



Published in final edited form as:

Nature. ; 483(7387): 70–73. doi:10.1038/nature10785.

Catalytic functionalization of unactivated primary C—H bonds directed by an alcohol

Eric M. Simmons^{1,†}, John F. Hartwig^{1,†}

¹Department of Chemistry, University of Illinois, Urbana, Illinois 61801, USA.

Abstract

New synthetic methods for the catalytic functionalization of C—H bonds have the potential to revolutionize the synthesis of complex molecules^{1–4}. However, the realization of this synthetic potential requires the ability to functionalize selectively one C—H bond in a compound containing many such bonds and an array of functional groups. The site-selective functionalization of aliphatic C—H bonds is one of the greatest challenges that must be met for C—H bond functionalization to be used widely in complex-molecule synthesis^{1,3,5,6}, and processes catalysed by transition-metals provide the opportunity to control selectivity^{7,8}. Current methods for catalytic, aliphatic C—H bond functionalization typically rely on the presence of one inherently reactive C—H bond^{9,10}, or on installation and subsequent removal of directing groups that are not components of the desired molecule⁸. To overcome these limitations, we sought catalysts and reagents that would facilitate aliphatic C—H bond functionalization at a single site, with chemoselectivity derived from the properties of the catalyst and site-selectivity directed by common functional groups¹¹ contained in both the reactant and the desired product. Here we show that the combination of an iridium-phenanthroline catalyst and a dihydrosilane reagent leads to the site-selective γ -functionalization of primary C—H bonds controlled by a hydroxyl group, the most common functional group in natural products¹². The scope of the reaction encompasses alcohols and ketones bearing many substitution patterns and auxiliary functional groups; this broad scope suggests that this methodology will be suitable for the site-selective and diastereoselective functionalization of complex natural products.

Our strategy for the functionalization of aliphatic C—H bonds directed by hydroxyl groups is outlined below:

Reprints and permissions information is available at www.nature.com/reprints.

Correspondence and requests for materials should be addressed to J.F.H. (jhartwig@berkeley.edu).

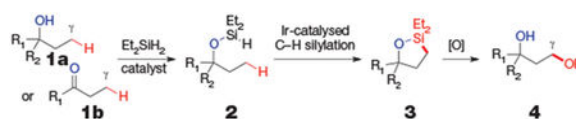
[†]Present address: Department of Chemistry, University of California, Berkeley, California 94720, USA.

Author Contributions E.M.S. and J.F.H. conceived the work and designed the experiments. E.M.S. performed the experiments. Both authors analysed the data and wrote the manuscript.

Supplementary Information is linked to the online version of the paper at www.nature.com/nature.

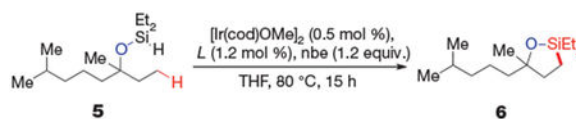
The authors declare no competing financial interests.

Readers are welcome to comment on the online version of this article at www.nature.com/nature.



In this approach, a single dihydridosilane reagent has two roles. First, the silane attaches to the oxygen atom of an alcohol (**1a**) or ketone (**1b**) by forming a (hydrido)silyl ether (**2**) to direct the C—H bond functionalization. The (hydrido)silyl ether is formed by dehydrogenative coupling with the alcohol or by hydrosilylation of the ketone. Second, the Si—H unit of the silyl ether undergoes dehydrogenative functionalization of a primary C—H bond without isolation of the intermediate (hydrido)silyl ether. Tamao-Fleming oxidation of the oxasilolane (**3**) formed by this process then yields a 1,3-diol (**4**) from a net 1,4-hydroxyl-directed, aliphatic C—H bond functionalization. On the basis of our recently developed, iridium-catalysed silylation of aromatic C—H bonds¹³, we anticipated that both silylation reactions could be catalysed by iridium complexes^{13,14}. However, successful implementation of this strategy would require the identification of a catalyst that is reactive for the silylation of unactivated aliphatic C—H bonds, not just the silylation of typically more reactive aromatic C—H bonds. It would also require that the directing effect be strong enough to ensure that intermolecular functionalization of aromatic C—H bonds would not interfere with the desired directed functionalization of an aliphatic C—H bond.

We began by evaluating iridium complexes containing a series of bipyridine ligands (*L*) as catalysts for the dehydrogenative cyclization of (hydrido)silyl ether (**5**), generated *in situ* by an iridium-catalysed dehydrogenative coupling of diethylsilane (Et₂SiH₂) with tetrahydrofuralol. The reaction is outlined below:



In the presence of 1.0 mol % of a combination of [Ir(cod)OMe]₂ (cod, 1,5-cyclooctadiene; Me, methyl group) and 1,10-phenanthroline (phen), with norbornene (nbe) as an H₂ acceptor¹³, we observed 77% conversion of **5** to form oxasilolane (**6**) in 68% yield (Table 1a). The same reaction conducted with 4,4'-di-*tert*-butylbipyridine (dtbpy), the most commonly used ligand for iridium-catalysed arene borylation¹⁵, occurred with only slightly higher conversion and yield (Table 1b). To probe systematically the effect of the electronic properties of ancillary ligands on iridium-catalysed aliphatic C—H bond silylation, we conducted reactions with catalysts generated from a series of 4,7-disubstituted phenanthroline derivatives (Table 1c-g). Reactions conducted with the more electron-donating ligands occurred to higher relative conversions and formed the silylation product in higher yields than did reactions conducted with the less electron-donating ligands¹⁶. Ultimately, we obtained the highest yield of **6** with a catalyst containing 3,4,7,8-tetramethyl-1,10-phenanthroline (Me₄phen, Table 1h), the most electron-donating phenanthroline derivative in this series¹⁶.

After identifying a suitable catalyst for aliphatic C—H bond silylation, we developed a telescoped procedure for transformation of a starting alcohol (**7**) or ketone (**8**) to a

1,3-diol (Fig. 1). Following iridium-catalysed aliphatic C—H silylation, we obtained the diol simply by adding MeOH, KHCO₃ and aqueous H₂O₂ to the crude silylation reaction mixture and heating at 50 °C. To provide compounds that were easily purified by silica-gel chromatography, we acylated the diols thus obtained before isolation. Figure 1 shows a series of products prepared by this sequence of C—H silylation and oxidation. Both tertiary (**9a**) and secondary acyclic alcohols (**9b, c**) underwent aliphatic C—H bond oxygenation with comparable efficiency. Under most conditions, oxygenation of a primary C—H bond in the presence of a secondary alcohol would be challenging because of competitive oxidation of the secondary alcohol to the corresponding ketone. Our strategy allows an overall oxidation of a primary C—H bond in the presence of a secondary alcohol because it uses a mildly reducing silane as the functionalizing reagent.

Reactions of phenols (**9d**) and cyclic aliphatic alcohols (**9e, f**) also occurred under these conditions in good yields. The C—H functionalization of cyclic alcohols proved insensitive to the stereochemistry of the ring fusion in the bicyclic oxasilolane intermediate; *trans*- and *cis*-2-methylcyclohexanol underwent this process in similar yields (**9e, f**). However, the reaction of an acyclic substrate bearing diastereotopic methyl groups formed **9g** as the major product with significant diastereoselectivity (82:18 dr), resulting from C—H bond silylation to form the less strained *trans*-disubstituted oxasilolane intermediate.

The products in Fig. 2 illustrate the range of functional groups that are tolerated by the aliphatic C—H bond oxygenation sequence. Aryl halides (**9h, i**), an aryl trifluoromethyl group (**9j**), and an internal carbon—carbon double bond (**9k**) were all compatible with the reaction conditions. The sequence also tolerated phenols protected as the corresponding benzyl or silyl ethers (**9l–n**); protected catechols (**9o**); and aliphatic alcohols protected with trialkylsilyl groups (**9p, q**). Although aldehydes were not compatible, the C—H functionalization occurred in high yield when this functionality was masked as an acetal (**9r**). None of the examples in Fig. 2 suffered from competing intra- or intermolecular aromatic C—H bond functionalization, an observation that is particularly striking for **9l**, which contains three unhindered aromatic C—H bonds. Because the catalyst for the present aliphatic C—H silylation is similar to that used most commonly for aromatic C—H borylation¹⁵, the absence of products from aromatic functionalization can be attributed to the powerful directing ability of the (hydrido)silyl group to promote selective functionalization of a δ-C—H bond.

Whereas a *tert*-butyl ester was tolerated by our standard conditions (**9s**), methyl ester, amide, ketone and carbamate functional groups underwent competitive hydrosilylation when forming the silyl ether in the presence of the iridium catalyst. However, diethyl(hydrido)silyl ethers formed from the coupling of Et₂SiH₂ with alcohols containing auxiliary methyl ester, ketone and carbamate moieties without competitive reduction of the carbonyl functionalities in the presence of 0.2 mol % of the ruthenium complex Ru(PPh₃)₃Cl₂ (ref. 17) in which Ph is a phenyl group. Moreover, the carbonyl groups in these compounds were compatible with the C—H silylation process and subsequent Tamao-Fleming oxidation; thus, we obtained diol derivatives **9t, 9v** and **9w** in good overall yield from the starting alcohols. A small amount of carbonyl hydrosilylation occurred during ruthenium-catalysed silylation of the

alcohol containing an amide functional group, but we still obtained diol product **9u** in 52% overall yield.

Because the iridium-catalysed C—H functionalization tolerates auxiliary functionality and is highly selective for reaction at a single C—H bond, it allows site-selective γ -functionalization of natural products bearing hydroxyl and carbonyl groups (Fig. 3). The reaction of (+)-fenchol (**10**) under our standard conditions led to selective functionalization of the C9 methyl group, directed by the C2 hydroxyl group, to generate 9-hydroxyfenchol diacetate (**11a**) in 66% yield (Fig. 3a). Previously, **11a** was accessed indirectly from other terpene skeletons by multi-step rearrangement sequences¹⁸; direct oxidation of (+)-fenchol at the C9 position by fermentation formed diol **11b** in only 4.0% yield and was accompanied by three further diol isomers¹⁹. *Exo*-selective hydrosilylation of (+)-camphor (**12**) catalysed by 0.05 mol % [Ir(coe)₂Cl]₂, in which coe is cyclooctene (92:8 *exo/endo*), followed by directed C—H functionalization at the C10 methyl group, gave **13a** in 57% yield. The previous synthesis of *exo*-2,10-camphanediol (**13b**) began with the significantly more expensive (+)-ketopinic acid²⁰.

Finally, we conducted the iridium-catalysed selective functionalization of a pair of triterpenoid saponin aglycons. Triterpenoid saponins (for example, **15**, in which R₃ = sugar, Fig. 3b) exhibit a range of biological activities, including anti-inflammatory, anti-fungal, anti-leishmanial and anti-tumour properties²¹. Together with the carbohydrate portions of saponins, the aglycon moiety is important in modulating biological activity; for example, C23-hydroxylated saponins possess strong haemolytic activity²¹. Because the extraction of saponins from natural sources can be time-consuming and low-yielding, laboratory synthesis from the corresponding aglycon is often the preferred method to gain material for biological studies²¹, and syntheses of both natural and non-natural saponins starting from methyl hederagenate (**15b**) have been described²¹. The potent biological activity of saponins bearing a C23-hydroxylated aglycon, coupled with the broader availability of the C23-unfunctionalized materials, suggest that a general method for chemoselective C23-oxygenation (for example, **14**→**15**) would provide a short synthesis of saponins that would otherwise be challenging to access. An earlier synthesis of hederagenin (**15a**) from oleanolic acid (**14a**) required ten steps and proceeded with 36% overall yield²².

As shown in Fig. 3b, our iridium-catalysed silylation of aliphatic C—H bonds converted methyl oleanate (**14b**) to methyl hederagenate (**15b**) in three steps and 61% overall yield, without isolation of any intermediates. Similarly, selective oxygenation of the C23 methyl group of methyl glycyrrhetinate (**16**) provided diol **17a** in 51% overall yield. C24-hydroxylated glycyrrhetinate derivative **17b** has previously been obtained from *Glycyrrhiza uralensis*²³, but the C23-hydroxylated diastereomer **17a** has not been reported. On the basis of these results, we anticipate that this iridium-catalysed C—H bond functionalization should be suitable for the hydroxyl-directed C23-functionalization of a series of triterpenoids, enabling the preparation of both natural and unnatural derivatives.

The hydroxyl-directed functionalization of primary C—H bonds that we have developed overcomes several limitations and complements the scope of current methods for aliphatic C—H bond functionalization. The regioselectivity is distinct from that of classical,

stoichiometric methods for 1,5-functionalization²⁴, which involve radical intermediates and often require strongly electrophilic reagents; the selectivity for reactions of primary C—H bonds distinguishes our method from more recent alcohol-directed 1,4-functionalizations, which occur only with weaker benzylic and tertiary C—H bonds^{25,26}. Furthermore, by our method, a single reagent docks at the existing functional group and effects the C—H functionalization process. Previous methods for catalytic, directed functionalization of aliphatic C—H bonds, which inspired the design of the current system, have led to regioselective functionalization of neighbouring C—H bonds but require installation and removal of a separate directing group before and after the C—H bond functionalization and purification of the intermediates^{27,28}. Finally, the iridium catalyst reacts with primary C—H bonds in preference to secondary C—H bonds, and this selectivity complements that of non-directed oxidations that typically occur at the weaker and more electron-rich C—H bonds^{9,10,29}. Considering the high selectivity of this process, the tolerance for auxiliary functionality, and the complementarity with radical-based reactions and direct oxidations, this method is suitable for both *de novo* synthesis of complex organic molecules and derivatization of natural products. It should inspire the development of related strategies for selective C—H bond functionalization with reagents that both dock at existing functional groups and deliver functionality to a single C—H bond³⁰.

METHODS SUMMARY

We assembled iridium-catalysed silylation reactions under a nitrogen atmosphere using oven-dried glassware and dry, deoxygenated solvents. We assembled Tamao-Fleming oxidation reactions under air using commercial-grade solvents. We monitored reactions using gas chromatography (with a mass spectral detector or a flame ionization detector) or ¹H nuclear magnetic resonance (NMR) spectroscopy.

General procedure for iridium-catalysed, directed aliphatic C—H bond functionalization.

We dissolved an alcohol or ketone substrate in tetrahydrofuran (THF) and treated it with a freshly prepared solution of [Ir(cod)OMe]₂ (0.05 mol %) in THF and then with neat Et₂SiH₂ (1.2 equiv.). We stirred the resulting solution at room temperature (23 °C) until we observed complete conversion of the alcohol or ketone to the corresponding diethyl(hydrido)silyl ether. We then placed the reaction mixture under high vacuum for 1 h. We treated the concentrated diethyl(hydrido)silyl ether sequentially with freshly prepared solutions of nbe (1.2 equiv.) in THF and [Ir(cod)OMe]₂ (0.5 mol %) in THF, and then with a slurry of Me₄phen (1.25 mol %) in THF. We stirred the resulting solution at room temperature for 1 h and then heated it at 80–120 °C until we observed complete conversion to the corresponding oxasilolane. We then treated the crude reaction mixture containing the oxasilolane sequentially with MeOH, KHCO₃ (2.5 equiv.) and H₂O₂ (30% solution in H₂O, 10 equiv.), and stirred the resulting mixture overnight at 50 °C. We carefully quenched the reaction with aqueous NaHSO₃, and extracted the resulting mixture with EtOAc. We washed the combined organic layers sequentially with 1 M HCl and saturated NaHCO₃, and then dried them with MgSO₄. We filtered the resulting organic layer through Celite and concentrated it to provide the crude diol, which we either purified directly or converted to the corresponding acetate derivative through treatment with Ac₂O and Et₃N. For full

experimental details and characterization of all new compounds, along with copies of ^1H and ^{13}C NMR spectra, see Supplementary Information.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We thank the US National Science Foundation (CHE-0910641 to J.F.H.) and the US National Institutes of Health (GM087901 to E.M.S.) for funding this work, and Johnson Matthey for a gift of $[\text{Ir}(\text{cod})\text{OMe}]_2$.

References

1. Gutekunst WR & Baran PS C—H functionalization logic in total synthesis. *Chem. Soc. Rev* 40, 1976–1991 (2011). [PubMed: 21298176]
2. McMurray L, O'Hara F & Gaunt MJ Recent developments in natural product synthesis using metal-catalysed C—H bond functionalisation. *Chem. Soc. Rev* 40, 1885–1898 (2011). [PubMed: 21390391]
3. Chen K & Baran PS Total synthesis of eudesmane terpenes by site-selective C—H oxidations. *Nature* 459, 824–828 (2009). [PubMed: 19440196]
4. Godula K & Sames D C—H bond functionalization in complex organic synthesis. *Science* 312, 67–72 (2006). [PubMed: 16601184]
5. Feng Y & Chen G Total synthesis of celogentin C by stereoselective C—H activation. *Angew. Chem. Int. Ed* 49, 958–961 (2010).
6. Giannis A, Heretsch P, Sarli V & Stöbel A Synthesis of cyclopamine using a biomimetic and diastereoselective approach. *Angew. Chem. Int. Ed* 48, 7911–7914 (2009).
7. Yu J-Q & Shi Z in *Topics in Current Chemistry* Vol. 292 (Springer, 2010).
8. Lyons TW & Sanford MS Palladium-catalyzed ligand-directed C—H functionalization reactions. *Chem. Rev* 110, 1147–1169 (2010). [PubMed: 20078038]
9. Chen MS & White MC A predictably selective aliphatic C—H oxidation reaction for complex molecule synthesis. *Science* 318, 783–787 (2007). [PubMed: 17975062]
10. Newhouse T & Baran PS If C—H bonds could talk: selective C—H bond oxidation. *Angew. Chem. Int. Ed* 50, 3362–3374 (2011).
11. Lu Y, Wang D-H, Engle KM & Yu J-Q Pd(II)-catalyzed hydroxyl-directed C—H olefination enabled by monoprotected amino acid ligands. *J. Am. Chem. Soc* 132, 5916–5921 (2010). [PubMed: 20359184]
12. Henkel T, Brunne RM, Müller H & Reichel F Statistical investigation into the structural complementarity of natural products and synthetic compounds. *Angew. Chem. Int. Ed* 38, 643–647 (1999).
13. Simmons EM & Hartwig JF Iridium-catalyzed arene *ortho*-silylation by formal hydroxyl-directed C—H activation. *J. Am. Chem. Soc* 132, 17092–17095 (2010). [PubMed: 21077625]
14. Boebel TA & Hartwig JF Silyl-directed, iridium-catalyzed *ortho*-borylation of arenes. A one-pot *ortho*-borylation of phenols, arylamines, and alkylarenes. *J. Am. Chem. Soc* 130, 7534–7535 (2008). [PubMed: 18494474]
15. Mkhaliid IAI, Barnard JH, Marder TB, Murphy JM & Hartwig JF C—H activation for the construction of C—B bonds. *Chem. Rev* 110, 890–931 (2010). [PubMed: 20028025]
16. Crotti C. et al. Evaluation of the donor ability of phenanthrolines in iridium complexes by means of synchrotron radiation photoemission spectroscopy and DFT calculations. *Dalton Trans.* 133–142 (2007). [PubMed: 17160183]
17. Corriu RJP & Moreau JJE Selective catalytic route to bifunctional silanes. *Catalysis by rhodium and ruthenium complexes of the alcoholysis of diarylsilanes and the hydrosilylation of carbonyl compounds. J. Chem. Soc. Chem. Commun* 38–39 (1973).

18. Bosworth N & Magnus PD Studies on terpenes. Part I. Rearrangement of 7-oxatricyclo[4,3,0,0]nonanes into 8-substituted 1,3,3-trimethylnorbornane derivatives. *J. Chem. Soc. Perkin Trans I* 943–948 (1972).
19. Miyazawa M & Miyamoto Y Biotransformation of (+)-(1*R*,2*S*)-fenchol by the larvae of common cutworm (*Spodoptera litura*). *Tetrahedron* 60, 3091–3096 (2004).
20. Deng JG, Jiang YZ, Liu GL, Wu LJ & Mi AQ A practical method for the synthesis of homochiral 2,10-camphanediols. *Synthesis* 963–965 (1991).
21. Plé K, Chwalek M & Voutquenne-Nazabadioko L Synthesis of α -hederin, δ -hederin, and related triterpenoid saponins. *Eur. J. Org. Chem* 2004, 1588–1603 (2004).
22. García-Granados A, López PE, Melguizo E, Parra A & Simeó Y Remote hydroxylation of methyl groups by regioselective cyclopalladation. Partial synthesis of hyptatic acid-A. *J. Org. Chem* 72, 3500–3509 (2007). [PubMed: 17402787]
23. Kitagawa I, Hori K, Sakagami M, Zhou JL & Yoshikawa M Saponin and sapogenol. XLVIII. On the constituents of the roots of *Glycyrrhiza uralensis* Fischer from northeastern China. (2). Licorice-saponins D3, E2, F3, G2, H2, J2, and K2. *Chem. Pharm. Bull. (Tokyo)* 41, 1337–1345 (1993). [PubMed: 8403082]
24. Majetich G & Wheless K Remote intramolecular free radical functionalizations: an update. *Tetrahedron* 51, 7095–7129 (1995).
25. Chen K, Richter JM & Baran PS 1,3-diol synthesis via controlled, radical-mediated C—H functionalization. *J. Am. Chem. Soc* 130, 7247–7249 (2008). [PubMed: 18481847]
26. Kasuya S, Kamijo S & Inoue M Direct construction of 1,3-diaxial diol derivatives by C—H hydroxylation. *Org. Lett* 11, 3630–3632 (2009). [PubMed: 19719200]
27. Desai LV, Hull KL & Sanford MS Palladium-catalyzed oxygenation of unactivated sp³ C—H bonds. *J. Am. Chem. Soc* 126, 9542–9543 (2004). [PubMed: 15291549]
28. Giri R. et al. Pd-catalyzed stereoselective oxidation of methyl groups by inexpensive oxidants under mild conditions: a dual role for carboxylic anhydrides in catalytic C—H bond oxidation. *Angew. Chem. Int. Ed* 44, 7420–7424 (2005).
29. Litvinas ND, Brodsky BH & Du Bois J C—H hydroxylation using a heterocyclic catalyst and aqueous H₂O₂. *Angew. Chem. Int. Ed* 48, 4513–4516 (2009).
30. Zalatan DN & Du Bois J in *Topics in Current Chemistry* Vol. 292 (eds Yu J-Q & Shi Z) 347–378 (Springer, 2010). [PubMed: 21500412]

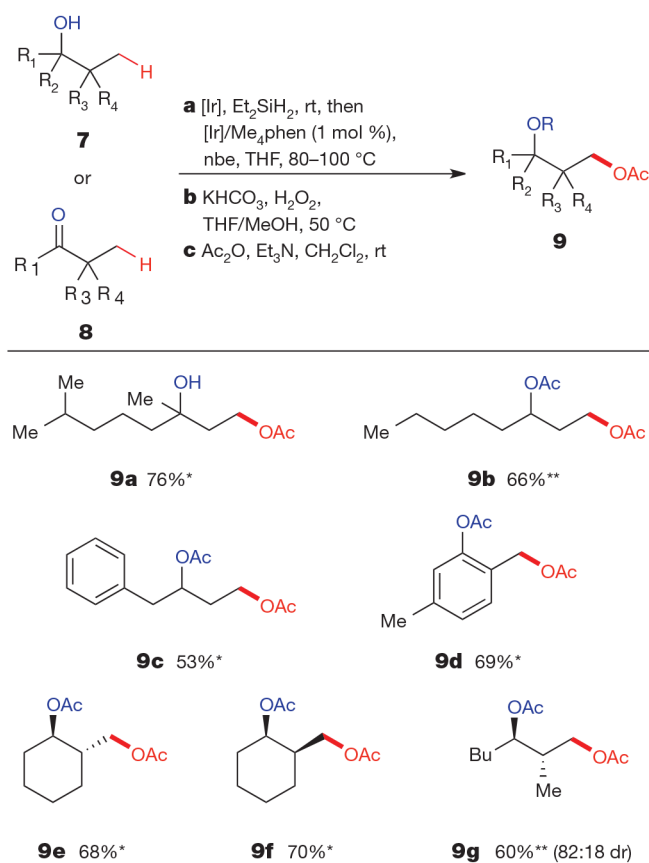


Figure 1 | Hydroxyl-directed γ -oxygenation of secondary and tertiary alcohols and ketones. Overall isolated yields for reactions conducted on a 1.0-mmol scale following purification by silica-gel chromatography. Reagents and conditions: **a**, **7** (to give products marked *) or **8** (products marked **) (1.0 equiv.), Et₂SiH₂ (1.2 equiv.), [Ir(cod)OMe]₂ (0.05 mol %), THF, room temperature (rt); removal of volatiles, then [Ir(cod)OMe]₂ (0.5 mol %), Me₄phen (1.2 mol %), nbe (1.2 equiv.), THF, 80–100 °C. **b**, KHCO₃ (2.5 equiv.), 30% aqueous H₂O₂ (10 equiv.), THF/MeOH, 50 °C. **c**, Ac₂O (1.5–3.0 equiv.), DMAP (0–0.05 equiv.), CH₂Cl₂/Et₃N, room temperature. Ac₂O, acetic anhydride; DMAP, 4-dimethylaminopyridine; Et₃N, triethylamine. For full experimental details, see the Supplementary Information.

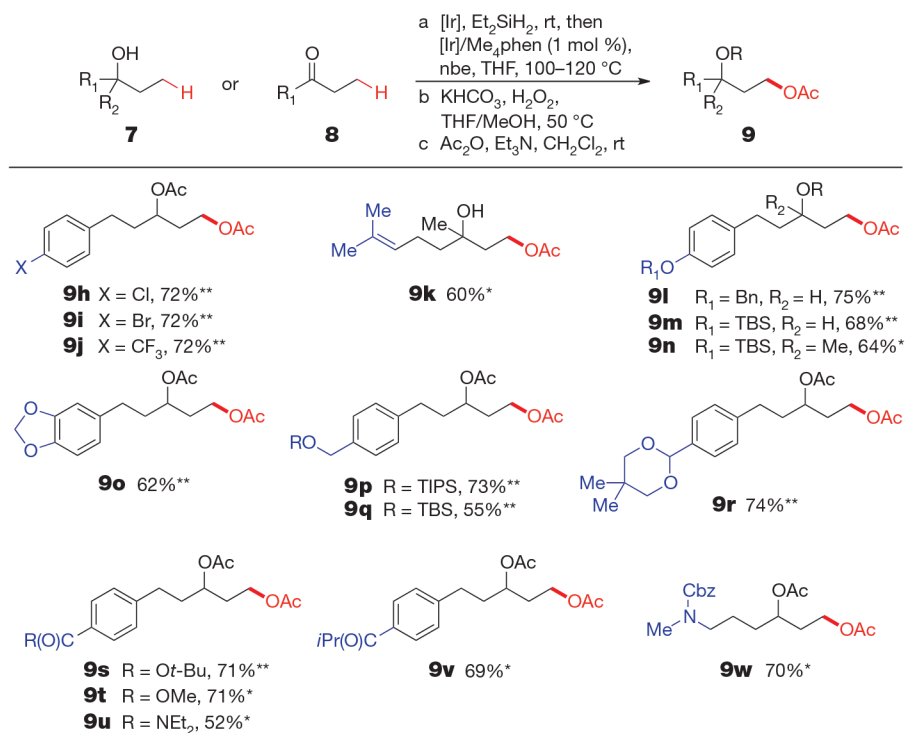


Figure 2 | Functional-group tolerance of hydroxyl-directed γ -oxygenation.

Overall isolated yields for reactions conducted on a 1.0-mmol scale following purification by silica-gel chromatography. Reagents and conditions: **a**, **7** (to give products marked *) or **8** (products marked **) (1.0 equiv.), Et₂SiH₂ (1.2 equiv.), [Ir(cod)OMe]₂ (0.05 mol %), THF, room temperature; removal of volatiles, then [Ir(cod)OMe]₂ (0.5 mol %), Me₄phen (1.2 mol %), nbe (1.2 equiv.), THF, 100–120 °C. **b**, KHCO₃ (2.5 equiv.), 30% aqueous H₂O₂ (10 equiv.), THF/MeOH, 50 °C. **c**, Ac₂O (1.5–3.0 equiv.), DMAP (0–0.05 equiv.), CH₂Cl₂/Et₃N, room temperature. For compounds **9t**, **9u**, **9v** and **9w**, step **a** (first half) used Ru(PPh₃)₃Cl₂ (0.2 mol %) in benzene or toluene at 50 °C. For compound **9u**, step **a** (second half) used 2 mol % [Ir]/Me₄phen. For full experimental details, see the Supplementary Information.

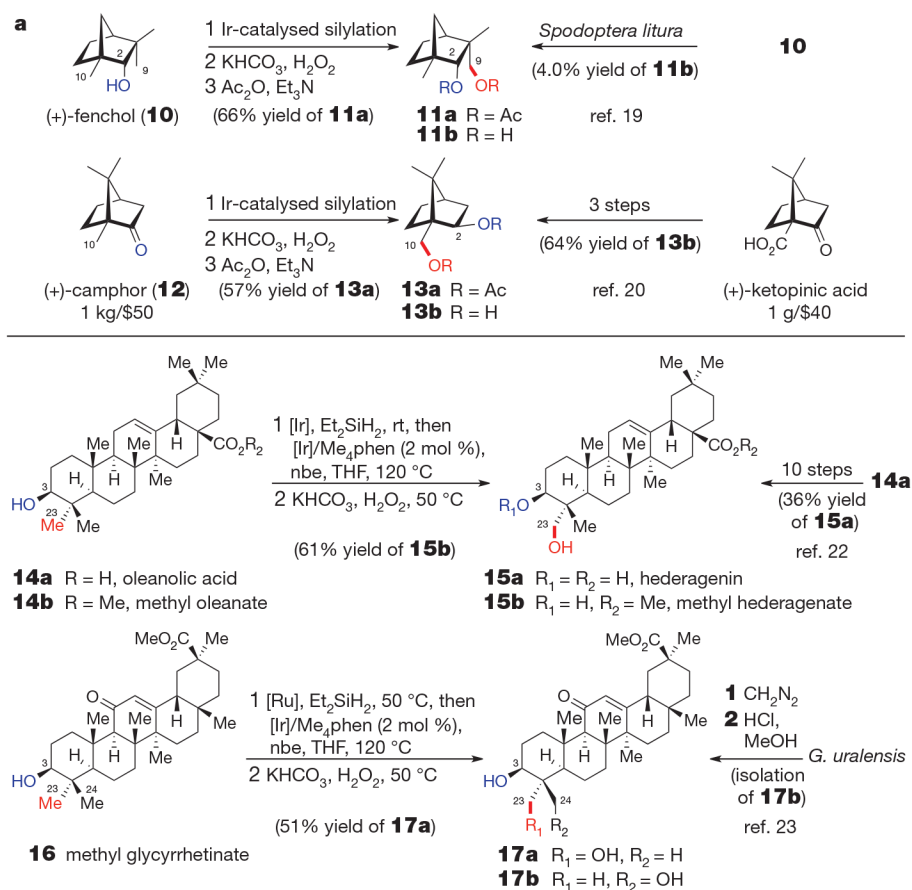


Figure 3 I. Directed aliphatic C—H functionalization of natural products.

a, Directed γ -functionalization of the monoterpenes fenchol (**10**) and camphor (**12**). **b**, Hydroxyl-directed γ -functionalization of the triterpenoid saponins methyl oleanate (**14b**) and methyl glycyrrhetinate (**16**). For full experimental details, see the Supplementary Information.

Table 1 |

Examination of bipyridine ligands for aliphatic C—H bond silylation (5→6)

	Ligand, <i>L</i>	Conversion	Yield
a	phen	77%	68%
b	dtbpy	83%	76%
c	4,7-Cl ₂ phen	13%	<2%
d	4,7-(HO) ₂ phen	33%	19%
e	4,7-Ph ₂ phen	82%	72%
f	4,7-Me ₂ phen	94%	85%
g	4,7-(MeO) ₂ phen	94%	87%
h	3,4,7,8-Me ₄ phen	100%	99%

Corrected, overall gas chromatography yields (0.25-mmol scale) with dodecane as an internal standard. Reagents and conditions: tetrahydrolinalool (1.0 equiv.), Et₂SiH₂ (1.2 equiv.), [Ir(cod)OMe]₂ (0.05 mol %), THF, room temperature, 17 h; removal of volatiles, then [Ir(cod)OMe]₂ (0.5 mol %), ligand (1.2 mol %), nbe (1.2 equiv.), THF, 80 °C, 15 h. For full experimental details, see the Supplementary Information.