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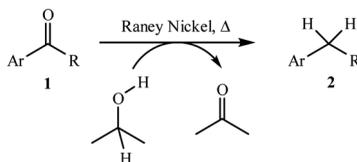
DEOXYGENATION OF AROMATIC KETONES USING TRANSFER HYDROGENOLYSIS WITH RANEY NICKEL IN 2-PROPANOL

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GRAPHICAL ABSTRACT



Abstract Aryl ketones are readily deoxygenated to their corresponding aryl alkanes upon treatment with Raney nickel catalyst in boiling 2-propanol.

Keywords Deoxygenation; hydrogenolysis; hydrogen transfer; ketone reduction; Raney nickel

The process of reducing an aryl ketone to an aryl alkane is a widely used and thoroughly studied synthetic technique.^[1–3] Conventional reduction methods commonly used to reduce the aryl ketone functional group to an aryl alkane include the Wolff–Kishner reduction and the Clemmensen reduction.^[1] The Wolff–Kishner reduction features basic conditions, whereas the Clemmensen reduction features acidic conditions. This often precludes use of precursors that are base- or acid-sensitive, respectively.

Catalytic transfer hydrogenolysis (CTH) has long been known as a method of reducing a variety of functional groups.^[4,5] This process features the catalytic transfer of hydrogen from a hydrogen donor—various combinations of catalysts and hydrogen donor agents have been studied for CTH and have been reviewed.^[5,6] Raney nickel has been shown to efficiently catalyze the transfer of hydrogen from various hydrogen donors to effect a wide variety of reductions—some of these include the conversion of aromatic nitro compounds to anilines,^[7] nitriles to

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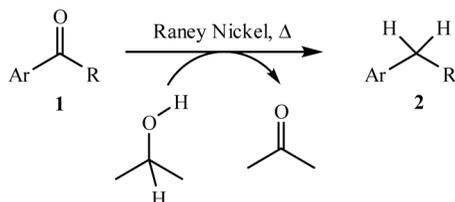


Figure 1. Deoxygenation of aryl ketones by treatment with Raney nickel in refluxing 2-propanol.

amines,^[8] and aryl carbonyl compounds to aryl methanes.^[9] This is the first time that 2-propanol has been used as a CTH donor with Raney nickel to reduce aryl ketones to aryl alkanes.

Mebane and coworkers have previously shown that ketones are readily reduced to secondary alcohols using CTH.^[10] Furthermore, Mebane and coworkers have also shown that benzylic alcohols can be deoxygenated to their corresponding aryl alkanes using CTH.^[11] It remained for us to demonstrate that the conversion from ketone to aryl alkane could be efficiently carried out as a one-pot procedure using Raney nickel and refluxing 2-propanol. Our results are described herein.

In this report, we describe a simple, mild alternative to the harsh conditions required in the Clemmensen and Wolff–Kishner reductions. Our procedure is carried out under neutral conditions in refluxing 2-propanol with the reaction vessel open to the atmosphere. The experimental procedure for this method of reduction is simple and straightforward and affords aryl alkanes in good yields. The overall reaction is described in Fig. 1, and a summary of our results is presented in Table 1. As seen in Table 1, isolated yields for the less volatile aryl alkanes were very good (entries 1–5). The more volatile aryl alkanes (entries 6 and 7) were not isolated because of extensive product loss while removing the 2-propanol solvent by rotary evaporation. Yields of all aryl alkanes as determined by GC were essentially quantitative. In a typical run, the aryl ketone (0.5 g) was refluxed (container open to the atmosphere) in a magnetically stirred suspension of Raney nickel (2.5 g) in 2-propanol (10 mL). The progress of the reaction was conveniently monitored by thin-layer chromatography (TLC). Good yields were generally achieved within a few hours at the most.

Table 1. Deoxygenation of aryl ketones by treatment with Raney nickel in refluxing 2-propanol

Entry	Aryl ketone	Reduction product	Time (h)	Yield (%)
1	Benzophenone	Diphenylmethane	1	98
2	Acetovanillone	4-Ethyl-2-methoxyphenol	1.5	82 ^a
3	Hexanophenone	Hexylbenzene	1	85
4	Decanophenone	1-Phenyldecane	0.3	99
5	o-Hydroxypropiophenone	2-Propylphenol	2.5	94
6	Valerophenone	Butylbenzene	1	— ^b
7	Acetophenone	Ethylbenzene	1	— ^b

^aAnalysis of the product revealed that 4-ethylphenol was formed in 17% yield.

^bNo isolated yield was determined because of the volatility of the product; gas chromatography indicated complete conversion to deoxygenated product.

Upon completion of the reaction, the aryl alkane could be isolated after suitable workup as described in the experimental section. All of the aryl alkanes prepared in this study are known. Therefore, product identities were confirmed by comparison of NMR and mass spectral data with authentic samples or literature spectra. In some instances, trace amounts of other reduction products were observed in addition to the deoxygenated aromatic compound. In these cases, the aromatic ring moiety underwent various degrees of reduction. As these products represented a very minor component of the product mixture (<5%), this did not cause yields to suffer on the reaction time scales we were using.

To demonstrate that the presence of Raney nickel was indeed required, a control experiment was run in which benzophenone (0.506 g, 2.78 mmol) was refluxed in 2-propanol (15 mL) for 3 h (no Raney nickel added). No conversion to diphenylmethane was observed. By comparison, in the presence of Raney nickel (2.5 g), after 1 h of heating, nearly quantitative conversion to diphenylmethane had been realized. This established that the presence of Raney nickel is necessary for the reaction to occur.

To verify that the mechanism of reduction was indeed CTH, an experiment was set up to verify that acetone was being generated as a by-product of the redox reaction. Hexanophenone (0.512 g, 2.64 mmol) was refluxed in a magnetically stirred suspension of Raney nickel (2.5 g) in 2-propanol (15 mL) for 0.5 h with the container open to the atmosphere. A Dean–Stark trap was used to collect distillate over the course of the reaction. The distillate was tested for the presence of acetone by mixing several drops of a 3% solution of 2,4-dinitrophenylhydrazine with a few drops of distillate. The formation of a yellow precipitate suggested a positive test for the presence of acetone. Examination of the melting point of the precipitate revealed a melting point identical to that of acetone 2,4-dinitrophenylhydrazone (126–128 °C).^[12] A source has reported that this test easily detects 1 part of acetone in 500 to 1000 parts of 2-propanol.^[13]

In our study, a 1:5 (*w/w*) substrate-to-catalyst ratio was used to deoxygenate the aryl ketones. Because this is a relatively large excess of Raney nickel, we were interested in determining whether the Raney nickel could be recycled. To verify that the deoxygenation reaction was indeed catalytic with respect to the Raney nickel, an experiment was set up to test whether the catalyst could be recycled without any loss of activity. We found that a given batch of Raney nickel catalyst could be used repeatedly (at least six times) without any loss of activity. Prior to reuse, the catalyst was washed with 2-propanol (3 × 10 mL). In a given run, benzophenone (0.50 g, 2.7 mmol) was refluxed in 2-propanol (10 mL) for 1 h. Yields for the reaction were greater than 93% for each run.

Since other Raney catalysts have been observed to be effective at reducing benzylic alcohols,^[11] we were curious to see if these would also be effective at reducing aryl ketones. The two additional Raney catalysts explored were Raney cobalt and Raney copper. For each catalyst, a reaction was set up in which benzophenone (0.25 g, 1.4 mmol) was refluxed in a magnetically stirred suspension of the Raney catalyst (1.25 g) in 2-propanol (10 mL) for 1 h with the container open to the atmosphere. No change was observed with either catalyst. The experiments were repeated twice, once using acid catalyst (1 drop conc. HCl) and once using base catalyst (1 pellet solid NaOH), but again, in each case, unreacted starting material was recovered.

In conclusion, aryl ketones are readily reduced to their corresponding aryl alkanes when refluxed in a suspension of Raney nickel in 2-propanol. This affords an attractive method of reducing ketones in that it offers cheap and readily available reagents, operational simplicity, easy product isolation, and excellent, clean product yields. Our laboratory continues to explore the CTH of aryl ketones using 2-propanol as a hydrogen donor source.

EXPERIMENTAL

Raney 2800 nickel was obtained from W. R. Grace Company, Chattanooga. The catalyst was washed prior to use with distilled water (3x) and 2-propanol (3x). Proton NMR spectra were recorded on a Varian 60-MHz spectrometer using tetramethylsilane (TMS) as an internal reference. Mass spectra (MS) were recorded on a ThermoElectron PolarisQ GC-MS. The proton NMR spectra and mass spectra of the aryl alkanes prepared in this work were identical to authentic spectra.

As an illustrative example of the deoxygenation procedure, benzophenone (0.499 g, 2.74 mmol) was refluxed in a magnetically stirred suspension of Raney nickel (2.5 g) in 2-propanol (10 mL) for 1 h with the container open to the atmosphere. After cooling to room temperature, the organic layer was decanted from the Raney nickel, and the catalyst was washed with 2-propanol (3×10 mL). Raney nickel is paramagnetic and clings to the magnetic stir bar, which facilitates decantation. The combined organic layers were filtered through celite and concentrated by rotary evaporation to yield a colorless oil (0.452 g, 2.69 mmol, 98.0%). Its spectral data (NMR, MS) were identical to those of authentic diphenylmethane.

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