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# Catalytic Synthesis of Saturated Oxygen Heterocycles by Hydrofunctionalization of Unactivated Olefins: "Unprotected" and "Protected" Strategies

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**ABSTRACT:** A mild, general, and functional group tolerant intramolecular hydroalkoxylation and hydroacyloxylation of unactivated olefins using a Co(salen) complex, an *N*-fluoropyridinium salt, and a disiloxane reagent is described. This reaction was carried out at room temperature and afforded five- and six-membered oxygen heterocyclic compounds, such as cyclic ethers and lactones. The Co-complex was optimized for previously rare medium-ring formation by hydrofunctionalization of unactivated olefins. The powerful Co-catalyst system also enables the deprotective hydroalkoxylation of *O*-protected alkenyl alcohol and hydroacyloxylation of alkenyl ester to afford cyclic ethers and lactones directly. The substrate scope and mechanistic proof of deprotection were investigated. The experimental evidence supports the concerted transition state of the bond-forming step involving a cationic Co complex.

## 1. Introduction

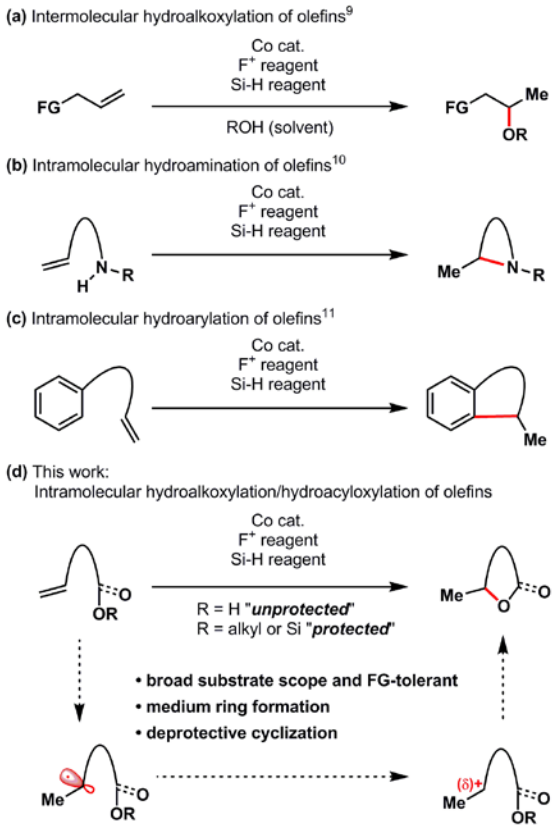
Saturated oxygen heterocycles, such as cyclic ethers and lactones, are found in the structures of many biologically active natural products.[1] Beyond the common five- and six-membered rings, rings of seven or more members, also called medium rings, have also been discovered; examples include polycyclic marine toxins (e.g., ciguatoxin), lauroxanes (e.g., laurencin), heliannuols (e.g., helianane), sodwanone S, zoapatanol, aphanamixoids (e.g., aphanamixoid A), and octalactins (e.g., octalactin A).[2] From a drug discovery perspective, there is still much room for the development of a chemical space derived from a medium-ring framework.[3]

In the field of organic synthesis, straightforward methods for accessing the motif of saturated oxygen heterocycles include catalytic regioselective intramolecular hydroalkoxylation and hydroacyloxylation, which refer to the direct coupling of olefins with hydroxyl groups and carboxyl groups, respectively. Consequently, many research groups have reported various examples of attractive Markovnikov-selective intramolecular hydroalkoxylation[4] and hydroacyloxylation[4b,4d,4e,5] over the past decade (Scheme 1). For example, some reactions are based on nucleophilic attack by OH-groups on the metal-coordinated olefins and protonation of the metal–carbon bond, as presented by Widenhoefer,[4a] He,[4b] and others.[4c-f] Non-metallic systems also enable the hydrofunctionalization of olefins.[4g,4i-k] Catalytic hydrofunctionalizations starting from *O*-nucleophile activation by a metal complex were also reported by Marks,[4l,4m] Duñach,[4n,4o] Hartung,[4p] and others.[4q,4r] Despite the development of these elegant approaches, the examples of medium-ring formation by hydroalkoxylation are quite limited, and these scant examples are further limited to the formation of rings of no more than seven members.[4d,4v,4aa] Recently, Tiefenbacher reported intramolecular hydroalkoxylation catalyzed by a self-assembled hexameric capsule affording seven-membered products; however, the substrate scope is fundamentally limited by the encapsulation.[4aa] Nicewicz reported an exclusive anti-Markovnikov selective hydroalkoxylation and an example of oxepane formation.[6] Meanwhile, to the best of our knowledge, the formation of rings of more than seven members in the hydroacyloxylation of olefins has not been reported. In contrast, haloetherification[7] and halolactonization[7b,8] have been thoroughly investigated. Although these approaches have the merit of enabling further manipulation on the halogen atom, removal of the terminal halogen, if unnecessary, entails an additional step.

Medium-ring formation is often fundamentally troublesome because of entropic factors (the approach frequency of two reactive sites), strain of the medium ring, and transannular interactions in the substrate. Therefore, a powerful and selective activation of the olefin in the reaction is highly desired for the development of a general and robust approach based on both hydroalkoxylation and hydroacyloxylation for medium-ring formation with good functional group tolerance.

We recently reported an intermolecular hydroalkoxylation,[9] an intramolecular hydroamination,[10] and a intramolecular hydroarylation[11] using Co(salen) complex **1**, an *N*-fluoro-2,4,6-trimethylpyridinium salt, and a 1,1,3,3-tetramethyldisiloxane [$(Me_2SiH)_2O$]. In these reactions, it is thought that a cationic intermediate enables bond formation between the olefins and nucleophile (Scheme 1a, b, c). The reaction demonstrated a broad substrate scope as a result of its high reactivity and functional group tolerance. In light of these previous observations and recent relevant examples,[12] we envisioned that intramolecular C-O bond formation may

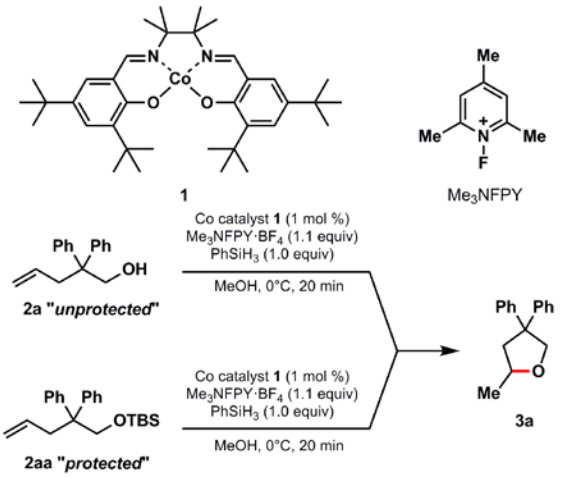
**Scheme 1. Our previous reports and this work**




occur under the identified or modified reaction conditions to yield both cyclic ethers and lactones with excellent functional group tolerance (Scheme 1d). Previously, we reported a preliminary result in which cyclization-biased alkenyl alcohol **2a** was used to obtain cyclic ether **3a** in excellent yield (Scheme 2).[9a] Furthermore, TBS-protected alkenyl alcohol **2aa** was directly cyclized to afford the same product **3a**. In the multistep synthesis of complex molecules, the use of protective group is often unavoidable because of the functional group reactivity, solubility, and high polarity of the compound. This deprotective cyclization approach has the advantage of being step-economical, allowing the deprotection step to be omitted. Nevertheless, there are few examples of deprotective cyclization for simple substrates under harsh conditions; Niggemann reported only one reaction of benzyl-deprotective hydroalkoxylation (dichloromethane, 80°C),[4f] and Duñach reported the hydroacyloxylation of alkenyl ester (dichloroethane or nitromethane, reflux).[13]

Herein, we developed a catalytic, mild, and functional group tolerant intramolecular hydroalkoxylation and hydroacyloxylation of unactivated olefins using a Co(salen) complex **1**, an *N*-fluoro-2,4,6-trimethylpyridinium salt, and $(Me_2SiH)_2O$ to produce a various five- and six-membered ring products. Next, the structure-reactivity relationship of the salen ligand was studied, identifying the optimum Co(salen) complex for medium-ring formation (seven- to nine-membered). It was then found that various cyclic ethers or lactones were directly obtained from *O*-protected alkenyl alcohol or alkenyl ester, respectively, by the Co-catalyst system at room temperature. The ultimate co-products of the protective group were also investigated to clarify the mechanism of the deprotection step. Finally, the experimental evidences

**Scheme 2. Preliminary result of hydroalkoxylation of olefins and deprotective cyclization[9a]**




supported the concerted transition state of the bond forming step involving a cationic Co complx.

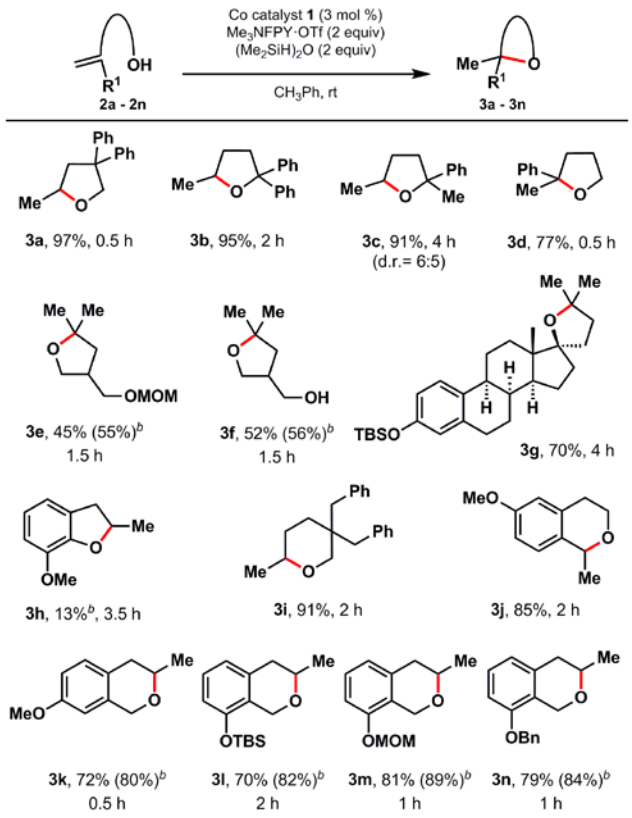
## 2. RESULTS AND DISCUSSION

### Synthesis of five- and six-membered cyclic ethers and lactones

First, the scope of alkenyl alcohol was investigated under the reaction conditions of the intramolecular hydroamination we previously reported: namely, Co complex **1** (3.0 mol%) in toluene and in the presence of *N*-fluoro-2,4,6-trimethylpyridinium trifluoromethanesulfonate ($Me_3NFPY{\cdot}OTf$, 2.0 equiv.)[14] and $(Me_2SiH)_2O$ (2.0 equiv.) (Table 1). We found that various five- to six-membered cyclic ethers were obtained in good-to-excellent yields. Alkenyl alcohol **2a** was smoothly cyclized to afford tetrahydrofuran **3a** in toluene. Substrates **2b** and **2c** (containing a bulky hydroxyl group) and **2d** (1,1-disubstituted olefin) were also subjected to cyclization to afford the desired products **3b**, **3c** (0% yield in ref 4i), and **3d**, respectively, in excellent yield. **3e** and **3f** were obtained from alkenyl alcohol containing the acid-sensitive acetal group **2e** and diol **2f**. A steroidal compound **3g** was also synthesized in good yield. Unfortunately, the phenolic hydroxyl group was found to be unsuitable for the cyclization, resulting in a complex product mixture (**2h**). Concerning the six-membered rings, tetrahydropyran **3i** and isochroman **3j**, **3k** could be synthesized. The investigation of the functional group tolerance of this method revealed that isochromans **3l**-**3n** were obtained from allyl-benzylalcohol-bearing, fluoro-anion-sensitive silyl ether (**2l**), acid-sensitive acetal (**2m**), and benzyl ether (**2n**). Unfortunately, the synthesis of three- or four-ring compounds was found to be ineffective in our conditions (see Supporting Information).

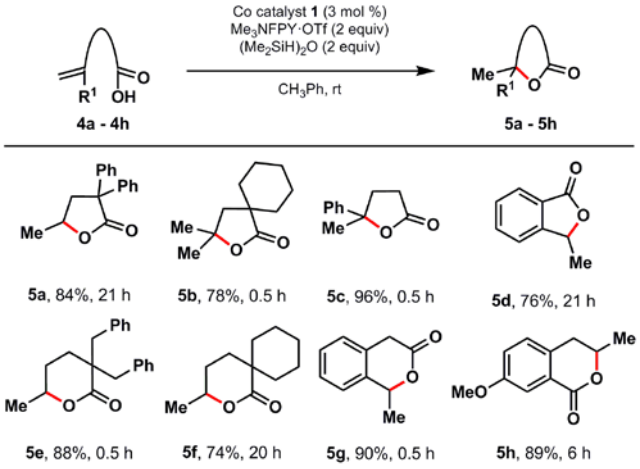
Encouraged by this result, we also investigated the hydroacyloxylation of olefins using a series of alkenyl carboxylicacids under the same reaction conditions (Table 2). To our delight, five-membered lactones were obtained from the substrate, including cyclization-biased **4a** and 1,1-disubstituted olefins **4b** and **4c** in excellent yield. Isobenzofuranone **5d** was obtained from benzoic acid derivative **4d**. Six-membered products, such as lactones **5e**, **5f**; 3-isochromanone **5g**; and 1-isochromanone **5h**, were obtained in good yield.

**Table 1. Scope of alkenyl alcohol for hydroalkoxylation of unactivated olefins**[a]




[a]Isolation yield (0.25 mmol scale, 0.1 M). [b]NMR yield using 1,4-bis(trifluoromethyl)benzene as the internal standard.

**Table 2. Scope of alkenyl carboxylic acid for hydroacyloxylation of unactivated olefins**[a]

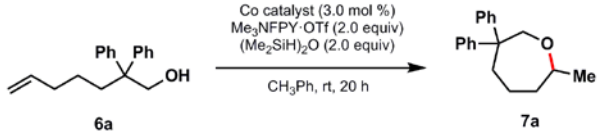



[a]Isolation yield (0.25 mmol scale, 0.1 M).

## Synthesis of medium-ring products

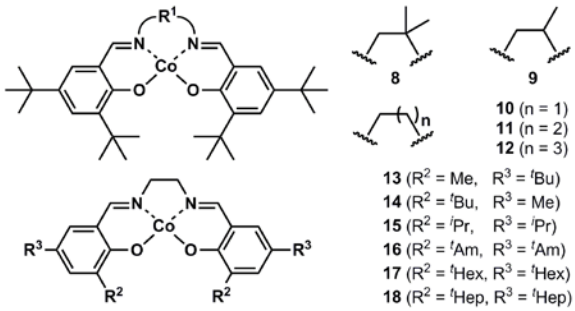
We explored the possibility of achieving unprecedented medium-ring formation by hydrofunctionalization under a Co-catalyst system. First, we investigated the hydroalkoxylation of alkenyl alcohol **6a** containing monosubstituted olefins (Table 3). Because the reaction condition for the synthesis of common ring sizes using complex **1** gave oxepane **7a** in only 30% yield along with considerable amounts of olefin isomers and recovered **6a** (entry 1), we conducted a systematic screening of the salen ligand in the Co-complex. We found that decreasing the bulkiness of diamine moiety improved the yield and that the ethylenediamine-containing salen ligand was effective (entry 2-4). Longer diamines gave worse results (entry 5, 6). Next, we examined the effect of substituents on the aromatic rings. It was found that using Co complexes possessing smaller methyl groups in either the 3 or 5 position (benzaldehyde numbering) dramatically decreased the yield of the desired product **7a** (entry 7, 8). Given the importance of both of the substituents on the aromatic ring, a kit of Co complexes containing substituents of different sizes was investigated (entry 9-12). Although further screening of Co complexes was investigated, we ultimately identified **17** as being optimal (see Supporting Information). Dilute conditions gave almost the same result (entry 13).

**Table 3. Optimization of reaction condition for medium ring formation by hydroalkoxylation of unactivated olefins**




| entry | Co cat | yield (%)[a] |
|---|---|---|
| 1 | **1** | 30 |
| 2 | **8** | 20 |
| 3 | **9** | 40 |
| 4 | **10** | 43, (41)[b] |
| 5 | **11** | 25 |
| 6 | **12** | <5 |
| 7 | **13** | <5 |
| 8 | **14** | 22 |
| 9 | **15** | 8 |
| 10 | **16** | 57 |
| 11 | **17** | **60**, (**50**)[c] |
| 12 | **18** | 57 |
| 13[d] | **17** | 60 |

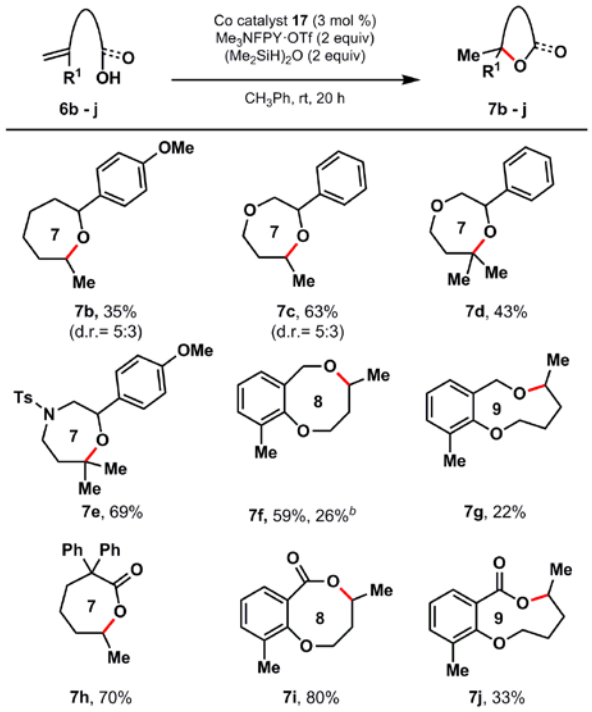
[a]NMR yield using 1,4-bis(trifluoromethyl)benzene as internal standard (0.25 mmol scale, 0.1 M). [b]$CF_3Ph$ was used [c]Isolation yield. [d]conc = 0.03 M.




Having demonstrated the catalytic activity of complex **17**, we next examined the scope of other substrates (Table 4). In the case of synthesizing seven-membered rings by hydroalkoxylation, oxepane **7b** and 1,4-dioxepane **7c**, **7d** were obtained from alkenyl alcohol containing mono- and disubstituted olefin. Nitrogen-containing 1,4-oxazepine **7e** was also syn-

thesized by this method. In the case of eight-membered ring formation affording **7f**, we reconfirmed the superiority of complex **17** in terms of yield. Furthermore, this method was applicable for nine-membered ring formation affording **7g**. Compared to hydroalkoxylation, hydroacyloxylation gave slightly higher yields of oxepanone **7h** (vs **7a**), benzodioxocanone **7i** (vs **7f**), and benzodioxonanone **7j** (vs **7g**). At this stage, some substrates were identified as being unsuitable even when using the optimum catalyst **17** because the isomerization of olefin was unavoidably faster than the cyclization (see Supporting Information). Although the yield of the medium-ring product was inferior to that of the small-ring product, various medium-ring products that had not been achieved previously were obtained by the hydrofunctionalization of olefins.

**Table 4. Scope of alkenyl alcohol and alkenyl carboxylic acid affording medium ring products**[a]

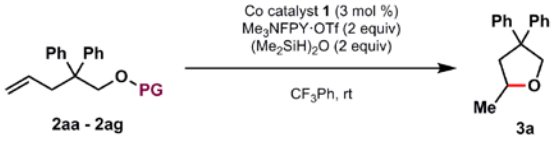



[a]Isolation yield (0.25 mmol scale, 0.1 M). [b]Catalyst **1** (3 mol %) was used.

**Deprotective intramolecular hydroalkoxylation of unactivated olefins**

We next investigated the scope of the protective group using cyclization-biased alkenyl alcohol **2aa** to **2ag** by the Co catalyst system (Table 5). In addition to the TBS group previously shown to be effective (Scheme 2), acetal (methoxymethyl acetal (MOM), methoxyethoxymethyl acetal (MEM), benzyloxymethyl acetal (BOM), and benzyl and methyl groups were found to be applicable. In contrast, the cyclization of **2ag** containing an acetyl group did not occur smoothly. Encouraged by this result, we next investigated the substrate scope for three protective groups per substrate (Table 6). Overall, it was found that MOM was much more effective for the deprotective cyclization than either TBS or benzyl groups.[15] For example, in the case of five-membered ring formation, tetrahydrofuran **3b** and **3d** were obtained in acceptable yield from MOM-protected **2bb**[16] and **2db**, respectively, whereas the other two protective groups provided the desired products in low yields, if at all. Among the bis-protected diol substrates **2fa**-**2fe**, the yield of the desired product was highest for the MOM-protected **2fb**. Although the phenolic hydroxyl group was unsuitable for substrate **2h** (Table 1), to our delight, the yield of benzofuran **3h** was excellent for any protective group (**2ha**-**2he**). More electron rich substrate **2hb'** was applicable. In the case of six-membered ring formation, the yield of tetrahydropyran **3i** was also quite high when using the MOM group (**2ib**) and exceptionally high when using the benzyl group (**2ie**). However, isochroman **3j** was only obtained in good yield from the MOM-group-containing substrate **2jb**. Considering the result of **3d** as well, it was concluded that the MOM group is required when using styrene-type substrates. Indeed, each protective group was effective for the synthesis of other types of isochroman **3k**. We next examined the functional group tolerance using the substrate, and various isochromans were obtained from substrate bearing TBS (**2lb**), MOM (**2mb**), and benzyl groups (**2nb**). Unfortunately, the synthesis of medium-ring compounds by deprotective hydroalkoxylation was found to be ineffective, even when using MOM groups. After continued investigation, only the eight-membered cyclic ether **7f** was obtained in 26% yield using MOM-protected **6fb**.

**Table 5. Scope of protective group for hydroalkoxylation of unactivated olefins**



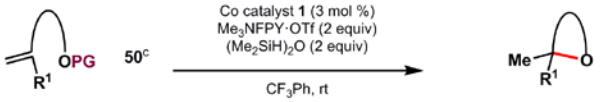

| entry | PG | time (h) | yield (%)[a] |
|---|---|---|---|
| 1 | TBS (**2aa**) | 0.5 | 99 |
| 2 | MOM (**2ab**) | 0.5 | 99 |
| 3 | MEM (**2ac**) | 0.5 | 97 |
| 4 | BOM (**2ad**) | 0.5 | 99 |
| 5 | Bn (**2ae**) | 1.5 | 93 |
| 6 | Me (**2af**) | 1.5 | 87 |
| 7 | Ac (**2ag**) | 6.5 | 27 |

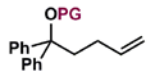
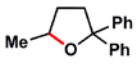
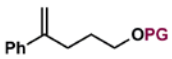
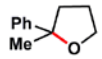
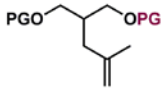
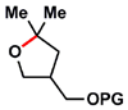
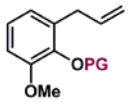
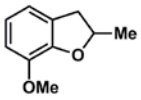
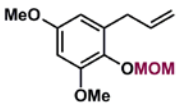
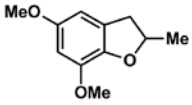
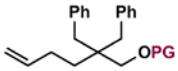
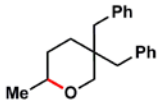
[a]Isolation yield (0.25 mmol scale, 0.1 M).

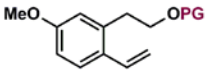
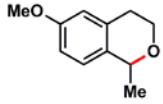
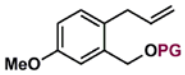
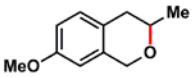
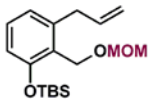
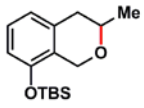
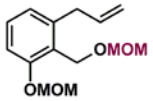
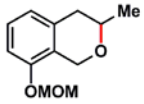
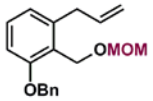
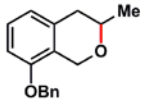
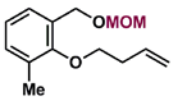
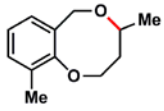
**Deprotective intramolecular hydroacyloxylation of unactivated olefins**

Furthermore, the method of deprotective cyclization was found to be applicable to alkenyl esters. The results of the hydroacyloxylation of alkenyl esters **4aa**-**4ae** are presented (Table 7). This method was applicable to all protective groups examined. In particular, the methyl group, being sterically smallest, gave the highest reactivity. We next investigated the substrate scope for various methyl esters (Table 8). The five-membered lactones **5b** and **5d** were obtained in good yield. However, **5c** was not obtained at all, and instread, the olefin isomer (tri-substituted olefin) was formed. C–O bond cleavage of the oxonium cation to afford a stable carbocation intermediate might be faster than the deprotection step in the case of 1,1-disubstituted styrene-type substrate. Indeed replacing the methyl group on olefin moiety of **4ba** to phenyl group did not afford the desired product **5b** at all. Six-membered lactones, such as **5e**-**5h**, were obtained in good to excellent yield. The desired product was obtained from styrene-type substrates **4ga** (mono-substituted olefin). The functional group tolerance was also investigated for hydroacyloxylation using alkenyl-ester-bearing TBS (**19aa**), MOM (**19ba**), acetyl (**19ca**), and hydroxyl groups (**19da**). The eight-membered ring lactone **7i**

**Table 6. Substrate scope of deprotective hydroalkoxylation of unactivated olefins**[a]




| entry | starting materials | products | yield (%) TBS | MOM | Bn |
|---|---|---|---|---|---|
| 1 |  **2ba** (PG=TMS) **2bb** (PG=MOM) **2be** (PG=Bn) |  **3b** | <10[b] 23 h | 50[c] 4.5 h | 0[b] 23 h |
| 2 |  **2da** (PG=TBS) **2db** (PG=MOM) **2de** (PG=Bn) |  **3d** | trace[b] 20 h | 59[c] 1.5 h | 0[b] 20 h |
| 3 |  **2fa** (PG=TBS) **2fb** (PG=MOM) **2fe** (PG=Bn) |  **3fa** (PG=TBS) **3e** (PG=MOM) **3fe** (PG=Bn) | 50[b] 21 h | 53[b] 1.5 h | trace[b] 21 h |
| 4 |  **2ha** (PG=TBS) **2hb** (PG=MOM) **2he** (PG=Bn) |  **3h** | 84[b] 19 h | 90[b] 1.5 h | 73[b] 2.5 h |
| 5 |  **2hb'** |  **3h'** | ND | 79[c] 1.5 h | ND |
| 6 |  **2ia** (PG=TBS) **2ib** (PG=MOM) **2ie** (PG=Bn) |  **3i** | trace 27 h | 84[c] 22 h | 80[c] 22 h |

| entry | starting materials | products | yield (%) TBS | MOM | Bn |
|---|---|---|---|---|---|
| 7 |  **2ja** (PG=TBS) **2jb** (PG=MOM) **2je** (PG=Bn) |  **3j** | 0[b] 20 h | 70[c] 2.0 h | 0[b] 20 h |
| 8 |  **2ka** (PG=TBS) **2kb** (PG=MOM) **2ke** (PG=Bn) |  **3k** | 82[b] 20 h | 90[b] 20 h | 70[b] 20 h |
| 9 |  **2lb** |  **3l** | ND | 96[b] 0.5 h | ND |
| 10 |  **2mb** |  **3m** | ND | 86[b] 0.5 h | ND |
| 11 |  **2nb** |  **3n** | ND | 89[b] 2.0 h | ND |
| 12[d] |  **6fb** |  **7f** | ND | 26[c] 20 h | ND |

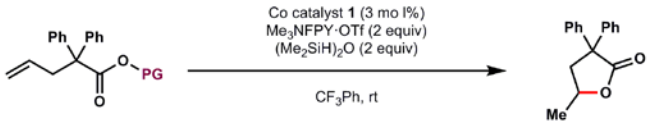
[a]0.25 mmol scale, 0.1 M. [b]NMR yield using 1,4-bis(trifluoromethyl)benzene as the internal standard. [c]Isolation yield. [d]Catalyst **17** (3 mol %) was used.

was also obtained from alkenyl ester **6ia**.

**Reaction mechanism**

The mechanistic implications of this deprotective cyclization merit discussion. First, in the case of the phenolic substrate (**2h** in Table 1 vs **2ha-2he** in Table 6), the yield of desired product **3h** was dramatically improved by using a protective group. Second, the investigation of the functional group tolerance using substrates **2lb-2nb** (Table 6) and **19aa-19ba** (Table 7) shows that the protective groups irrelevant to the cyclization remained intact under the reaction condition. Therefore, cyclization should begin with the formation of an oxonium intermediate, followed by deprotection. The experimental results show that the protective group was trapped by 2,4,6-trimethylpyridine (collidine) to generate the alkylpyridinium salt in the cases of MOM, benzyl, and methyl groups,

**Table 7. Scope of protective group for hydroacyloxylation of unactivated olefins**

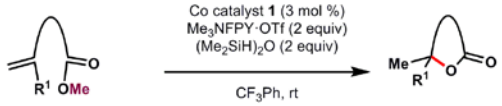


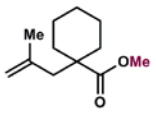
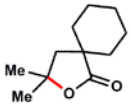
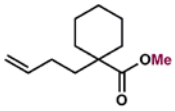
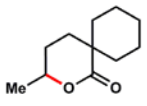
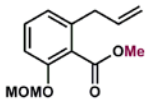
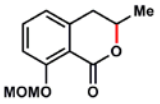
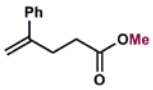
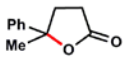
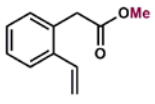
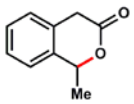
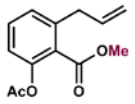
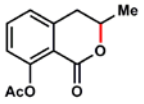
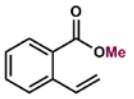
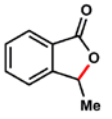
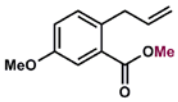
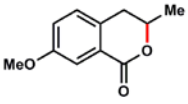
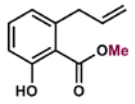
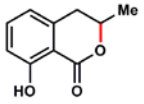
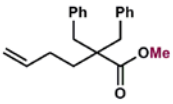
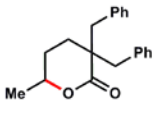
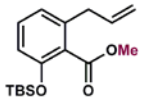
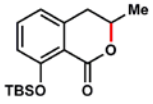
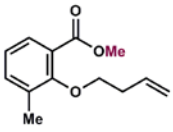
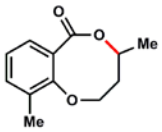

4aa - 4ae 5a

| entry | PG | time (h) | yield (%)[a] |
|---|---|---|---|
| 1 | Me (**4aa**) | 0.5 | 99 |
| 2 | Et (**4ab**) | 1.0 | 99 |
| 3 | Bn (**4ac**) | 19 | 97 |
| 4 | PMB (**4ad**) | 3 | 99 |
| 5 | $^t$Bu (**4ae**) | 19 | 93 |

[a]Isolation yield (0.25 mmol scale, 0.1 M).

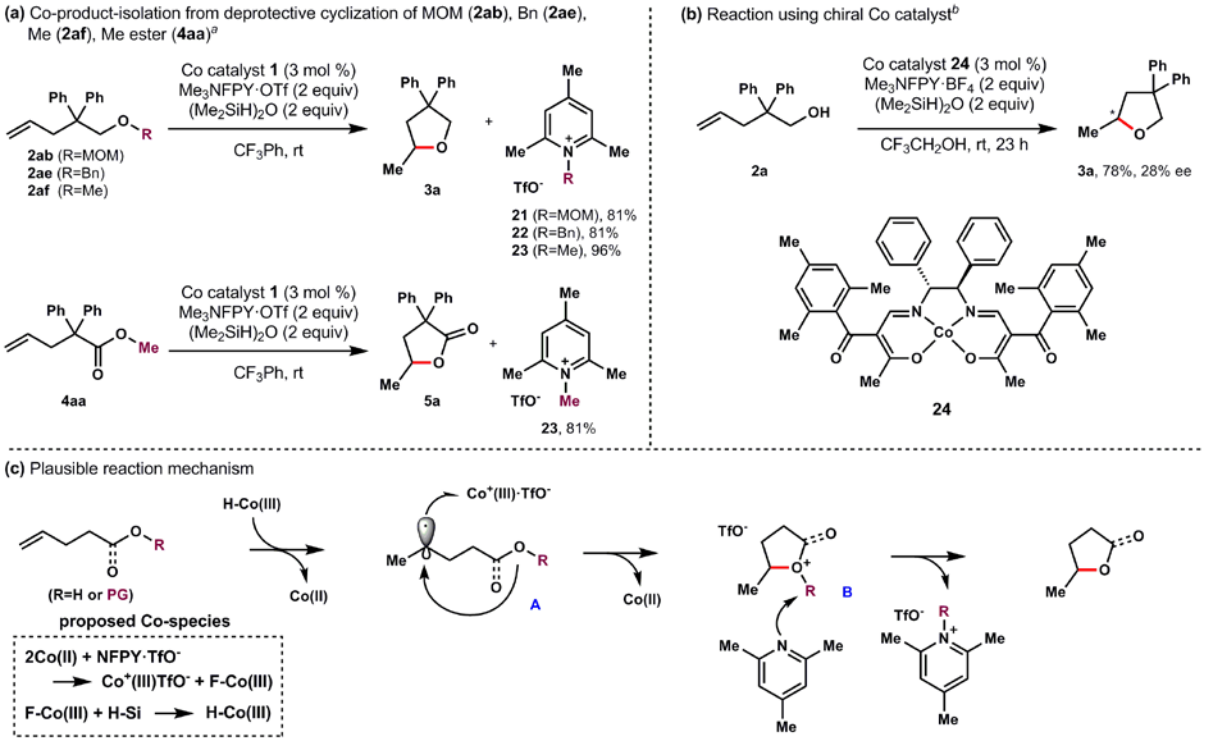
**Table 8. Scope of alkenyl methylester for hydroacyloxylation of unactivated olefins**[a]




| entry | starting materials | products | entry | starting materials | products | entry | starting materials | products |
|---|---|---|---|---|---|---|---|---|
| 1 |  |  | 5 |  |  | 9 |  |  |
| | **4ba** | **5b**, 74%, 5.5 h | | **4fa** | **5f**, 53%, 15 h | | **19ba** | **20b**, 91%, 3 h |
| 2 |  |  | 6 |  |  | 10 |  |  |
| | **4ca** | **5c**, 0%, 20 h | | **4ga** | **5g**, 47%, 0.5 h | | **19ca** | **20c**, 93%, 0.5 h |
| 3 |  |  | 7 |  |  | 11[b] |  |  |
| | **4da** | **5d**, 63%, 0.5 h | | **4ha** | **5h**, 88%, 15 h | | **19da** | **20d**, 86%, 2 h |
| 4 |  |  | 8 |  |  | 12[c] |  |  |
| | **4ea** | **5e**, 60%, 3 h | | **19aa** | **20a**, 79%, 0.5 h | | **6ia** | **7i**, 25%, 20 h |

[a]Isolation yield (0.25 mmol scale, 0.1 M). [b]Conc = 0.03 M [c]Catalyst **17** (3 mol %) was used.

**Scheme 3. Plausible reaction mechanism**




[a]NMR yield using dimethylsulfone as the internal standard (0.25 mmol scale). [b]Isolation yield (0.25 mmol scale, 0.1 M).

although the final product for the TBS group is still unclear (Scheme 3a).

The ligand optimization affected the yield of the desired product, as shown in Table 3, which sheds additional light on

the reaction mechanism. Furthermore, the measurable enantioselectivity was observed when using a chiral Co catalyst **24**[17] (Scheme 3b, not fully optimized). We propose that the Co complex could significantly interfere with the transition state of the C–O bond-forming step.

A proposed mechanism that is consistent with the experimental data is provided in Scheme 3c. In this mechanism, hydrogen atom transfer[18] to generate the carbon radical intermediate **A**[19] along with the recovery of the Co complex, is plausible according to Shenvi and Herzon's insightful discussions.[12f,12g] Notably in our mechanism, both single-electron oxidation of the carbon radical by the cationic Co species and intramolecular nucleophilic trapping by the oxygen atom could occur simultaneously to generate oxonium intermediate **B** via a concerted transition state.[20] Finally, the protective group (or proton in the case of an unprotected substrate) was transferred from intermediate **B** to 2,4,6-trimethylpyridine, with the formation of the desired product and co-product.

### 3. Conclusion

We developed Co-catalyzed intramolecular hydroalkoxylation and hydroacyloxylation to afford five- and six-membered saturated oxygen heterocycles. The mild reaction condition realized a broad substrate scope and excellent functional group tolerance. The use of the optimum catalyst **17** paved the way for the synthesis of medium rings by the hydrofunctionalization of unactivated olefins. It was found that the high reactivity of this Co catalyst system enabled the deprotective cyclization of protected alkenyl alcohol and alkenyl ester to directly afford oxygen heterocycles. The experimental evidence supported the concerted transition state of the bond-forming step involving a cationic Co complex. Based on the results of this study, improving the enantioselectivity is ongoing.

## Associated Content

**Supporting Information**. Experimental procedures and analytical data ($^{1}$H and $^{13}$C NMR) for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Funding Sources

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### Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENT

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(14) *N*-fluoro-2,4,6-trimethylpyridinium trifluoromethanesulfonate was used instead of tetrafluoroborate to avoid hydrofluorination. See ref 12j.

(15) The desired bond cleavage is hypothesized to not occur from the posturated oxonium intermediate in the case of TBS and benzyl groups, whereas C–O bond cleavage is assisted by lone pair of electrons on the oxygen atom of the MOM group.

(16) Use of NFPY·OTf instead of $Me_3$NFPY·OTf did not improve the yield of the desired product (45% yield with NFPY·OTf).

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(18) A deuterium experiment was conducted to determine the source of terminal hydrogen. See ref 9a.

(19) The existence of a carbon radical intermediate was supported by radical clock and $O_2$ uptake experiments. See ref 9a.

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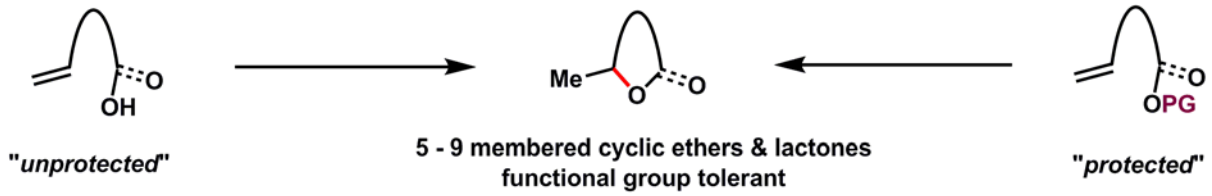
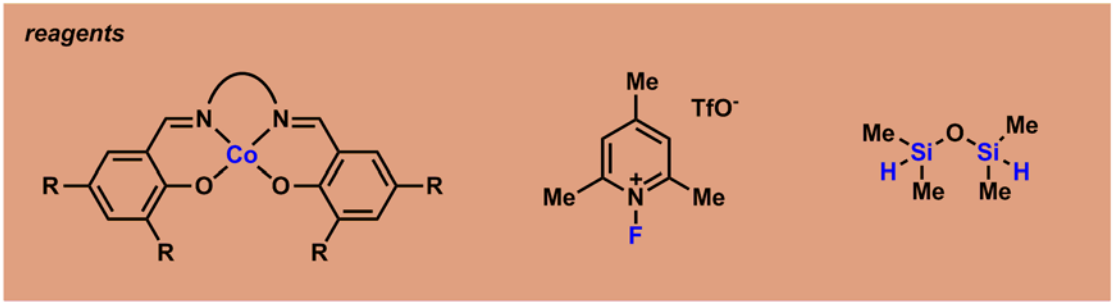
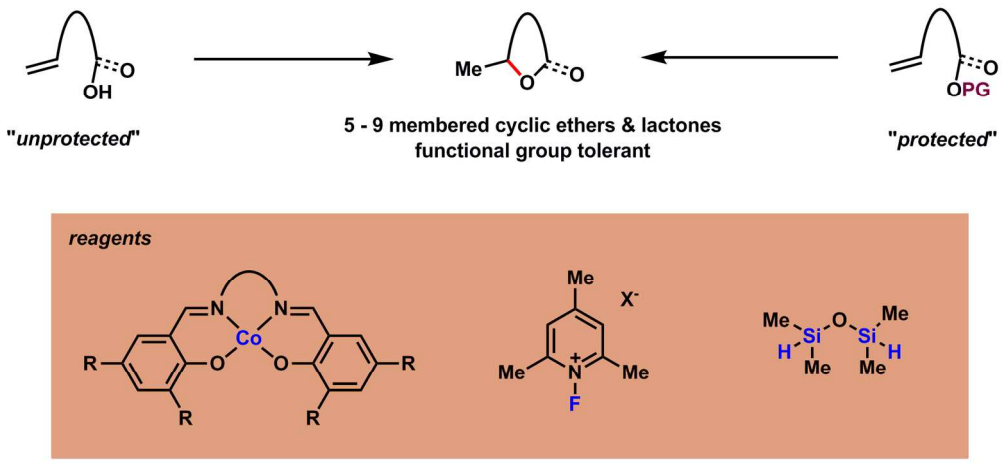
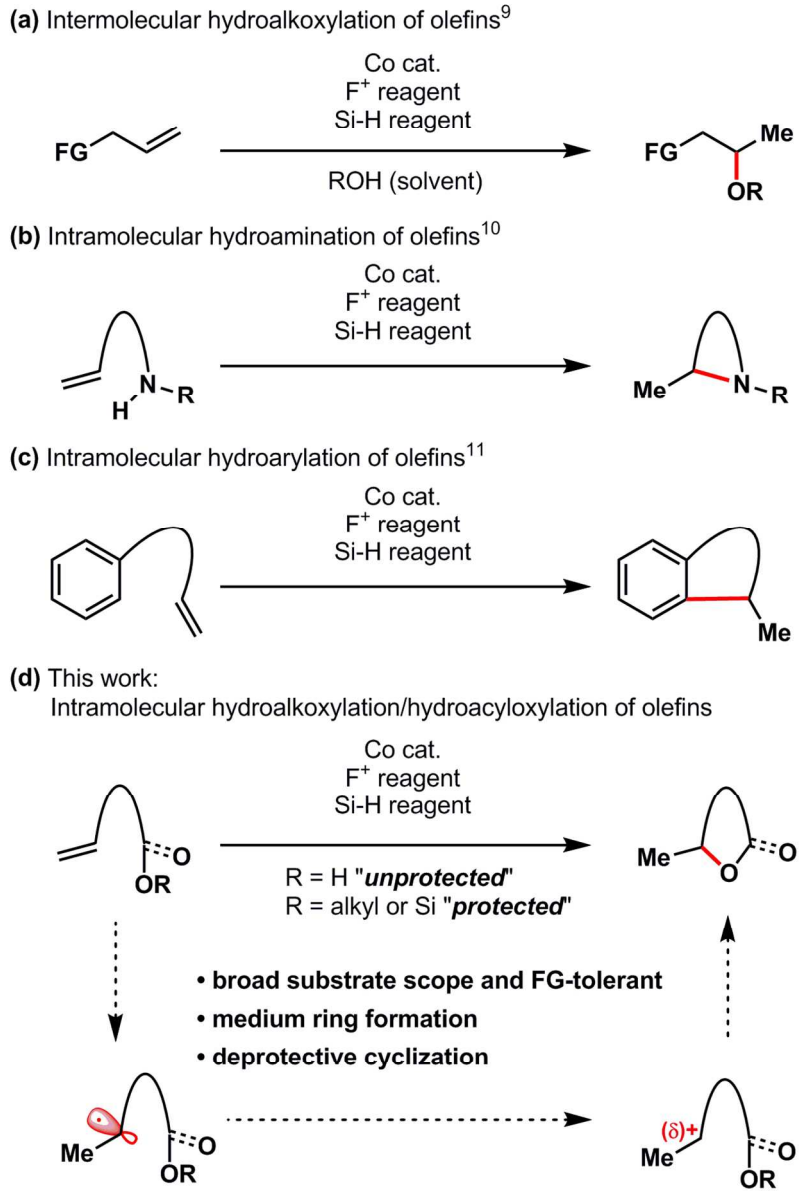




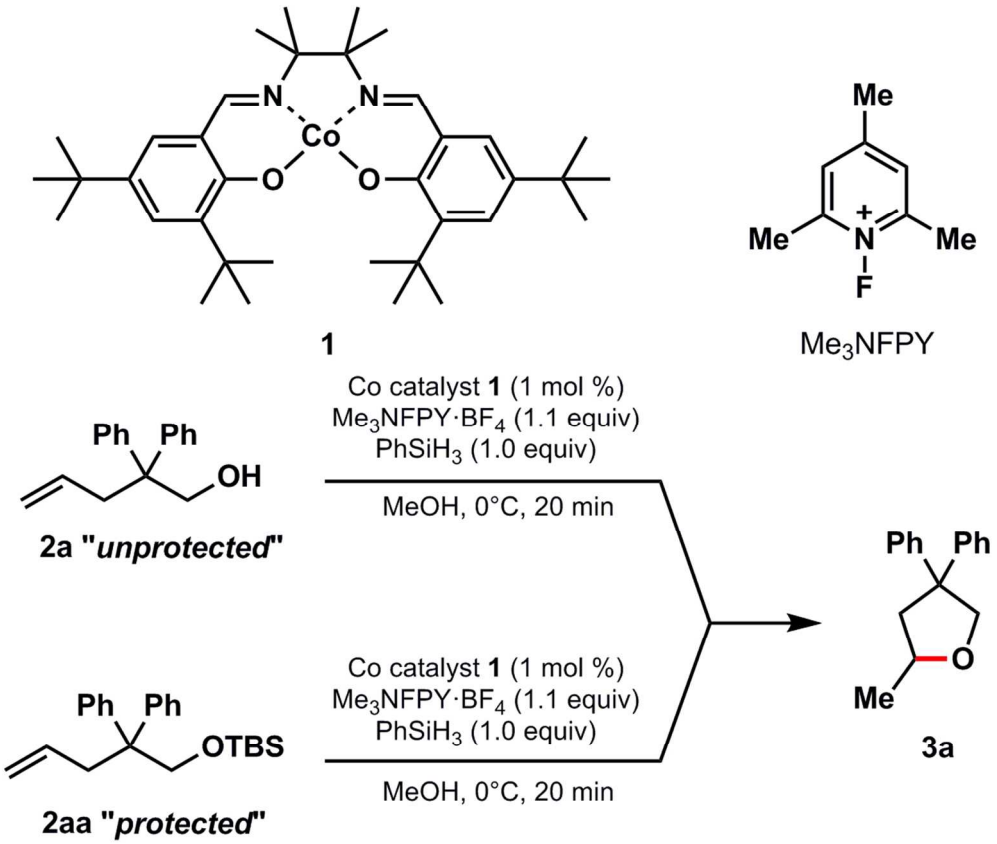

Graphical abstract

159x73mm (300 x 300 DPI)



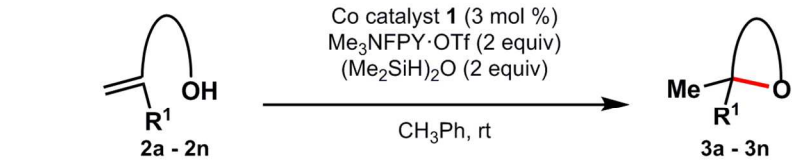

Scheme 1

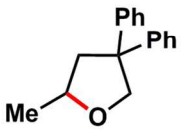
103x156mm (300 x 300 DPI)



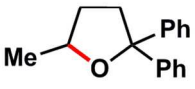

Scheme 2

105x89mm (300 x 300 DPI)

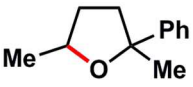


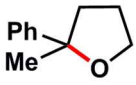

**3a**, 97%, 0.5 h



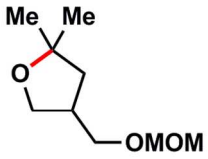

**3b**, 95%, 2 h



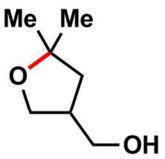

**3c**, 91%, 4 h
(d.r.= 6:5)



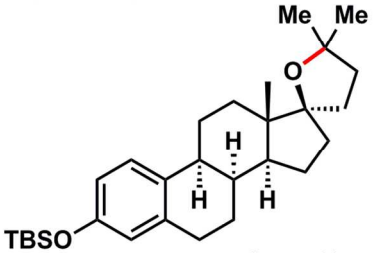

**3d**, 77%, 0.5 h



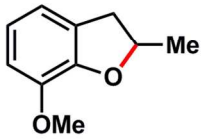

**3e**, 45% (55%)[b]
1.5 h



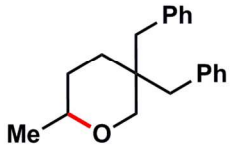

**3f**, 52% (56%)[b]
1.5 h



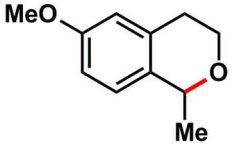

**3g**, 70%, 4 h



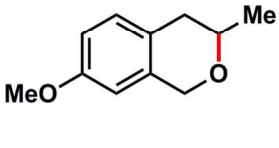

**3h**, 13%[b], 3.5 h



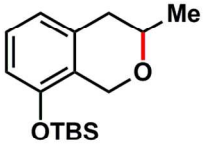

**3i**, 91%, 2 h



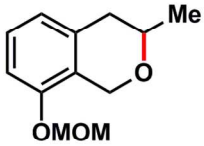

**3j**, 85%, 2 h



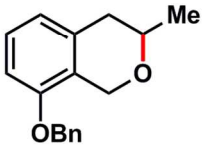

**3k**, 72% (80%)[b]
0.5 h




**3l**, 70% (82%)[b]
2 h



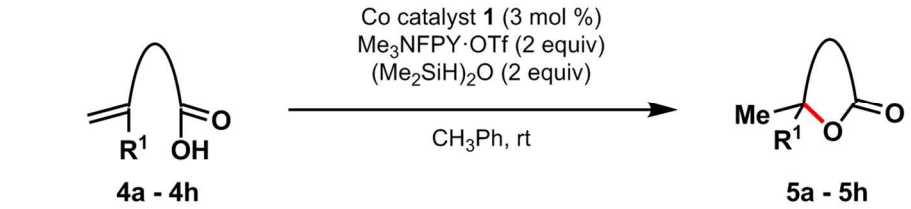

**3m**, 81% (89%)[b]
1 h




**3n**, 79% (84%)[b]
1 h

Table 1

119x154mm (300 x 300 DPI)



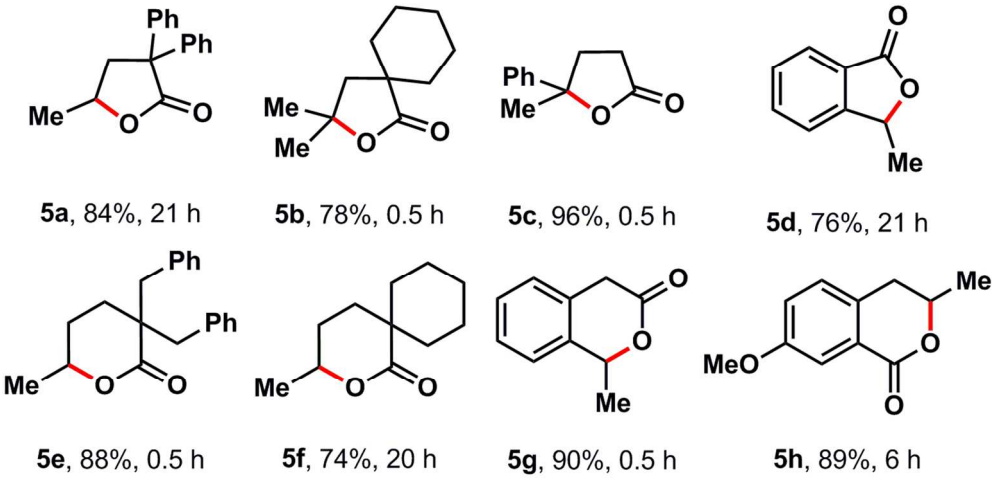




Table 2

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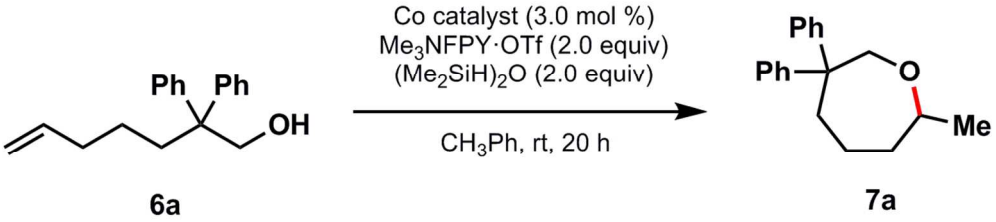


6a 7a

Table 3

112x26mm (300 x 300 DPI)

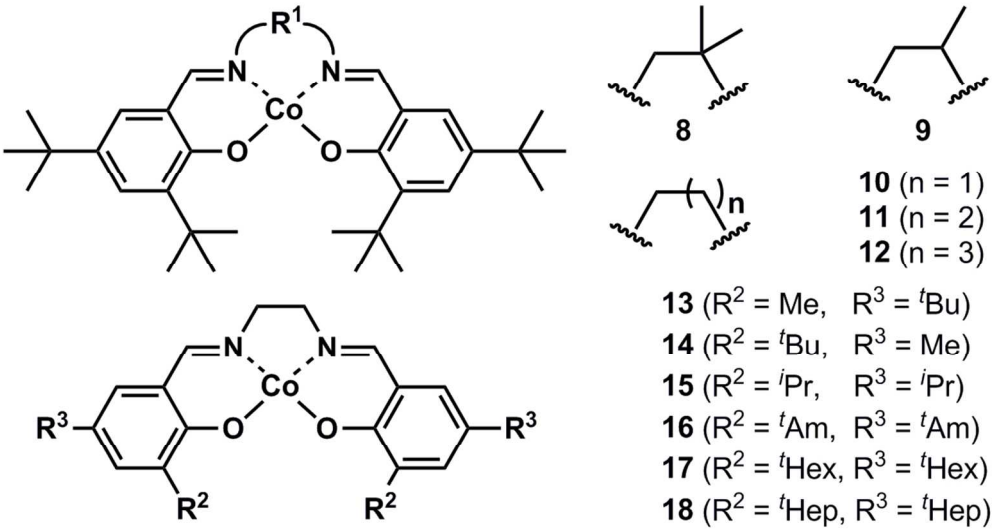


Table 3

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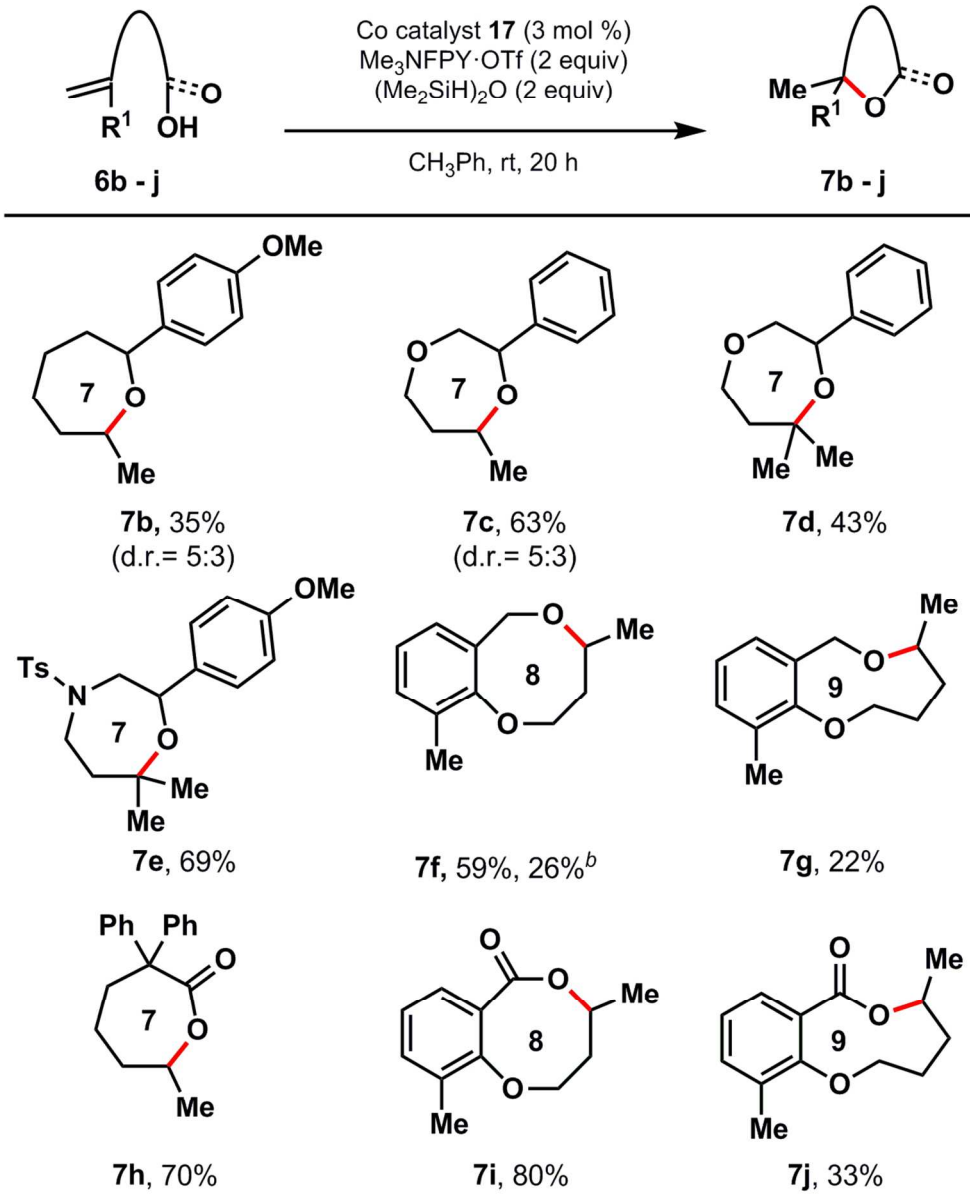



Table 4

111x134mm (300 x 300 DPI)

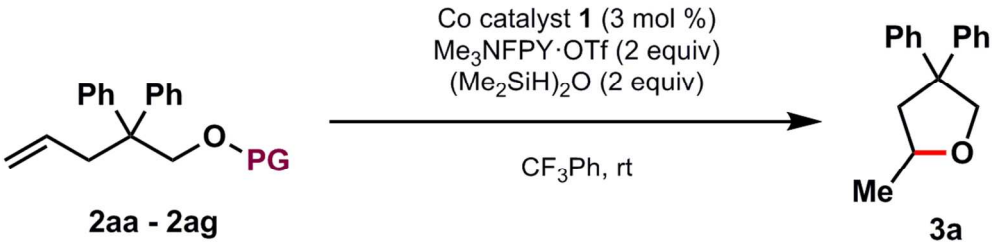
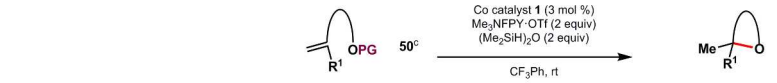



Table 5

104x27mm (300 x 300 DPI)



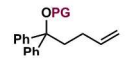
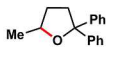
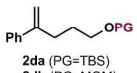
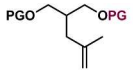
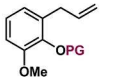
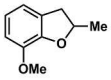
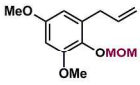
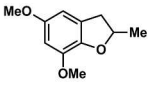
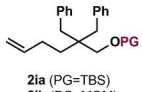
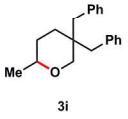
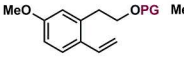
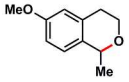
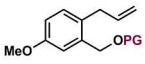
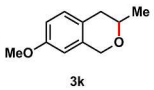
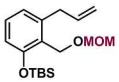
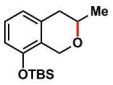
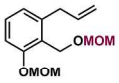
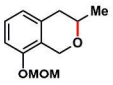
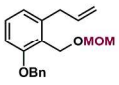
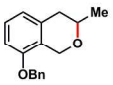
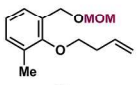
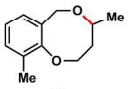

| entry | starting materials | products | yield (%) TBS | MOM | Bn |
|---|---|---|---|---|---|
| 1 |  **2ba** (PG=TMS) **2bb** (PG=MOM) **2be** (PG=Bn) |  **3b** | <10[b] 23 h | **50**[c] 4.5 h | 0[b] 23 h |
| 2 |  **2da** (PG=TBS) **2db** (PG=MOM) **2de** (PG=Bn) |  **3d** | trace[b] 20 h | **59**[c] 1.5 h | 0[b] 20 h |
| 3 |  **2fa** (PG=TBS) **2fb** (PG=MOM) **2fe** (PG=Bn) |  **3fa** (PG=TBS) **3e** (PG=MOM) **3fe** (PG=Bn) | 50[b] 21 h | **53**[b] 1.5 h | trace[b] 21 h |
| 4 |  **2ha** (PG=TBS) **2hb** (PG=MOM) **2he** (PG=Bn) |  **3h** | 84[b] 19 h | **90**[b] 1.5 h | 73[b] 2.5 h |
| 5 |  **2hb'** |  **3h'** | ND | **79**[c] 1.5 h | ND |
| 6 |  **2ia** (PG=TBS) **2ib** (PG=MOM) **2ie** (PG=Bn) |  **3i** | trace 27 h | **84**[c] 22 h | **80**[c] 22 h |
| 7 |  **2ja** (PG=TBS) **2jb** (PG=MOM) **2je** (PG=Bn) |  **3j** | 0[b] 20 h | **70**[c] 2.0 h | 0[b] 20 h |
| 8 |  **2ka** (PG=TBS) **2kb** (PG=MOM) **2ke** (PG=Bn) |  **3k** | 82[b] 20 h | **90**[b] 20 h | 70[b] 20 h |
| 9 |  **2lb** |  **3l** | ND | **96**[b] 0.5 h | ND |
| 10 |  **2mb** |  **3m** | ND | **86**[b] 0.5 h | ND |
| 11 |  **2nb** |  **3n** | ND | **89**[b] 2.0 h | ND |
| 12[d] |  **6fb** |  **7f** | ND | **26**[c] 20 h | ND |

Table 6

242x227mm (300 x 300 DPI)

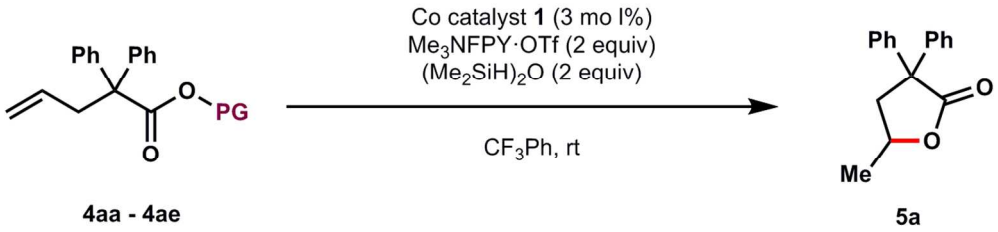



Table 7

121x28mm (300 x 300 DPI)

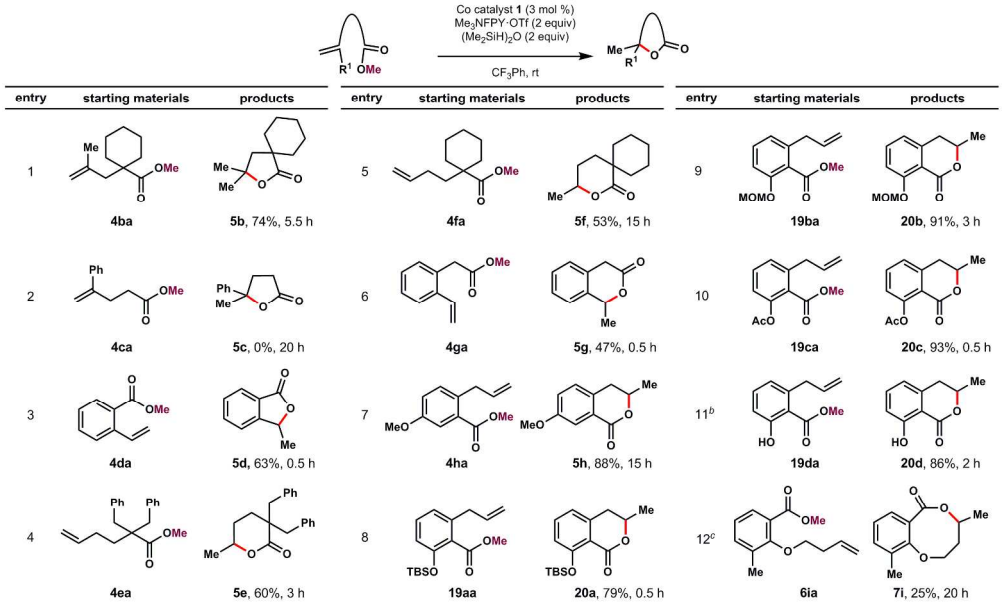
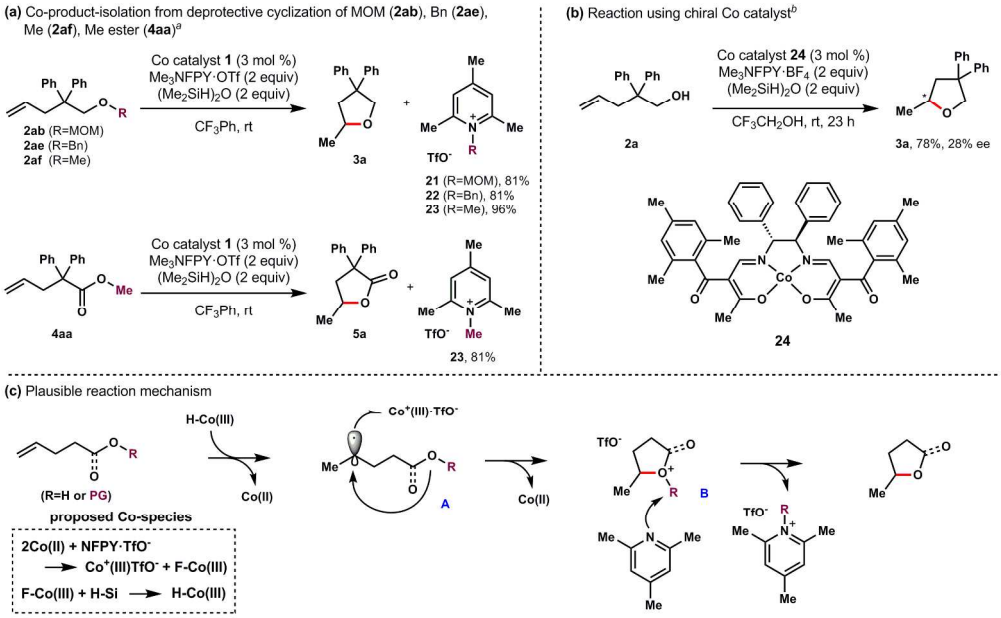



Table 8

248x149mm (300 x 300 DPI)




Scheme 3

226x140mm (300 x 300 DPI)