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Reduction of alkylarylketones to alkylbenzenes with zinc dust and hydrochloric acid: comparison with zinc amalgam reduction.

Vladimir N. Bulavka

Slavich Company,
Mendeleev sq. 2, Pereslavl-Zalesskiy, Yaroslavl region, 152020, Russian Federation.
E-mail: nifti-drum@slavich.ru

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Abstract: The new method of arylalkylketones Clemmensen reduction to alkylbenzenes with zinc dust and hydrochloric acid was elaborated. A comparison of arylalkylketones Clemmensen reduction with zinc amalgam literature method was made. The direction of reaction is the same, the yield of alkylbenzenes is often slightly higher. The conditions of reaction are the same or slightly milder than classic conditions.

Reduction of carbonyl group to methylene group with zinc amalgam and hydrochloric acid is known as the Clemmensen reaction [1, 2, 3]. At the present time this method becomes less of value due to pollution with mercuric compounds, undesirable for ecologic reason.

Earlier, the Clemmensen reduction with non-amalgamated granulated zinc and hydrochloric acid in ethanolic medium on heating was used for the reduction of ketosteroids [4-12].

The first example of Clemmensen reduction with non-amalgamated zinc dust and hydrochloric acid in ethanolic medium on heating described is the reduction of the ketosteroid compound allopregnanedione-3,20 to allopregnanone-20 (72%) [13]. The Clemmensen reduction with zinc dust and hydrochloric acid in methanolic medium at heating was used for transformation of some substituted dihydrobenzopyran-4-ones to corresponding tetrahydroderivatives [14]. So, non-amalgamated zinc was used for reduction of natural compounds and their analogs at mild conditions. However, the chemists who used last modification of Clemmensen reaction believed that said reaction is not Clemmensen reduction, but another reaction.

Earlier we have described reduction of 4-hydroxyacetophenone to 4-ethylphenol with zinc dust and aqueous hydrochloric acid at reflux, the yield was almost quantitative [15].

We have elaborated an extension of this method for other phenolic and non-phenolic alkylarylketones. Their reduction proceeds readily and yields are 85-99% (Table).

Here we present a study of arylalkylketones reduction with zinc dust in comparison with literature method of reduction with zinc amalgam. The conditions in each run were similar to literature conditions for classical Clemmensen reduction.

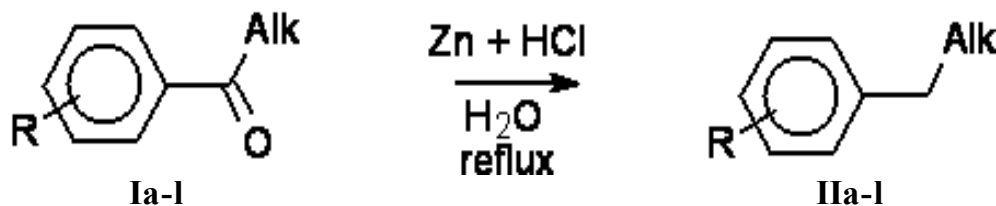


Table.

Starting compound No.	Alk	R	Obtained compound No., b.p. or m.p. (b.p. or m.p. [lit]), °C	Yield, %, Zn (dust)	Yield, %, ZnHg _n [lit.]
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Ia	CH ₃	H	IIa , b.p. 135-137 (135-136 [1])	90	80 [1]
Ib	CH ₃	4-OH	IIb , m.p. 46-48 (47-48 [2])	99 [15]	99 [2]
Ic	CH ₃	2,4-(OH) ₂	IIc , m.p. 97-99 (98-99 [17])	99	99 [2]
Id	CH ₃	3,4-(OH) ₂	IIId , m.p. 36-38 (39 [17])	85	75 [2]
Ie	CH ₃	2,5-(OH) ₂	IIe , m.p. 111-113 (113-114 [17])	86	70 [2]
If	CH ₃	2,3,4-(OH) ₃	IIIf , m.p. 106-108 (106 [2])	94	95 [2]
Ig	CH ₃	4-CH ₃	IIg , b.p. 160-163 (162,5 [16])	92	- [16]
Ih	CH ₃	4-OCH ₃	IIh , b.p. 195-197 (196-197 [17])	93	59 [17]
Ii	CH ₃	4-OC ₂ H ₅	IIi , b.p. 206-209 (208 [17])	93	- [17]
Ij	C ₂ H ₅	H	IIj , b.p. 155-158 (155-160 [1])	92	90 [1]
Ik	C ₂ H ₅	4-OH	IIk , m.p. 20-22 (21-22 [2])	98	99 [2]
Il	n-C ₃ H ₇	H	III , b.p. 180-183 (180-185 [1])	91	88 [1]

The reaction proceeds with high velocity at the temperature higher than 80°C and the products produced are identical (b. p. or m. p., ¹H NMR) with those produced with ZnHg_n procedure. Generally, the conditions are some milder than at reduction with zinc amalgam. In our previous work we have discussed the role of mercury in Clemmensen reaction and the conditions for carrying out of said reaction without mercury [18].

The monophenolic and *meta*-diphenolic alkylarylketones **Ib**, **Ic**, **Ik** are the most reactive. Oxidation during isolation of reaction products significantly decreased the yields of *ortho*- and *para*-diphenolic compounds **IIId-f**. Reduction of non-phenolic alkylarylketones **Ia**, **Ig-i**, **Il** proceeds more slowly and with some lower yields than monophenolic and metha-diphenolic ones.

Experimental

General procedure for reduction of non-phenolic arylalkylketones. To 0.1 mol of alkylarylketone and 0.7 mol of zinc dust 50 ml of water and 50 ml (0.6 mol) of concentrated hydrochloric acid were added. The reaction mixture was heated with reflux condenser at reflux during 5-8 hr. Each hour 5 ml of concentrated hydrochloric acid was added. The reaction mixture was monitored with TLC. After the end of reaction the mixture was cooled and extracted with ethyl ether. After drying with sodium sulphate, filtration and removing of solvent the residue was purified by distillation (from 12.02g of **Ia** 9.54g, 90% of **IIa** was obtained, b. p. 135-137°C, ¹H.NMR: 1.27 (3H, t, CH₃), 2.68 (2H, q, CH₂), 7.2-7.4 (5H, m, C₆H₅)).

General procedure for reduction of phenolic arylalkylketones. To 0.1 mol of alkylarylketone and 0.3 mol of zinc dust 50 ml of water and 50 ml (0.6 mol) of concentrated hydrochloric acid were added. The reaction mixture was heated with reflux condenser at reflux during 2-5 hr. The reaction mixture was monitored with TLC. After the end of reaction the mixture was cooled, saturated with NaCl, and extracted with ethyl ether. After drying with sodium sulphate, filtration and removing of solvent, the residue was purified by crystallisation from dichloromethane, chloroform or benzene.

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