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FULL PAPER

Lewis Base Catalysis Enables the Activation of Alcohols by means of Chloroformates as Phosgene Substitutes

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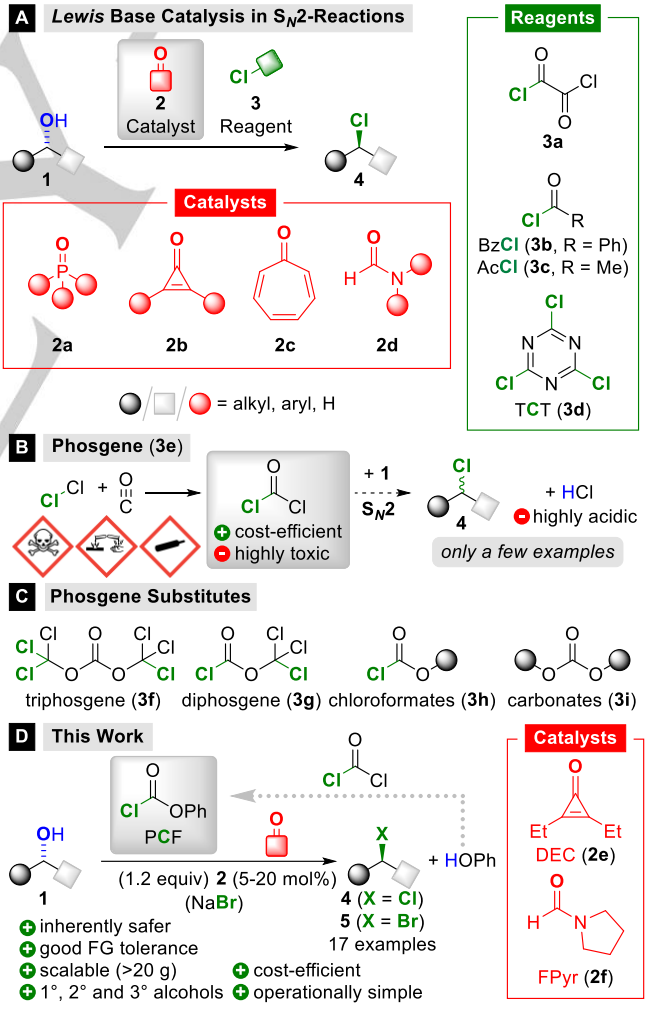
Abstract: Nucleophilic substitutions (S_N) are typically promoted by acid chlorides as sacrificial reagents to improve the thermodynamic driving force and lower kinetic barriers. However, the cheapest acid chloride phosgene ($COCl_2$) is a highly toxic gas. Against this background, phenyl chloroformate (PCF) was discovered as inherently safer phosgene substitute for the S_N-type formation of C-Cl and C-Br bonds using alcohols. Thereby, application of the Lewis bases 1-formylpyrroldine (FPyr) and diethylcyclopropenone (DEC) as catalysts turned out to be pivotal to shift the chemoselectivity in favor of halo alkane generation. Primary, secondary and tertiary, benzylic, allylic and aliphatic alcohols are appropriate starting materials. A variety of functional groups are tolerated, which includes even acid labile moieties such as *tert*-butyl esters and acetals. Since the by-product phenol can be isolated, a recycling to PCF with inexpensive phosgene would be feasible on a technical scale. Eventually, a thorough competitive study demonstrated that PCF is indeed superior to phosgene and other substitutes.

Introduction

Nucleophilic substitutions (S_N) engaging alcohols **1** belong to the most elementary and crucial chemical transformations.[1-3] Lewis base catalysis provides an effective technology for the activation of alcohols to alkyl chlorides of type **4**, for example (Scheme 1 **A**).[1,4-9] Especially phosphane oxides **2a**,[4] cyclopropenones **2b**,[5a,b,d] tropone (**2c**)[5c] and formamides **2d**[6] have been discovered as potent catalysts for C-Cl, C-Br and C-O bond formations. Actually, these OH group exchanges are promoted by acid chlorides like oxalyl chloride (**3a**), BzCl (**3b**), AcCl (**3c**) and TCT (**3d**). Importantly, without a suitable catalyst the reaction of alcohols **1** with the aforementioned acid chlorides typically afford the respective esters. Notably, alkyl halides like **4** are important intermediates for the generation of C-O, C-S, C-N and C-C bonds. This type of catalysis is also applicable to carboxylic acids,[5c,7] aldehydes and epoxides[8] and culminated recently into the development of a fully catalytic Mitsunobu reaction.[9]



Scheme 1. A Lewis base catalyzed S_N2-type transformations with alcohols, **B** synthesis of phosgene and activation of alcohols, **C** phosgene surrogates and **D** this work. AcCl = acetyl chloride, BzCl = benzoyl chloride, DEC = diethylcyclopropenone, FPyr = 1-formylpyrrolidine, PCF = phenyl chloroformate TCT = 2,4,6-trichloro-1,3,5-triazine.

Actually, OH groups as in alcohols are rather poor leaving groups, because a highly Brønsted basic hydroxide anion emerges from a S_N-reaction.[1-3] Therefore, sacrificial reagents like acid chlorides are commonly applied, which enable the conversion of hydroxy functions into improved leaving groups (for examples see above). Consequently, not only kinetic barriers are reduced but also the thermodynamic driving force is tremendously enhanced.

In fact, the by far cheapest acid chloride is gaseous phosgene ($COCl_2$), which is produced from the commodity chemicals CO and Cl_2 (Scheme 1 **B**).[10] Surprisingly, examples for transformations of alcohols into chloro alkanes that rely on carbonyldichloride are rare and mainly available in the patent literature.[11,12] This might be in part reasoned by the high toxicity of $COCl_2$, which had been utilized as warfare agent in the first world war.[10] Furthermore, alkyl chloroformates, which are amenable from alkanols using phosgene (or **3f**),[10] are transformed into alkyl chlorides through heating.[13] Actually, Lewis bases like dimethylformamide (DMF) accelerate this decomposition reaction.[14,15]

To solve the severe safety issues associated with the handling of phosgene, several substitutes[10a,b,16] have been introduced: Examples are tri- and diphosgene **3f** and **3g**,[17] chloroformates of type **3h**,[18] carbonates **3i**[19] and CO_2[20] (Scheme 1 **C**). As described by Kartika, the use of triphosgene (**3f**) enables the synthesis of type **4** substitution products in high levels of functional group tolerance, when either pyridine or NEt_3 are engaged as base and catalyst.[21] Worthy of note, tri- and diphosgene are synthesized in industry from Cl_2 and dimethyl carbonate and methyl chloroformate, respectively.[10a,b,17]

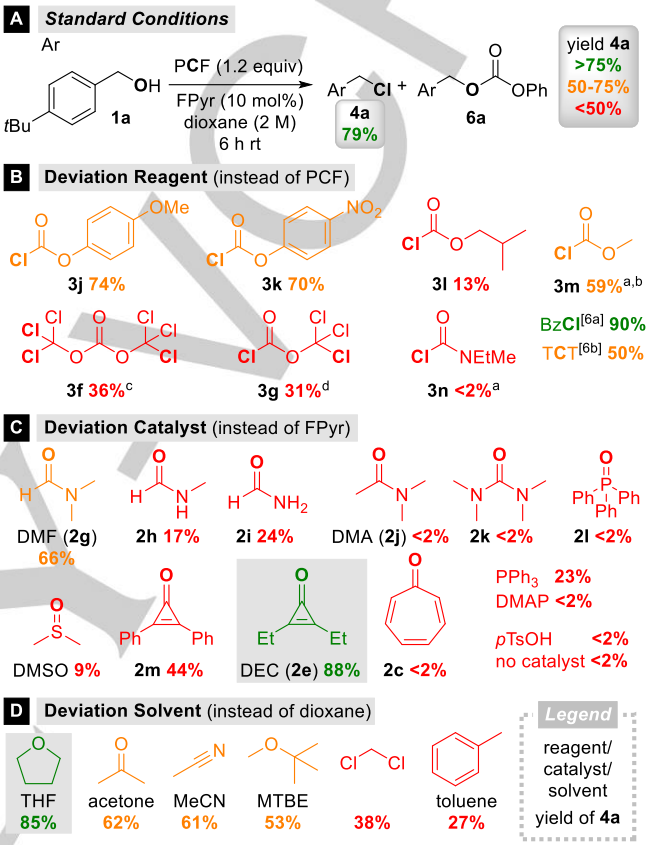
Indeed, chloroformates **3h** have to the best of our knowledge so far not been applied as reagents to forge C-Cl and C-Br motifs.[22] However, their use as reagents for S_N-processes would enable a recycling of the corresponding alcohol by-product by means of phosgene. Under consideration of the high cost-efficiency of phosgene (and its inherently hazardous nature), the formation of C-X bonds by means of chloroformates constitutes a highly attractive target (X = halogen). Unfortunately, reaction of alcohols with type **3h** agents usually furnishes the respective carbonates.[18] Herein, we demonstrate that formamide and cyclopropenone catalysts enable the activation of alcohols with phenyl chloroformate (PCF) in a highly efficient manner (Scheme 1 **D**).

Results and Discussion

Method Development

Benzylic alcohol **1a** was chosen as simplified model compound for the optimization of the reaction conditions (Scheme 2). In the presence of 10 mol% 1-formylpyrrolidine (FPyr), chloride **4a** was formed in 79% yield upon reaction with PCF in dioxane at room temperature (Scheme 2 **A**). The respective carbonate **6a** was only observed in trace amounts (ratio **4a**/**6a** 93:7). Based on these standard conditions as reference point, the influence of deviations will be discussed in the following. In Scheme 2, the structures of the applied acid chlorides, Lewis bases and solvents, respectively, are displayed. Below these formulas the yields of **4a** that have been accomplished under the respective deviation from the standard conditions are stated. In addition, ranges of yields are clearly visualized with the aid of a traffic light color code. Worthy of note, an increase of the reaction duration from 6 to 20 h effected an enhanced yield of **4a** of 92%, because the starting material was completely consumed (see Table S1 in the Supporting Information = SI).

Substitution of PCF by more complex electron rich and electron poor chloroformates **3j** and **3k** caused slightly deteriorated yields (Scheme 2 **B**, see Table S1 and S2 in the SI for further information on the reagent screen). Use of aliphatic acid chloride **3l** afforded model product **4a** in a very low yield of 13%.



Scheme 2. Optimization of reactions conditions. Yields were determined by means of internal NMR standard. a. Reaction time 24 h instead of 6. b. Reaction temperature 40 °C. c. 40 mol% reagent used. d. 60 mol% reagent used. Ar = 4-*tert*-butylphenyl, DMA = dimethylacetamide, DMAP = 4-(dimethylamino)pyridine, DMF = dimethylformamide, MTBE = methyl-*tert*-butylether, *p*TsOH = *para*-tolylsulfonic acid, THF = tetrahydrofurane.

With plain methyl chloroformate (**3m**) a moderate yield of 59% was accomplished, when the reaction duration and time were increased to 40 °C and 24 h, respectively. Since the yield was still lower than in the case of PCF and the MeOH released as by-product could potentially result in diminished chemoselectivities **4**/**6**, aliphatic chloroformates were ruled out. Importantly, in the absence of a NEt_3 and pyridine[21] both, tri- and diphosgene (**3f** and **3g**) turned out to be rather poor reagents for the preparation of chloro alkanes. Nevertheless, FPyr exerted a catalytic effect, because in the absence of this formamide formation of halide **4a** was not observed (see SI). A comparative assessment against phosgene was included in Table 1 below. Interestingly, reaction of substrate **1a** with carbamoyl chloride **3n** did not furnish any product at all. According to our previous method[6a] the utilization of BzCl instead of PCF gave **4a** in an enhanced yield of 90%, which is comparable to the yields accomplished after reaction with

PCF after 20 h (see above). However, chloride **4a** emerged from the reaction of **1a** with TCT[6b] in a clearly mitigated yield of 50%.

After identification of PCF as optimal chloroformate, different Lewis bases were probed regarding their catalytic proficiency (Scheme 2 **C**). DMF (**2g**) turned out to be a less feasible catalyst, because the benzylic chloride **4a** was formed in a reduced yield of 66%. The test of **2h**, **2i**, dimethylacetamide (DMA, **2j**) and **2k** furnished the desired S_N-product in very low yields ≤24%. These finding prove that the formyl proton cannot be replaced by another group and that two alkyl moieties on the N-atom are required.

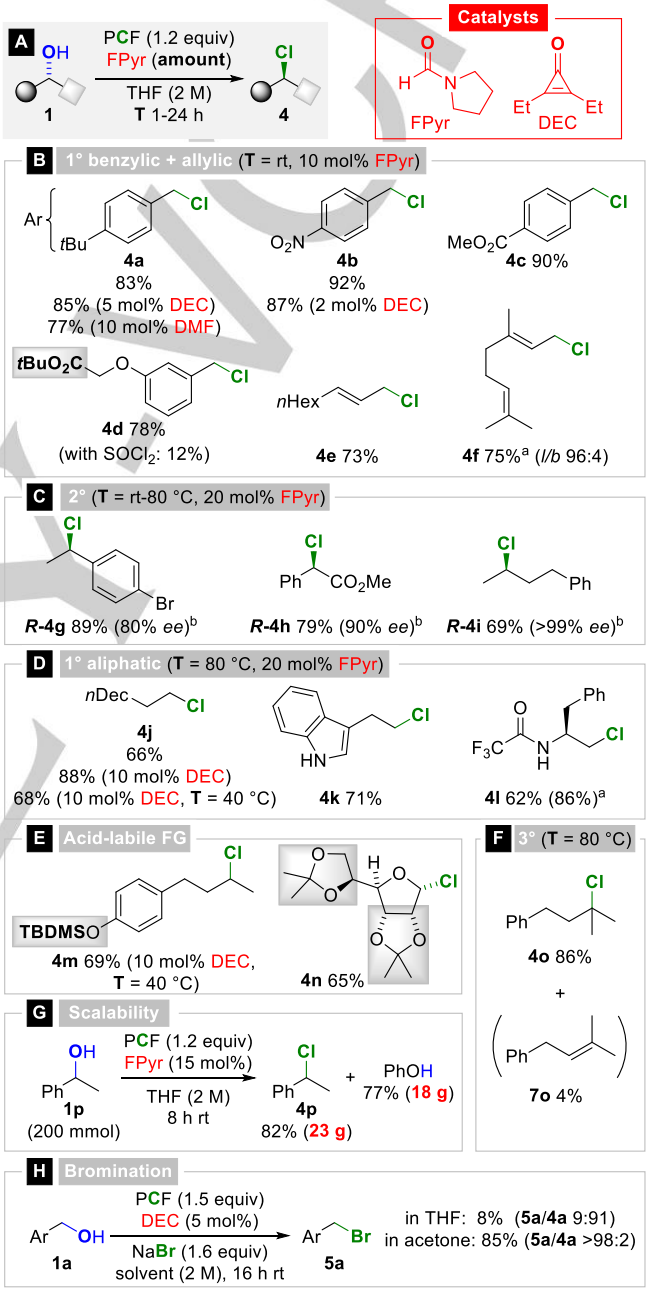
In addition, phosphaneoxide **2l**, which has been reported as powerful catalyst in concert with oxalyl chloride for related transformations,[4] did not allow for the synthesis of **4a**. Usage of dimethylsulfoxide (DMSO) was realized as ineffective Lewis base, too. While halide **4a** formed in the presence of diphenylcyclopropenone (**2m**) in moderate yield, application of the sterically less shielded diethyl derivative diethylcyclopropenone (DEC, **2e**) enabled the production of **4a** in an improved yield of 88%. In agreement with our previous findings,[5d] cyclopropenones were realized as more competent catalysts than formamides. Despite reports on tropone (**2c**) promoted S_N-transformations with $(COCl)_2$,[5c,7a] in the case of the reagent PCF no product **4a** could be detected. In addition, engagement of the widespread Lewis bases PPh_3 and DMAP and the Brønsted acid *p*TsOH did not entail generation of chloroalkane **4a**. As an important aspect, reaction of alcohol **1a** with PCF in the absence of a viable catalyst only affords carbonate **6a** as exclusive product. In conclusion, the assessment of various Lewis bases showed that only specific compounds, namely FPyr and DEC, enable the production of alkyl chlorides with PCF in synthetically meaningful yields. Further details on the catalyst survey are located in Table S3 in the SI.

Ultimately, an investigation of the reaction solvent certified THF as superior reaction medium, which facilitated an increased yield of 85% (in comparison to 79% yield with dioxane, Scheme 2 **D**, see also chp. 1.3 in the SI). Usage of the aprotic polar solvents acetone and MeCN allowed to access **4a** in moderate yields of 61-62%, albeit an extended reaction duration made yields up to 89% possible (see Table S4 in the SI). Pleasingly, non environmental-friendly dichloromethane was recognized as poor solvent, which also accounts for non-polar toluene. To summarize the solvent screening, aprotic, highly polar solvents are the best choice for the preparation of alkyl chlorides with PCF.

Substrate Scope

After the determination of the optimal reaction conditions, we explored the substrate scope (Scheme 3). While the syntheses of benzylic and allylic chlorides were conducted at room temperature (Scheme 3 **B**), less reactive aliphatic starting materials required heating to 80 °C (Scheme 3 **D**). The elevated reaction temperatures **T** are needed to allow for a catalytic turn-over.[6a,b] Whereas THF had been realized as optimal solvent for benzylic and allylic alcohols (see Scheme 2 **D**), transformations of aliphatic substrates were carried out preferentially in 1,4-dioxane due to its higher boiling point. In the case of primary starting materials full conversion was accomplished within 6 h. However, sterically more demanding secondary substrates typically required stirring overnight to ensure full consumption. A detailed reaction conditions guide based on the type of starting material and a representative graphical procedure are located in the SI (chp. 4 and 5.2.4).

In the case of benzylic alcohols, utilization of DEC allowed to decrease the catalyst loading from 10 down to 2 mol% (examples **4a** and **4b**). In addition, FPyr could also be replaced by the common organic solvent DMF in substoichiometric quantities, which furnished chloride **4a** in a slightly diminished yield of 77% (compared to 83% with FPyr). The remarkably mild reaction conditions are witnessed by the preparation of acid-labile *tert*-butyl ester **4d**. In contrast, attempted production of **4d** using thionyl chloride gave rise of chloro alkane **4d** in only 12% yield.



Scheme 3. Substrate scope. For detailed reaction conditions see SI. Yield determined after chromatographic purification. a. Prepared from the respective *S*-configured alcohols in ≥99% *ee*. b. Yield determined with the aid of an internal NMR standard. *b* = branched, *ee* = enantiomeric excess, *l* = linear, rt = room temperature, T = temperature, TBDMS = *tert*-butyldimethylsilyl.

In the instance of $SOCl_2$ highly acidic HCl is formed as by-product, whereas the present approach affords phenol and CO_2 as neutral

by-products. The less acidic reaction medium explains the compatibility with acid-sensitive moieties. Additionally, volatile allylic chloride **4e** was obtained as a single regio- and diastereomer according to NMR. Nevertheless, when the allylic alcohol geraniol was reacted with PCF in the presence of FPyr, a 96:4 mixture of geranyl chloride (**4f**) and its branched regioisomer was obtained (see SI for details). Since chlorinations of geraniol with thionyl chloride basically take place without any selectivity,[6a] PCF is superior. Nevertheless, the combination of BzCl and FPyr[6a] or DEC[5d] enabled improved selectivities even on a >100 g scale. Transformations involving secondary, non-racemic alcohols (≥99% *ee*) proceeded under stereochemical inversion in high levels of stereospecificity (Scheme 3 **C**). In order to accelerate the consumption of these substrates, the amount of FPyr was raised to 20 mol%. The benzylic and an electron-deficient alkyl chloride ***R*-4g** and **4h**, respectively, were formed in 80-90% *ee*, while in the case of the volatile aliphatic product **4i** no erosion of enantiopurity was observed. A change of the solvent from THF to less polar EtOAc facilitated an improvement of the *ee* of **4h** from 83 to 90% (see SI).

Moreover, aliphatic chloride **4j** was isolated in a yield of 66%, when 20 mol% of FPyr were engaged as catalyst at 80 °C (Scheme 3 **D**). The moderate yield is rationalized by formation of dodecyl phenyl carbonate (**6j**) as side-product in increased amounts (**4j**/**6j** 76:24). In the case of BzCl and TCT better yields up to 87% were reached.[6a,b] This example may display the higher electrophilicity of PCF in comparison to BzCl and TCT. Nevertheless, application of the Lewis base DEC[5d] (10 mol%) furnished 1-chloro dodecane in an excellent yield of 88% (**4j**/**6j** 92:8). With DEC the reaction temperature could even be lowered to 40 °C, although **4j** arose in a lower yield of 68% alongside with increased quantities of dodecyl phenyl carbonate (**4j**/**6j** 70:30).

The tolerance of functional groups that are labile towards acidic reaction conditions is highlighted by the production of silyl ether **4m** and the sugar derived α-chloro ether **4n**, which contains two acetal moieties, and **4d** (Scheme 3 **E**). Other compatible functional group are esters (**4c**, **4h**), nitro substituents (**4b**) alkenes (**4e**, **4f**) indoles (**4k**) and a secondary amide (**4l**). Remarkably, even tertiary chloride **4o** was created in an excellent yield of 86% (Scheme 3 **F**). Thereby, the use of MeCN as solvent allowed to minimize formation of undesired elimination side-products like alkene **7o**. This may be reasoned by the slightly acidic reaction medium. With triphosgene and pyridine tertiary chlorides are not amenable due to rivalling olefin formation.[21c,d]

General limitations of Lewis base catalyzed syntheses of chloro alkanes are (1) sterically encumbered substrates like cyclohexanol derivatives.[6a] (2) Highly acid-sensitive functions like methoxymethyl ethers (MOM) are only tolerated when N*i*Bu$_3$ is used as base.[5d] And (3) basic functional groups like amines are incompatible, because the direct condensation of alcohols **1** with the acid chloride reagent is accelerated. In addition, cyclopropenone catalysis is not amenable to certain polar functional groups including indoles and secondary amides with an NH motif.[5d]

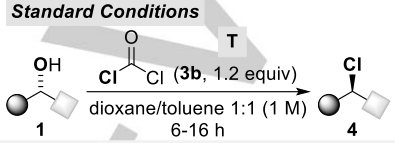
As an important feature, scalability was verified by means of the synthesis of chloro alkane **4p** on a >20 g scale (Scheme 3 **G**). Besides chloride **4p**, also phenol was isolated, which proves the opportunity to recycle this by-product with inexpensive phosgene. In addition, this example, highlights the operational simplicity of the current approach: No strict exclusion of water and air was necessary to access **4p** on a 200 mmol scale (see chp. 5.2.6 in the SI for an exemplary graphical procedure). Finally, even alkyl bromides of type **5** can be synthesized under Finkelstein-type reaction conditions using NaBr (Scheme 3 **H**). Significantly, the alteration of the reaction solvent from THF to acetone enabled very high levels of chemoselectivity in favor of bromide **5a** (**5a**/**4a** 9:91→≥98:2).

Comparative Study

Since only limited data regarding activation of alcohols by means of phosgene is available,[11.21b] a thorough comparative assessment using four different starting materials was conducted (Table 1, see chp. 2 in the SI). In Table 1 ranges of yields are again illustrated by a traffic light color code. At the outset, a solution of the respective alcohol in dioxane was combined with a commercial 20 wt% solution of phosgene in toluene, which resulted in a 1:1 mixture of these solvents, and stirred at the reaction temperature **T** for 6-16 h (entry 1).

Table 1. Comparative study using phosgene.

Standard Conditions



Products		4a	4f	*R*-4g[a]	4j
Entry	Deviations T =	rt	rt	rt	80 °C
1	/	<2%	64% (*l*/*b* 81:19)	10% (n.d.)	<2%
2	FPyr (cat.)	20%	83% (*l*/*b* 86:14)	71% (36% *ee*)[b]	67%
3	NEt_3	74%	59% (*l*/*b* >98:2)	54% (88% *ee*)	75%[c]
4	**this work**	78%	63% (*l*/*b* 94:6)	85% (89% *ee*)	72%

For detailed reaction conditions see SI. Yields were determined by means of an internal NMR standard. a. Prepared from the respective *S*-configured alcohol in ≥99% *ee*. b. Carried out at 40 °C instead of rt. c. Performed at rt instead of 80 °C.

Indeed, under these "standard conditions" mainly the respective chloroformates were formed, while the requested alkyl chlorides of type **4** were only observed in trace amounts. The only exception is highly reactive allylic geraniol, which gave **4f** as a mixture of regioisomers in a moderate yield of 64%. Next, the syntheses of chlorides **4a**, **4f**, ***R*-4g** and **4j** were repeated in the presence of FPyr (10-20 mol%, entry 2): Improved yields for type **4** products verified a significant catalytic effect. Nevertheless, benzylic halide **4a** arose in a low yield of 20%. In order to reach high levels of conversion the reaction affording ***R*-4g** had to be heated to 40 °C. This in turn resulted in severe racemization (99%→36% *ee*). In comparison to tri- and diphosgene (Scheme 2 **B**), a clearly enhanced outcome was accomplished. This may be traced back to the higher electrophilicity of phosgene in comparison to afore-mentioned surrogates.

The use of NEt_3 in the absence of FPyr promoted the synthesis of all four chlorides with phosgene in moderate to good yields of 54-75% (entry 3). A surprisingly good regioselectivity and stereospecificity were observed in the case of geranyl chloride (**4f**, *l*/*b* ≥98:2) and chiral chloride ***R*-4g** (99%→88% *ee*), respectively. For the reason of comparability, the four model products were also prepared according to the current approach but using a 1:1 mixture of dioxane and toluene as solvent system (entry 4). In fact,

higher yields in the case of the benzylic chlorides **4a** and ***R*-4g** (and a comparable enantiopurity) evidenced that the present approach is superior to phosgene activation. Reaction in dioxane/toluene 1:1 instead of more polar THF using PCF afforded ***R*-4g** even in an *ee* of 89% (see also Scheme 3 **C**).

Interestingly, the chemical yield for the preparation of geranyl chloride (**4f**) is higher, when phosgene and FPyr are engaged (83% vs. 63%). Nevertheless, a lower regioselectivity was accomplished (*l*/*b* 86:14 compared to 94:6). Only when the synthesis of **4f** was carried out with phosgene and NEt_3, a better regioselectivity was reached than with this work (*l*/*b* ≥98:2 against 94:6). In the event of aliphatic chloride **4j** the present protocol and phosgene in conjunction with NEt_3 allowed for comparable yields (72% vs. 75%). In conclusion, the present approach enables comparable or even better yields and selectivities with the exception of highly isomerization sensitive geraniol. Furthermore, chlorinations with phosgene in the absence of a base give rise of HCl as by-product like in the case of thionyl chloride. Therefore, lower levels of functional group compatibility can be anticipated (see example **4d** in Scheme 3 **B**).

Sensitivity Assessment

To easily evaluate the sensitivity of chemical methods towards deviations from the standard conditions, the so-called sensitivity assessment has been coined by Glorius.[23] Thereby, a set of experiments is carried out, in which one reaction parameter is varied at the time. The change in terms of product yield in comparison to the standard reaction conditions as reference point is illustrated by means of a radar diagram (Figure 1).[23] This facilitates the identification of pivotal reaction parameters with a large impact on the reaction outcome, which is decisive for the reproducibility.

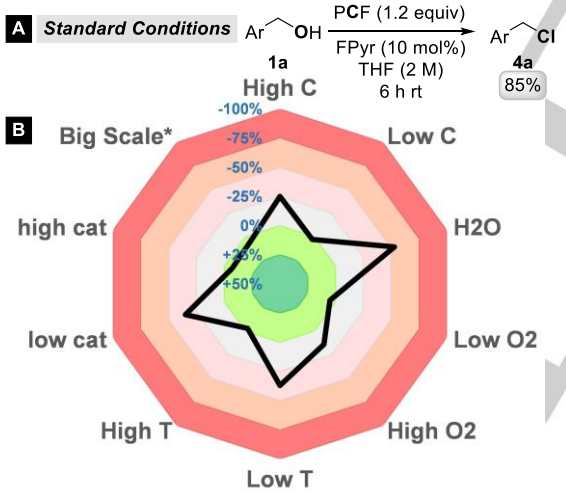


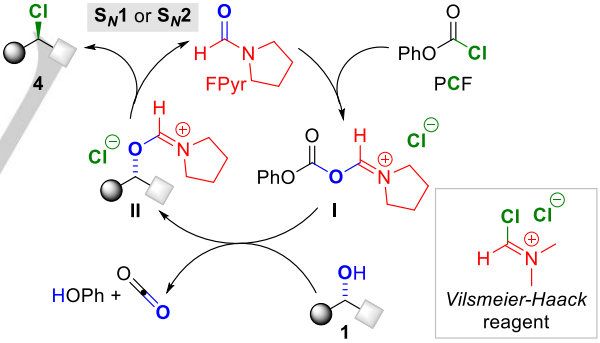
Figure 1. Sensitivity assessment according to Glorius. *Upscaling was demonstrated with the reaction in Scheme 3 **G**. Ar = 4-*tert*-butylbenzyl, C = concentration.

Investigated parameters are substrate concentration (entries "low C" and "high C"), water content ("H2O") and oxygen ("low O2" and "high O2"), reaction temperature ("low T" and "high T") and scalability ("big scale"). The light intensity in the original protocol was exchanged by the catalyst amount ("high cat." and "low cat."). For the assessment of the current method we mostly choose stronger differences from the standard conditions as originally suggested (see chp. 4 in SI). The findings of the sensitivity assessment in the instance of the model reaction **1a**→**4a** (see Figure 1 **A**) demonstrated a relatively low sensitivity towards alterations of the conditions, because the standard yield of 85% turned out to be well reproducible (Figure 1 **B**).

Addition of water (1 vol%, entry "H2O"), a lower catalyst amount (5 mol%, "low cat") and a decreased reaction temperature **T** (10 instead of 25 °C, "Low T") resulted in deteriorated yields. Water likely causes hydrolysis of PCF and electrophilic intermediates, while the lower catalyst loading and temperature result in diminished reaction rates and therefore lower levels of conversion. In addition, also a lower solvent amount (= high concentration of the substrate, "High C") had a negative impact on the product yield, since pronounced phenyl carbonate **6a** formation was detected (**4a**/**6a** 73:27 instead of 90:10). Finally, scalability was evidence by a 100-fold upscaling in the production of chloride **4p** (Scheme 3 **G**).

Reaction Mechanism

In accordance with our previous reports,[5d,6a,b] a plausible mechanism with FPyr as catalyst is proposed in Scheme 4. In the beginning, a condensation of the Lewis basic catalyst **3** with the *Lewis* acidic reagent PCF is expected. The forming intermediate **I** is structural related with the *Vilsmeier-Haack* reagent. Indirect evidence for **I** was gathered by the reaction of PCF with DMF in MeCN, which mainly afforded phenol and phenyl formate. Both are probable products of the hydrolysis of **I**. Since BzCl does not seem to react with FPyr even at elevated temperatures,[6a] type **I** intermediates are most likely generated in a rapid and endothermic equilibrium. In addition, benzoyloxyiminium triflates related to **I** have been accessed using BzCl, DMF and silver triflate,[24] which substantiates the current mechanistic proposal.



Scheme 4. Proposed mechanism exemplified with FPyr.

Next, nucleophilic attack of the alcohol **1** onto electrophilic species **I** should yield phenol, gaseous CO_2 and alkoxyiminium chloride **II** which have been witnessed in our previous report.[6a] Finally, **II** most likely undergoes a S_N1 or S_N2-substitution, which is influenced by the carbon backbone of the substrate **1**, to furnish the final product **4** and the catalyst **3** for another turn-over.[25]

Conclusion

Herein, a novel catalytic method for the activation of alcohols to chloro and bromo alkanes, which is promoted by phenyl chloroformate (PCF) as phosgene substitute, has been implemented. Since reaction of chloroformates with alcohols

typically furnishes the respective carbonates, a Lewis base catalyst is pivotal to switch chemoselectivity in favor for C-Cl and C-Br bond formation. Indeed, 1-formylpyrrolidine (FPyr) and diethylcyclopropenone (DEC) were identified as potent catalysts, which is evidenced by turn-over numbers up to 40. Remarkably, primary, secondary and even tertiary substrates are suitable regardless if they are benzylic, allylic or aliphatic.

As an important aspect, acid labile functions like *tert*-butylesters, acetals and silylethers are compatible. This is reasoned by the emergence of neutral phenol and CO_2 as by-products instead of strongly acidic HCl like in the case of chlorinations exploiting phosgene ($COCl_2$) and thionyl chloride ($SOCl_2$). The isolation of phenol attested that a recycling using phosgene, which is the cheapest reagent for the activation of OH groups, would be reasonable in a technical scale. In addition, these nucleophilic substitutions proceed under stereochemical inversion in high levels of stereospecificity. Actually, a comparative survey verified that PCF is superior to tri- and diphosgene and even $COCl_2$. Finally, a sensitivity assessment according to Glorius revealed that the reaction conditions are not very sensitive towards alterations. Currently, other S_N-type bond formations relying on PCF are under investigation and will be reported in due course.

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Keywords: organocatalysis • nucleophilic substitutions • phosgene substitutes • stereochemical inversion • homogenous catalysis

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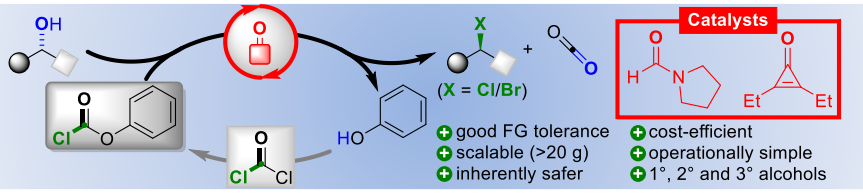

As substitute for hazardous and gaseous phosgene, phenyl chloroformate enables the activation of alcohols to halo alkanes in the presence of an appropriate Lewis base catalyst. Indeed, 1-formylpyrrolidine (FPyr) or diethylcyclopropenone (DEC) are crucial as catalytic species to drive the chemoselectivity from phenyl carbonate to the desired alkyl halide formation. The isolation of the by-product phenol shows that conceptually a recycling by means of inexpensive phosgene is feasible.

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