

Raney Nickel: An Efficient Reagent to Achieve the Chemoselective Hydrogenation of α,β -Unsaturated Carbonyl Compounds

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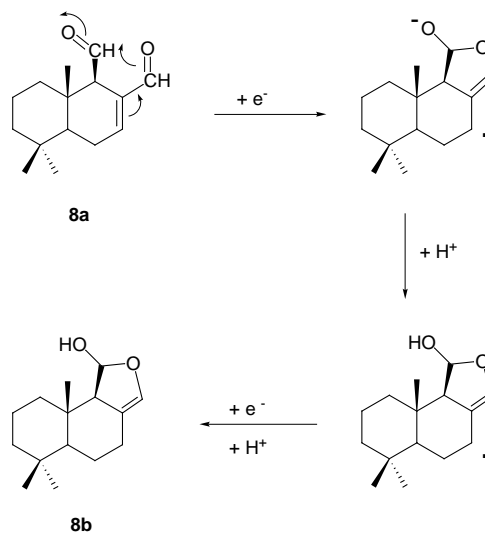
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Abstract: Raney Nickel is an effective reagent to achieve the chemoselective reduction of conjugated olefins in α,β -unsaturated carbonyl compounds that also contain isolated double bonds. Its use is also compatible with a variety of other functional groups.

Key words: hydrogenation, 1,4-addition

The selective reduction of conjugated olefins in α,β -unsaturated carbonyl compounds, that also contain isolated carbon-carbon double bonds, constitutes an important challenge in organic synthesis. This can be achieved by treating the carbonyl derivative with triethylsilane, in the presence of catalytic amounts of (tris(triphenylphosphine)rhodium chloride); **2a** was converted in **2b** following this procedure.¹ Some organic hydrides also allow this transformation to be carried out. Thus, L-, K-selectride and lithium triethylborohydride have been used to reduce α,β -unsaturated esters and ketones; however, this reactivity is not general and depends upon the steric hindrance of the alkene and of the ring size in cyclic ketones, β -alkylation usually completely suppresses the 1,4-reduction. For example, treatment of **1a** with an equivalent of K-selectride afforded **1b** in a quantitative yield;² **2a** gave the dienic alcohol as the only product under similar conditions.² Enantioselective reduction of α,β -unsaturated carboxylates with sodium borohydride in the presence of cobalt complexes has been reported.³ Semmelhack et al have demonstrated that copper salts modify the reactivity of lithium and sodium hydridoaluminate derivatives so that the reagents deliver hydride in a 1,4 fashion to alkenones.⁴ Other copper hydrides have also been successfully used for this purpose.⁵⁻⁸ Keinan et al described that a three-component system comprised of a soluble palladium catalyst, hydrosilane and zinc chloride is capable of efficient conjugate reduction of α,β -unsaturated carbonyl compounds.⁹ A ruthenium complex combined with cyanoborohydride has also been reported for carrying out this transformation.¹⁰ Very recently the selective 1,4-reduction of α,β -unsaturated carbonyl compounds by combined use of bis(1,3-diketonate)cobalt(II) complex and diisobutylaluminium hydride has been described.¹¹ On the other hand, conventional catalytic hydrogenation, using platinum or palladium, is not suitable to achieve the conjugate reduction because of its low selectivity, procuring in most cases the complete reduction of carbon-carbon double bonds.^{12,13}



Scheme

Following the authors' research into the synthesis of valuable compounds from available natural terpenes we have found that Raney Nickel exhibited a good selectivity to carry out the conjugate reduction of α,β -unsaturated carbonyl compounds bearing other isolated carbon-carbon double bonds. In order to establish the scope and synthetic applications of this reaction, the behaviour of Raney Nickel against different α,β -unsaturated carbonyl compounds has been studied and compared with that of palladium over carbon (Table). In most cases, treatment with Raney Nickel in tetrahydrofuran for 20-30 minutes at room temperature afforded the 1,4-reduction compound in a high yield, without reduction of the isolated double bond. (-)-Carvone (**1a**) was reduced after 15 minutes at -0°C ; the isomerization of the isolated double bond took place when the temperature or reaction time was increased, affording carvacrol in a high yield. α,β - γ,δ -unsaturated compounds, such as **4a**, were converted into the completely saturated compound; the α,β -unsaturated compound was obtained when the temperature or reaction time was decreased.

The hydrogenation of conjugated olefin in the presence of palladium over carbon is slower. Moreover, this reaction is less selective: in most cases the 1,4-addition took place with simultaneous reduction of the isolated carbon-carbon double bond. Thus, compounds **2a**, **3a**, **5a**, **6a** and **13a** re-

Table 1,4-Reduction of Conjugated Enones and Related Compounds with Raney Nickel

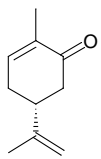
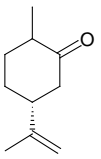
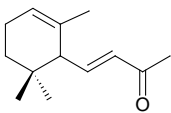
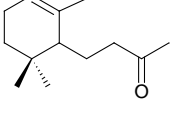
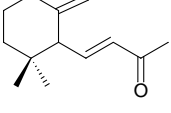
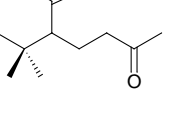
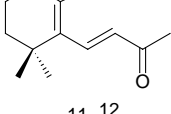
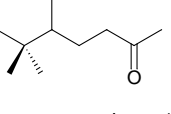
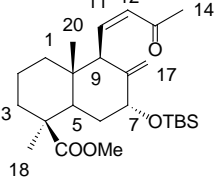
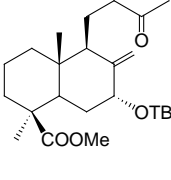
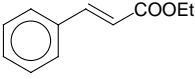
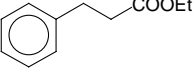


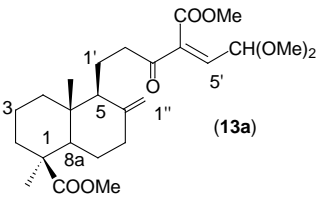
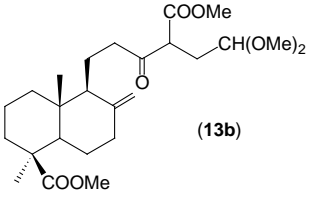
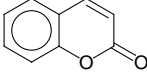
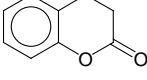
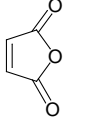
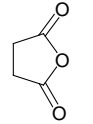
Substrate	Product	Reaction Time	Yield
 (1a)	 (1b)	20 min.	90%
 (2a)	 (2b)	30 min.	95%
 (3a)	 (3b)	30 min.	92%
 (4a)	 (4b)	15 min.	quantitative
 (5a)	 (5b)	25 min.	96%
 (11a)	 (11b)	60 min.	93 %
 (12a)	 (12b)	30 min.	90 %
 (13a)	 (13b)	30 min.	96 %
 (14a)	 (14b)	15 min.	90 %
 (15a)	 (15b)	20 min.	92 %

Table (continued)

Substrate	Product	Reaction Time	Yield
 (6a)	 (6b)	30 min.	90 %
 (7a)	 (7b)	10 min.	quantitative
 (8a)	 (8b)	20 min.	95 %
 (9a)	 (9b)	30 min.	93 %
 (10a)	 (10b)	30 min.	90 %
 (16a)	 (16b)	15 min.	93 %
 (17a)	 (17b)	60 min.	80 %
 (18a)	 (18b)	5 min.	quantitative

main unaltered after treating for 30 min with palladium over carbon under hydrogen atmosphere, and complete hydrogenation of all the carbon-carbon double bond was observed at longer reaction time: however prolonged treatment of these compounds with Raney Nickel did not affect the isolated double bond, so making easier the reaction control.

Although the mechanism for this reaction has not been studied yet, it seems probable that the reaction starts when an electron is transferred from the metal to the β -olefinic carbon. The formation of the hemiketal **8b** from poligodol (**8a**) is in accordance with this supposition (Scheme).

In summary, Raney Nickel is an efficient reagent to carry out selective 1,4-reduction of α,β -unsaturated carbonyl compounds that also contain isolated carbon-carbon double bonds. A variety of other functional groups remain unaltered under the reaction conditions.

Acknowledgement

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References and notes

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- (14) All new compounds were fully characterized spectroscopically and had satisfactory high resolution mass spectroscopy data. Compounds **5a**, **6a** and **13a** are intermediates of our synthetic research and are a part of unpublished results. **8a** is described in the reference 15, and **8b** is reported in the reference 16.
- Selected data:**
- 5a** ¹H NMR (400 MHz, CDCl₃) δ: 0.01 (s, 3H, Me-Si-CH₃), 0.07 (s, 3H, Me-Si-CH₃), 0.68 (s, 3H, Me-10), 0.89 (s, 9H, CH₃-Bu^tSi), 1.17 (s, 3H, Me-4), 1.73-2.02 (m, 3H), 2.29 (s, 3H, Me-13), 2.99 (d, J=10.4 Hz, 1H, H-9), 3.65 (s, 3H, Me-COOCH₃), 4.30 (t, J=2.8 Hz, 1H, H-7), 4.48 (s, 1H, H-17), 4.90 (s, 1H, H-17'), 6.09 (d, J=15.8 Hz, 1H, H-12), 6.82 (dd, J=15.8 and 10.4 Hz, H-11).
- 5b** ¹H NMR (300 MHz, CDCl₃) δ: 0.00 (s, 3H, Me-Si-CH₃), 0.05 (s, 3H, Me-Si-CH₃), 0.48 (s, 3H, Me-10), 0.87 (s, 9H, CH₃-Bu^tSi), 1.01 (ddd, J=17.5, 13.2 and 4.2 Hz, 1H, H-1_{ax}), 1.12 (s, 3H, Me-4), 2.09 (s, 3H, Me-13), 2.16 (da, J=15 Hz, 1H, H-9), 2.26 (ddd, J=15.2, 9.0 and 6.7 Hz, 1H, H-12B), 2.51 (ddd, J=14, 9.2 and 4.7 Hz, 1H, H-12A), 3.61 (s, 3H, Me-COOCH₃), 4.28 (d, J=3.0 Hz, 1H, H-7), 4.46 (s, 1H, H-17), 4.92 (s, 1H, H-17').
- 6a** ¹H NMR (400 MHz, CDCl₃) δ: -0.01 (s, 3H, Me-Si-CH₃), 0.04 (s, 3H, Me-Si-CH₃), 0.47 (s, 3H, Me-4a), 0.86 (s, 9H, CH₃-Bu^tSi), 1.12 (s, 3H, Me-1), 1.13 (ddd, J=17.4, 13.4 and 4.1 Hz, 1H, H-4_{ax}), 1.48-1.55 (m, 2H), 1.77-1.98 (m, 6H), 2.15 (da, J=12.2 Hz, 1H, H-1_{eq}), 2.40 (ddd, J=15.7, 9.2 and 6.6 Hz, H-2'A), 2.67 (ddd, J=14.0, 9.2 and 4.6 Hz, H-2'B), 3.32 (s, 6H, Me-CH(OCH₃)₂), 3.59 (s, 3H, Me-COOCH₃), 4.28 (t, J=2.9 Hz, 1H, H-7), 4.47 (s, 1H, H-1'A), 4.92 (s, 1H, H-1'B), 4.93 (d, J=4.1 Hz, 1H, H-6'), 6.31 (dd, J=16.1 and 1.3 Hz, 1H, H-4'), 6.54 (dd, J=16.1 and 4.1 Hz, 1H, H-5').
- 6b** ¹H NMR (300 MHz, CDCl₃) δ: -0.04 (s, 3H, Me-Si-CH₃), 0.06 (s, 3H, Me-Si-CH₃), 0.47 (s, 3H, Me-4a), 0.87 (s, 9H, CH₃-Bu^tSi), 1.12 (s, 3H, Me-1), 1.49-1.54 (m, 2H), 1.81-1.96 (m, 6H), 2.09 (sa, 1H, H-5), 3.33 (s, 6H, Me-CH(OCH₃)₂), 3.60 (s, 3H, Me-COOCH₃), 4.28 (t, J=3.0 Hz, 1H, H-7), 4.35 (t, J=5.6 Hz, H-6'), 4.46 (s, 1H, H-1'A), 4.91 (s, 1H, H-1'B).
- 13a** ¹H NMR (400 MHz, CDCl₃) δ: 0.50 (s, 3H, Me-4a), 1.04 (ddd, J=17.5, 13.9 and 4.3 Hz, 1H, H-4_{ax}), 1.15 (s, 3H, Me-1), 1.27 (dd, J=12.2 and 2.9 Hz, 1H, H-8a), 1.50 (dt, J=10.8 and 3.5 Hz, 1H, H-1_{eq}), 1.54-1.61 (m, 3H), 1.69-1.90 (m, 4H), 1.91-1.99 (m, 2H), 2.14 (da, J=13.4 Hz, 1H, H-5_{eq}), 2.36 (dt, J=11.9 and 3.3 Hz, 1H, H-7), 2.42-2.55 (m, 1H, H-2'A), 2.75-2.85 (m, 1H, H-2'B), 3.27 (s, 6H, Me-CH(OCH₃)₂), 3.58 (s, 3H, Me-COOCH₃), 3.73 (s, 3H, Me-COOCH₃), 4.44 (s, 1H, H-1'A), 4.82 (s, 1H, H-1'B), 5.0 (d, J=4.3, 1H, H-6'), 6.64 (d, J= 4.3 Hz, 1H, H-5').
- 13b** ¹H NMR (300 MHz, CDCl₃) δ: 0.51 (s, 3H, Me-4a), 1.06 (ddd, J=17.5, 13.4 and 4.1 Hz, 1H, H-4_{ax}), 1.18 (s, 3H, Me-1), 1.29 (dd, J=12.2 and 2.9 Hz, 1H, H-8a), 1.54-1.56 (m, 2H), 1.81 (dt, J=9.8 and 3.3 Hz, H-4_{eq}), 1.85-1.92 (m, 4H), 2.13-2.20 (m, 2H), 2.38-2.41 (m, 2H), 3.31 (s, 6H, Me-CH(OCH₃)₂), 3.61 (s, 3H, Me-COOCH₃), 3.70 (s, 3H, Me-COOCH₃), 4.33 (t, J=5.3 Hz, 1H, H-6'), 4.43 (s, 1H, H-1'A), 4.85 (s, 1H, H-1'B).
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- (17) **Typical experimental procedure:**
0.8 g of an aqueous suspension of Raney Nickel (Fluka, cat. no. 83440) was added to a stirred solution of compound (1.0 mmol) in tetrahydrofuran (10 ml) and the mixture was further stirred at room temperature (except for compound **1a**, which was reacted at 0°C) for the specified time (Table). The mixture was diluted with ether and filtered through silica gel, and the solvent was evaporated to yield the reduced compound.

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