ (M + H) $^+$: 264.1725, Found: 264.1728.

1-Chloro-5-phenylpentan-3-yl dimethylcarbamate (6u): Yellow liquid, 215.7 mg, 76% yield (**5u**:**6u** > 1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.35 – 7.27 (m, 3H), 7.25 – 7.17 (m, 3H), 5.05 – 4.96 (m, 1H), 3.65 – 3.54 (m, 2H), 2.95 (s, 3H), 2.90 (s, 3H), 2.76 – 2.64 (m, 2H), 2.19 – 2.04 (m, 2H), 2.04 – 1.87 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.3, 141.6, 128.5, 128.4, 126.1, 72.5, 41.1, 37.9, 36.6, 36.4, 35.9, 31.8. HRMS-ESI (m/z): Calculated for $C_{14}H_{21}{}^{35}ClNO_2$ (M + H) $^+$: 270.1255, Found: 270.1254.

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Supplementary Material

Supplementary data (experimental information and characterisation data for vicinal diols (**1**) as well as the spectra copies of the diols and the products) associated with this article can be found, in the online version, at.

Selective monochlorination of unsymmetrical vicinal diols with chlorinated iminium chlorides

Liqun Yang [a], Xiaotong Li [a], Yu Wang [a], Chengyang Li [a], Xiaoyu Wu [a], Zhaoguo Zhang [a,b], and Xiaomin Xie [a,*]

[a] *School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, China*

[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Fenglin Road, Shanghai 200032, China

Highlights

- **Easily available chlorination reagents**
- **Mild conditions and medium to excellent yields**
- **High chemo- and regio-selectivity**
- **Chlorohydrins and chlorohydrin carbamates as the products**
- **The monochlorinated products with retained enantiopure**

* Corresponding author. Tel.: +86-021-5474-8925; fax: +86-021-5474-8925; e-mail: xiaominxie@sjtu.edu.cn

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: