Reduction of Olefins Using Ruthenium Carbene Catalysts and Silanes

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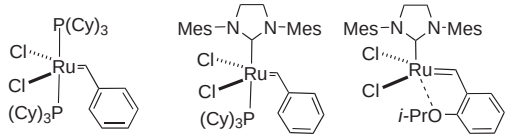
Abstract: Ruthenium carbene complexes are able to mediate reduction of olefins in the presence of trialkylsilanes. Under these reduction conditions, when kinetically favorable ring-closing metathesis is possible, a one-pot cyclization–reduction sequence can be performed.

Key words: reduction, hydrosilylation, stereoselective synthesis

One of the most important advancements in synthetic organic chemistry in the last ten years is the development of efficient catalysts for metathesis reactions.[1] While an impressive array and variety of catalysts have been devised for carbon–carbon double bond formation, some attention has been paid to the non-metathetic reactions of such complexes.[2] Ruthenium carbene complexes were distinguished in mediating halogenation,[3] cyclopropanation,[4] alkylative[5a] and radical cyclizations,[5b,c] intramolecular [3+2]-cycloaddition of alkynilidene cyclopropanes,[6] isomerization[7] and reduction of olefins,[8a] including hydrosilylation of carbonyl compounds[8a] and alkynes.[8b,c] Somewhat surprisingly, the capacity in mediating these reactions sequentially was seldom considered.[2,4,7e,8]

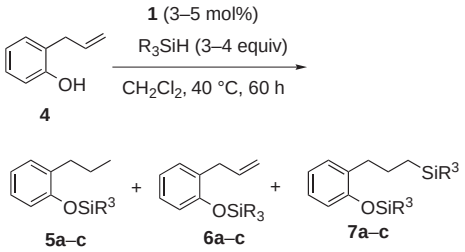


1 **2** **3**

Scheme 1

As ruthenium complexes are generally considered to be poor hydrogen-transfer agents toward olefins and alkynes,[9] these mild hydrogen donors can be exploited advantageously in selective transformations. Here, we wish to describe the selective hydrogenation of olefins using complexes **1**–**3** in the presence of silanes (Scheme 1).[10]

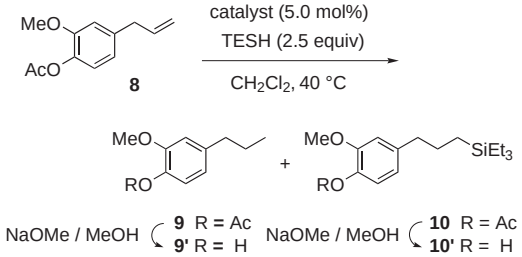
When olefin **4** was treated with a mixture of triethylsilane (TESH, 3–4 equiv) and ruthenium complex **1** (3–5 mol%), in refluxing CH_2Cl_2, a slow conversion of olefin **4** was observed (Scheme 2). After 60 hours, the saturated O-silylated phenol **5a** was obtained, accompanied by a small amount of unsaturated O-silylated product **6a** and hydrosilylated compound **7a** in a ratio of 91/4/5 and in 94% yield.[11] Similar results were observed when TESH was replaced by triphenylsilane (Ph_3SiH) or *tert*-butyldimethylsilane (TBSH), even though compounds **7b** and **7c** were not formed, the reduction was more sluggish, and compounds **5b** and **5c** were obtained after 60 hours accompanied by the O-silylated products **6b** and **6c**, respectively, in a ratio of 32/68 and 86/14 (Scheme 2). As the best results were obtained with triethylsilane, this reagent was selected for further studies.



Reagent	Ratio **5**/**6**/**7**[11]	Yield
a $R^3SiH = Et_3SiH$	91/4/5	(94%)
b $R^3SiH = t\text{-}BuMe_2SiH$	32/68/0	(74%)
c $R^3SiH = Ph_3SiH$	86/14/0	(79%)

Scheme 2

In order to optimize the reaction conditions, different ruthenium complexes **1**–**3** (5 mol%) were compared in the reduction of eugenol acetate **8** in the presence of TESH (2.5 equiv) in refluxing CH_2Cl_2 (Scheme 3). In the presence of catalyst **1** (5.0 mol%) and after 16 hours, compound **8** was transformed to a mixture of **9** and **10** in 79% global yield, and in a ratio of 96/4.[11] When catalyst **2** was used, the reaction was also complete after 16 hours and compounds **9** and **10** were isolated in 71% yield (95/5).[11]



Catalyst	Time	Ratio **9**/**10**[11]	Yield of **9**+**10**
1	16 h	96/4	(79%)
2	16 h	95/5	(71%)
3	3 h	68/32	(74%)

Scheme 3

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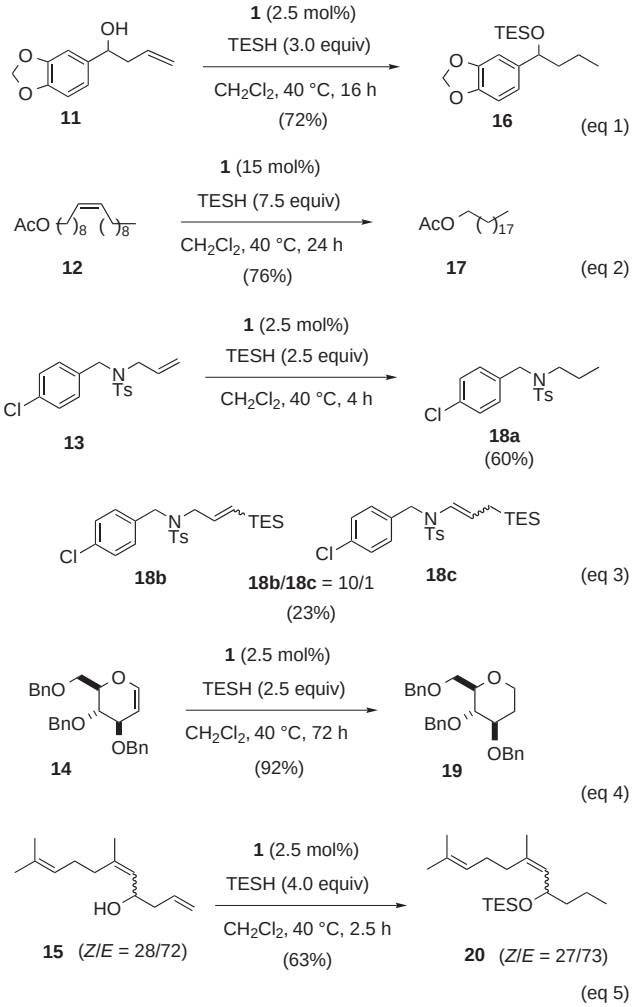
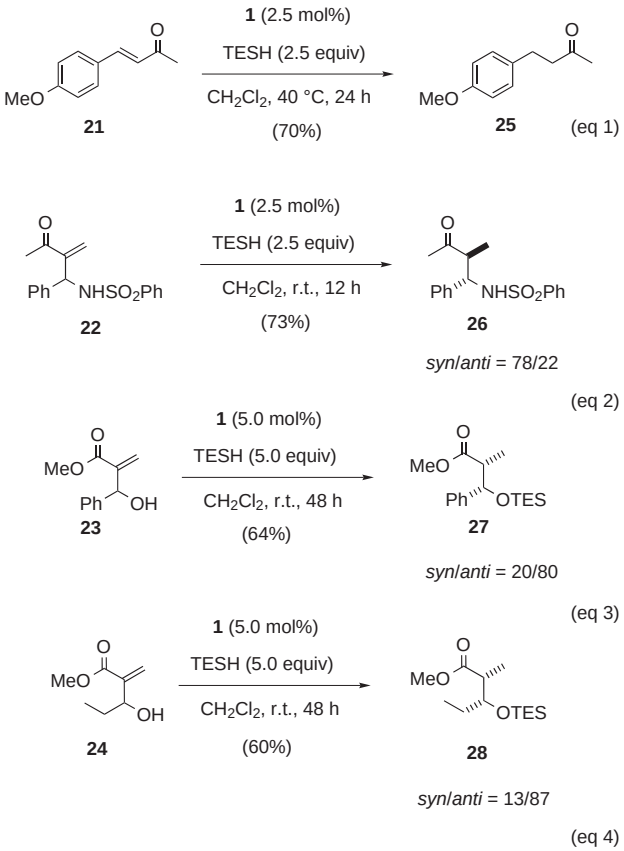
When catalyst **3** (2.5 mol%) was employed the reaction was faster although less selective than with catalysts **1** and **2**, as after 3 hours, compounds **9** and **10** were isolated in 74% yield in a ratio of 68/32.[11] It is worth noting that compounds **9** and **10** could not be separated. However, after cleavage of the acetate using a catalytic amount of NaOMe in MeOH, the corresponding phenol derivatives **9′** and **10′** were obtained in quantitative yield, separated and characterized (Scheme 3).



Scheme 4

The reaction is general and the results are reported in Scheme 4. Olefins **11**–**15** were treated with catalyst **1** (2.5–15 mol%) and TESH (3.0–7.5 equiv) in refluxing CH_2Cl_2.[12] Compound **11**, having a terminal olefin, was converted to the corresponding saturated compound **16** in 72% yield [**1** (2.5 mol%), TESH (3.0 equiv), 16 h (Scheme 4, eq 1)]. The reduction of disubstituted olefins such as **12** was more sluggish (24 h) and required 15 mol% of catalyst to afford **17** in 76% yield (Scheme 4, eq 2). It is worth noting that unsaturated aryl chloride derivatives can be reduced without concomitant dehalogenation under the reaction conditions. The reduction of olefin **13** afforded the saturated compound **18a** in 60% yield, accompanied by a small amount of **18b** and **18c** (23%) issued from the competing oxidative addition of TESH to the double bond (Scheme 4, eq 3). Furthermore, the reduction conditions are compatible with the presence of a benzyl protecting group as D-glucal (**14**) was converted to the corresponding dideoxy D-glucose derivative **19** in 92% yield without detectable loss of the benzyl groups (Scheme 4, eq 4). The fact that trisubstituted olefins are inert under the reaction conditions can be used advantageously in chemoselective reductions (Scheme 4, eq 5). For example, triene **15** was converted to the selectively reduced product **20** with the concomitant silylation of the free alcohol in 63% yield (Scheme 4, eq 5). We have to point out that the stereochemistry of the trisubstituted double bond remained unchanged under the reaction conditions.[11]

The reduction conditions of alkenes by TESH in the presence of catalyst **1** can be applied to the selective transformation of α,β-unsaturated carbonyl compounds to the corresponding saturated products (Scheme 5).[13] In these transformations a catalytic amount of **1** (2.5 mol%) and TESH (2.5 equiv) was used either in refluxing CH_2Cl_2 or at room temperature for 12–48 hours.[14]

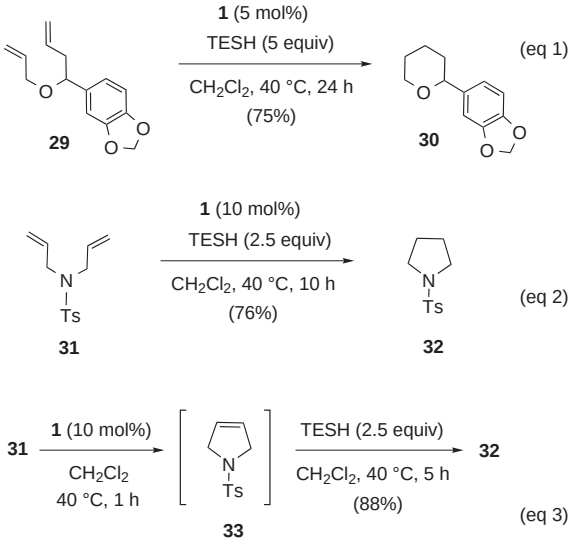


Scheme 5

After 24 hours, compound **21** was transformed to ketone **25** in 70% yield (Scheme 5, eq 1). The reduction of the ketone under the reaction conditions was not observed. The diastereoselectivity of the transformation was studied in the reduction of acyclic enone **22** and α,β-unsaturated

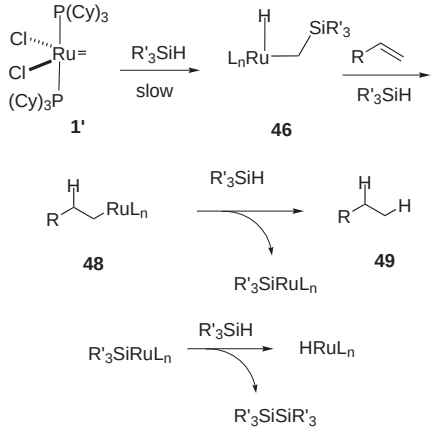
esters **23** and **24** (Scheme 5, eq 2–4). The saturated products **26**, **27** and **28** were formed in 73%, 64% and 60% yield, respectively. We have to point out, that *syn* selectivity was observed in reducing amide **22** (dr = 78/22), while the *anti* products were formed as the major isomers from alcohols **23** and **24** (dr = 20/80 and 13/87).[15]

Furthermore, the ability in mediating tandem metathesis reaction–reduction under the reaction conditions was tested. Even in the presence of trialkylsilanes the metathetic activity of ruthenium complex **1** was retained, as **29** was transformed to tetrahydropyran **30** in 75% yield in a one-pot cyclization–reduction sequence using a catalytic amount of **1** (5 mol%) and TESH (5 equiv) in refluxing CH_2Cl_2 for 24 hours (Scheme 6, eq 1).[16] Likewise, *N*-tosyl-*N*,*N*-diallylamine (**31**) was converted to the pyrrolidine derivative **32** in a one-pot sequence in 76% yield (Scheme 6, eq 2). It is interesting to compare the efficiency of this transformation with the sequential addition of the carbene catalyst **1** followed by the addition of the triethylsilane reagent. The two processes afforded **32** in a comparable yield (76% vs. 88%, Scheme 6, eq 2 and 3).



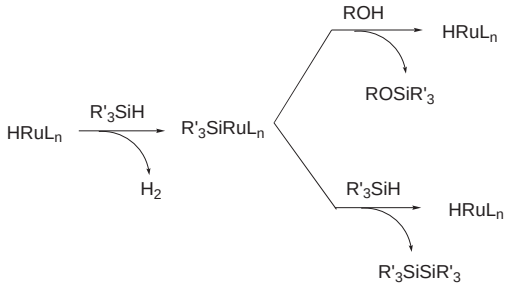
Scheme 6

The mechanism of the transformation is the subject of speculation. It is difficult to account all the observed events to a single organometallic complex, and they are probably the consequence of competing processes. Unfortunately, we were unable to characterize any of these complexes by different ^1H NMR techniques, and at present we can only speculate on the plausible intermediates involved in the process. The first step of the mechanism can be the addition of the silane to the metal-carbene, which produces **46** (Scheme 7). The methylidene complex **1′** derived from **1** reacts probably slowly with silanes under the reaction conditions, which would explain the sustained metathetic activity of the mixture even after extended reaction time. The addition of L_nRuH to olefins can then follow a classical oxidative addition–reductive elimination pathway. Accordingly, the addition will provide **48**, which in the presence of Si–H is reduced, and gives raise to the alkane and $L_nRuSiR'_3$. The starting RuH is regenerated by further reduction with the silane, forming disilane as a by-product.



Scheme 7

A secondary reaction is the dimerization of the silanes forming disilanes or disiloxanes and molecular H_2, when water is present (Scheme 8). In fact, in all the reactions the corresponding disiloxane was the major secondary product, suggesting that water is required for the process. Due to this competing reaction an excess of silane is necessary for completing the desired reduction.



Scheme 8

In summary, a method allowing the selective reduction of non-activated, and activated olefins in the presence of ruthenium–carbene catalysts and silanes was presented. The selectivity of the reduction is essentially steric: terminal olefins are reduced preferentially in the presence of di-, tri- or tetrasubstituted olefins. This selectivity, and the fact that no molecular hydrogen at higher pressure is required should be of interest in synthesis. The ability in mediating sequential transformations such as ring-closing metathesis and reductions contributes to the fascinating array of reactions of the ruthenium carbene complexes. The study of the mechanism and the structure of the active complex are the subject of further investigations and will be reported in due course.

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(11) Product ratio was determined by GC-MS.

(12) **2,6-Dimethyl-8-triethylsilyloxyundec-2,6-diene (20).** To a solution of olefin **15** (200 mg, 1.03 mmol, 1 equiv) in degassed CH_2Cl_2 (2 mL) were added the silane reagent (0.65 mL, 4.12 mmol, 4 equiv) and catalyst **1** (21 mg, 25.7 μmol, 2.5 mol%) at r.t. The reaction was stirred at reflux until total conversion of the starting material. The solution was concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel using a gradient of eluent (pentane–EtOAc). Colorless oil (200 mg, 0.65 mmol, 63%); R_f = 0 .57 (pentane–EtOAc, 95:1). IR (neat): 1475, 1400, 1260, 1080, 760 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, *E*- and *Z*-isomers): δ = 5.10–5.00 (m, 2 H), 4.30–4.20 (m, 1 H), 2.05–1.89 (m, 4 H), 1.61 (dd, *J* = 4.9, 1.1 Hz, 3 H), 1.54 (dd, *J* = 4.5, 1.5 Hz, 6 H), 1.35–1.15 (m, 4 H), 0.87 (t, *J* = 7.9 Hz, 9 H), 0.84 (t, *J* = 6.4 Hz, 3 H), 0.49 (q, *J* = 7.5 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$): *E*-isomer δ = 134.4, 131.4, 129.5, 124.1, 69.3, 40.9, 39.6, 26.3, 25.6, 18.6, 17.5, 16.4, 14.1, 6.8, 5.0. *Z*-Isomer: δ = 134.6, 131.7, 130.3, 124.1, 68.9, 41.2, 32.4, 26.5, 23.4, 18.8, 17.6, 16.4, 14.1, 6.8, 4.9. MS (EI, 70 eV): *E*-isomer *m/z* (%) = 310 (8) [M^+], 267 (100), 173 (24), 75 (39), 69 (40). MS (EI, 70 eV): *Z*-isomer *m/z* (%) = 310 (20) [M^+], 267 (25), 173 (97), 135 (59), 115 (38), 107 (32), 103 (100), 75 (54), 69 (45).

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(14) **4-(4-Methoxyphenyl)butan-2-one (25).** To a solution of compound **21** (42 mg, 0.24 mmol, 1 equiv) in degassed CH_2Cl_2 (0.5 mL) at r.t. were added triethylsilane (0.10 mL, 0.70 mmol, 2.5 equiv) and catalyst **1** (5 mg, 7 mol, 2.5 mol%). The resulting solution was stirred until total conversion of the starting material. The solution was concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel using a gradient of eluent (pentane–EtOAc). Colorless oil (30 mg, 0.17 mmol, 70%); R_f = 0.63 (pentane–EtOAc, 4:1). IR (neat): 1720, 1610, 1510, 1250, 1035 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.05 (d, *J* = 8.7 Hz, 2 H), 6.75 (d, *J* = 8.7 Hz, 2 H), 3.70 (s, 3 H), 2.70 (m, 4 H), 2.05 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.0, 157.8, 132.9, 129.1, 113.8, 55.1, 45.3, 29.9, 28.7. MS (EI, 70 eV): *m/z* (%) = 178 (39) [M^+], 121 (100).

(15) The relative stereochemistry of the major isomers was attributed on the basis of the *J* values observed in the ^1H NMR spectra. Moreover, **28** was transformed to the known β-hydroxy ester (TBAF, overnight), and the spectral data of the desilylated compound was compared with the literature data: Bouzide, A. *Org. Lett.* **2002**, *4*, 1347.

(16) As one of our referees pointed out, it is likely that hydrogenation occurred by the metathesis-inactive catalyst after the RCM reaction was completed, because the RCM was much faster than the modification of carbene catalyst by silanes or hydrogen, generated from dimerization of silanes.