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Intermolecular Halogenation/Esterification of Alkenes with N–Halosuccinimide and Acetic Acid Catalyzed by DABCO

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Abstract. DABCO (1,4-diazabicyclo[2.2.2]octane) is a suitable Lewis base that acts as an organocatalyst in the activation of N–chlorosuccinimide (NCS) towards chlorination of alkenes. The chloriranium ion formed from NCS and the alkene, can be intermolecularly opened by a nucleophile, such as acetic acid, to produce highly functionalized *trans*-chloroesters in high yields. The protocol is also applied to the synthesis of chlorohydrins and chloroethers using water or methanol as nucleophiles instead of acetic acid. Brominated analogs can also be synthesized from alkenes and N–bromosuccinimide (NBS) in the presence of various basic catalysts. However, the reaction pattern seems to be remarkably different. The catalytic performance of bases in the bromoesterification of alkenes was found to be strongly affected by their Brønsted-basicity, suggesting that acetyl hypobromite, formed *in situ* from NBS and acetic acid, acts as a real brominating agent in these systems.

Keywords: *Alkenes; Bromination; Chlorination; Chloroester; N–Chlorosuccinimide; Organocatalysis*

Introduction

Catalytic halenium ion (e.g., Cl^+, Br^+) transfer to an alkene followed by nucleophilic ring opening of the haliranium ion is a powerful tool to produce highly functionalized organic compounds.[1] In the past years, much effort has been devoted toward the monohalogenation of alkenes. Perhaps, the most studied transformation is the intramolecular halolactonization and haloetherification of organic substrates employing haloimide-based reagents (e.g., N-halosucciminide, N-halophthalimide).[2] These processes have been extensively explored and nowadays represent a consolidated method for the alkene functional group transformation, even in an asymmetric fashion.[3]

The intermolecular version of these reactions delivers halohydrin, haloether or haloester derivatives. Collectively, these substances represent a class of privileged natural and synthetic compounds, which find broad application in chemical and biological processes.[4] Even though new approaches and methodologies for the synthesis of bromohydrin and related compounds have been well explored,[5] the research for efficient ways to produce chlorinated analogs still has plenty of room for improvement. For instance, chloroester derivatives are most commonly prepared by the catalytic ring opening of epoxides with acid chlorides.[6] Diols can also be used as substrates to prepare various chlorohydrin derivatives whose nature depends on the reaction conditions and reagents used.[7] Alternatively, these compounds can be synthesized from alkenes by treatment with chlorinating agents such as acetyl hypochlorite (AcOCl),[8] chromyl chloride in acetyl chloride,[9] trichloroisocyanuric acid[10] or with $PhICl_2$ in wet DMF.[11] Oxidation of chloride salts by (diacetoxyiodo)benzene in the presence of a phase transfer catalyst has also been reported for alkene chloroesterification.[12]

Despite the recent advent of potent chlorinating agents such as CDSC ($Et_2SCl{\bullet}SbCl_6$)[13] and Palau'chlor®,[14] N-chlorosuccinimide (NCS) remains to be a useful, inexpensive and reliable reagent for the electrophilic chlorination of organic substrates.[15] NCS is a mild chlorine transfer agent and in most cases it is not capable to chlorinate alkenes in uncatalyzed reactions. This feature opens up the possibility to better control the regio-, diastereo-, and stereochemical outcome of the process by the activation of NCS with an appropriate organocatalyst (Lewis acid or base).[3b] Surprisingly just a few reports in the literature account for the chlorination and intermolecular functionalization of alkenes with NCS: products such as chlorohydrins,[16] chloroethers[17] and chloroamides[18] have been prepared using this approach.

Accordingly, as part of our interest in the halofunctionalization of organic substrates,[19] we

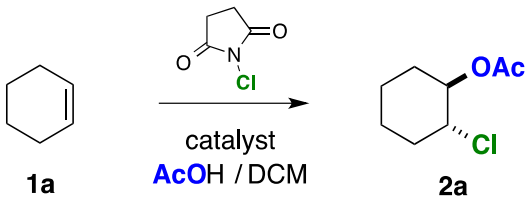
describe herein a simple, straightforward and efficient protocol for the synthesis of chloroester starting from alkenes. The method consists of the treatment of starting materials with NCS in acetic acid in the presence of catalytic amounts of DABCO. The protocol can also be applied to the synthesis of chlorohydrins, chloroethers and bromoesters from alkenes (using in this case *N*-bromosuccinimide as a source of bromine).

Results and Discussion

As a model reaction, the chloroesterification of cyclohexene **1a** was investigated using *N*–chlorosuccinimide, acetic acid as the nucleophile and 10 mol–% of different Lewis bases as organocatalysts. Representative results are shown in Table 1. All experiments were performed in the dark at 20 ± 2 ºC employing dichloromethane as the solvent. The progress of the reaction was monitored by gas chromatography using undecane as the internal standard. Initially, a set of phosphorus, sulfur and selenium-based organocatalysts was tested. Unfortunately none of them was effective to promote the desired conversion (Entries 1–3). Next, we turned out our attention to nitrogen-based catalysts. Pyridine, 2,4,6-trimethylaniline, 4-methylmorpholine, triethylamine and DMAP (4-dimethylamino-pyridine) were tested and again, little if any catalytic activity was observed after two hours of reaction (Entries 4–8).

An encouraging result was obtained using 10 mol–% of DABCO (1,4-diazabicyclo[2.2.2]octane) and two equivalents of acetic acid: *trans*–chloroacetate **2a** was obtained in 46% yield (Entry 9). Increasing the amount of acetic acid to five equivalents related to cyclohexene as well as extending the reaction time to 6 hours resulted in higher yields of product (Entries 10 and 11). It can be seen that the reaction occurs faster in the presence of increased amounts of AcOH (Entries 9 and 10). The best reaction condition to obtain chloroester **2a** was achieved with 20 mol–% of DACBO, a slight excess of NCS and 10 equivalents of acetic acid. After a two-hour reaction, product **2a** was obtained in 95% yield (Entry 12). In a control experiment under identical conditions, but without the catalyst, no substrate conversion and no formation of product **2a** were detected (Entry 13). Other catalysts and solvents were also screened, but unfortunately, chloroacetate **2a** was produced in lower yields (the results are presented in the supporting information). Noteworthy is that the catalytic activity of organic bases in the chloroesterification of cyclohexene did not correlate at all with their Brønsted basicity. For example, DMAP and pyridine showed much lower activity than DABCO (Entries 4, 6 and 7).

Table 1. Optimization of the reaction conditions for the synthesis of chloroacetate **2a.**[a]



1a **2a**

Entry	catalyst (mol–%)	AcOH (equiv.)	Yield (%)[b]
1	Ph_3P (10)	2	2 ± 0
2	Ph_3PS (10)	2	3 ± 0
3	Ph_3PSe (10)	2	NR[c]
4	Pyridine (10)	2	NR[c]
5	2,4,6-Trimethylaniline (10)	2	NR[c]
6	DMAP (10)	2	6 ± 0
7	4-Methylmorpholine	2	4 ± 0
8	Triethylamine	2	11 ± 1
9	DABCO (10)	2	46 ± 1
10	DABCO (10)	5	64 ± 0
11[d]	DABCO (10)	5	76 ± 1
12[e]	DABCO (20)	10	95 ± 1
13[e]	None	10	NR[c]

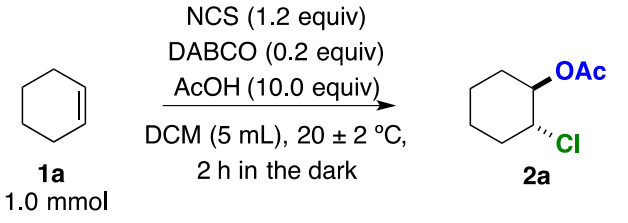
[a] Reaction conditions: cyclohexene (1.0 mmol), NCS (1.0 mmol), AcOH (2.0 – 10.0 mmol), catalyst (10.0 – 20.0 mol–%, related to cyclohexene), undecane (internal standard, 0.5 mmol) and dichloromethane (5.0 mL). Reactions were performed during two hours, in the dark (in an amber flask wrapped with an aluminium foil) at 20 ± 2 ºC (water bath). [b] GC yield (average for duplicate runs). [c] NR = no reaction within two hours. [d] Six hours of reaction. [e] Reaction with 1.2 mmol of NCS. DMAP = 4-dimethylamino-pyridine; DABCO = 1,4-diazabicyclo[2.2.2]octane.

With the optimized reaction conditions in hands, control experiments were designed to better understand the reaction mechanism (Scheme 1). It was observed that after two hours of reaction the experiments conducted in the dark or under the daylight gave essentially the same yield of chloroacetate **2a**: 95% and 94%, respectively. A similar result was obtained in the presence of 0.2 equivalents of BHT (butylated hydroxytoluene), which is a radical inhibitor, suggesting that the process involves the formation of ionic rather than radical intermediates. These results point out for a process that occurs mainly by an ionic pathway.

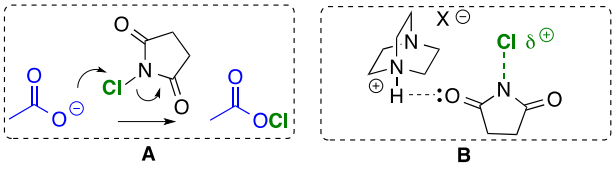
As the reaction occurs in acidic media and is accelerated by DABCO, which can also act as a Brønsted base and deprotonate acetic acid, one can speculate that the chlorine transfer agent could be acetyl hypochloride (AcOCl)[8] formed *in situ* from NCS and the acetate ion, as shown in Scheme **1** (dotted box **A**). To check this hypothesis, we swapped the organocatalyst/base DABCO by cesium carbonate, an inorganic base strong enough to deprotonate acetic acid and soluble in the reaction media. However, in the reaction conducted with Cs_2CO_3 instead of DABCO, no formation of product **2a** was detected at all. This result suggests that acetyl

hypochloride is not the real chlorinating agent acting in our reaction.

Another plausible explanation for the reaction outcome could be the activation of NCS by the interaction with a protonated DABCO species as shown in Scheme **1** (dotted box **B**). The difference in the pK_a values of the compounds involved in the reaction allows the formation, in appreciable concentrations, only of the monoprotonated DABCO derivative (pk_a of AcOH = 4.8 *vs* 3.0 and 8.8 for protonated DABCO species). On the other hand, the use of a stronger acid such as trifluoroacetic acid (pK_a of TFA = – 0.3) would permit the protonation of both nitrogen atoms in the DABCO molecule making it even more effective in the activation of NCS by this manner. To verify this supposition, we performed the reaction in the presence of various amounts of TFA. At equimolar TFA/DABCO concentration, chloroester **2a** was formed in a yield considerable lower than in the absence of TFA.[20] Moreover, further increase in the TFA concentration virtually shouted down the chloroesterification of cyclohexene catalyzed by DABCO. These results ruled out the assumption that the activation of NCS could occur by the interaction of N-chlorosuccinimide's oxygen atoms with the protonated molecule of the catalyst.

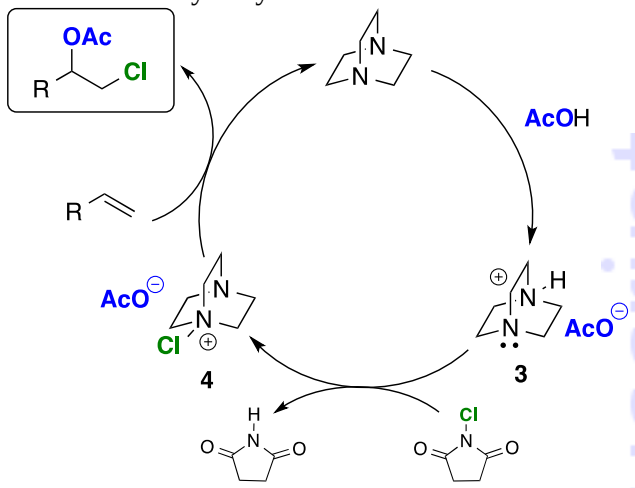


change in the reaction condition:	GC Yield (%)
none	95 ± 1
reaction exposed to daylight	94 ± 1
addition of BHT (0.2 equiv)	90 ± 1
Cs_2CO_3 (0.2 equiv) instead of DABCO	NR [a]
addition of TFA (0.2 equiv)	74 ± 2
addition of TFA (0.4 equiv)	1 ± 1



Scheme 1. Effect of additives and/reaction conditions on the chloroesterification of cyclohexene **1a**. [a] NR = no reaction within two hours. BHT = butylated hydroxytoluene; TFA = trifluoroacetic acid.

Based on the obtained experimental evidences, we proposed the following mechanism for the DABCO catalyzed chloroesterification of alkenes with NCS (Scheme **2**). The first event in the sequence is probably the Brønsted acid/base reaction between DABCO and AcOH producing protonated species **3**, which seems to be the truly catalyst in this system. The remaining nitrogen's lone pair on **3** could act as a Lewis base [21] and attack the chlorine atom of NCS to produce succinimide and intermediate **4**, the actual chlorinating agent in the process. [22] The formation of the chloroester can be rationalized by the subsequent attack of the nucleophile (acetate or acetic acid) on the chloriranium ion formed between **4** and the alkene, delivering the final product and DABCO to resume the catalytic cycle.



Scheme 2. Proposed reaction mechanism.

The proposed mechanism is additionally supported by the observation that nitrogen-based compounds which lack the second tertiary amine fragment (such as 4-methylmorpholine and triethylamine, were inefficient catalysts for this reaction (Table 1, Entries 7 and 8). Protonation by acetic acid seems to inactivate these compounds toward the interaction with NCS. It should also be mentioned that formation of acetyl hypochlorite in the reaction solution cannot be completely ruled out. However, the results obtained indicate that the contribution of the reaction pathway involving acetyl hypochlorite is not significant under the conditions used.

To verify the substrate scope and limitations, experiments with a set of different alkenes were conducted under the conditions optimized for cyclohexene. A small but important change in the reaction conditions was made: instead of DCM, the reactions were performed in glacial acetic acid, thus avoiding the use of a strongly regulated chlorinated solvent (Table 2). A two-hour reaction with cyclohexene produced *trans*-chloroester **2a** in 84% yield. Methyl-cyclohexene, 1-octene and 2-hexene (mixture of *cis* and *trans*) gave under the same conditions the corresponding chloroacetates **2b**, **2c** and **2d** in a range of 53–95% yield. The product derived from 1-octene was detected as a 3:1 mixture of two regioisomers **2c** and **2c'** isolated in a 95% combined yield. On the hand, the reaction with 2-hexene produced a complex mixture of isomers **2d**.

Table 2. Substrate scope for the synthesis of chloroacetate **2**.[a]

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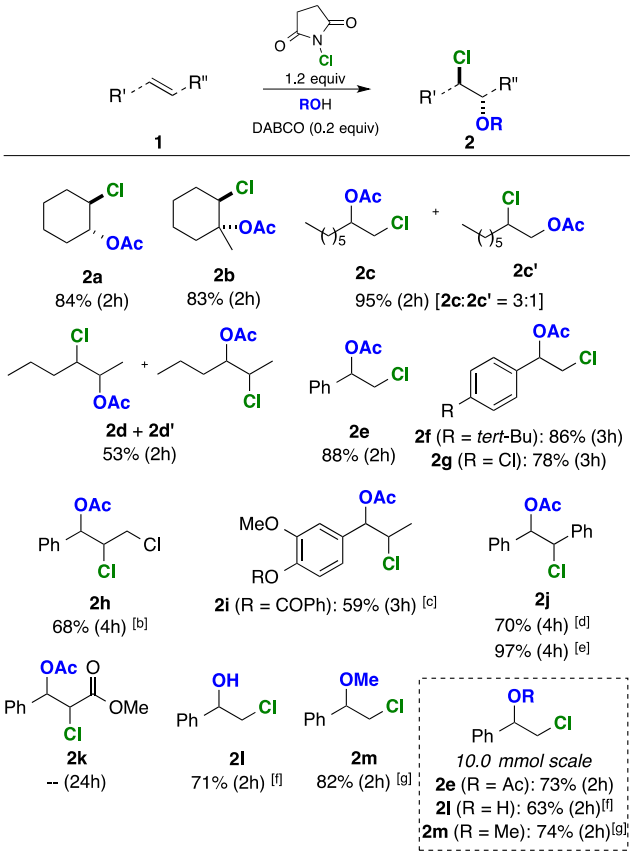
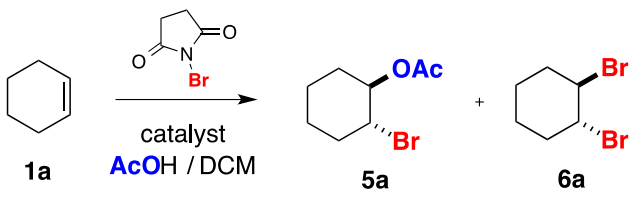


[a] Reaction conditions: substrate (1.0 mmol), glacial acetic acid (2.0 mL), DABCO (22 mg, 0.2 mmol) NCS (160 mg, 1.2 mmol) at 20 ± 2 ºC (water bath, under the daylight). Reaction times are given in parenthesis and yields are of pure, isolated products. [b] Product obtained as a 2/1 mixture of diastereoisomers. [c] Product obtained as a 2.5/1 mixture of diastereoisomers. [d] Starting material: *E*–stilbene, solvent: DCM/AcOH (1/1 v/v; 4.0 mL total), product ratio: syn/anti = 1/1. [e] Starting material: *Z*–stilbene, product ratio: syn/anti = 1/1. [f] Solvent = H_2O/THF (1/1 v/v; 2.0 mL total). [g] Solvent: MeOH (2.0 mL).

Styrene derivatives were also subjected to the reaction producing the corresponding chloroacetates **2e–g** in ca. 80–90 % yields. Cinnamyl chloride was also a suitable substrate for the reaction. Highly functionalized dichloride acetate **2h** was isolated in 68% yield after 4 hours of reaction. An attempt to employ isoeugenol as substrate did not show encouraging results. Formation of numerous products was observed by GC with low selectivity. Due to the complexity of the reaction mixture these products were not identified. We suppose that the concomitant chlorination at the aromatic ring occurs along with the desired oxidation of the alkene. Converting isoeugenol to its *O*-benzoyl derivative allowed to perform the oxidation of the olefinic bond with an acceptable selectivity: product **2j** was isolated in 59% yield. Reactions with *E* and *Z* stilbenes were also efficient. It is noteworthy that from both stilbenes a 1:1 mixture of the corresponding *syn* and *anti*–chloroesters **2j** was obtained suggesting a freely rotating opened carbocation rather than a cyclic chloriranium ion as the preferred intermediate of the electrophilic addition of chlorine to these substrates. Additionally, *E*-stilbene was sparingly soluble in the reaction media, even after the addition of DCM, furnishing the product in a lower yield. A limitation of the process was evidenced when an electron poor alkene, methyl cinnamate, was tested as the starting material: product **2k** was not detected in the reaction solution even after 24 hours. On the other hand, the scope of this reaction can be extended to other chlorohydrin derivatives by changing the solvent (nucleophile) nature. Styrene gave the corresponding chlorohydrin **2l** and chloroether **2m** in 71 and 82% yields when the reaction was performed in aqueous THF or in methanol, respectively. Preparative reactions were successfully performed using 10 mmol of styrene as starting material. Chlorinated products **2e**, **2l** and **2m** were obtained in 63–74% yield.

Lastly, we investigated the bromoesterification of cyclohexene with *N*–bromosuccinimide (NBS) and AcOH[23] and compared the results with the chlorination protocol. Cyclohexene was treated with NBS in DMC solutions containing acetic acid and catalytic amounts of various organic and inorganic bases. In the blank reaction, without the catalyst added, the main product detected after 60 minutes was *trans*-1,2-dibromocyclohexane **6a** obtained in 21% yield along with 4% of bromoacetate **5a** (Table 3, Entry 1). The addition of catalytic amounts of DMAP or DABCO (5 mol–%) resulted in drastic changes in the reaction kinetics and product distribution: after 15 minutes bromoacetate **5a** was obtained in 84% and 81% yields, respectively along with small amounts of the dibrominated product **6a** (Entries 2 and 3). Pyridine, a less basic compound than DMAP and DABCO, proved to be an inefficient organocatalyst for this transformation showing nearly the same results as the reaction without the catalyst (Entries 4 vs. 1). The increase in the amount of DABCO to 10 mol–% affected not only the reaction rate, but also the product selectivity: bromoacetate **5a** was obtained in 93% yield along with only 1% of the dibromide (Entry 5 vs. entry 3). On the other hand, in a sharp contrast with the chlorination process, the catalytic performance of cesium carbonate was similar to those of DMAP and DABCO (cf. entry 6 with entries 2, 3 and 5). Moreover, sodium acetate, sparingly soluble in the reaction mixture, was also able to activate NBS and promote the formation of bromoacetate **5a** from cyclohexene in 55% yield (Entry 7).

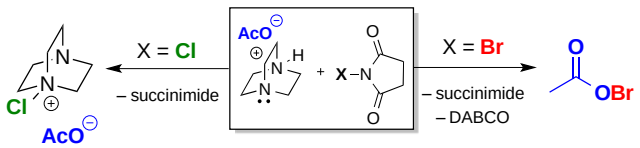
Table 3. Optimization of the reaction conditions for the synthesis of bromoacetate **5a.**[a]



Entry	catalyst (mol–%)	Time (min)	Yield (%)[b]	
			5a	**6a**
1	none	60	4 ± 0	21 ± 1
2	DMAP (5)	15	84 ± 2	3 ± 0
3	DABCO (5)	15	81 ± 1	6 ± 1
4	Pyridine (5)	15	5 ± 1	19 ± 0
5	DABCO (10)	15	93 ± 1	1 ± 0
6	Cs_2CO_3 (10)	15	76 ± 2	2 ± 1
7	AcONa (10)	15	55 ± 2	1 ± 0

[a] Reaction conditions: cyclohexene (1.0 mmol), NBS (1.0 mmol), AcOH (2.0 mmol), catalyst (5.0 – 10.0 mol–%, related to cyclohexene), undecane (internal standard, 0.5 mmol) and DCM (5.0 mL). Reactions were performed in the dark (in an amber flask wrapped with an aluminium foil) at 20 ± 2 ºC (water bath). [b] GC yield (average for duplicate runs).

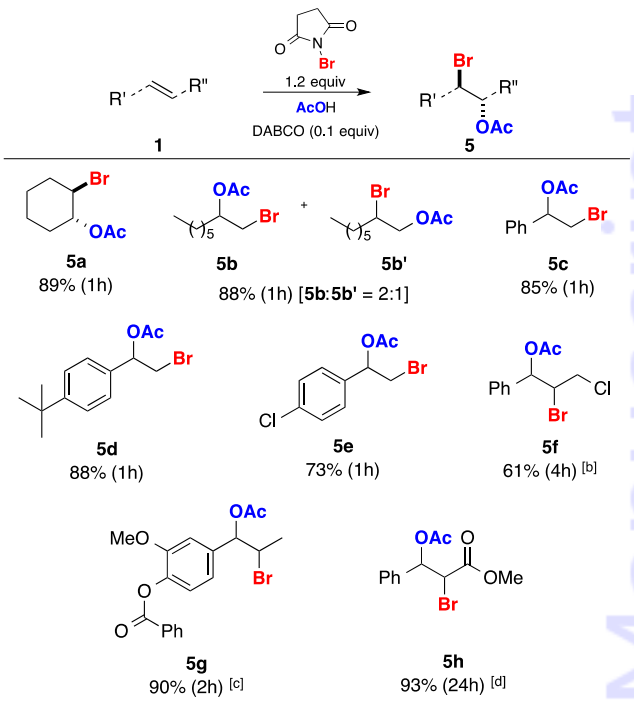
These results indicate that differently from the chloroesterification process, in the bromoacetoxylation of alkenes with NBS and acetic acid, the catalyst efficiency and product distribution are directly related to the Brønsted-basicity of the catalyst employed. The formation of bromoacetate **5a** seems to be the result of the reaction between cyclohexene and acetyl hypobromite,[24] formed *in situ* by the reaction between the acetate ion and NBS. In other words, the role of the organocatalyst in the bromination process more likely consists in the deprotonation of acetic acid (thus favoring the formation of acetyl hypobromite) rather than in the direct participation in the halogen atom transfer from NBS to alkene (Scheme **3**).



Scheme 3. Different activation types of NBS and NCS with an organocatalyst (DABCO for instance) towards haloesterification of alkenes.

Representative examples of brominated products synthesized are depicted in Table 4. Likewise in the reactions for the chlorination of alkenes, the use of the strongly regulated chlorinated solvent DCM was avoided. All the experiments were conducted in glacial acetic acid solutions (substrate concentration of 0.5 M) with 1.2 equivalents of NBS and 10 mol% of the catalyst, in the dark at 20 ± 2 ºC. *Trans*-bromoacetate **5a** was isolated in 89% yield after the oxidation of cyclohexene. The reaction with 1-octene gave a 2/1 mixture of isomers **5b** in 88% yield. Styrene and its derivatives were successfully converted to the corresponding bromoacetates **5c–e**. An interesting product, compound **5f**, was obtained in 61% yield from cinnamyl chloride after a 4-hour reaction. Product **5g** was produced in a high yield from *O*-benzoyl-isoeugenol. Differently from what was observed in the chloroacetoxylation, electron poor methyl cinnamate was effectively converted to the corresponding bromoacetate. Although a longer reaction time was required for the full conversion of the starting material, product **5h** was isolated in 93% yield.

Table 4. Substrate scope for the synthesis of bromoacetate **5.**[a]



[a] Reaction conditions: substrate (1.0 mmol), glacial acetic acid (2.0 mL), DABCO (11 mg, 0.1 mmol) NBS (214 mg, 1.2 mmol) at 20 ± 2 ºC (water bath, in the dark: amber flask wrapped with aluminum foil). Reaction times are given in parenthesis and yields are of pure, isolated products. [b] Product obtained as a 5/1 mixture of diastereoisomers. [c] Product obtained as a 14/1 mixture of diastereoisomers. [d] Product obtained as an 11/1 mixture of diastereoisomers.

Conclusion

In summary, a simple and straightforward protocol for the intramolecular chloro and bromoesterification of alkenes employing acetic acid and *N*-halosuccinimide was conceived. One of the advantages of the developed procedure is the use of acetic acid as solvent as well as the acetoxylating reagent. In this regard, the use of an organic co–solvent, particularly a chlorinated one can be avoided. Among several organocatalysts tested, commercially available DABCO proved to be a superior catalyst in the chloroacetoxylation of cyclohexene. Control experiments indicate that DACBO acts as a Lewis base in the activation of NCS and is the "truly chlorinating agent" in the process, participating directly in the chlorine atom transfer from NCS to the alkene molecule. The protocol can also be

conveniently extended to the preparation of chloroethers or chlorohydrins by changing the solvent by alcohols or water. On the other hand, bromoesterification of alkenes using NBS is affected to a greater extent by the Brønsted-basicity of the catalyst, suggesting acetyl hypobromite as the real brominating agent.

Experimental Section

Optimization of the Chloroacetoxylation of Cyclohexene: in an amber, screw capped 3 dram vial, wrapped with aluminium foil, *N*-chlorosuccinimide (1.0 – 1.2 mmol) was added to a solution of catalyst (0.1 – 0.2 mmol), undecane (107 µL, 0.5 mmol), glacial acetic acid (2.0 – 10.0 mmol) and cyclohexene (101 µL, 1.0 mmol) in dichloromethane (5.0 mL). The reaction was performed at 20 ± 2 ºC (reaction vessel immersed in a water bath). No precautions were taken to exclude oxygen or water from the reaction media. After two hours, the reaction was quenched with $NaHSO_3$ 2M (0.5 mL). The organic phase was separated, dried over $MgSO_4$, filtered and injected in the GC. The reported yields represent an average of duplicate runs.

Procedure for Chloroacetoxylation Of Alkenes: a 25 mL one-neck flask was charged with substrate (1.0 mmol), glacial acetic acid (2.0 mL), DABCO (22 mg, 0.2 mmol) and *N*-chlorosuccinimide (160 mg, 1.2 mmol). No precautions were taken to avoid light, oxygen or water on the reaction media. The mixture was then stirred at 20 ± 2 ºC (water bath) for the appropriate amount of time (the progress of the reaction was followed by gas chromatography). At the end of the reaction, it was diluted with hexanes (25 mL) and extracted with distilled water (3 x 10 mL). The organic phase was washed with Na_2CO_3 1M (1 x 10 mL), dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The product was purified by silica gel chromatography.

Procedure for Chlorohydroxylation of Styrene: in a 25 mL one-neck flask, *N*-chlorosuccinimide (160 mg, 1.2 mmol) was added to a mixture of DABCO (22 mg, 0.2 mmol) and styrene (115 µL, 1.0 mmol) in a mixture of distilled water (1.0 mL) and THF (1.0 mL). No precautions were taken to avoid light, oxygen or water on the reaction media. The mixture was stirred at 20 ± 2 ºC (water bath) during 2 hours. The reaction mixture was then diluted with 30 mL of AcOEt and washed with water (2 x 20 mL). The combined organic phase was dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The product was purified by silica gel chromatography.

Procedure for Chloromethoxylation of Styrene: in a 25 mL one-neck flask *N*-chlorosuccinimide (160 mg, 1.2 mmol) was added to a solution of DABCO (22 mg, 0.2 mmol) and styrene (115 µL, 1.0 mmol) in methanol (2.0 mL). No precautions were taken to avoid light, oxygen or water on the reaction media. The mixture was then stirred at 20 ± 2 ºC (water bath) during 2 hours. The solvent was removed under reduced pressure, and the product purified by silica gel chromatography.

Optimization of the Bromoacetoxylation of Cyclohexene: in an amber, screw capped 3 dram vial, wrapped with aluminium foil, *N*-bromosuccinimide (178 mg, 1.0 mmol) was added to a solution of catalyst (0.05 – 0.10 mmol), undecane (107 µL, 0.5 mmol), glacial acetic acid (114 µL, 2.0 mmol) and cyclohexene (101 µL, 1.0 mmol) in dichloromethane (5.0 mL). The reaction was performed at 20 ± 2 ºC (reaction vessel immersed in a water bath). No precautions were taken to exclude oxygen or water from the reaction media. After 15 minutes, the reaction was quenched with $NaHSO_3$ 2M (0.5 mL). The organic phase was separated, dried over $MgSO_4$, filtered and injected in the CG. The reported yields represent an average of duplicate runs.

General Procedure for Bromoacetoxylation of Alkenes: an amber, screw capped 3 dram vial, wrapped with aluminium foil, was charged with substrate (1.0 mmol), glacial acetic acid (2.0 mL), DABCO (11 mg, 0.10 mmol) and *N*-bromosuccinimide (214 mg, 1.2 mmol). The mixture was then stirred at 20 ± 2 ºC (water bath) for the appropriate amount of time (the progress of the reaction was followed by gas chromatography). At the end of the reaction, it was diluted with hexanes (25 mL) and extracted with distilled water (3 x 10 mL). The organic phase was washed with Na_2CO_3 1M (1 x 10 mL), dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The product was purified by silica gel chromatography.

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