



*Dedicated to the memory of Professor Margareta Avram
on the remembrance of her 100th anniversary*

REDUCTION OF α,β -UNSATURATED CARBONYL COMPOUNDS AND 1,3-DIKETONES IN AQUEOUS MEDIA, USING A RANEY Ni-AL ALLOY

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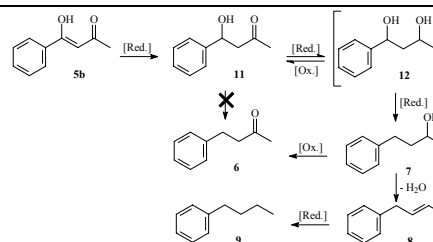
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Received May 7, 2019

The treatment of α,β -unsaturated carbonyl compounds and 1,3-diketones with Raney Ni-Al alloy in aqueous media yielded as major reaction products the corresponding saturated alcohols and/or the corresponding hydrocarbons, in a complete transformation of the starting material.



INTRODUCTION

In light of the **Green Chemistry** principles, an interesting and appealing tool for organic chemists is aqueous two-phases homogenous organometallic catalysis.¹ One of the first applications of this method regarded hydrogenation processes using either molecular hydrogen or any other hydrogen donor.²⁻⁵ Thus, numerous carbon-heteroatom double bonds were successfully reduced.⁶⁻⁹ One application of these catalytic systems is the regioselective reduction of α,β -unsaturated aldehydes to unsaturated alcohols or saturated aldehydes.¹⁰⁻¹⁷ However, these catalysts proved to be quite sensitive and their recycling difficult because of poisoning adsorption of organic compounds on their surface. Mechanistic studies on the hydrogenation reaction in these systems clearly

showed that water was not an inert solvent, but influenced both the rate and the selectivity of the processes, actively participating in the process as a hydrogen donor. In the recent years, simpler catalysts were tested in the same purpose: reduction processes in aqueous media. Thus, Ni and various other Raney alloys were tested in aqueous media for the reduction of carbonyl compounds,¹⁸⁻²⁰ aromatic rings,²¹ nitroderivatives²² and even halogenated compounds, in a hydrodehalogenation process.²³⁻²⁵

Consequently to our investigation of the aqueous reduction of cinnamaldehyde,²⁶ we considered opportune to extend this particulate research to the reduction of other α,β -unsaturated carbonyl compounds as well as of 1,3-dicarbonyl compounds (since these species exist in 85% proportion as α,β -unsaturated carbonyl compounds

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through enolization of one of the carbonyl moieties) using Raney Ni-Al and water as solvent and hydrogen donor.

RESULTS AND DISCUSSION

Mesityl oxide **1a**, cyclohexenone **1b** and 3-methylcyclohexenone **1c** were the key-compounds chosen for this study. The results of the aqueous reduction of these compounds are summarized in Table 1.

A notable result is the complete transformation in every experiment of all 3 starting materials. A second result is the confirmation of the higher sensitivity toward reduction of the >C=C< double bond than of the carbonyl moiety; this fact is more relevant in the case of mesityl oxide, when, according to the reaction time, either 4-methyl-2-pentanone or 4-methyl-2-pentanol is obtained as major product. A faster transformation seemed to occur when working in a sealed environment. On the other hand, total reduction of cyclic α,β -unsaturated carbonyl compound proceeds much

more rapidly, the corresponding alcohol being formed in less than 1 hour. This result is in accordance with already reported results for the reduction of C=C bond of unsaturated carbonyl compounds over Ni/C catalyst, in organic solvents.²⁷

Moreover, when the methyl group is present on the C3 of cyclohexenone, the reduction is even swifter, confirming thus our previous results for substituted cinnamaldehydes,²⁶ when the existence of an electron-donating substituent such as a methyl group on the carbon double bond accelerated the process.

This specific transformation is accomplished with a good stereoselectivity, the *cis* form of the methylcyclohexanol being recorded with a good diastereomeric excess (approximately 3:1, exactly the opposite of the one recorded through a more classical reduction, with a phosphine catalyst, in *t*-BuOH:C₆H₆ mixture and molecular H₂ as reagent²⁸). This ratio between *cis* and *trans* isomers doesn't seem to be influenced by the reaction time, nor by the reaction conditions (open or sealed tube).

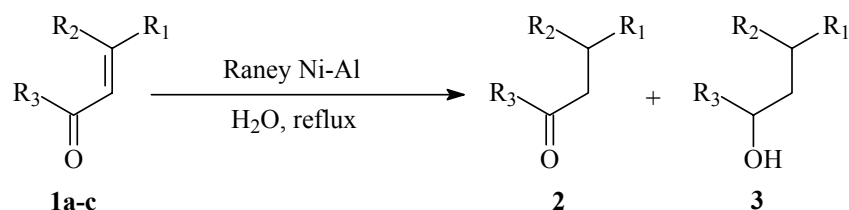


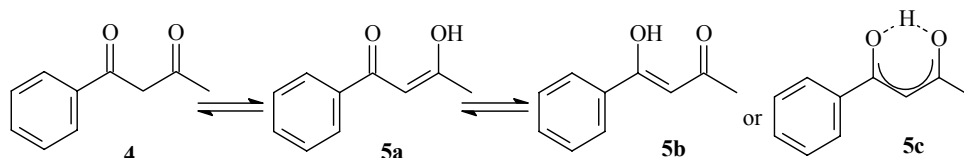
Table 1

Reduction of various α,β -unsaturated carbonyl compounds with Raney Ni-Al

Entry	Substrate	Reaction vessel	Reaction time (h)	Result (yield, %) ^a		
				1	2	3
1	 1a	open flask	1/3	-	97.2	2.8
2			1/2	-	97.1	2.9
3			1	-	90.3	9.7
4			10	-	61.0	39.0
5		24	-	18.0	82.0	
6		sealed flask	1/3	-	64.7	35.3
7			2/3	-	40.6	59.4
8			1	-	7.7	92.3
9	 1b		open flask	1/6	9.8	49.0
10		1/3		-	18.4	81.6
11		1/2		-	2.9	97.1
12		2/3		-	-	100
13		1, 3, 5, 24		-	-	100
14	 1c	open flask	1/3	-	-	73.8 <i>cis</i> + 26.2 <i>trans</i>
15			1	-	1	71.9 <i>cis</i> + 27.1 <i>trans</i>
16			2	-	0.9	72.8 <i>cis</i> + 26.3 <i>trans</i>
17			3	-	4.2	72.5 <i>cis</i> + 23.3 <i>trans</i>
18			5	-	0.9	73.5 <i>cis</i> + 25.6 <i>trans</i>
19			24	-	-	74.5 <i>cis</i> + 25.5 <i>trans</i>
20			sealed flask	24	-	-

^aGC-MS yields

In all cases, the final reaction product is the corresponding alcohol. No further transformation products from here were recorded: neither oxidation or Clemmensen-type reduction compounds were formed (as in the case of cinnamaldehyde²⁶), assessing the greater stability of the secondary alcohol.



When submitted to the reductive process with Raney Ni-Al alloy, in the same conditions as the α,β -unsaturated carbonyl compounds previously used, benzoylacetone afforded a wider distribution

In order to thoroughly investigate this aspect, we turned our attention to a 1,3-dicarbonyl compound, benzoylacetone **4**. Benzoylacetone is a β -diketone that upon enolization forms a *cis*- β -keto-enol structure with an intramolecular hydrogen bond, which potentially can be either asymmetrical as in **5a** and **5b** or symmetrical as in **5c**.²⁹⁻³²

of products, including hydrocarbons **8** and **9** (but no aromatic ring reduction products), without any recovery of the starting diketone. Complete results are presented in Table 2.

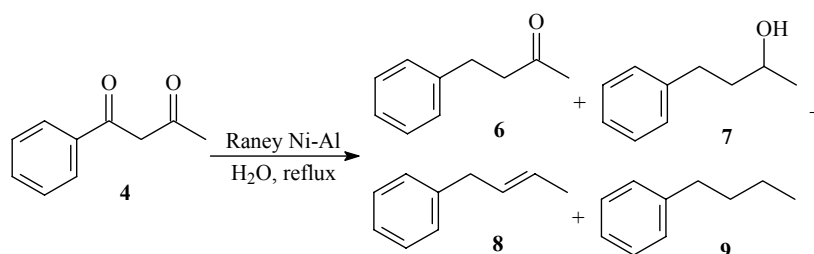


Table 2

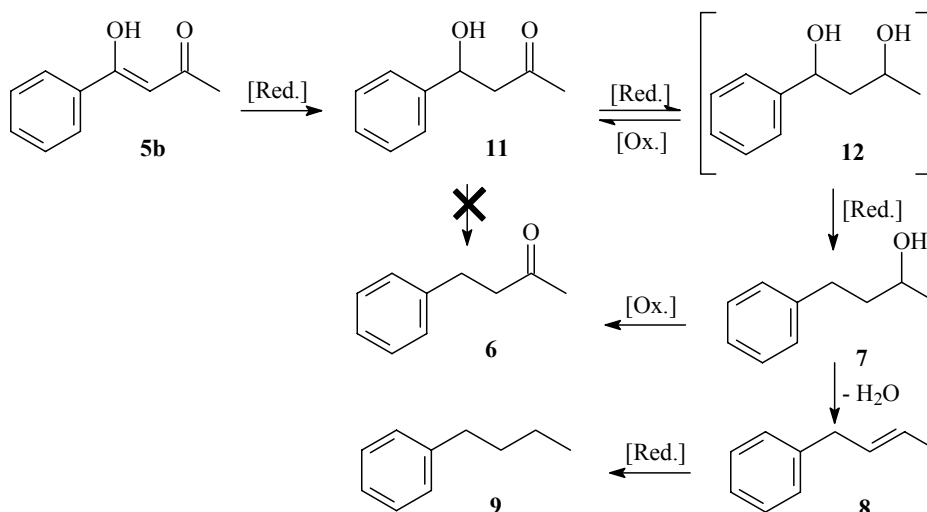
Reduction of benzoylacetone with Raney Ni-Al^a

Entry	Reaction time (h)	Result (yield, %) ^b				
		4	6	7	8	9
1	1	-	8.9	46.9	7.3	28.0
2	2	-	7.3	48.5	13.2	35.7
3	3	-	2.6	41.8	6.2	47.7
4	5	-	3.9	40.3	6.7	51.4
5	10	-	1.9	25.1	11.8	60.9

^aOpen flask only; ^bGC-MS yields

It is interesting to note that the main reaction products are the alcohol **7** and *n*-butylbenzene **9**, and longer the reaction time, the higher the proportion of the latter. Taking into account that the starting 1,3-diketone is in its enolic form, the electron-donating $-OH$ group will accelerate the reduction of the $>C=C<$ double bond;^{33,34} since the result of this first step is the 4-phenyl-2-butanol **7**, then the starting structure must be **5b**. Indeed, it has been proved that in aqueous media 1,3-diketones exist mostly in their enolic tautomer³⁵ (e.g. dimedone **10a** has 85% enolic form **10b** in water). The intermediate of this process would be a β -keto-alcohol of type **11** that suffered a subsequent reduction process. It would be easier to accept a Clemmensen-type reduction of the hydroxyl group,

but the $>C=O$ group is more likely to be transformed in this case into a $-OH$ function. Therefore, a 1,3-diol would be formed. Now, the most sensitive of the two $-OH$ groups toward reduction will be transformed into a methylene group, while the most sensitive $-OH$ group toward oxidation will regenerate a $>C=O$ group, yielding finally the ketone **6**. Indeed, we have previously established that the treatment of a substrate such as cinnamaldehyde with Raney alloys is in fact an oxido-reductive process, and not a simple reduction.²⁶ Subsequent dehydration of the alcohol **7** (with formation of the alkene **8**) and the reduction of the newly formed $>C=C<$ double bond will yield the final *n*-butylbenzene **9**. A general reaction pathway is proposed in the following scheme:



In the spirit of confirmation of the product distribution and comparison with the results of the treatment of cyclic α,β -unsaturated ketones, we

submitted dimedone **10** to the same reaction protocol (Table 3). The expected reaction products for dimedone are presented in the following scheme.

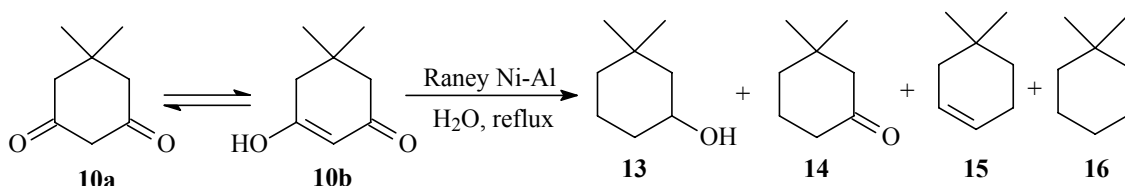


Table 3

Reduction of dimedone with Raney Ni-Al^a

Entry	Reaction time (h)	Result (yield, %) ^b				
		10 (recovery)	13	14	15	16
1	1	47	53	-	-	-
2	2	22	62	12	-	4
3	5	14	69	11	-	6
4	10	3	73	4	-	20

^aOpen flask only; ^bGC-MS yields

Interestingly, no alkene was observed. The main product was dimethyl cyclohexanol **13** (the alcohol was also the main reaction product in α,β -unsaturated ketones reduction), along with small amounts of ketone and of the corresponding hydrocarbon, dimethylcyclohexane **16** (as for the reduction of the other 1,3-diketone used in this study, benzoylacetone **4**). For a comparison, in much earlier processes involving dimedone same reaction products were obtained: in a catalytic hydrogenation on Ni Raney, Henshall obtained ca 72% 3,3-dimethylcyclohexanol,³⁶ while Wibaut and Gitsels, upon catalytic reduction (Adam's Pt) in 96% ethanol containing 1% HCl, obtained about 58% 3,3-dimethylcyclohexanol and 10% of 1,1-dimethylcyclohexane.³⁷

The advantage of this procedure is that it obviously doesn't need gaseous hydrogen, water serving as hydrogen donor. Such a methodology, associated with our previous study on cinnamaldehyde,²⁶ shows that aqueous treatment with Raney alloys of various phenyl keto-compounds can be a useful tool for the generation of substituted benzenes with linear hydrocarbonated chain, an interesting alternative to the more classical Friedel-Crafts alkylation that is generally accompanied by isomerization processes.

EXPERIMENTAL

All reagents were used as purchased (3-methyl-2-cyclohexenone, Aldrich, 98%; 2-cyclohexen-1-one, Wako,

>98%, 4-methyl-3-penten-2-one, Aldrich, analytical grade, dimedone, Wako, >99%, benzoylacetone, Wako, >98%), with no prior purification step. Distilled water was used in all experiments. Reactions were carried out in an usual reflux installation (50 mL round-bottom flask, reflux condenser) or in sealed and pressure-resistant tube of 35 mL (i.v.).

In the reaction flask (open flask or sealed tube, as specified for each case in the "Results and discussion" part), the carbonyl compound (5 mmoles) was introduced along with the Raney Ni-Al alloy (50:50; 5 g) and 9 mL of water. Powerful magnetic stirring (400 rpm) was applied for the specified refluxing time for all experiments in all Tables. After completion of the process, the reaction mixture was extracted with 3 portions of ethyl ether. The organic layers were dried over MgSO_4 , filtrated, evaporated and submitted to GC-MS analysis (Hewlett-Packard HP6890 GC, carrier gas He, flow 1.5 mL/min, velocity 48 cm/s and pressure 10.3 psi, J&W Scientific DB-1 fused silica capillary column and Jeol Automass system II MS, init. temp = 35°C, rate 2°C/min to 220°C, maintained 10 min).

CONCLUSION

Ni-Al alloy aqueous reduction of α,β -unsaturated ketones afforded the alcohol as main reaction product. In the same time, reduction of 1,3-diketones, which in water present an enolic α,β -unsaturated ketone structure, yielded both an alcohol and a hydrocarbon as reaction products.

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