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Selective reduction of mono- and disubstituted olefins by $NaBH_4$ and catalytic $RuCl_3$

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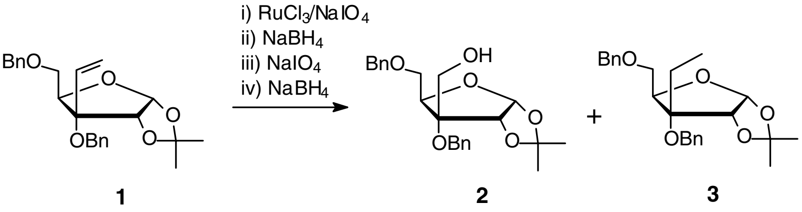
Abstract—Direct use of the relatively inexpensive reagent, $RuCl_3 \times H_2O$, as a catalyst for the reductions of olefins in the presence of water is reported. The combination of cheap and readily available sodium borohydride and a catalytic amount of $RuCl_3 \times H_2O$ selectively reduces mono- and disubstituted olefins, whereas trisubstituted olefins, unless activated, and benzyl ethers remain inert.

Catalytic hydrogenation is usually the method of choice for the reduction of alkenes, which is an important transformation in organic synthesis.[1] The standard conditions are atmospheric or high pressure hydrogen and a Pd or Pt catalyst. Hydrogenation is also the most important method for cleaving benzyl ethers. Several other hydrogenation reagents such as Caubere's nickel complex reducing reagent (NiCRA),[2] P-2 Ni[3] and Ni_2B-BER[4] are well known for the reduction of alkenes. Some other systems such as FeCRA,[5] LiH–VCl,[6] $LaNi_5H_6$[7] and $CoCl_2$–$NaBH_4$[8] have also been reported to be good hydrogenation systems. Besides toxicity issues associated with some of these metals, major drawbacks associated with these hydrogenation systems are long and complex procedures required for their preparation[2–7] and/or the use of a stoichiometric amount or more of costly transition metal salts.[8] The requirement of a hydrogen atmosphere in some cases further complicates the procedures.

We report in this Letter the serendipitous discovery of an extremely simple and novel system for the selective hydrogenation of mono- and disubstituted olefins using $RuCl_3$ and $NaBH_4$. Recently, we developed a new protocol for cleavage of terminal olefins to primary alcohols (**1** → **2**, Scheme 1) based on RuO_4-mediated dihydroxylation, reduction, $NaIO_4$-mediated diol cleavage, and $NaBH_4$-mediated reduction.[9] The introduction of a reducing step before the diol cleavage was a key step in this protocol as it prevents the formation of byproducts and improves the yield significantly.[9] While developing this protocol we were optimizing the time required for the first step, that is, the dihydroxylation of olefin **1**, by reducing the reaction time by 15 s in successive trials. In this optimization study we found the optimum time for full conversion of the olefin to the diol to be 90 s. A few experiments using less than 90 s for dihydroxylation revealed, however, small amounts of the hydrogenated product, **3**. Looking for



Scheme 1.

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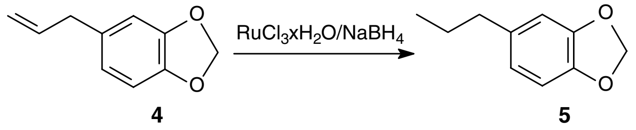


Scheme 2.

the explanation, we subjected alkene **1** to reduction with $NaBH_4$, but no reaction was observed even after overnight stirring. This led us to believe that it might be the small amount of active ruthenium species from the first step, that was responsible for the hydrogenation in the presence of $NaBH_4$. On the basis of these observations, we treated alkene **1** with $NaBH_4$ (1 equiv) and $RuCl_3 \times H_2O$[10] (25 mol %), and were pleasantly surprised to find that alkene **1** was cleanly hydrogenated to **3** in excellent yield. The remarkable success of this reaction protocol inspired us to apply it to various other carbohydrate substrates (including allyl and vinyl substituents) as well as simple substrates such as styrene and allylphenyl ether.

Optimization studies were performed using safrol (**4**) as the substrate (Scheme 2). Complete conversion of **4** into **5** was observed while using $RuCl_3 \times H_2O$ down to 10 mol % along with two equivalents of $NaBH_4$. Although hydrogenation of **4** to **5** was complete even while using one equivalent of $NaBH_4$, the results were most consistent in the majority of cases (Table 2) while using two equivalents of $NaBH_4$.

Subsequently, the influence of solvent on the reaction course was investigated (Table 1). There was virtually no difference in yield on using aqueous conditions or non-aqueous conditions. However, the reaction time increased in the absence of water (entries 3 and 6). It seems reasonable when we consider that a proton source such as water is required for the hydrolysis of $NaBH_4$. Thus longer reaction times in the absence of water is simply a reflection that the amount of water present was limited. We did not examine a larger series of different solvents, as $RuCl_3$ is known to accept a wide range of solvents, whereas the scope and limitations of $NaBH_4$ are well known.[11,12] Concerning the influence of temperature, we found that the addition of $RuCl_3$ was exothermic with rapid evolution of hydrogen,[13] and hence, cooling was needed. However, the reactions proceeded well at room temperature.

Having developed optimized conditions, we next investigated the scope and limitations of the method (Table 2). Monosubstituted terminal olefins were readily reduced by this reagent (entries 1–8). The reactions for monosubstituted alkenes were complete in one hour except for styrene (entry 6). Disubstituted olefins (entries 9 and 10) were also reduced completely, but more slowly compared to monosubstituted olefins. Importantly, mono- and disubstituted olefins were efficiently reduced while more highly substituted olefins (entries 11–13) were virtually inert to these reducing conditions. Interestingly, in the case of 3-benzoyl-1-allylthymine (entry 16), the monosubstituted olefin was selectively reduced over the endocyclic double bond of the heterocycle. It is pertinent to mention here that this endocyclic double bond in a similar thymidine analogue reacts with the $RuCl_3/NaIO_4$ system and is dihydroxylated.[9] Activated trisubstituted alkenes (entries 14 and 15) were efficiently reduced by this reagent system. The conditions employed for the transformations are compatible with a variety of functional groups. Benzyl ethers were not affected under the reaction conditions, which make this protocol potentially appealing for carbohydrate and nucleoside chemistry. Esters, amides and alkyl/aryl ethers were also found to be stable.

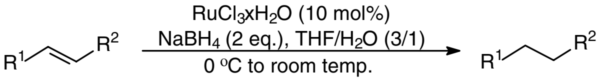
All these features in combination give the present reducing agent a broad and general synthetic utility. Ruthenium is neither poisonous nor explosive.[14] $RuCl_3 \times H_2O$ has been used extensively in organic chemistry for oxidations/oxidative degradations of unsaturated organic compounds.[15,16] It has long been known that transition metal salts catalyze the hydrolysis of borohydride ions under aqueous conditions[13] to generate hydrogen that can be used in combination with transition metal salts for the reductions. There are several reports using ruthenium complexes, sometimes prepared using long and tedious processes under anhydrous conditions, for various reductive applications.[17–19] Reduction of alkenes using $NaBH_4$ as the reducing agent in combination with dihydridoruthenium(II) complex has also recently been reported.[20] However, the direct use of this relatively inexpensive reagent as a catalyst for reductions is, to the best of our knowledge, reported here for the first time. It is reasonable to assume that the species responsible for the selective reduction of mono- and disubstituted alkenes is most likely a ruthenium hydride or active ruthenium in the presence of hydrogen generated under the reaction conditions.

Table 1. Influence of solvent

Entry[a]	Solvent	Reaction time (h)	Conversion[b] (%)	**5** (% Yield)[c]
1	THF (3 mL)/H_2O (1 mL)	1	100	96
2	THF (3 mL)/H_2O (0.5 mL)	1	100	95
3	THF (3 mL)	3	100	96
4	CH_3CN (3 mL)/H_2O (1 mL)	1	100	96
5	CH_3CN (3 mL)/H_2O (0.5 mL)	1	100	96
6	CH_3CN (3 mL)	4	100	95

[a] All reactions were performed at room temperature on a 1 mmol scale using 10 mol % $RuCl_3 \times H_2O$ and 2 equiv $NaBH_4$.
[b] Determined by NMR.
[c] Isolated yield.

Table 2. Reduction of olefins



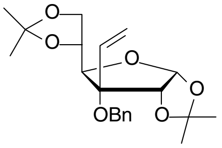
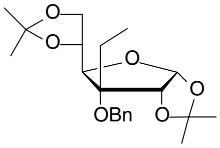
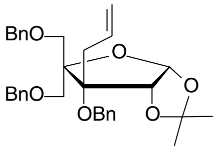
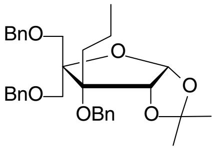
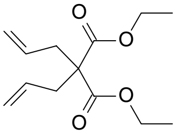
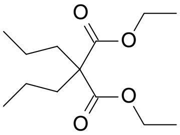
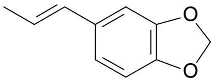
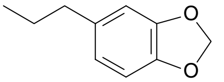
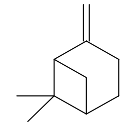
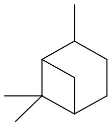
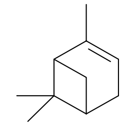
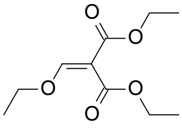
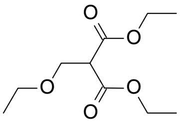
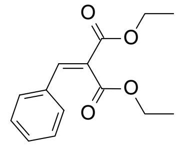
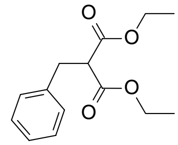
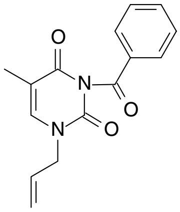
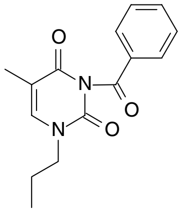
Entry	Substrate[a]	Product	Time [h]	Conversion[b] (%)	Yield[c] (%)
1	**1**	**3**	1	100	93
2	**4**	**5**	1	100	96
3	 **6**	 **7**	1	100	94
4	 **8**	 **9**	1	100	100
5	1-Decene (**10**)	Decane (**11**)	1	100	90[d]
6	Styrene (**12**)	Ethyl benzene (**13**)	2	100	nd
7	Allylphenyl ether (**14**)	Phenylpropyl ether (**15**)	1	100	90[d]
8	 **16**	 **17**	1	100	93
9	 **18**	 **5**	2	100	97
10	 **19**	 **20**	5	100	88
11	 **21**	No reaction	20	0	93[e]
12	Cholesterol (**22**)	No reaction	20	0	98[e]
13	1-Methylcyclohexene (**23**)	No reaction	20	0	nd
14.	 **24**	 **25**	5	100	99

Table 2 (*continued*)

Entry	Substrate[a]	Product	Time [h]	Conversion[b] (%)	Yield[c] (%)
15	 **26**	 **27**	5	100	99
16	 **28**	 **29**	1	100	96

nd—Not determined.

[a] All reactions were run on 1 mmol scale in a solvent mixture of THF (3 mL)/water (1 mL) at 0 °C using 10 mol % $RuCl_3 \times H_2O$.

[b] Determined by NMR.

[c] Isolated yield.

[d] Yield may partly be low due to the volatile nature of the product.

[e] Only starting material recovered.

The experimental procedure[21] involves the addition of $RuCl_3 \times H_2O$ (10 mol %) and $NaBH_4$ to a stirred solution of the olefin in THF and water at 0–5 °C, stirring the reaction mixture at room temperature for 1–5 h followed by dilution with water and extraction to give the reduced product in high yield.

In conclusion, the combination of cheap and readily available sodium borohydride and a catalytic amount of $RuCl_3 \times H_2O$ provides a method for the selective reduction of mono- and disubstituted olefins, whereas trisubstituted olefins and benzyl ethers remain inert. Activated trisubstituted olefins can be reduced under the same reaction conditions. As the complex species responsible for the reductions is generated in situ, and as the reductions are performed under aqueous conditions, this reagent system offers a mild, convenient, efficient and cost effective alternative over other reducing systems.

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References and notes

1. Rylander, P. N. In *Catalytic Hydrogenation in Organic Syntheses*; Academic Press: New York, 1979; pp 1–81.
2. Brunet, J. J.; Gallois, P.; Caubere, P. *J. Org. Chem.* **1980**, *45*, 1937–1945.
3. Brown, C. A.; Ahuja, V. K. *J. Org. Chem.* **1973**, *38*, 2226–2230.
4. Choi, J.; Yoon, N. M. *Synthesis* **1996**, 597–599.
5. Brunet, J. J.; Caubere, P. *Tetrahedron Lett.* **1977**, 3947–3950.
6. Ashby, E. C.; Noding, S. A. *J. Org. Chem.* **1980**, *45*, 1041–1044.
7. Imamoto, T.; Mita, T.; Yokoyama, M. *J. Org. Chem.* **1987**, *52*, 5695–5699.
8. Chung, S. K. *J. Org. Chem.* **1979**, *44*, 1014–1016.
9. Sharma, P. K.; Nielsen, P. *J. Org. Chem.* **2004**, *69*, 5742–5745.
10. $RuCl_3 \times H_2O$ (40.6% Ru) was obtained from ChemPure, Germany.
11. Plietker, B.; Niggemann, M.; Pollrich, A. *Org. Biomol. Chem.* **2004**, *2*, 1116–1124.
12. Griffith, W. P.; Kwong, E. *Synth. Commun.* **2003**, *33*, 2945–2951.
13. Brown, H. C.; Brown, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 1493.
14. Frunzke, J.; Loschen, C.; Frenking, G. *J. Am. Chem. Soc.* **2004**, *126*, 3642–3652.
15. Martin, V. S.; Palazon, J. M.; Rodriguez, C. M. In *Oxidizing and Reducing Agents-Handbook of Reagents for Organic Synthesis*; Burke, S. D., Danheiser, R. L., Eds.; Wiley-VCH: Weinheim, New York, 1999; p 346.
16. Courtney, J. L. In *Organic Syntheses by Oxidation with Metal Compounds*; Mijs, W. J., de Jonge, C. R. H. I., Eds.; Plenum Press: New York, London, 1986; p 445.
17. Lee, H. M.; Smith, D. C., Jr.; He, Z.; Stevens, E. D.; Yi, C. S.; Nolan, S. P. *Organometallics* **2001**, *20*, 794–797.
18. Forman, G. S.; Ohkuma, T.; Hemms, W. P.; Noyori, R. *Tetrahedron Lett.* **2000**, *41*, 9471.
19. Yi, C. S.; Lee, D. W. *Organometallics* **1999**, *18*, 5152–5196.
20. Adair, G. R. A.; Kapoor, K. K.; Scolan, A. L. B.; Williams, J. M. J. *Tetrahedron Lett.* **2006**, *47*, 8943–8944.
21. *Typical experimental procedure*: To a stirred solution of **1**[9] (396 mg, 1 mmol) in a mixture of THF (3 mL) and water (1 mL) at 0–5 °C was added $RuCl_3 \times H_2O$ (31 mg, 0.1 mmol). $NaBH_4$ (76 mg, 2 mmol) was added slowly

and a flocculent black powder began to separate after a few minutes. The mixture was stirred for 1 h at room temperature, water was added and the mixture was extracted with dichloromethane or ethyl acetate (3 × 10 mL). The combined organic phase was washed with a saturated aqueous solution of $NaHCO_3$ (3 × 5 mL), dried (Na_2SO_4), filtered through Celite and concentrated under reduced pressure to give **3** as a white solid. The identity and the purity of the reaction products were established from their spectral (^1H NMR, ^{13}C NMR and MS) data and by comparison with authentic samples, when available.