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Selective, Catalytic Carbon−Carbon Bond Activation and Functionalization Promoted by Late Transition Metal Catalysts

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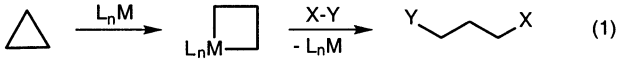
The selective cleavage and subsequent elaboration of aliphatic carbon−carbon bonds into more valuable commodity and specialty chemicals presents a fundamental challenge in synthesis.[1] Relatively high bond strengths (typically 85 kcal/mol) and directional σ orbitals provide both thermodynamic and kinetic obstacles to C−C bond activation. Relief of ring strain with substrates such as cyclopropane[2] and cubane[3] has provided favorable conditions for stoichiometric carbon−carbon bond cleavage. This strategy has recently evolved to include catalytic hydrogenation,[4] decarbonylation,[5] and ring expansion/opening[6] reactions of strained substrates.

Despite these significant advances, the general applicability of carbon−carbon bond activation in synthetically useful transformations remains limited.[5,7] Although the ring opening hydrosilylation of methylenecyclopropanes has been described, these reactions provide mixtures of products and are believed to proceed via olefin insertion into a metal hydrogen bond followed by β-alkyl elimination.[8] To achieve hydrocarbon cleavage and derivatization for a range of functional groups, methodologies that couple carbon−carbon activation with other bond-forming processes are desirable. Considering the metallocyclobutane product of C−C bond oxidative addition as a typical metal alkyl suggests that traditional organometallic bond-forming reactions (insertion, elimination, etc.) may be coupled to bond activation processes (eq 1). Such a pairing may extend the utility of numerous catalytic reactions to otherwise inert substrates.



(1)

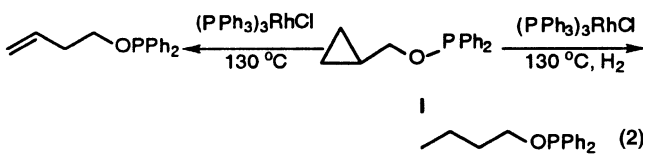
In this communication, we describe the regioselective catalytic hydrogenation, olefination, and, in one case, hydrosilylation, of aliphatic carbon−carbon bonds for a range of substituted cyclopropane derivatives. Each reaction may be performed under typical laboratory conditions with commercially available transition metal catalysts. The regioselectivity of the C−C cleavage and subsequent functionalization reaction can be controlled by the appropriate choice of cyclopropyl substituent.

Initial studies focused on the hydrogenation of the [$SiMe_3$]-protected cyclopropylcarbinol, $^cPrCH_2OSiMe_3$, with a series of commercially available late transition metal catalysts (Table S1, Supporting Information). The hydrogenation reactions proceeded readily at 130 °C with 1−4 atm of dihydrogen and with low (0.5−2 mol %) catalyst loadings. To compare relative rates, hydrogenation reactions were carried out under standard conditions of 4 atm of H_2, 2 mol % catalyst, and were assayed at 18 h. In each case, $Me_2CHCH_2OSiMe_3$ was the sole product formed, arising from cleavage of the most sterically accessible C−C bond. The activity of the hydrogenation reaction showed only a modest dependence on the metal catalyst and was unaffected by the addition of elemental mercury, consistent with a homogeneous process.[9] The observed turnover frequencies (∼1 mol/h for the best cases) are some of the most active catalytic C−C hydrogenation reactions reported to date.[4]

The scope of the catalytic hydrogenation reaction was explored with a series of substituted cyclopropane substrates (Table 1). Wilkinson's catalyst, $(PPh_3)_3RhCl$, was chosen for subsequent experiments because it displays good activity and is the most readily available. In general, the hydrogenation reactions are tolerant of a range of functional groups including alcohols, ethers, carbonyls, and thiophenes with little influence on activity. Notable exceptions are the presence of long alkyl chains (entries 4 and 7). Pure hydrocarbon substrates such as cyclopropylbutane (entry 7) as well as butyl ethers (entry 4) undergo preferential C−H activation and dehydrogenation[10] of the alkyl chain, even in the presence of dihydrogen,[11] forming a mixture (∼1:1) of 2-olefins. Catalytic, acceptorless alkane dehydrogenation at 130 °C represents one of the lowest temperatures reported for this process.[12] Interestingly, ethyl ethers (entry 5) are compatible with the C−C cleavage reaction, participating in ring opening and hydrogenation with no complications arising from C−H activation.

Performing the C−C bond activation reactions with $(PPh_3)_3RhCl$ under an atmosphere of N_2 rather than H_2 results in catalytic alkane olefination (Table 2). In each case, *gem*-olefins arising from C−C activation of the least hindered face of the cyclopropane are formed. Olefination most likely occurs via C−C oxidative addition followed by both β-hydrogen and reductive eliminations, respectively. Unlike hydrogenation, the olefination procedure is not effective for alcohol substrates (entry 2) or for the dehydrogenation of the butyl ether derivative (entry 4). However, $(PPh_3)_3RhCl$ does promote the dehydrogenation, albeit with low activity, of the alkyl chain of cyclopropylbutane (entry 7).

In principle, the regioselectivity of both catalytic hydrogenation and olefination can be altered by incorporation of functional groups that can serve as ligands for rhodium and direct the activation of the *most hindered* C−C bond.[4c,13] Because oxygen[14] and sulfur donors are ineffective in providing chelate-assisted selectivity, a [PPh_2] group was chosen given the high affinity of rhodium for phosphine-based ligands.[15] This approach was successfully applied in both the catalytic hydrogenation and the olefination of the [PPh_2]-substituted cyclopropylcarbinol (**I**), resulting in exclusive cleavage of the most hindered C−C bond (eq 2). As observed previously in Table 2, the terminal olefin is formed initially but undergoes isomerization to a mixture (∼1:1) of 2-olefins during the course of the reaction.



(2)

In addition to altering the kinetic selectivity, chelate assistance is also effective in providing a lower energy pathway for C−C cleavage. The reactions presented in Table 2 take place over the

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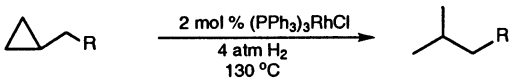
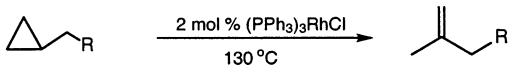
Table 1. Catalytic Hydrogenation of Cyclopropyl Substrates with $(PPh_3)_3RhCl$



entry[a]	R	tof[b]
1	$OSiMe_3$	0.98
2	OH	0.25
3	OAc	0.56
4	$OCH_2CH_2CH_2CH_3$[c]	2.4
5	OCH_2CH_3	0.21
6	$C(O)(2\text{-}C_4H_3S)$	0.25
7	$CH_2CH_2CH_3$[c]	0.25

[a] 2.75 mM $(PPh_3)_3RhCl$ and 0.138 M substrate in anhydrous toluene. [b] Turnover frequency determined with 4 atm of H_2 at 18 h. [c] Undergoes alkane dehydrogenation of the alkyl chain to a mixture of internal olefins.

Table 2. Catalytic Olefination of Cyclopropyl Substrates with $(PPh_3)_3RhCl$



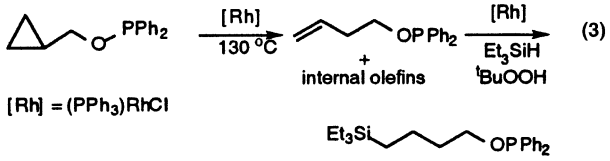
entry[a]	R	tof[b]
1	$OSiMe_3$	1.78
2	OH	no reaction
3	OAc	0.28
4	$OCH_2CH_2CH_2CH_3$[c]	no reaction
5	OCH_2CH_3	0.68
6	$C(O)(2\text{-}C_4H_3S)$	0.92
7	$CH_2CH_2CH_3$	0.05

[a] 2.75 mM $(PPh_3)_3RhCl$ and 0.138 M substrate in anhydrous toluene. [b] Turnover frequency determined at 18 h. [c] Undergoes alkane dehydrogenation of the alkyl chain to a mixture of internal olefins.

course of 55 h, whereas the catalytic hydrogenation or olefination of **I** is complete within 6 h. Likewise, both of these catalytic processes can be conducted at temperatures as low as 100 °C. In addition to $(PPh_3)_3RhCl$, other catalysts such as $[Rh(COD)Cl]_2$ and $Pd(PPh_3)_4$ are effective for the chelate-assisted hydrogenation or olefination protocol.

Catalytic carbon−carbon bond activation may also be coupled to hydrosilylation. In a one-pot procedure, olefination of **I** followed by addition of Et_3SiH under conditions where $(PPh_3)_3RhCl$ is active for hydrosilylation[16] produced the terminal silane in >95% yield (eq 3). As typically observed with olefin hydrosilylation reactions, mixtures of internal alkenes undergo isomerization and hydrosilylation to the terminal product.[16]

In summary, we have successfully coupled carbon−carbon bond activation to reactions traditionally available to metal alkyls. Using commercially available catalysts under convenient laboratory conditions, we have achieved catalytic hydrocarbon functionalization. Introduction of functional groups such as $[PPh_2]$ is effective in promoting accelerated reactions with exclusive selectivity for the most hindered carbon−carbon bond. Further studies aimed at elucidating the mechanistic details of both catalytic reactions as well as coupling them to additional organometallic bond-forming reactions are now in progress.



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Supporting Information Available: Results for catalytic hydrogenation of $^cPrCH_2OSiMe_3$ as a function of metal catalyst and all experimental procedures (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) (a) For alkane dehydrogenation that is dependent on the presence of dihydrogen for activity, see: Goldman, A. S. *J. Am. Chem. Soc.* **1991**, *113*, 6706. (b) The terminal olefin is formed initially, undergoing isomerization under the reaction conditions.
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(14) It is important to note in the case of entry 3 (Tables 1 and 2), coordination of the carbonyl group and C−C oxidative addition would provide a [3.1.1] bicyclo intermediate, whereas a [2.1.1] intermediate is anticipated for **I**.
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