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A practical and mild Peterson olefination protocol mediated by $CuCl_2 \cdot 2H_2O$

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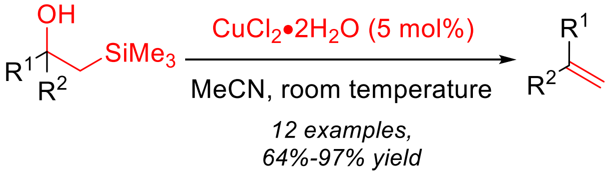
Abstract

The Peterson olefination is a versatile method for converting ketones and aldehydes to alkenes with stereochemical control. An operationally simple and mild Peterson olefination is facilitated by the use of $CuCl_2$•$2H_2O$ to promote the dehydrative desilylation reaction. Various β-hydroxysilanes have been converted to olefins in yields of up to 97%. $CuCl_2$•$2H_2O$ Acts as an easily handled, and inexpensive precursor, of Brønsted acid that promotes the elimination, yielding alkenes. Many acid-sensitive compounds are stable under these conditions in which a low, and controlled, amount of Brønsted acid is produced *in situ*.



- Inexpensive reagent
- Commercially available
- Mild conditions
- Operationally simple

Keywords: Methylenation, Peterson olefination, desilylative elimination, alkene

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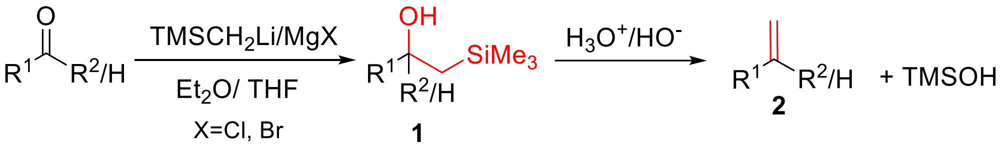
Introduction

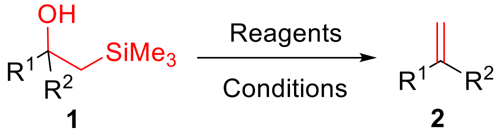
The Peterson olefination is a well-known, versatile, transformation method to convert ketones or aldehydes to alkenes with stereochemical control. It involves two steps: trimethylsilylalkyl addition to the carbonyl group, followed by the elimination of trimethylsilanol (Scheme 1).[1] The β-hydroxysilanes **1** resulting from addition to the carbonyl group can be induced to eliminate silanol under acidic or basic conditions to provide methylenated products **2**, which are often the less thermodynamically stable olefins. Thus, mild conditions for the elimination are desirable to prevent isomerization to the more substituted and stable alkenes. The utility of this reaction can be seen by its application in various contexts, including the synthesis of natural products where functional group compatibilities are particularly demanding, such as in the enantioselective total synthesis of (−)-taxol,[2] (+)-arboridinine,[3] and *ent*-callilongisin B.[4] Since its discovery,[5] there have been efforts to increase the scope and applications of this olefination reaction. Studies include developing reagents to obtain the β-hydroxysilanes, eg., $TMSCH_2Li$, $TMSCH_2MgX$, $TMSCH_2CeCl_2$,[6] and substituted α-lithiosilanes that would enable the generation of *tri*- or *tetra*-substituted olefins.[1]



Scheme 1. Classical Peterson olefination

Another series of efforts involves finding milder and more effective silanol-elimination conditions that are tolerant of a wider range of functional groups. Recent work reported the development of alternative acidic conditions to induce the dehydrative desilylation reaction by using catalytic amounts of triflimide ($HNTf_2$) at room temperature[7] or TMSOTf in DCM at room temperature to 45 °C (Schemes 2Aand 2B).[8] Both of these methods demonstrated that the dehydrative desilylation reaction is practicable under relatively mild conditions, in contrast to the classical reaction conditions (eg., KH, AcOH, TFA) where stoichiometric or even super-stoichiometric amounts of reagents and heating have been employed for the conversion.[9-11] That catalytic amounts induce elimination is not surprising since ,mechanistically, the dehydrative desilylation process is catalyzed by acid. In the classical Peterson reactions, relatively simple compounds had been employed, so that the use of an excess of acid or base, instead of catalytic amounts, had not been detrimental. Addition of super-stoichiometric amounts of acids had probably also been an issue of practicality since it is not easy to measure and introduce precise, and minute, amounts of acid conveniently to most smaller-scale reactions. Thus, practicality is an important consideration in implementing this reaction effectively.

Herein, we report a simple and straightforward protocol to promote the second step of the Peterson reaction, using $CuCl_2 \bullet 2H_2O$ as the dehydrative desilylating reagent (Scheme 2C). We found that treating **1** with catalytic amounts of $CuCl_2 \bullet 2H_2O$ induced a facile elimination of TMSOH in **1** to afford the corresponding olefins cleanly in excellent yields.



A. Leadbeater (2014)	B. McLaughlin (2020)	C. This work
TMSOTf -Liquid -Hygroscopic	**$HNTf_2$** -Sticky solid -Deliquescent	**$CuCl_2 \bullet 2H_2O$** -Crystalline solid -Bench stable
10 mol%, r.t.- 45 °C	0.1 mol%, r.t. in DCE Used stock solution of $HNTf_2$ in DCE	≤ 5 mol%, r.t. in MeCN Weighed out by mass

This work: $CuCl_2 \bullet 2H_2O + H_2O \rightleftharpoons [Cu^{2+}(OH)(H_2O)_{x-1}Cl_y] + H^+$

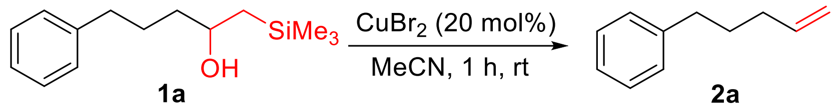
Scheme 2. Recent catalytic Peterson olefination methods (columns A and B) and our method (column C)

Since $CuCl_2 \bullet 2H_2O$ is a benchtop solid that does not require special handling precautions, weighing and using it in this reaction is extremely convenient (Scheme 2C), making it more desirable to use than other reagents. For example, $HNTf_2$ is used as a stock solution in DCE, which must also be prepared and stored in the cold.[7]

Results and Discussion

In selecting a model compound for studying this reaction, we avoided benzylic or tertiary alcohol derivatives which would be already conducive to elimination. We selected as the model substrate β-hydroxysilane **1a**, which is readily prepared from 4-phenylbutyraldehyde. Treatment of **1a** with 20 mol% of $CuBr_2$ in untreated MeCN provided olefin **2a** in >99% conversion (Table 1, entry 1). The olefination reaction did not occur when rigorously dried MeCN was employed as the solvent under dry argon (Table 1, entry 2). However, when 20 mol% of water was added to the anhydrous reaction (Table 1, entry 3), the olefination proceeded again in >99% conversion. As it was apparent that a trace amount of water is crucial to the success of the reaction, we speculated that $CuBr_2$ undergoes hydrolysis in water to generate, in addition to the hydrated copper(II) species, an acid that promoted the elimination (Scheme 2C above). Consistent with this theory, the reaction was completely shut down when the acid scavenger pyridine or 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) were added. Since equilibrium favors the formation of the weakest acid, the acid that actually catalyzed the elimination reaction in acetonitrile is not HBr, but, rather, should be the predominantly protonated acetonitrile. Alternatively, methanol can also serve as the proton source instead of water (Table 1, entry 4). THF Was ineffective as the solvent in this reaction, and **1a** remained completely inert, likely due to the insolubility of $CuCl_2 \bullet 2H_2O$ in THF (Table 1, entry 5). On the other hand, **1a** was completely consumed when acetone was used as the solvent (Table 1, entry 6); however, the formation of bromoacetone was also obtained as a side product under these conditions, and, thus, it is not a solvent of choice. [12]

Table 1. Optimization studies *[a]*

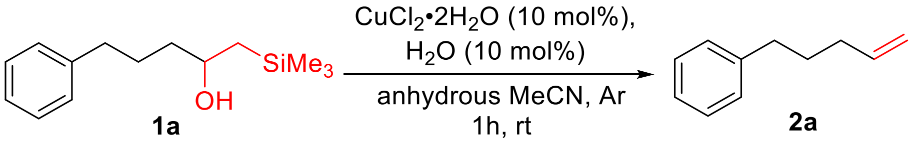


entry [a]	deviation from std. conditions	conv.(%) [b]
1	$CuBr_2$	>99%
2	anhydrous MeCN, Ar	0%
3	20 mol% H_2O, anhydrous MeCN, Ar	>99%
4	20 mol% MeOH, anhydrous MeCN, Ar	>99%
5	20 mol% H_2O, anhydrous THF, Ar	0%
6	20 mol% H_2O, anhydrous acetone, Ar	>99% [c]
7	CuBr	0%
8	CuCl	0%
9	$FeBr_2$	>99% [d]
10	$FeBr_3$	>99%
11	CuF_2	0%
12	CuF_2•$2H_2O$	0%
13	$Cu(TFA)_2$	0%
14	$Cu(OAc)_2$	0%
15	$Cu(OTf)_2$	>99%
16	$CuCl_2$•$2H_2O$	>99%

[a] Reaction conditions: **1a** (0.21 mmol, 1.0 equiv.), salt (0.20 equiv.), solvent (1.1 mL, 0.19 M). [b] Conversion after 1 h: [(**2a**)/(**1a+2a**) X 100%] determined by crude ^{1}H-NMR after filtration of an aliquot through a short plug of silica gel. [c] 1-bromopropan-2-one and precipitation of Cu(I)Br was observed. [d] Reaction time: 20 h.

The olefination reaction did not occur when **1a** was treated with CuBr or CuCl, salts (Table 1, entries 7 and 8) which should, in principle, also hydrolyze to generate Brønsted acids for inducing the dehydrative desilylation. This is due to the poor solubility of copper (I) halides in water,[13] which results in an inefficient reaction to generate a Brønsted acid. Both $FeBr_2$ and $FeBr_3$ are also effective in inducing elimination, consistent with both salts being water soluble (Table 1, entries 9 and 10).[14-15] However, $FeBr_2$ and $FeBr_3$ are less easy to handle, e.g., $FeBr_3$ is very hygroscopic[16] and reactive, so that, during the weighing process, it was progressively being hydrolyzed and transformed in open air. We screened other copper salts to investigate the counter-ion effect. No dehydrative desilylation occurred when **1a** was treated with CuF_2, CuF_2•$2H_2O$, $Cu(TFA)_2$, or $Cu(OAc)_2$ (Table 1, entries 11-14), whereas, $CuBr_2$, $Cu(OTf)_2$, and $CuCl_2$•$2H_2O$ were similarly effective (Table 1, entries 1, 15-16). This suggests that the conjugate acids generated by the salts need to be sufficiently acidic to promote the reaction efficiently. Amongst all of the salts, $CuCl_2$•$2H_2O$ became the reagent of choice due to its bench-top stability towards moisture, ease of handling and reaction efficiency, providing a convenient, and also cost-effective, solution for this application.

Table 2. Optimization of water content and catalyst loading



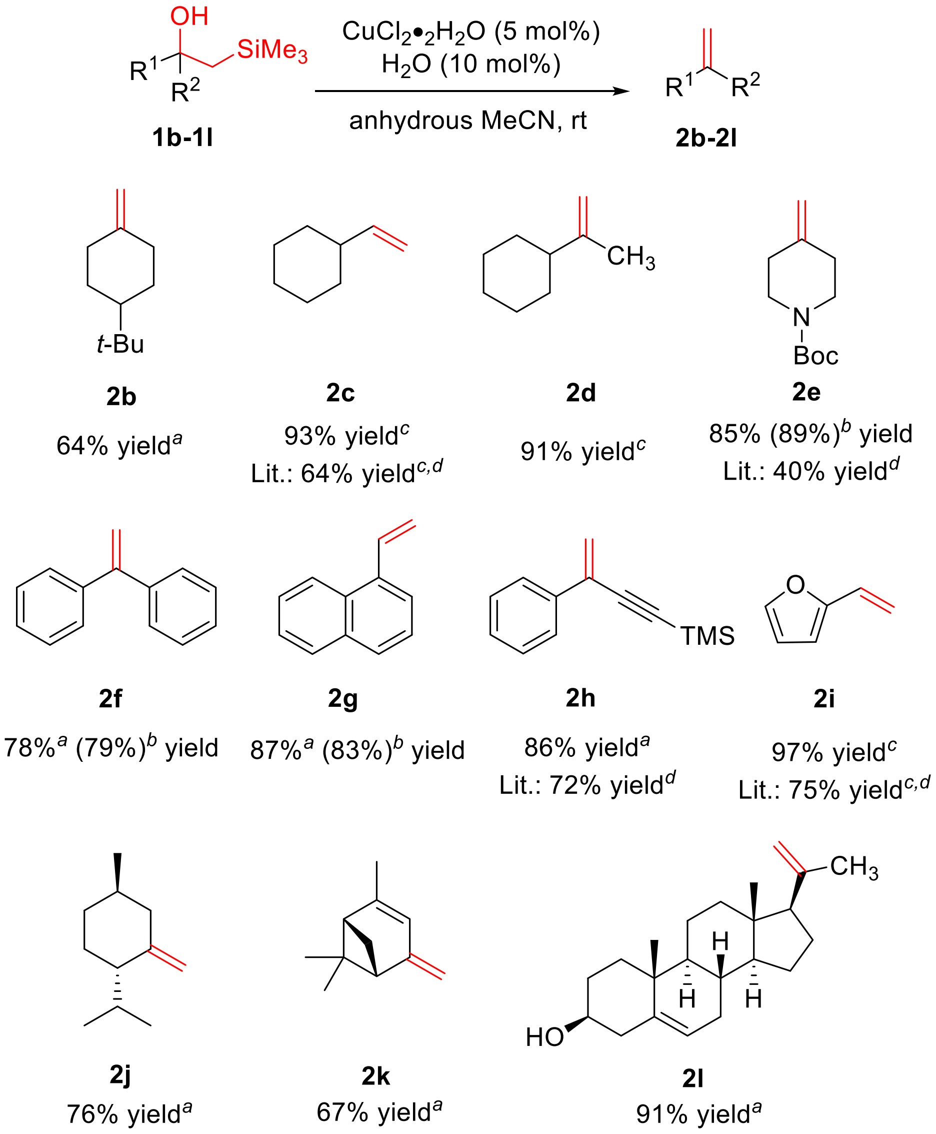
entry [a]	*deviation from std. conditions*	*conv.(%)* [b]
1	/	>99%
2	50 mol% H_2O	>99%
3	100 mol% H_2O	>99%
4	500 mol% H_2O	>99%
5	1000 mol% H_2O	45% (74%)[c](83%)[d]
6	3000 mol% H_2O	0%
7	5 mol% $CuCl_2\bullet 2H_2O$, 5 mol% H_2O	>99%
8	2.5 mol% $CuCl_2\bullet 2H_2O$, 2.5 mol% H_2O	9% (17%)[d]
9	1 mol% $CuCl_2\bullet 2H_2O$, 1 mol% H_2O	0%
10	5 mol% $CuCl_2\bullet 2H_2O$, 10 mol% H_2O	>99% [85%] [e]
11	5 mol% HBr (48% wt in H_2O)	>99% [82%] [e]

[a] Reaction conditions: **1a** (0.21 mmol, 1.0 equiv.), salt (0.01-0.20 equiv.), solvent (1.1 mL, 0.19 M). [b]Conversion after 1 h: [(**2a**)/(**1a+2a**) X 100%] determined by crude ^{1}H-NMR after filtration of an aliquot through a short plug of silica gel**.** [c]Conversion after 2 h. [d]Conversion after 3 h. [e]Isolated yield, work up: Add $NaHCO_3$ (aq), then extraction with diethyl ether as the organic solvent, followed by column chromatography.

We investigated the amount of water required for this reaction by conducting the reaction in anhydrous MeCN and under a dry, inert atmosphere. The use of $CuCl_2\bullet 2H_2O$, albeit in hydrated form, was insufficient to introduce enough water to promote the reaction. This reaction was found to be able to tolerate 0.1 equiv. to 10 equiv. of water with respect to **1a** (Table 2, entries 1-5), where conversion after 3 h reached 83% (Table 2, entry 5). Too much water in the reaction (30 equiv.), however, was detrimental (Table 2, entry 6). As for the catalyst loading, we found that the reaction proceeded to full conversion down to 5 mol% of a 1:1 $CuCl_2\bullet 2H_2O$: H_2O (Table 2, entry 7) in one hour. Below this, ie., the use of 2.5 mol% of 1:1 $CuCl_2\bullet 2H_2O$:H_2O (Table 2, entry 8) substantially decreased the conversion, and no reaction was observed at 1 mol% (Table 2, entry 9). We surmise that the concentrations of the acid generated at these loadings were too low to induce elimination effectively. Thus, in practice, 5 mol% of $CuCl_2\bullet 2H_2O$ with 10 mol% water ensured that a high enough concentration of acid was generated to promote and complete the reaction within a reasonable time frame.

In these analytical studies, in order to track, precisely, the amount of water needed to promote the elimination reaction, the reaction was performed in anhydrous MeCN, and water was added as a reagent (Table 2, entry 10). However, in practice, we typically use $CuCl_2\bullet 2H_2O$ in “wet” benchtop MeCN as received, which yielded excellent results as well as being very convenient. In comparison, treatment of **1a** with 5 mol% of 48% HBr also delivers **2a** in 82% yield (Table 2, entry 11). While a similar outcome is obtained with HBr, its corrosive nature, which eats away needles, makes its handling more difficult, and precise delivery more challenging, particularly when working with small-scale reactions. On the other hand, $CuCl_2\bullet 2H_2O$ is a bench-top stable reagent which can be measured out by mass very accurately, and delivered conveniently to reactions of all scales.

This convenient protocol demonstrated very good results experimentally. Therefore, we decided to evaluate the effectiveness of this dehydrative desilylation approach on different β-hydroxysilanes (Scheme 3, **1b-1l**). We were particularly interested to see how substrates and products bearing more acid-sensitive functional groups might fare under these reaction conditions. Scheme 3 shows the products that are obtained using this protocol, along with, where available, the yields of the same products obtained under alternative reaction conditions reported in the literature.[7]



[a] Isolated yield. [b] Reaction performed in untreated MeCN, isolated yield. [c] Yield determined by ^{1}H-NMR spectroscopy using 1,3,5- trimethoxybenzene as the internal standard, due to volatility or stability of the products. [d] Literature yield (Ref 7, reagent: $HNTf_2$ in 1,2-DCE).

Scheme 3. Substrate scope

A range of substrates underwent effective reactions with up to 97% yields, with the exception of 1-(*tert*-butyl)-4-methylenecyclohexane (**2b**), which was isolated in moderate yield, despite complete conversion, due to its volatility.[17] Therefore, for other volatile olefins, e.g., **2c**, **2d**, and **2i**, NMR yields were adopted for yield determinations. This method also enables fair comparison with the existing literature, which also utilized NMR yield for certain olefin products. Even the highly sensitive 2-vinylfuran (**2i**) was obtained in a very good yield

(97%). This method provided enynes like **2h** in improved yields compared to the literature (86% vs. 72%). Notably, the *N*-Boc protected **2e** was isolated in 85% yield with the acid-labile protecting group remaining intact. This compares favorably against **2e** being obtained in a reported 40% yield using 0.1 mol% of $HNTf_2$ in 1,2-DCE.[7] We attribute the higher yields to being able to weigh and charge the reaction with a precise mass of acid precursor so that the reaction proceeds with a controlled "just-enough" amount and low concentration of acid generated in situ. Methylenation of natural product scaffolds such as menthone (**2j**), verbenone (**2k**), which represents the olefination of an enone, as well as pregnenolone (**2l**) also proceeded smoothly.

Conclusions

The Peterson reaction remains a useful reaction to synthesize olefinic compounds with good stereochemical control. We have outlined a modified Peterson protocol by employing 5-10 mol% $CuCl_2•2H_2O$, as the dehydrative desilylating catalyst, to complete the reaction conveniently and efficiently. This salt reacts with trace amounts of water in acetonitrile to generate a protic acid in situ, to catalyze the dehydrative desilylation process. While the use of a Bronsted acid to accomplish this transformation is not new, this paper outlines a practical protocol to carry this out in which a precise, controlled, amount of acid is generated in situ, with the result that comparatively better yields of products have been obtained. In practice, this reaction uses a benchtop solvent and an inexpensive, readily available salt. The aqueous workup is also simple and convenient to perform. Besides the present reaction, it should also be possible to use $CuCl_2•2H_2O$ in acetonitrile in lieu of the direct addition of protic acids, to induce additional acid-promoted transformations.[18-20] This may allow such reactions to be conveniently accomplished under more controlled conditions. Besides the present reaction, it should also be possible to use $CuCl_2•2H_2O$ in acetonitrile in lieu of the direct addition of protic acids, to induce additional acid-promoted transformations. This may allow such reactions to be conveniently accomplished under more controlled conditions.

Experimental Section

1. General information:

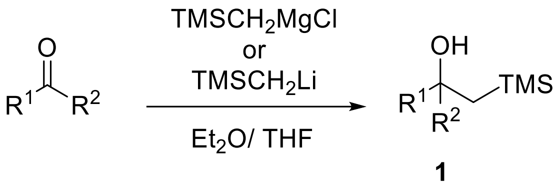
<u>Preparative:</u> All anhydrous reactions were performed in oven-dried round-bottomed flasks under a positive pressure of dry argon. Air and moisture-sensitive compounds were introduced via syringes or cannula using standard inert-atmosphere techniques. Reactions were monitored by thin layer chromatography (TLC) using E. Merck silica gel plates, Kieselgel 60 F_{254} with 0.2 mm thickness. Components were visualized by illumination with short-wavelength ultra-violet light and/or staining with phosphomolybdic acid (PMA). Flash-column chromatography was performed with E. Merck silica gel 60 (230-400 mesh ASTM). Solvents and chemicals were purchased from commercial sources and used without prior purification. All anhydrous solvents (THF, Et_2O, MeCN) used for reactions were distilled or dried by passing through drying columns. Anhydrous acetonitrile was distilled from CaH_2 under argon, followed by storage over 4 Å molecular sieves.

<u>Analytical:</u> ^1H and ^{13}C NMR spectra were recorded in deuterochloroform ($CDCl_3$) or trideuteroacetonitrile (CD_3CN), with tetramethylsilane (TMS) as an internal standard, at ambient temperature on a

Bruker Advance 400 spectrometer or Bruker DX 500 spectrometer operating at 400 MHz or 500 MHz respectively for ^{1}H, 100 MHz or 125 MHz respectively for ^{13}C, and at 376 MHz for ^{19}F. All spectra were calibrated using the respective solvent-resonance internal standard ($CDCl_3$, δ 7.26 and 77.16 ppm; CD_3CN, δ 1.94 and 118.26 ppm). Splitting patterns were designated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR absorption spectra were recorded on a PerkinElmer-Spectrum Two FT-IR Spectrometer from 4000 cm^{-1} to 400 cm^{-1}. Electron-impact mass spectrometry was recorded on a Finnigan MAT 95 mass spectrometer or API QSTAR PULSAR iLC/MS/TOF System for both low resolution and high resolution, with accurate mass reported for the molecular ion (M^+) or next largest fragment. Optical rotations were recorded as solutions in $CHCl_3$ on a Bellingham & Stanley ADP440+ polarimeter.

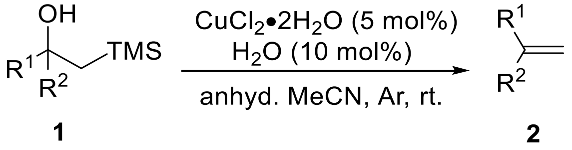
2. General Experimental Procedures

General Procedure A: Preparation of β-hydroxysilanes (1a-1l)



(Trimethylsilyl)methyllithium in hexanes or (trimethylsilylmethyl)magnesium chloride in Et_2O or THF (1-4 equiv) was added to a round-bottomed flask under argon. A solution of aldehyde or ketone (1 equiv) in anhydrous Et_2O (0.2-0.4 M) or anhydrous THF (0.2-0.4 M) was added by cannula dropwise to the round-bottomed flask containing the organometallic reagent at 0 °C. The reaction mixture was allowed to stir at room temperature until the reaction was complete (as judged by TLC analysis). The reaction mixture was then quenched with sat. NH_4Cl, and the phases were separated. The aqueous layer was back-extracted with Et_2O three times. The combined organics were washed with brine, dried over anhydrous $MgSO_4$, and concentrated by rotary evaporation to give the crude β-hydroxysilane **1**. The residue was purified by flash chromatography using an appropriate solvent system, which is described in the corresponding individual procedures.

General procedure B: Desilylative elimination by addition of a controlled amount of water to the reaction



A stock solution of H_2O in anhydrous MeCN (0.019 M, 0.034% v/v H_2O in acetonitrile) was prepared. To a solution of the β-hydroxysilane **1** (1 equiv) in this anhydrous acetonitrile stock solution (0.19 M) was added $CuCl_2•2H_2O$ (0.05 equiv) under argon. The reaction mixture was allowed to stir at room temperature until the reaction was complete as judged by TLC analysis.

General procedure C: Routine method for desilylative elimination using bench-top MeCN

In open air, to a solution of β-hydroxysilane **1** (1 equiv) in MeCN (not pre-dried) was added $CuCl_2•2H_2O$ (0.05 equiv). The flask was capped with a septum. The reaction mixture was stirred at room temperature until the reaction was complete, as determined by TLC analysis.

Workup and Purification Method I (For volatile olefins):

Pentane and H_2O (1:1) were added to the reaction mixture, and the two phases were separated. The aqueous layer was back-extracted with pentane three times. The combined organics were washed with brine, dried over anhydrous $MgSO_4$ and concentrated by rotary evaporation to afford the crude olefin **2**, which was purified by flash chromatography using an appropriate eluent system described in the corresponding individual procedures.

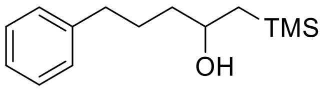
Workup and Purification Method II:

Saturated $NaHCO_3$ (aq.) was added to the reaction mixture, and the two phases were separated. The aqueous layer was back-extracted with Et_2O three times. The combined organics were washed with brine, dried over anhydrous $MgSO_4$ and concentrated by rotary evaporation to afford the crude olefin **2**, which was purified by flash chromatography using an appropriate eluent system described in the corresponding individual procedures.

Method III: Yield determination by NMR for volatile olefins:

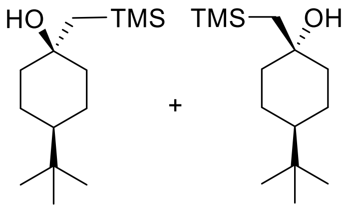
1,3,5-Trimethoxybenzene (NMR standard) was weighed and added to the reaction mixture for analysis. An aliquot (~ 0.2mL) of the reaction mixture was withdrawn and filtered through a short pad of silica plug, using CD_3CN as the eluent. The eluate was analyzed by ^1H NMR spectroscopy (relaxation *t* d1 = 10 s). The peaks in question were integrated. The amount of the alkene product was quantified by the following equation: $n_A = r_A/r_{IS} \times n_{IS}$, where n_A = mmol of analyte, n_{IS} = mmol of internal standard, and r_A/r_{IS} = ratio of analyte to internal standard.

3. Characterizations of β-hydroxysilanes 1a-1l and alkenes 2a-2l



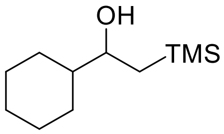
(**1a**)

5-Phenyl-1-(trimethylsilyl)pentan-2-ol (1a). According to general procedure A, 4-phenylbutanol (0.549 g, 3.70 mmol, 1.00 equiv) in anhydrous THF (9 mL, 0.4 M) was treated with $TMSCH_2MgCl$ (0.36 M in THF, 26 mL, 9.3 mmol, 2.5 equiv) . β-Hydroxysilane **1a** (0.724 g, 3.06 mmol, 91%) was obtained as a colorless oil after purification by flash chromatography (5% EtOAc in hexane). R_f (15% EtOAc in hexane) 0.64; IR (neat, ν/cm^{-1}) 3378, 2948, 1623, 1247, 993; ^1H NMR (500 MHz, $CDCl_3$): δ_H 7.27 (d, *J* 7.2 Hz, 2H), 7.21 – 7.16 (m, 3H), 3.81 (m, *J* 7.2, 4.7 Hz, 1H), 2.63 (t, *J* 9.2, 6.8 Hz, 2H), 1.84 – 1.60 (m, 2H), 1.55 – 1.42 (m, 2H), 0.91 – 0.78 (m, 2H), 0.02 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 142.4, 128.4, 127.8, 125.7, 70.0, 40.2, 35.8, 27.6, 26.6, -0.7 ppm; HRMS (EI, 40eV) *m/z* $[M-H_2O]^+$ calcd for $C_{14}H_{22}Si$ 218.1485, found 218.1482.



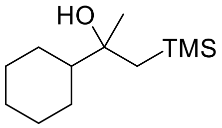
(**1b**)

***(1r,4r)*- and *(1s,4s)*-4-(*tert*-Butyl)-1-((trimethylsilyl)methyl)cyclohexan-1-ol (1b).** According to general procedure A, 4-(*tert*-butyl)cyclohexan-1-one (0.589 g, 3.81 mmol, 1.00 equiv) in anhydrous THF (3 mL, 2 M) was treated with $TMSCH_2Li$ (0.56 M in hexanes, 7.5 mL, 4.2 mmol, 1.1 equiv). β-Hydroxysilane **1b** (0.608 g, 2.51 mmol, 66%) was obtained as a 2.8:1 diastereomeric mixture, in the form of a white solid after purification by flash chromatography (5% EtOAc in hexane). R_f (15% EtOAc in hexane) 0.82; Major diastereomer (*1r,4r*)-**1b**: ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.74 (s, 1H), 1.55 (m, *J* 3.9, 3.2 Hz, 1H), 1.39 (m, *J* 3.5 Hz, 3H), 1.34 – 1.20 (m, 3H), 1.12 – 0.98 (m, 1H), 0.95 (s, 2H), 0.85 (s, 9H), 0.06 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 71.9, 47.7, 40.8, 34.8, 32.5, 27.7, 23.0, 0.7 ppm. The spectral characteristics are consistent with those of (*1r,4r*)-**1b** reported in the literature.[21]



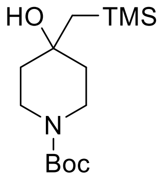
(**1c**)

1-Cyclohexyl-2-(trimethylsilyl)ethan-1-ol (1c). According to general procedure A, 4 cyclohexanecarbaldehyde (0.855 g, 7.62 mmol, 1.00 equiv) in anhydrous Et_2O (18 mL, 0.4 M) was treated with $TMSCH_2MgCl$ (1.0 M in Et_2O, 19 mL, 19 mmol, 2.5 equiv). β-Hydroxysilane **1c** (1.36 g, 6.78 mmol, 89%) was obtained as a pale-yellow oil after purification by flash chromatography (5% EtOAc in hexane). R_f (10% EtOAc in hexane) 0.47; ^1H NMR (400 MHz, $CDCl_3$): δ_H 3.56 (s, 1H), 1.84 – 1.73 (m, 2H), 1.64 (s, 1H), 1.31 – 0.93 (m, 8H), 0.84 (dd, *J* 14.7, 4.5 Hz, 1H), 0.74 (dd, *J* 14.7, 9.6 Hz, 1H), 0.05 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 74.5, 46.3, 29.6, 27.5, 26.7, 26.5, 26.3, 22.8, -2.1 ppm. The spectral characteristics are consistent with those of **1c** reported in the literature.[22]



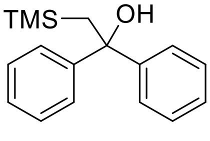
(**1d**)

2-Cyclohexyl-1-(trimethylsilyl)propan-2-ol (1d). According to general procedure A, 1-cyclohexylethan-1-one (0.832 g, 6.34 mmol, 1.00 equiv) in anhydrous Et_2O (16 mL, 0.4 M) was treated with $TMSCH_2MgCl$ (1.0 M in Et_2O, 16 mL, 16 mmol, 2.5 equiv). β-Hydroxysilane **1d** (1.04 g, 4.85 mmol, 76%) was obtained as a pale-yellow oil after purification by flash chromatography (5% EtOAc in hexane). R_f (15% EtOAc in hexane) 0.82; IR (neat, ν/cm^{-1}) 3481, 2925, 2854, 1246, 836; ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.84 – 1.71 (m, 4H), 1.69 – 1.63 (m, 1H), 1.29 – 1.04 (m, 7H), 1.04 – 0.96 (m, 1H), 0.94 (s, 2H), 0.07 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 75.8, 50.9, 30.1, 27.8, 27.4, 27.2, 26.9, 26.8, 26.6, 0.8 ppm; HRMS (EI, 40eV) *m/z* $[M-H_2O]^+$ calcd for $C_{12}H_{24}Si$ 196.1642, found 196.1642.



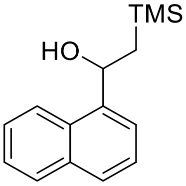
(**1e**)

***tert*-Butyl 4-hydroxy-4-((trimethylsilyl)methyl)piperidine-1-carboxylate (1e).** According to general procedure A, *tert*-butyl 4-oxopiperidine-1-carboxylate (0.503 g, 2.53 mmol, 1.00 equiv) in anhydrous Et_2O (6 mL, 0.4 M) was treated with $TMSCH_2MgCl$ (1.0 M in Et_2O, 6.3 mL, 6.3 mmol, 2.5 equiv). β-Hydroxysilane **1e** (0.539 g, 1.87 mmol, 74%) was obtained as a white solid after purification by flash chromatography (20% EtOAc in hexane). m.p. 63.2 – 65.9 °C; R_f (20% EtOAc in hexane) 0.27; IR (neat, ν/cm^{-1}) 3469, 2948, 1667, 1246, 1049; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.74 (d, 2H), 3.22 – 3.11 (m, 2H), 1.56 (s, 4H), 1.46 (s, 9H), 0.99 (s, 2H), 0.08 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 155.0, 79.5, 70.9, 39.9, 33.6, 28.6, 0.7 ppm; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{14}H_{29}NNaO_3Si$ 310.1814, found 310.1809.



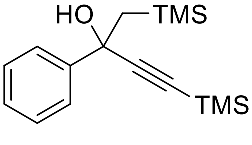
(**1f**)

1,1-Diphenyl-2-(trimethylsilyl)ethan-1-ol (1f). According to general procedure A, benzophenone (1.05 g, 5.76 mmol, 1.00 equiv) in anhydrous THF (28 mL, 0.2 M) was treated with $TMSCH_2MgCl$ (1.0 M in Et_2O, 14 mL, 14 mmol, 2.5 equiv). β-Hydroxysilane **1f** (1.52 g, 5.61 mmol, 97%) was obtained as a white solid after purification by flash chromatography (15% EtOAc in hexane). R_f (20% EtOAc in hexane) 0.72; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.48 – 7.43 (m, 4H), 7.33 – 7.22 (m, 4H), 7.22 – 7.15 (m, 2H), 1.83 (s, 2H), -0.18 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 149.3, 128.2, 126.7, 125.8, 78.6, 32.7, 0.1 ppm. The spectral characteristics are consistent with those of **1f** reported in the literature.[23]



(**1g**)

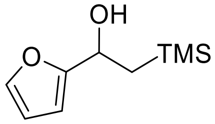
1-(Naphthalen-1-yl)-2-(trimethylsilyl)ethan-1-ol (1g). According to general procedure A, 1-naphthaldehyde (0.531 g, 3.39 mmol, 1.00 equiv) in anhydrous Et_2O (8 mL, 0.4 M) was treated with $TMSCH_2MgCl$ (0.63 M in Et_2O, 13 mL, 8.5 mmol, 2.5 equiv). β-Hydroxysilane **1g** (0.7118 g, 2.912 mmol, 86%) was obtained as a pale-yellow oil after purification by flash chromatography (5% EtOAc in hexane). R_f (15% EtOAc in hexane) 0.56; IR (neat, ν/cm^{-1}) 3376, 2951, 1509, 1247, 1008; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.21 (dd, *J* 8.4, 1.5 Hz, 1H), 7.87 (dd, *J* 7.8, 1.8 Hz, 1H), 7.77 (d, *J* 8.2 Hz, 1H), 7.63 (t, *J* 7.1, 0.8 Hz, 1H), 7.58 – 7.39 (m, 3H), 5.77 – 5.54 (m, 1H), 1.87 (dt, *J* 3.7, 1.7 Hz, 1H), 1.46 – 1.31 (m, 2H), 0.01 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 142.5, 134.1, 130.4, 129.1, 128.1, 126.0, 125.6, 125.6, 123.7, 122.7, 70.0, 27.6, -0.8 ppm; HRMS (EI, 40eV) *m/z* $[M]^+$ calcd for $C_{15}H_{20}OSi$ 244.1278, found 244.1281.



(**1h**)

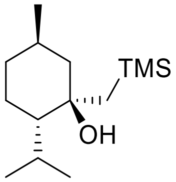
2-Phenyl-1,4-bis(trimethylsilyl)but-3-yn-2-ol (1h). According to general procedure A, 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-one (0.186 g, 0.919 mmol, 1.00 equiv) in anhydrous Et_2O (2.3 mL, 0.4 M) was treated with $TMSCH_2MgCl$ (1.0 M in Et_2O, 2.7 mL, 2.7 mmol, 3.0 equiv). β-Hydroxysilane **1h** (0.148 g, 0.509 mmol, 55%)

as obtained as a pale-yellow oil after purification by flash chromatography (2% Et_2O in pentanes). R_f (5% EtOAc in hexane) 0.52; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.66 (dd, *J* 8.3, 1.3 Hz, 2H), 7.33 (d, *J* 7.9 Hz, 2H), 7.32 – 7.23 (m, 1H), 2.34 (s, 1H), 1.58 (d, *J* 14.3 Hz, 1H), 1.50 (dd, *J* 14.2, 0.8 Hz, 1H), 0.22 (s, 9H), -0.08 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ_C 146.4, 128.3, 127.7, 125.3, 109.4, 90.4, 72.5, 36.3, -0.0, -0.3 ppm. The spectral characteristics are consistent with those of **1h** reported in the literature.[7]



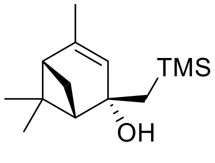
(**1i**)

1-(Furan-2-yl)-2-(trimethylsilyl)ethan-1-ol (1i). According to general procedure A, furan-2-carbaldehyde (0.510 g, 5.31 mmol, 1.00 equiv) in anhydrous THF (12 mL, 0.4 M) was treated with $TMSCH_2MgCl$ (1.0 M in THF, 13 mL, 13 mmol, 2.5 equiv). β-Hydroxysilane **1i** (0.860 g, 4.67 mmol, 88%) was obtained as a pale-yellow oil after purification by flash chromatography (10% EtOAc in hexane). R_f (10% EtOAc in hexane) 0.29; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.36 (dd, *J* 1.9, 0.8 Hz, 1H), 6.33 – 6.24 (m, 1H), 6.21 (s, 1H), 4.85 (m, *J* 7.7, 5.0 Hz, 1H), 1.78 (d, *J* 5.2 Hz, 1H), 1.39 – 1.17 (m, 2H), -0.05 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 157.9, 141.8, 110.3, 105.6, 65.8, 24.9, -1.0 ppm. The spectral characteristics are consistent with those of **1i** reported in the literature.[24]



(**1j**)

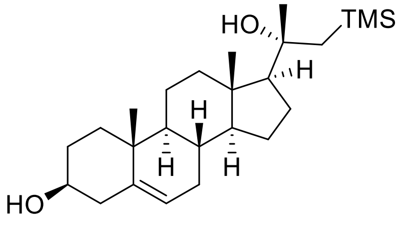
(*1R,2S,5R*)-2-Isopropyl-5-methyl-1-((trimethylsilyl)methyl)cyclohexan-1-ol (1j). According to general procedure A, (–)-menthone (0.560 g, 3.63 mmol, 1.00 equiv) in anhydrous Et_2O (16 mL, 0.2 M) was treated with $TMSCH_2MgCl$ (0.52 M in Et_2O, 15 mL, 9.1 mmol, 2.5 equiv). β-Hydroxysilane **1j** (0.787 g, 3.25 mmol, 90%) was obtained as a colorless oil after purification by flash chromatography (10% EtOAc in hexane). R_f (10% EtOAc in hexane) 0.14; $[\alpha]_D^{23}$ +8.9 (*c* 0.01, $CHCl_3$); IR (neat, ν/cm^{-1}) 3504, 2951, 1446, 1248, 835; ^1H NMR (400 MHz, $CDCl_3$): δ_H 2.17 (m, *J* 7.1 Hz, 1H), 1.75 (m, *J* 13.0, 3.4 Hz, 1H), 1.70 – 1.60 (m, 2H), 1.54 – 1.45 (m, 1H), 1.36 (m, *J* 13.0, 3.5 Hz, 1H), 1.22 – 0.99 (m, 5H), 0.96 – 0.80 (m, 11H), 0.07 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 76.3, 51.0, 50.7, 31.6, 28.5, 26.1, 23.7, 22.6, 20.9, 18.3, 0.8 ppm; HRMS (EI, 40eV) *m/z* $[M]^+$ calcd for $C_{14}H_{30}OSi$ 242.2063, found 242.2060.



(**1k**)

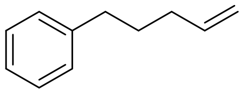
(*1S,2S,5S*)-4,6,6-Trimethyl-2-((trimethylsilyl)methyl)bicyclo[3.1.1]hept-3-en-2-ol (1k). According to general procedure A, *(S)*-(–)-verbenone (0.530 g, 3.53 mmol, 1.00 equiv) in anhydrous THF (11 mL, 0.3 M) was treated with $TMSCH_2MgCl$ (0.46 M in Et_2O, 19 mL, 8.8 mmol, 2.5 equiv). The reaction mixture was heated to reflux for 19 hours, after which the reaction was complete as judged by TLC analysis. The reaction mixture was cooled to

0 °C. The reaction mixture was then quenched with sat. NH_4Cl, and the phases were separated. The aqueous layer was back-extracted with Et_2O three times. The combined organics were washed with brine, dried over anhydrous Na_2SO_4, and concentrated by rotary evaporation to give the crude β-hydroxysilane **1k**. β-Hydroxysilane **1k** (0.18 g, 0.76 mmol, 22%) was obtained as a colorless oil after purification by flash chromatography (3% EtOAc in hexane). R_f (10% EtOAc in hexane) 0.7; $[\alpha]_D^{25}$ -25.5 (*c* 0.002, $CHCl_3$); IR (neat, ν/cm^{-1}) 3518, 2923, 1641, 1246, 836; ^1H NMR (500 MHz, $CDCl_3$): δ_H 5.29 (s, 1H), 2.44 (m, *J* 9.2, 5.2 Hz, 1H), 2.09 (m, *J* 6.0, 2.3 Hz, 1H), 1.96 – 1.90 (m, 1H), 1.70 (d, *J* 1.6 Hz, 3H), 1.40 (d, *J* 9.1 Hz, 1H), 1.34 (s, 3H), 1.08 (s, 4H), 0.99 – 0.89 (m, 1H), 0.07 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 144.1, 124.6, 78.5, 55.4, 47.8, 42.7, 36.2, 31.3, 27.3, 23.5, 22.7, 0.8 ppm; HRMS (EI, 40eV) *m/z* $[M-H_2O]^+$ calcd for $C_{14}H_{24}Si$ 220.1642, found 220.1640.



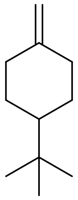
(**1l**)

***(3S,8S,9S,10R,13S,14S,17S)-17-((S)-*2-hydroxy-1-(trimethylsilyl)propan-2-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-ol (1l).** According to general procedure A, pregnenolone (0.500 g, 1.58 mmol, 1.00 equiv) in anhydrous THF (15 mL, 0.2 M) was treated with $TMSCH_2MgCl$ (0.46 M in THF, 14 mL, 6.3 mmol, 2.5 equiv). The reaction mixture was heated to reflux for 3 hours, after which the reaction was complete as judged by TLC analysis. The reaction mixture was cooled to 0 °C. The reaction mixture was then quenched with sat. NH_4Cl, and the phases were separated. The aqueous layer was back-extracted with Et_2O three times. The combined organics were washed with brine, dried over anhydrous $MgSO_4$, and concentrated by rotary evaporation to give the crude β-hydroxysilane **1l.** β-Hydroxysilane **1l** (0.19 g, 0.47 mmol, 30%) was obtained as a white solid after purification by flash chromatography (15% EtOAc in hexane). The configuration of **1l** was assigned based on the stereochemical outcome of the addition of other Grignard reagents to pregnenolone.[25] m.p. 150.1-152.5 °C; R_f (50% EtOAc in hexane) 0.74; $[\alpha]_D^{24}$ -36.0 (*c* 0.002, $CHCl_3$); IR (neat, ν/cm^{-1}) 3234, 2944, 1460, 1371, 1246, 1061, 835; ^1H NMR (400 MHz, $CDCl_3$): δ_H 5.35 (d, *J* 5.2 Hz, 1H), 3.52 (m, 1H), 2.36 – 2.05 (m, 4H), 2.03 – 1.57 (m, 6H), 1.53 – 1.40 (m, 5H), 1.36 (s, 3H), 1.28 – 1.02 (m, 5H), 1.01 (s, 3H), 1.00 – 0.87 (m, 2H), 0.85 (s, 3H), 0.06 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 140.9, 121.6, 76.2, 71.8, 61.0, 57.1, 50.1, 42.9, 42.4, 40.3, 37.3, 36.6, 34.7, 31.8, 31.7, 31.4, 29.9, 23.9, 23.1, 21.0, 19.5, 13.5, 0.7 ppm; HRMS (EI, 40eV) *m/z* $[M-H_2O]^+$ calcd for $C_{25}H_{42}OSi$ 386.2999, found 386.3002.



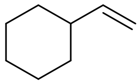
(**2a**)

Pent-4-en-1-ylbenzene (2a). According to general procedure B, **1a** (0.156 g, 0.661 mmol, 1.00 equiv) in 3.5 mL of the MeCN stock solution (0.19 M in **1a**) was treated with $CuCl_2•2H_2O$ (5.6 mg, 0.033 mmol, 0.05 equiv). Alkene **2a** (82 mg, 0.56 mmol, 85%) was obtained as a colorless oil, after workup and purification by flash chromatography using 0.5% Et_2O in pentanes as eluent, according to Method I. R_f (5% EtOAc in hexane) 0.86; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.27 (d, *J* 7.3 Hz, 2H), 7.18 (d, *J* 7.2 Hz, 3H), 5.91 – 5.76 (m, 1H), 5.13 – 4.86 (m, 2H), 2.62 (t, *J* 7.8 Hz, 2H), 2.10 (m, *J* 7.3 Hz, 2H), 1.72 (m, *J* 7.7 Hz, 2H) ppm; $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ_C 142.6, 138.7, 128.6, 128.4, 125.8, 114.8, 35.4, 33.4, 30.8 ppm. The spectral characteristics are consistent with those of **2a** reported in the literature.[26]



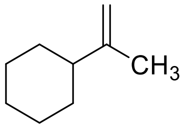
(**2b**)

1-(*tert*-Butyl)-4-methylenecyclohexane (2b). According to general procedure B, **1b** (0.150 g, 0.619 mmol, 1.00 equiv) in 3.3 mL of the MeCN stock solution (0.19 M in **1b**) was treated with $CuCl_2•2H_2O$ (5.3 mg, 0.031 mmol, 0.05 equiv). Alkene **2b** (60.4 mg, 0.395 mmol, 64%) was obtained as a colorless oil, after workup and purification by flash chromatography using pentanes as eluent, according to Method I. R_f (5% EtOAc in hexane) 0.80; ^1H NMR (500 MHz, $CDCl_3$): δ_H 4.58 (s, *J* 1.8 Hz, 2H), 2.33 (d, *J* 1.8 Hz, 2H), 1.99 (m, *J* 1.8 Hz, 2H), 1.86 (m, *J* 2.0 Hz, 2H), 1.23 – 0.99 (m, 3H), 0.85 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ_C 150.5, 106.2, 48.0, 35.5, 32.6, 29.1, 27.8 ppm. The spectral characteristics are consistent with those of **2b** reported in the literature.[27]



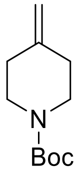
(**2c**)

Vinylcyclohexane (2c). According to general procedure B, **1c** (0.207 g, 1.03 mmol, 1.00 equiv) in 5.4 mL of the MeCN stock solution (0.19 M in **1c**) was treated with $CuCl_2•2H_2O$ (8.8 mg, 0.052 mmol, 0.05 equiv). After the reaction was complete as judged by TLC analysis, 1,3,5-trimethoxybenzene (13.4 mg) was added to the reaction mixture for analysis. Alkene **2c** (0.964 mmol, 93% NMR yield) was obtained, according to Method III. R_f (5% EtOAc in hexane) 0.93; ^1H NMR (400 MHz, $CDCl_3$) δ_H 5.75 (ddd, *J* 17.1, 10.4, 6.5 Hz, 1H), 4.91 (d, *J* 17.4, 1H), 4.84 (d, *J* 10.5, 1H), 1.99 – 1.84 (m, 1H), 1.74 – 1.58 (m, 5H), 1.32 – 0.98 (m, 5H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ_C 145.1, 111.7, 41.8, 32.7, 26.4, 26.2 ppm. The spectral characteristics are consistent with those of **2c** in the literature.[7]



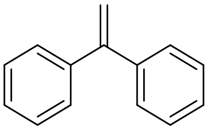
(**2d**)

Prop-1-en-2-ylcyclohexane (2d). According to general procedure B, **1d** (0.204 g, 0.952 mmol, 1.00 equiv) in 5.0 mL of the MeCN stock solution (0.19 M in **1d**) was treated with $CuCl_2•2H_2O$ (8.1 mg, 0.047 mmol, 0.05 equiv). After the reaction was complete as judged by TLC analysis, 1,3,5-trimethoxybenzene (11.5 mg) was added to the reaction mixture for analysis. Alkene **2d** (0.866 mmol, 91% NMR yield) was obtained, according to Method III. R_f (5% EtOAc in hexane) 0.76; ^1H NMR (400 MHz, $CDCl_3$) δ_H 4.66 (s, , 2H), 1.86 (tt, *J* 11.3, 3.0 Hz, 1H), 1.81 – 1.61 (m, 8H), 1.36 – 1.05 (m, 5H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 151.5, 108.0, 45.7, 32.1, 26.8, 26.5, 21.1 ppm. The spectral characteristics are consistent with those of **2d** in the literature.[28]



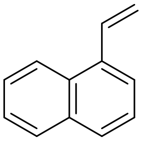
(**2e**)

***tert*-Butyl 4-methylenepiperidine-1-carboxylate (2e).** According to general procedure B, **1e** (0.165 g, 0.572 mmol, 1.00 equiv) in 3.0 mL of the MeCN stock solution (0.19 M in **1e**) was treated with $CuCl_2•2H_2O$ (4.9 mg, 0.029 mmol, 0.05 equiv). Alkene **2e** (96 mg, 0.49 mmol, 85%) was obtained as a colorless oil, after workup and purification by flash chromatography using 5% EtOAc in hexane as eluent, according to Method II (Drying agent: Na_2SO_4). According to general procedure C, **1e** (0.153 g, 0.532 mmol, 1.00 equiv) in MeCN (2.8 mL, 0.19 M) was treated with $CuCl_2•2H_2O$ (4.5 mg, 0.027 mmol, 0.05 equiv). Alkene **2e** (93.7 mg, 0.475 mmol, 89%) was obtained as a colorless oil, after workup and purification by flash chromatography using 5% EtOAc in hexane as eluent, according to Method II (Drying agent: Na_2SO_4). R_f (15% EtOAc in hexane) 0.64; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 4.74 (d, *J* 1.1 Hz, 2H), 3.42 (t, *J* 5.8 Hz, 4H), 2.18 (t, *J* 5.8 Hz, 4H), 1.47 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 154.9, 145.5, 109.2, 79.6, 45.5, 34.7, 28.6 ppm. The spectral characteristics are consistent with those of **2e** in the literature.[7]



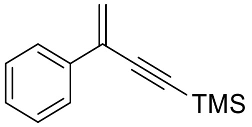
(**2f**)

Ethene-1,1-diyldibenzene (2f). According to general procedure B, **1f** (0.121 g, 0.447 mmol, 1.00 equiv) in 2.4 mL of the MeCN stock solution (0.19 M in **1f**) was treated with $CuCl_2•2H_2O$ (3.8 mg, 0.022 mmol, 0.05 equiv). Alkene **2f** (63 mg, 0.35 mmol, 78%) was obtained as a colorless oil, after workup and purification by flash chromatography using pentanes as eluent, according to Method II. According to general procedure C, **1f** (0.127 g, 0.469 mmol, 1.00 equiv) in MeCN (2.5 mL, 0.19 M) was treated with $CuCl_2•2H_2O$ (4.0 mg, 0.023 mmol, 0.05 equiv). Alkene **2f** (67.1 mg, 0.372 mmol, 79%) was obtained as a colorless oil, after workup and purification by flash chromatography using pentanes as eluent, according to Method II. R_f (5% EtOAc in hexane) 0.83; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.34 (s, 10H), 5.46 (d, *J* 1.9 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ_C 150.2, 141.6, 128.4, 128.3, 127.8, 114.4 ppm. The spectral characteristics are consistent with those of **2f** in the literature.[29]



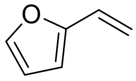
(**2g**)

1-Vinylnaphthalene (2g). According to general procedure B, **1g** (0.207 g, 0.845 mmol, 1.00 equiv) in 4.4 mL of the MeCN stock solution (0.19 M in **1g**) was treated with $CuCl_2•2H_2O$ (7.2 mg, 0.042 mmol, 0.05 equiv). Alkene **2g** (0.113 g, 0.733 mmol, 87%) was obtained as a colorless oil, after workup and purification by flash chromatography using 1% Et_2O in pentanes as eluent, according to Method II. According to general procedure C, **1g** (0.200 g, 0.772 mmol, 1.00 equiv) in MeCN (4.3 mL, 0.19 M) was treated with $CuCl_2•2H_2O$ (6.9 mg, 0.041 mmol, 0.05 equiv). Alkene **2g** (99 mg, 0.64 mmol, 83%) was obtained as a colorless oil, after workup and purification by flash chromatography using 1% Et_2O in pentanes as eluent, according to Method II. R_f (15% EtOAc in hexane) 0.64; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 8.23 – 8.11 (m, 1H), 7.87 (dd, *J* 7.2, 2.1 Hz, 1H), 7.81 (d, *J* 8.2 Hz, 1H), 7.65 (d, *J* 7.2 Hz, 1H), 7.58 – 7.43 (m, 4H), 5.82 (dd, *J* 17.3, 1.7 Hz, 1H), 5.50 (dd, *J* 10.9, 1.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 135.7, 134.5, 133.7, 131.2, 128.6, 128.2, 126.2, 125.9, 125.8, 123.9, 123.8, 117.2 ppm; The spectral characteristics are consistent with those of **2g** in the literature.[30]



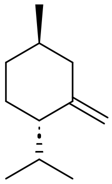
(**2h**)

Trimethyl(3-phenylbut-3-en-1-yn-1-yl)silane (2h). According to general procedure B, **1h** (76.1 mg, 0.262 mmol, 1.00 equiv) in 1.4 mL of the MeCN stock solution (0.19 M in **1h**) was treated with $CuCl_2 \bullet 2H_2O$ (2.2 mg, 0.013 mmol, 0.05 equiv). Alkene **2h** (45.3 mg, 0.225 mmol, 86%) was obtained as a colorless oil, after workup and purification by flash chromatography using pentanes as eluent, according to Method I. R_f (15% EtOAc in hexane) 0.64; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.68 – 7.62 (m, 2H), 7.39 – 7.33 (m, 2H), 7.34 – 7.27 (m, 1H), 5.94 (s, 1H), 5.72 (s, 1H), 0.26 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ_C 137.1, 130.8, 128.5, 128.4, 126.2, 121.6, 104.2, 96.1, 0.1 ppm. The spectral characteristics are consistent with those of **2h** in the literature.[7]



(**2i**)

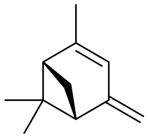
2-Vinylfuran (2i). According to general procedure B, **1i** (50.6 mg, 0.275 mmol, 1.00 equiv) in 1.4 mL of the MeCN stock solution (0.19 M in **1i**) was treated with $CuCl_2 \bullet 2H_2O$ (2.3 mg, 0.014 mmol, 0.05 equiv). After the reaction was complete as judged by TLC analysis, 1,3,5-trimethoxybenzene (11.1 mg) was added to the reaction mixture for analysis. Alkene **2i** (0.266 mmol, 97% NMR yield) was obtained, according to Method III. R_f (10% EtOAc in hexane) 0.67; ^{1}H NMR (500 MHz, CD_3CN): δ_H 7.44 (s, 1H), 6.61 – 6.52 (m, *J* 17.8, 11.5 Hz, 1H), 6.43 (d, *J* 3.1, 1.4 Hz, 1H), 6.35 (d, *J* 3.3 Hz, 1H), 5.65 – 5.58 (d, *J* 17.8 Hz, 1H), 5.19 – 5.13 (d, *J* 11.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (100 MHz, CD_3CN): δ_C 154.0, 143.3, 126.0, 112.6, 112.3, 109.2 ppm. The spectral characteristics are consistent with those of **2i** in the literature.[7]



(**2j**)

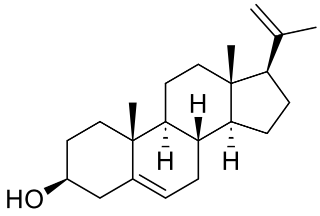
(*1S,4R*)-1-Isopropyl-4-methyl-2-methylenecyclohexane (2j). According to general procedure B, **1j** (0.210 g, 0.867 mmol, 1.00 equiv) in 4.5 mL of the MeCN stock solution (0.19 M in **1j**) was treated with $CuCl_2 \bullet 2H_2O$ (7.4 mg, 0.043 mmol, 0.05 equiv). Alkene **2j** (0.100 g, 0.658 mmol, 76%) was obtained as a colorless oil, after workup and purification by flash chromatography using pentanes as eluent, according to Method I. R_f (5% EtOAc in hexane) 0.86; $[\alpha]_D^{24}$ -36.5 (*c* 0.004, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.70 (s, 1H), 4.58 (s, 1H), 2.28 (dd, *J* 12.6, 4.1 Hz, 1H), 1.96 (h, *J* 6.7 Hz, 1H), 1.77 (dt, *J* 9.2, 4.1 Hz, 2H), 1.71 – 1.63 (m, 2H), 1.62 – 1.53 (m, 1H), 1.24 – 1.02

(m, 2H), 0.94 – 0.86 (m, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ_C 151.3, 106.2, 49.5, 44.6, 34.2, 33.5, 27.5, 27.2, 22.3, 21.5, 19.1 ppm. The spectral characteristics are consistent with those of **2j** in the literature.[31]



(**2k**)

(*1S,5S*)-2,6,6-Trimethyl-4-methylenebicyclo[3.1.1]hept-2-ene (2k). According to general procedure B, **1k** (0.104 g, 0.435 mmol, 1.00 equiv) in 2.3 mL of the MeCN stock solution (0.19 M in **1k**) was treated with $CuCl_2$•$2H_2O$ (3.7 mg, 0.022 mmol, 0.05 equiv). Alkene **2k** (43.1 mg, 0.291 mmol, 67%) was obtained as a colorless oil, after workup and purification by flash chromatography using pentanes as eluent, according to Method I. R_f (10% EtOAc in hexane) 0.9; $[\alpha]_D^{23}$ -17.2 (*c* 0.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 5.77 (d, *J* 2.4 Hz, 1H), 4.56 (s, 2H), 2.59 (td, *J* 5.9, 1.5 Hz, 1H), 2.51 (dt, *J* 8.5, 5.4 Hz, 1H), 2.10 (td, *J* 5.8, 1.5 Hz, 1H), 1.78 (s, *J* 1.6 Hz, 3H), 1.45 (d, *J* 8.5 Hz, 1H), 1.35 (s, 3H), 0.82 (s, 3H) ppm; $^{13}C\{^1H\}$ (125 MHz, $CDCl_3$) δ_C 150.3, 148.6, 120.7, 104.5, 51.4, 48.3, 43.7, 35.7, 26.3, 23.0, 21.9.ppm. The spectral characteristics are consistent with those of **2k** in the literature.[32]



(**2l**)

(*3S,8S,9S,10R,13S,14S,17R*)- (2l). According to general procedure B, **1l** (49.2 mg, 0.122 mmol, 1.00 equiv) in a mixture of 0.64 mL of the MeCN stock solution (0.19 M in **1l**) and anhydrous DCM (0.8 mL), was treated with $CuCl_2$•$2H_2O$ (1 mg, 0.006 mmol, 0.05 equiv). Alkene **2l** (35 mg, 0.11 mmol, 91%) was obtained as a white solid, after workup and purification by flash chromatography using 25% EtOAc in hexane as eluent, according to Method II. R_f (25% EtOAc in hexane) 0.47; $[\alpha]_D^{24}$ -53.2 (*c* 0.004, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 5.35 (dt, *J* 4.9, 2.0 Hz, 1H), 4.85 (s, 1H), 4.75 – 4.65 (s, 1H), 3.61 – 3.44 (m, 1H), 2.34-2.18(m, 2H), 2.07 – 1.94 (m, 2H), 1.91 – 1.78 (m, 3H), 1.78-1.72 (s, 4H), 1.73 – 1.59 (m, 3H), 1.59 – 1.36 (m, 5H), 1.27 – 1.02 (m, 4H), 1.02 – 0.91 (m, 4H), 0.58 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ_C 145.8, 140.9, 121.7, 110.8, 71.9, 57.4, 56.6, 50.4, 43.2, 42.4, 38.8, 37.4, 36.7, 32.4, 32.0, 31.8, 25.5, 24.8, 24.4, 21.3, 19.6, 12.8 ppm. The spectral characteristics are consistent with those of **2l** in the literature.[28]

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Supplementary Material

Copies of ^{1}H and ^{13}C NMR spectra of and ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra for compounds **1a-1l, 2a-2l** are available in the supplementary material file associated with this paper.

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