

Deoxygenative Insertion of Carbonyl Carbon into a C(sp³)–H Bond: Synthesis of Indolines and Indoles

Sobi Asako,^{*,†,‡} Seina Ishihara,[†] Keiya Hirata,[†] and Kazuhiko Takai^{*,†}

[†]Division of Applied Chemistry, Graduate School of Natural Science and Technology, Okayama University, 3-1-1 Tsumishanaka, Kita-ku, Okayama 700-8530, Japan

[‡]Present address: RIKEN Center for Sustainable Resource Science, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan

Supporting Information Placeholder

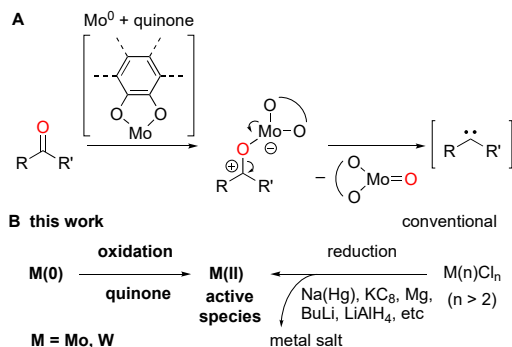
ABSTRACT: A simple deoxygenation reagent prepared in situ from commercially available Mo(CO)₆ and *ortho*-quinone has been developed for the synthesis of indoline and indole derivatives. The Mo/quinone complex efficiently deoxygenates carbonyl compounds bearing a neighboring dialkylamino group and effects intramolecular cyclizations with the insertion of a deoxygenated carbonyl carbon into a C(sp³)–H bond, in which a carbonyl group acts as a carbene equivalent. The reaction also proceeds with a catalytic amount of Mo/quinone in the presence of Me₃SiSiMe₃ as an oxygen atom acceptor.

Diazo compounds are convenient precursors of carbene species in organic synthesis because dinitrogen extrusion takes place easily upon photoirradiation, heating, or interaction with metals.¹ However, the inherent explosive and toxic nature of diazo compounds often limits their synthetic applications, which has attracted much attention to the identification of stable and safe surrogates.² Carbonyl compounds, sometimes used as precursors of diazo compounds, are stable and readily available; therefore, they are attractive candidates. However, they have been scarcely used as carbene equivalents upon deoxygenation in organic synthesis, except a few notable examples using stoichiometric reagents such as Sm/SmI₂³ and Zn(Hg)/R₃SiCl.⁴ Meanwhile, the carbene generation from carbonyl compounds has attracted some attention from the inorganic chemistry community; and several transition-metal complexes such as Zr/Fe,⁵ Zr/Co,⁶ W₂(OR)₆py₂,⁷ and MCl₂(PR₃)₄ (M = Mo, W)⁸ have been reported to be effective for the transformation. However, poor stability or tedious preparation of these complexes, including the necessity for specially designed ligands^{5,6} and reduction steps using Na(Hg)^{6,8} have hampered their use in organic synthesis.

We became particularly interested in M(II)Cl₂(PR₃)₄ complexes (M = Mo, W)⁸ and envisioned that a low-

valent molybdenum(II) simultaneously possessing Lewis acidity and reducing ability would be prepared by the partial oxidation of easy-to-handle zero-valent Mo(CO)₆ with *ortho*-quinone^{9,10} and that it would remove an oxygen atom from a carbonyl compound in a pull–push manner to afford a carbon unit that functions as a carbene equivalent (Scheme 1A). This strategy contrasts with the widely employed approaches for the generation of low-valent active species by reducing the corresponding high-valent metals (Scheme 1B), examples of which include the preparation of deoxygenation reagents such as MCl₄(PR₃)_n/Na(Hg) (M = Mo, W)⁸ and WCl₆/RLi,¹¹ often with the concomitant formation of metal salts.^{12,13} Our oxidative approach using commercially available Mo(CO)₆/quinone for the generation of low-valent active species is simple and clean without forming such byproducts, which may cause undesired side reactions.

Scheme 1. Deoxygenation of Carbonyl Compounds with Low-Valent Molybdenum Prepared by Oxidation of Mo(0) with Quinone.



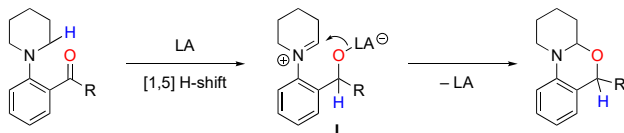
To test the hypothesis, we turned our attention to a [1,5]-hydrogen shift for the functionalization of C(sp³)–H bonds.¹⁴ The process is accelerated by introducing a heteroatom adjacent to the carbon atom and increasing the electrophilicity of the acceptor moiety using Lewis

acids. *N,N*-Dialkyl-2-aminobenzaldehydes are typical substrates employed in such reactions, and dihydrobenzoxazine products are obtained through a [1,5]-H shift/C–O bond formation sequence (Scheme 2A). We considered that the molybdenum/quinone complex, which initially acts as Lewis acid to trigger [1,5]-H shift, would remove an oxygen atom from **I** and that a C–C bond would form instead of a C–O bond to afford indoline derivatives, compounds of importance for medicinal chemistry (Scheme 2B).¹⁵ The overall process is the insertion of a deoxygenated carbonyl carbon into a C(sp³)–H bond, in which a carbonyl group acts as a carbene equivalent. The same net transformation has been achieved by C–H insertion of a diazo-derived carbene, but then has required two-step sequences of hydrazone formation/base treatment (Scheme 2C).¹⁶ A rhodium-catalyzed C–H insertion of diazo-derived metal carbene has also been recently reported.^{17,18} In continuation of our interest in the use of simple molybdenum complexes for deoxygenation¹⁹ and other transformations,²⁰ we report here that Mo(CO)₆ combined with *ortho*-quinone effects transformations such as those described in Scheme 2B, which enables the direct use of readily available carbonyl compounds as carbene equivalents without recourse to high energy diazo compounds.

Scheme 2. Strategies for Intramolecular C(sp³)–H Bond Functionalization.

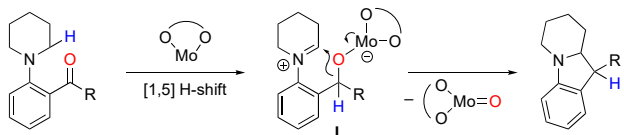
A Redox-neutral C(sp³)–H functionalization

via [1,5] H-shift/C–O bond formation promoted by Lewis acids (ref. 14)

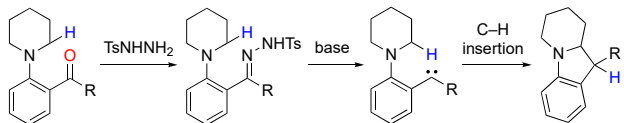


B Deoxygenative C(sp³)–H functionalization

via [1,5] H-shift/C–C bond formation promoted by Mo/quinone (this work)



C Deoxygenative C(sp³)–H functionalization via hydrazone intermediate (ref. 16)



A typical reaction procedure is described first (Eq. 1). A toluene solution of Mo(CO)₆ (1.2 equiv) and 3,5-di-^tBu-1,2-benzoquinone (**L1**, 1.2 equiv) was heated at 160 °C for 15 min to form a Mo(CO)_n/quinone complex, whose intense purple color was suggestive of charge transfer from the Mo center to the quinone. 2-(1-Piperidinyl)benzophenone (**1a**) was added to the reaction mixture, and heating the solution at 135 °C for 24 h afforded indoline **2a** as a mixture of diastereomers and indole **3a**, in 68% and 22% yields, respectively. Use of

1.0 equiv of Mo/**L1** slightly reduced the reaction efficiency to afford the products in 61% (**2a**) and 18% (**3a**) yields, respectively (Table 1, entry 2). Treatment of the crude mixture with *p*-chloranil afforded **3a** as the sole product in 83% yield.²¹ We noticed that the introduction of a small amount of air into the reaction mixture after the preparation of the Mo/**L1** complex slightly improved the reaction efficiency when this quinone was used, the reason for which remains unclear at the moment^{22,23}

Brief screening of other commercially available quinones revealed that *o*-chloranil (**L2**) and 9,10-phenanthrenequinone (**L3**) were less efficient (Table 1, entries 3 and 4). The deoxygenative cyclization did not proceed at all in the absence of either Mo(CO)₆ or quinones, and **1a** was largely recovered (entries 5 and 6). Consistent with the latter, the reaction efficiency decreased when Mo(CO)₆, **L1**, and **1a** were mixed at the same time (entry 7), highlighting the importance of pre-complexation of Mo and **L1**. The 1:1 ratio of Mo/**L1** was found optimal (Table S7). Other Mo(0) precursors such as Mo(CO)₃(MeCN)₃ and Mo(benzene)₂ also worked,²⁰ while other metal carbonyl complexes such as Cr(CO)₆, W(CO)₆, Mn₂(CO)₁₀, and Re₂(CO)₁₀ were less efficient or ineffective for the transformation (Table S9).

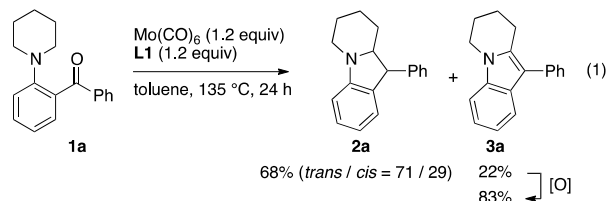


Table 1. Deoxygenative Cyclization of **1a**

entry	quinone	yield / % ^b		quinone structure
		2a (<i>trans</i> / <i>cis</i>)	3a	
1 ^c	L1	68 (71 / 29)	22	
2	L1	61 (69 / 31)	18	
3	L2	15 (100 / 0)	28	
4	L3	12 (67 / 33)	8	
5 ^d	L1	0	0	
6	none	0	0	
7 ^{ce}	L1	51 (75 / 25)	25	

^aThe reaction was performed on a 0.2 mmol scale in toluene (1.0 mL) at 135 °C for 24 h. ^b¹H NMR yields using 1,1,2,2-tetrachloroethane as an internal standard. ^cMo(CO)₆/**L1** (1.2 equiv). ^dIn the absence of Mo(CO)₆. ^eMo(CO)₆, **L1**, and **1a** were mixed at the same time.

The scope of the reaction was investigated under the optimized conditions (Table 2). Both an electron-donating group and a withdrawing group on the benzene rings were tolerated, and the corresponding indoles were obtained after oxidation of the crude reaction mixture containing indolines (entries 1–9). Consistent with the reluctance of molybdenum to undergo oxidative addition with aryl halides,²⁴ halogen groups remained intact during the reaction. While *tert*-butyl 2-(1-piperidinyl)phenyl ketone gave indoline **2j** (trans only) and indole **3j** in moderate yields (entry 10), indolines or indoles could not be obtained from ketones with a smaller alkyl substituent such as a methyl group or 2-(1-piperidinyl)benzaldehyde because of the decomposition of substrates or products to intractable compounds. Benzofused substrates such as 2-naphthyl phenyl ketone with a 1-piperidinyl group and benzophenone with a 2-tetrahydroisoquinolinyl group afforded the tetracyclic compounds in good yields (entries 11 and 12). The latter substrate underwent a selective C(sp³)–H bond functionalization at the more reactive benzylic position to afford **3l** as a major product. 4-Substituted piperidinyl groups were tolerated, while morpholinyl and piperazinyl groups were less efficient (entries 13–16). Ketones possessing other cyclic amino groups with different ring sizes and a noncyclic amino group such as a dibutylamino group also participated in the reaction, although modifications of the reaction conditions by replacing **L1** with **L2** or **L3** and increasing the reaction temperature were necessary to obtain the products in reasonable yields (entries 17–19). 2-Cylohexylbenzophenone did not participate in the reaction and the starting material was largely recovered, indicating the importance of a nitrogen atom adjacent to a C(sp³)–H bond.

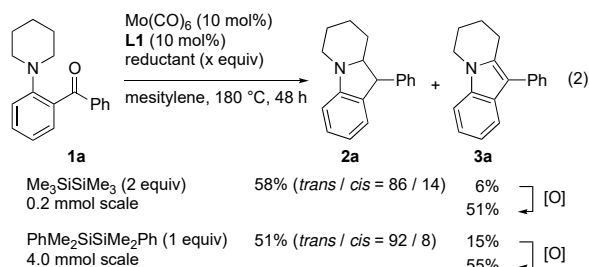
Table 2. Deoxygenative Cyclization with C(sp³)–H Bond Cleavage for the Synthesis of Indoles^a

entry	substrates	products	Yield ^b / %
1			83 (3a , Ar = Ph)
2			80 (3b , Ar = 4-MeC ₆ H ₄)
3			77 (3c , Ar = 4-MeOC ₆ H ₄)
4			73 (3d , Ar = 4-FC ₆ H ₄)
5			81 (3e , Ar = 4-ClC ₆ H ₄)
6			71 (3f , Ar = 4-BrC ₆ H ₄)
7			74 (3g , Ar = 4-IC ₆ H ₄)
8			35 (3h , X = OMe)
9			84 (3i , X = F)
10 ^{cd}			34 (2j) + 8 (3j)
11			50 (3k)
12 ^e			62 (3l)
13			69 (3m , X = CHMe)
14			77 (3n , X = CHPh)
15			0 (3o , X = O)
16 ^f			33 (3p , X = NMe)
17 ^g			58 (3q , n = 1)
18 ^g			36 (3r , n = 3)
19 ^h			16 (3s)

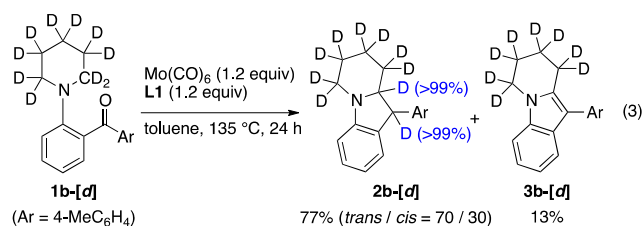
^aThe reaction was performed with Mo(CO)₆/L1 (1.2 equiv) on a 0.2 mmol scale in toluene (1.0 mL) at 135 °C for 24 h, followed by oxidation with *p*-chloranil. ^bIsolated yields. ^cReaction at 160 °C for 24 h. ^dThe crude product was not treated with *p*-chloranil because of the difficulty in oxidizing **2j**. ^eA regioisomer, 12-phenyl-6,11-dihydroindolo[1,2-*b*]isoquinoline (**3l'**) was obtained in 2% yield. ^fReaction in mesitylene at 180 °C for 72 h. ^gReaction with Mo(CO)₆/L3 (1.2 equiv) at 160 °C for 24 h. ^hReaction with W(CO)₆/L2 (1.2 equiv) at 160 °C for 24 h.

We next attempted the deoxygenative cyclization reaction in a catalytic manner by decreasing the amount of the Mo/quinone complex in the presence of an oxygen atom acceptor. While phosphines, which we used as a reductant for the stereospecific deoxygenation of epoxides,¹⁹ completely shut off the reaction, the use of a non-coordinating disilane, Me₃SiSiMe₃, effected the catalytic deoxygenative cyclization with 10 mol% catalyst to afford **2a** and **3a** in 58% and 6% yields, respectively,²⁵ which after treatment with *p*-chloranil afforded **3a** as the sole product in 51% yield (Eq. 2). The reaction could be

similarly performed on 1 gram scale (4.0 mmol of **1a**) using PhMe₂SiSiMe₂Ph as a reductant.



To confirm that the carbonyl carbon had indeed been inserted into a C(sp³)-H bond, decadeuterated substrate **1b-[d]** was subjected to the standard reaction conditions, to find almost quantitative transfer of the α-D atom to the carbonyl carbon (Eq. 3). The result is consistent with the mechanistic scenario shown in Scheme 2B. However, with the precedent of carbene generation via C=O double bond cleavage by related complexes, MCl₂(PR₃)₄ (M = Mo, W) in mind,⁸ we cannot yet exclude the reaction path initiated by carbene generation followed by insertion into a C(sp³)-H bond (Scheme S3).



In summary, we found that the Mo(CO)₆/quinone reagent, which is easily prepared in situ using commercially available compounds without purification or specially designed ligands, effects deoxygenative insertion of a carbonyl carbon into a C(sp³)-H bond, where the carbonyl carbon acts as a carbene equivalent. The deoxygenative cyclization also proceeded with a catalytic amount of a Mo/quinone complex using Me₃SiSiMe₃ as an oxygen atom acceptor. This new protocol allows the direct use of carbonyl compounds as carbene equivalents upon deoxygenation and omits the transformation of carbonyl groups to hydrazones or related diazo compounds, streamlining the overall process. Further studies toward diazo-free syntheses by replacing diazo compounds with carbonyl compounds and mechanistic studies are in progress.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:
Experimental procedures and physical properties of the compounds (PDF)

X-ray crystallographic data for *cis*-**2b** (CIF)

AUTHOR INFORMATION

Corresponding Author

*asako@cc.okayama-u.ac.jp, sobi.asako@riken.jp

*ktakai@cc.okayama-u.ac.jp

ORCID

Sobi Asako: 0000-0003-4525-5317

Kazuhiko Takai: 0000-0002-2572-0851

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank MEXT for financial support (KAKENHI Grant-in-Aid for Scientific Research (A) No. 26248030 and No. 18H03911 to K.T., Grant-in-Aid for Young Scientists (B) No. 15K21180 and Challenging Research (Exploratory) No. 17K19122 to S.A.). We are grateful to Dr. Masahito Murai for X-ray crystal structure analysis.

REFERENCES

- (a) Doyle, M. P. Catalytic methods for metal carbene transformations. *Chem. Rev.* **1986**, *86*, 919–939. (b) Ye, T.; McKervy, M. A. Organic synthesis with α-diazo carbonyl compounds. *Chem. Rev.* **1994**, *94*, 1091–1160. (c) Doyle, M. P.; Forbes, D. C. Recent advances in asymmetric catalytic metal carbene transformations. *Chem. Rev.* **1998**, *98*, 911–936. (d) Davies, H. M. L.; Beckwith, R. E. J. Catalytic Enantioselective C–H Activation by Means of Metal–Carbenoid-Induced C–H Insertion. *Chem. Rev.* **2003**, *103*, 2861–2904. (e) Davies, H. M. L.; Manning, J. R. Catalytic C–H functionalization by metal carbenoid and nitrenoid insertion. *Nature* **2008**, *451*, 417–424. (f) Zhang, Z.; Wang, J. Recent studies on the reactions of α-diazocarbonyl compounds. *Tetrahedron* **2008**, *64*, 6577–6605. (g) Zhang, Y.; Wang, J. Recent development of reactions with α-diazocarbonyl compounds as nucleophiles. *Chem. Commun.* **2009**, 5350–5361. (h) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. Catalytic carbene insertion into C–H bonds. *Chem. Rev.* **2010**, *110*, 704–724. (i) Xia, Y.; Zhang, Y.; Wang, J. Catalytic cascade reactions involving metal carbene migratory insertion. *ACS Catal.* **2013**, *3*, 2586–2598. (j) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKervy, M. A. Modern Organic Synthesis with α-Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115*, 9981–10080. (k) Xia, Y.; Qiu, D.; Wang, J. Transition-Metal-Catalyzed Cross-Couplings through Carbene Migratory Insertion. *Chem. Rev.* **2017**, *117*, 13810–13889.

² Jia, M.; Ma, Shengming. New approaches to the synthesis of metal carbenes. *Angew. Chem. Int. Ed.* **2016**, *55*, 9134–9166.

³ (a) Ogawa, A.; Takami, N.; Sekiguchi, M.; Ryu, I.; Kambe, N.; Sonoda, N. The first deoxygenative coupling of amides by an unprecedented samarium/samarium diiodide system. *J. Am. Chem. Soc.* **1992**, *114*, 8729–8730. (b) Ogawa, A.; Nanke, T.; Takami, N.; Sekiguchi, M.; Kambe, N.; Sonoda, N. A new reduction system by the combination of lanthanoid metals (Ln) and LnI₂: Deoxygenative coupling of amides tovic-diaminoalkenes. *Appl. Organomet. Chem.* **1995**, *9*, 461–466. (c) Ogawa, A.; Takami, N.; Nanke, T.; Ohya, S.; Hirao, T.; Sonoda, N. A novel C–H insertion via deoxygenation of amides by a Sm/SmI₂ mixed system. *Tetrahedron* **1997**, *53*, 12895–12902.

⁴ (a) Motherwell, W. B. Direct deoxygenation of alicyclic ketones. A new olefin synthesis. *J. C. S. Chem. Comm.* **1973**, 935. (b) Motherwell, W. B. On the evolution of organozinc carbenoid chemistry from carbonyl compounds – a personal account. *J. Organomet. Chem.* **2001**, 624, 41–46.

⁵ Lutz, M.; Haukka, M.; Pakkanen, T. A.; Gade, L. H. Structural characterization of the product of intramolecular oxygen transfer from a ketone to CO within the coordination sphere of a Zr–Fe heterodimetallic complex. *Organometallics* **2001**, 20, 2631–2634.

⁶ (a) Marquard, S. L.; Bezpalko, M. W.; Foxman, B. M.; Thomas, C. M. Stoichiometric C=O bond oxidative addition of benzophenone by a discrete radical intermediate to form a cobalt(I) carbene. *J. Am. Chem. Soc.* **2013**, 135, 6018–6021. (b) Marquard, S. L.; Bezpalko, M. W.; Foxman, B. M.; Thomas, C. M. Interaction and activation of carbon–heteroatom π bonds with a Zr/Co heterobimetallic complex. *Organometallics* **2014**, 33, 2071–2079. (c) Zhang, H.; Wu, B.; Marquard, S. L.; Little, E. D.; Dickie, D. A.; Bezpalko, M. W.; Foxman, B. M.; Thomas, C. M. Investigation of ketone C=O bond activation processes by heterobimetallic Zr/Co and Ti/Co tris(phosphinoamide) complexes. *Organometallics* **2017**, 36, 3498–3507.

⁷ (a) Chisholm, M. H.; Klang, J. A. The reductive cross-coupling of ketones and aldehydes to olefins by ditungsten hexaalkoxides. *J. Am. Chem. Soc.* **1989**, 111, 2324–2325. (b) Chisholm, M. H.; Folting, K.; Klang, J. A. Reductive cleavage of ketonic carbon–oxygen bonds in the reactions between ketones and ditungsten hexaalkoxides. Structural characterization of a ditungsten μ -propylidene derivative. *Organometallics* **1990**, 9, 602–606. (c) Chisholm, M. H.; Folting, K.; Klang, J. A. Reaction between benzophenone and ditungsten hexaalkoxides. Molecular structure and reactivity of $W(OCH_2-t-Bu)_4(py)(\eta^2-OCPh_2)$. *Organometallics* **1990**, 9, 607–613.

⁸ (a) Bryan, J. C.; Mayer, J. M. Oxidative addition of cyclopentanone to $WC1_2(PMePh_2)_4$ to give a tungsten(VI) oxo-alkylidene complex. *J. Am. Chem. Soc.* **1987**, 109, 7213–7214. (b) Bryan, J. C.; Mayer, J. M. Oxidative addition of carbon–oxygen and carbon–nitrogen double bonds to $WC1_2(PMePh_2)_4$. Synthesis of tungsten metallaoxirane and tungsten oxo- and imido-alkylidene complexes. *J. Am. Chem. Soc.* **1990**, 112, 2298–2308. (c) Bryan, J. C.; Arterburn, J. B.; Cook, G. K.; Mayer, J. M. Deoxygenative coupling of ketones and alkenes by tungsten(II) compounds. *Organometallics* **1992**, 11, 3965–3970. (d) Hall, K. A.; Mayer, J. M. Reactions of ML_4C1_2 (M = Mo, W; L = PMe_3 , $PMePh_2$) with epoxides, episulfides, CO_2 , heterocumulenes, and other substrates: A comparative study of oxidative addition by oxygen atom, sulfur atom, or nitrene group transfer. *J. Am. Chem. Soc.* **1992**, 114, 10402–10411.

⁹ The reduction of O_2 with a related but π -bound molybdenum/quinone complex has been recently reported: Henthorn, J. T.; Lin, S.; Agapie, T. Combination of redox-active ligand and Lewis acid for dioxygen reduction with π -bound molybdenum–quinonoid complexes. *J. Am. Chem. Soc.* **2015**, 137, 1458–1464.

¹⁰ $Mo(CO)_6$ is known to react with 3 equiv of **L1** to form 0.5 equiv of a dinuclear complex, Mo_2L1_6 : (a) Randolph, A. H.; Seewald, N. J.; Rickert, K.; Brown, S. N. Tris(3,5-di-*tert*-butylcatecholato)molybdenum(VI): Lewis acidity and nonclassical oxygen atom transfer reactions. *Inorg. Chem.* **2013**, 52, 12587–12598. (b) Cass, M. E.; Pierpont, C. G. Synthesis of tris(3,5-di-*tert*-butylcatecholato)molybdenum(VI) and its reaction with molecular oxygen. *Inorg. Chem.* **1986**, 25, 122123.

¹¹ (a) Sharpless, K. B.; Umbreit, M. A.; Nieh, M. T.; Flood, T. C. Lower valent tungsten halides. A new class of reagents for deoxygenation of organic molecules. *J. Am. Chem. Soc.* **1972**, 94, 6538–6540. (b) Fujiwara, Y.; Ishikawa, R.; Akiyama, F.; Teranishi, S. Reductive coupling of carbonyl compounds to olefins by tungsten hexachloridelithium aluminum hydride and some tungsten and molybdenum carbonyls. *J. Org. Chem.* **1978**, 43, 2477–2480.

¹² $TiCl_n/Zn$ system: (a) McMurry, J. E. Carbonyl-coupling reactions using low-valent titanium. *Chem. Rev.* **1989**, 89, 1513–1524. (b) Fürstner, A.; Bogdanović, B. New developments in the chemistry of low-valent titanium. *Angew. Chem. Int. Ed. Engl.* **1996**, 35, 2443–2469.

¹³ Salt-free reduction of WCl_n with formation of R_3SiCl : (a) Tsurugi, H.; Tanahashi, H.; Nishiyama, H.; Fegler, W.; Saito, T.; Sauer, A.; Okuda, J.; Mashima, K. Salt-free reducing reagent of bis(trimethylsilyl)cyclohexadiene mediates multielectron reduction of chloride complexes of W(VI) and W(IV). *J. Am. Chem. Soc.* **2013**, 135, 5986–5989. (b) Tanahashi, H.; Tsurugi, H.; Mashima, K. Synthesis of alkyl and alkylidene complexes of tungsten bearing imido and redox-active α -diimine or *o*-iminoquinone ligands and their application as catalysts for ring-opening metathesis polymerization of norbornene. *Organometallics* **2015**, 34, 731–741. (c) Mouglet, V.; Chan, K.-W.; Siddiqi, G.; Kawakita, K.; Nagae, H.; Tsurugi, H.; Mashima, K.; Safonova, O.; Copéret, C. Low temperature activation of supported metathesis catalysts by organosilicon reducing agents. *ACS Cent. Sci.* **2016**, 2, 569–576. (d) Tanahashi, H.; Ikeda, H.; Tsurugi, H.; Mashima, K. Synthesis and characterization of paramagnetic tungsten imido complexes bearing α -diimine ligands. *Inorg. Chem.* **2016**, 55, 1446–1452.

¹⁴ (a) Tobisu, M.; Chatani, N. A catalytic approach for the functionalization of $C(sp^3)$ –H bonds. *Angew. Chem. Int. Ed.* **2006**, 45, 1683–1684. (b) Pan, S. C. Organocatalytic C–H activation reactions. *Beilstein J. Org. Chem.* **2012**, 8, 1374–1384. (c) Wang, M. Enantioselective intramolecular 1,5-hydride transfer/cyclization through the direct functionalization of $C(sp^3)$ –H bonds adjacent to a heteroatom: from nitrogen to oxygen. *ChemCatChem* **2013**, 5, 1291–1293. (d) Peng, B.; Maulide, N. The redox-neutral approach to C–H functionalization. *Chem. Eur. J.* **2013**, 19, 13274–13287. (e) Platonova, A. Y.; Glukhareva, T. V.; Zimovets, O. A.; Morzherin, Y. Y. *tert*-Amino effect: the Meth-Cohn and Reinholdt reactions. *Chem. Heterocycl. Compd.* **2013**, 49, 357–385. (f) Haibach, M. C.; Seidel, D. C–H bond functionalization through intramolecular hydride transfer. *Angew. Chem. Int. Ed.* **2014**, 53, 5010–5036. (g) Wang, L.; Xiao, J. Advancement in cascade [1,*n*]-hydrogen transfer/cyclization: A method for direct functionalization of inactive $C(sp^3)$ –H bonds. *Adv. Synth. Catal.* **2014**, 356, 1137–1171.

¹⁵ (a) *Modern Alkaloids*; Fattorusso, E., Tagliatalata-Scafati, O., Eds.; Wiley-VCH: Weinheim, 2008. (b) *Anticancer Agents from Natural Products*; Cragg, G. M., Kingstom, D. G. I., Newman, D. J., Eds.; CRC: Boca Raton, FL, 2005. (c) Crich, D.; Banerjee, A. Chemistry of the hexahydropyrrolo[2,3-*b*]indoles: Configuration, conformation, reactivity, and applications in synthesis. *Acc. Chem. Res.* **2007**, 40, 151–161. (d) Boger, D. L.; Boyce, C. W.; Garbaccio, R. M.; Goldberg, J. A. CC-1065 and the Duocarmycins: Synthetic studies. *Chem. Rev.* **1997**, 97, 787–828.

¹⁶ (a) Garner, R. A Facile Synthesis of Indoline-systems Involving an Intramolecular Cyclisation via Arylcarbenes. *Tetrahedron Lett.* **1968**, 9, 221–224 (b) Krogsgaard-Larsen, N.; Begtrup, M.; Herth, M. M.; Kehler, J. Novel, versatile three-step synthesis of 1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indoles by intramolecular carbene-mediated C–H insertion. *Synthesis* **2010**, 24, 4287–4299. (c) Mahoney, S. J.; Fillion, E. *N*-Fused indolines through non-carbonyl-stabilized rhodium carbenoid C–H insertion of *N*-aziridinyl imines. *Chem. Eur. J.* **2012**, 18, 68–71.

¹⁷ Souza, L. W.; Squitieri, R. A.; Dimirjian, C. A.; Hodur, B. M.; Nickerson, L. A.; Penrod, C. N.; Cordova, J.; Fettinger, J. C.; Shaw, J. T. Enantioselective Synthesis of Indolines, Benzodihydrothiophenes, and Indanes by C–H Insertion of Donor/Donor Carbenes. *Angew. Chem. Int. Ed.* **2018**, 57, 15213–15216.

¹⁸ C–H insertion of diazo esters: (a) Lim, H.-J.; Sulikowski, G. A. Enantioselective Synthesis of a 1,2-Disubstituted Mitosene by a Copper-Catalyzed Intramolecular Carbon–Hydrogen Insertion Reaction of

a Diazo Ester. *J. Org. Chem.* **1995**, *60*, 2326–2327. (b) Lee, S.; Lim, H.-J.; Cha, K. L.; Sulikowski, G. A. Asymmetric Approaches to 1,2-Disubstituted Mitosenes Based on the Intramolecular Cyclization of Diazoesters. *Tetrahedron* **1997**, *53*, 16521–16532. (c) Sulikowski, G. A.; Lee, S. Kinetic isotope effects in the intramolecular insertion of a metal carbene into a C–H bond adjacent to nitrogen. *Tetrahedron Lett.* **1999**, *40*, 8035–8038. (d) Santi, M.; Müller, S. T. R.; Folgueiras-Amador, A. A.; Utry, A.; Hellier, P.; Wirth, T. Enantioselective Synthesis of trans-2,3-Dihydro-1*H*-indoles Through C–H Insertion of α -Diazocarbonyl Compounds *Eur. J. Org. Chem.* **2017**, 1889–1893;

¹⁹ Asako, S.; Sakae, T.; Murai, M.; Takai, K. Molybdenum-catalyzed stereospecific deoxygenation of epoxides to alkenes. *Adv. Synth. Catal.* **2016**, *358*, 3966–3970.

²⁰ (a) Asako, S.; Ishikawa, S.; Takai, K. Synthesis of linear allylsilanes via molybdenum-catalyzed regioselective hydrosilylation of allenes. *ACS Catal.* **2016**, *6*, 3387–3395. (b) Asako, S.; Kobashi, T.; Takai, K. Use of cyclopropane as C1 synthetic unit by directed retrocyclopropanation with ethylene release. *J. Am. Chem. Soc.* **2018**, *140*, 15425–15429.

²¹ Indole synthesis from similar substrates via a radical-based mechanism: (a) Wei, W.-t.; Dong, X.-j.; Nie, S.-z.; Chen, Y.-y.; Zhang, X.-j.; Yan, M. Intramolecular dehydrative coupling of tertiary amines and ketones promoted by KO-*t*-Bu/DMF: A new synthesis of indole derivatives. *Org. Lett.* **2013**, *15*, 6018–6021. (b) Yuan, X.; Wu,

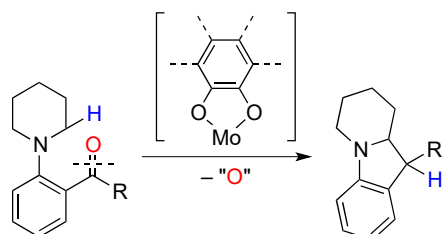
X.; Dong, S.; Wu, G.; Ye, J. Intramolecular addition of diaryl-methanols to imines promoted by KO-*t*-Bu/DMF: A new synthetic approach to indole derivatives. *Org. Biomol. Chem.* **2016**, *14*, 7447–7450.

²² The presence of air or oxygen was not absolutely essential to the reaction. It contributed to the prevention of the products from decomposing. See SI for the details.

²³ A beneficial effect of O₂ on the deoxygenative homocoupling of alkoxyvanadium: Kataoka, Y.; Akiyama, H.; Makihira, I.; Tani, K. A novel C–C single bond formation accompanying C–O bond cleavage by use of a ketone, an alkylating reagent, and a low-valent vanadium complex in the presence of a catalytic amount of molecular oxygen. *J. Org. Chem.* **1997**, *62*, 8109–8113.

²⁴ (a) Sangu, K.; Watanabe, T.; Takaya, J.; Iwasawa, N. Intermolecular addition reaction to alkenes of acylmolybdenum complexes generated by oxidative addition of aryl or alkenyl halides with molybdenum(0) carbonyl complexes. *Synlett* **2007**, 929–933. (b) Takaya, J.; Sangu, K.; Iwasawa, N. Molybdenum(0)-promoted carbonylative cyclization of *o*-haloaryl- and β -haloalkenylimine derivatives by oxidative addition of a carbon(sp²)-halogen bond: Preparation of two types of γ -lactams. *Angew. Chem. Int. Ed.* **2009**, *48*, 7090–7093.

²⁵ A small amount of Me₃SiOSiMe₃ was detected. See Scheme S2 for the details.



carbonyl compounds as carbene equivalents
diazo-free

C(sp³)-H bond functionalization
synthesis of indolines and indoles