Raney Nickel: An Effective Reagent for Reductive Dehalogenation of Organic Halides

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Abstract: Raney Nickel is an effective reagent to achieve the chemoselective reductive dehalogenation of organic halides. Fluorides and vinyl halides are unreactive under the used experimental conditions.

Key words: reduction, halides, chemoselectivity

The present authors have previously reported the effectiveness of Raney nickel to accomplish the chemoselective reduction of aldehydes in the presence of ketones and the reduction of conjugated olefins in α,β−unsaturated carbonyl compounds, which also contain isolated carbon-carbon double bonds.[1,2] Our recent studies have revealed that this reagent may also be very effective in carrying out the chemoselective reduction of organic halides.

The replacement of halogen by hydrogen has attracted great interest among organic chemists, stimulating considerable investigation, and a number of methods have been reported hitherto.[3] A variety of reducing agents are now available, and many of them are successfully applied to practical organic synthesis. Metallic zinc in acetic acid has been efficiently used for reductive dehalogenation.[4] The use of metal hydrides has also been found effective. Thus, lithium aluminum hydride reduces alkyl halides to the corresponding hydrocarbons, with good yields.[5] Sodium borohydride in aprotic polar solvents reduces primary, secondary, tertiary and benzyl halides, in the presence of nitro, ester or carboxylic groups, which remain unaltered.[6] Stannanes have been used extensively to replace halogen by hydrogen.[7] Tri-n-butyltin hydride is able to reductively replace iodides and bromides at room temperature, and chlorides under more extreme conditions; fluorides are not reactive. This reagent exhibits high chemoselectivity and is compatible with a variety of other functional groups. A drawback of this reagent is its toxicity.

Catalytic hydrogenation has also been used to achieve the reductive dehalogenation of organic halides, the reaction rate being dependent on the structural feature and the halogen involved. For example, alkyl iodides and alkyl bromides are converted into the corresponding hydrocarbons by hydrogenation over palladium on carbon.[8] Williams et al. reported that the Raney nickel catalyst is readily deactivated by the halide during hydrogenation and, therefore, massive amounts of the catalyst are usually required in order to improve yields.[9,10] Recently, Yus et al. have described that $NiCl_2 \cdot 2H_2O$-Li-DTBB (cat.) reduces organic halides in high yields.[11]

During our research into the use of Raney nickel as a chemoselective reductor we found that activated Raney nickel is an effective reagent in the reduction of organic halides. Some representative examples are summarized in the table, which shows that benzyl halides (**5a-8a**) and α-halocarbonyl and related compounds (**1a-3a**, **9a-11a**) are easily reduced after treating with Raney nickel in tetrahydrofuran at room temperature for 45 min-2 h. The treatment of a solution of bromolactone **4a** in tetrahydrofuran with Raney nickel at room temperature for 5 min yielded γ−lactone **4b** in 80%; the carbon-carbon double bond was also reduced when the reaction was allowed to proceed for longer times (1 h), and the lactone **4c** was obtained in 90%. Alkyl iodides (**12a-15a**) react under the same reaction conditions after 1-6 h. Alkyl bromides (**16a-22a**) exhibit lower reactivity. Alkyl chlorides (**23a-26a**) were reduced under refluxing tetrahydrofuran, in the presence of an excess of Raney nickel (double the quantity used for the other halides); under these conditions the carbonyl group of **25a** was also reduced. Reductive dehalogenation of chloride **23a** was carried out at room temperature after 1.5 h; under these conditions, the quinoline ring was also reduced.

Allyl halides exhibited a different behavior which will be reported in a forthcoming paper.

In summary, a new synthetic application of Raney nickel has been developed. This reagent reduces organic halides with high chemoselectivity; it has some advantages over other methods, such as easy manipulation and mild conditions. The order of reactivity is benzyl = α-halocarbonyl > iodides > bromides > chlorides. Fluorides and vinyl halides do not react.

Typical experimental procedure

1.5 g of a slurry of commercial aqueous Raney nickel (Fluka, cat. no. 83440)* was added to a solution of halide (150 mg) in THF (10 mL) and the mixture was further vigorously stirred at room temperature or under reflux (except for chlorides, which were refluxed in the presence of double amount of Raney nickel) for the especified time. The mixture was diluted with ether and filtered through silica gel, and the solvent was evaporated to yield the reduced compound.

* The Raney nickel was weighed as an aqueous slurry after removing four fifth of water.

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Table Reduction of Halides with Raney Nickel

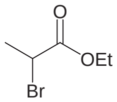
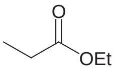
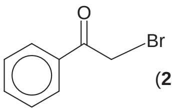
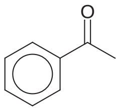
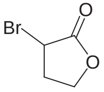
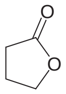
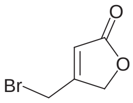
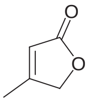
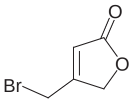
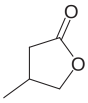
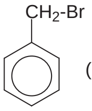
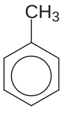
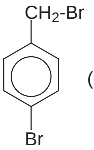
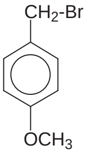
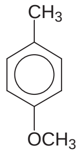
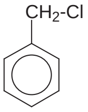
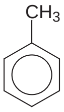
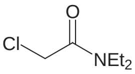
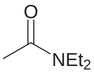
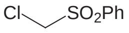
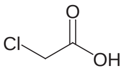
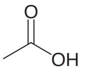
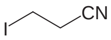
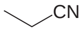
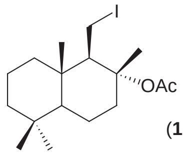
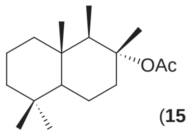
Substrate		Product		Reaction Time	Yield
	(**1a**)		(**1b**)	45 min.	>90 %[a]
	(**2a**)		(**2b**)	45 min.	90 %
	(**3a**)		(**3b**)	45 min.	95 %
	(**4a**)		(**4b**)	5 min.	80 %
	(**4a**)		(**4c**)	1 h.	90 %
	(**5a**)		(**5b**)	1 h.	>90 %[a]
	(**6a**)		(**6b**)	1 h.	90 %
	(**7a**)		(**7b**)	1 h.	97 %
	(**8a**)		(**8b**)	1 h.	>90 %[a]
	(**9a**)		(**9b**)	2 h.	>90 %[a]
	(**10a**)	CH_3-SO_2Ph	(**10b**)	2 h.	>90 %[a]
	(**11a**)		(**11b**)	2 h.	90 %
I-$(CH_2)_{10}$-I	(**12a**)	CH_3-$(CH_2)_8$-CH_3	(**12b**)	6 h.	92 %
I-$(CH_2)_8$-I	(**13a**)	CH_3-$(CH_2)_6$-CH_3	(**13b**)	6 h.	>90 %[a]
	(**14a**)		(**14b**)	6 h.	>90 %[a]
	(**15a**)		(**15b**)	1 h 45 min.	100 %

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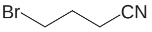
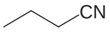
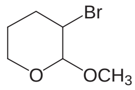
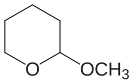
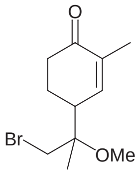
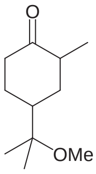
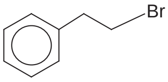
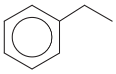
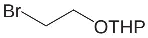
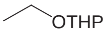
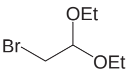
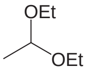
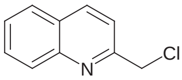
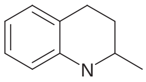
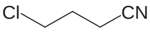
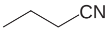
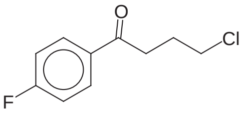
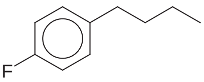
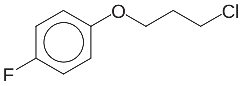
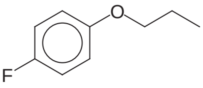
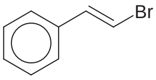
Table (continued)

Substrate	Product	Reaction Time	Yield
Br-(CH$_2$)$_8$-Br (**16a**)	CH$_3$-(CH$_2$)$_6$-CH$_3$ (**16b**)	12 h.	>90 %[a]
 (**17a**)	 (**17b**)	12 h.	85 %
 (**18a**)	 (18b)	12 h.	90 %
 (**19a**)	 (**19b**)	12 h.	87 %[b]
 (**20a**)	 (**20b**)	12 h.	89 %
 (**21a**)	 (**21b**)	12 h.	95 %
 (**22a**)	 (**22b**)	12 h.	>90 %[a]
 (**23a**)	 (**23b**)	1 h 30 min.	85 %
 (**24a**)	 (**24b**)	15 h., reflux	75%
 (**25a**)	 (**25b**)	15 h., reflux	95 %
 (**26a**)	 (**26b**)	15 h., reflux	30 %[c]
Cl$_2$CH-CHCl$_2$ (**27a**)	ClCH$_2$-CH$_2$Cl (**27a**)	4 h.	>90 %[a]
 (**28a**)	No Reaction	24 h.	----

[a] Yields based on ^{1}H NMR data of crude containing residual solvent.

[b] Double amount of Raney Nickel was used.

[c] Yield based on the ^{1}H NMR spectrum of crude.

References and Notes

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