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Effect of Cyclodextrin Complexation on the Reduction of Menthone and Isomenthone

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Abstract. The β- and γ-cyclodextrin complexation of menthone and isomenthone was found to modify the ratio of epimeric menthol products formed upon a $NaBH_4$/MeOH reduction of these ketones.

Key words: Stereoselectivity, selective reduction, menthol menthone cyclodextrin complex.

1. Introduction

The presence of cyclodextrins in reaction mixtures often results in the alteration of well known chemical transformations, due either to their catalytic activities or by controlling the formation of certain reaction products. This latter may lead to the alteration of the ratio of products, formed, and to the improvement of the selectivities and yield of the reactions [1]. Characteristic examples are the selective chlorination of anisole [2] and the selective formylation of phenol [3].

The present work reports preliminary data on the $NaBH_4$ reduction of menthone and isomenthone in the free and cyclodextrin complexed form.

The reduction of these terpenketones results in a mixture of epimeric products which are difficult to separate [4, 5, 6] (Figure 1). A reduction method with improved selectivity would be of practical importance, especially in the production of menthol from menthone.

2. Experimental

The reduction of menthone and isomenthone or their CD-complexes with $NaBH_4$ was carried out in methanol according to Hedin [7]. The cyclodextrin complexes were only suspended. The process was followed by TLC on a silica layer using a benzene-ethylacetate 95:5 mixture.

The end product was analyzed by GLC. The β- and γ-cyclodextrin complexes of menthone and isomenthone were prepared by co-crystallization, as previously described [8, 9]. Menthone and isomenthone were purchased from Dragoco Co. (Holzminden, West, Germany).

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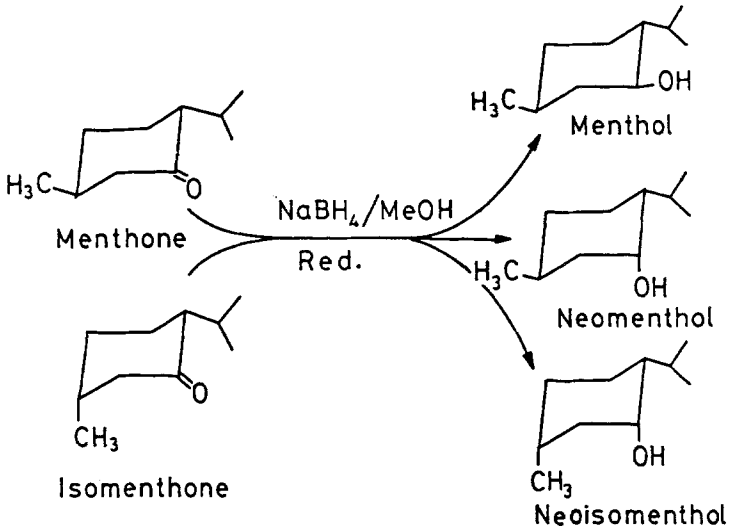

Fig. 1.

β-and γ-cyclodextrin are produced by Chinoin Pharm. and Chem. Works Ltd. (Budapest, Hungary).

3. Results and Discussion

It has earlier been reported, that both menthones and menthols form inclusion complexes with cyclodextrins [8, 9]. It is presumed that the ketones and the isomer alcohols formed upon reduction, show different affinities towards inclusion complexation by cyclodextrins.

3.1. REDUCTION OF FREE AND CYCLODEXTRIN COMPLEXED MENTHONE

The $NaBH_4$-reduction of menthone and its β- and γ-cyclodextrin complex suspended in methanol at 22 °C for 2 hours gave the reaction mixture of menthol epimeric products as listed in Table I, according to gas-chomatographic analysis.

Table I. Products obtained by reducing menthone or cyclodextrin-complexed menthone with $NaBH_4$

Ketone	Menthol (%)	Neomenthol (%)	Neoisomenthol (%)	Isomenthol (%)
Free Menthone	42.06	43.47	13.86	not detectable
Menthone-β-cyclodextrin	64.60	29.94	8.37	not detectable
Menthone-γ-cyclodextrin	68.58	23.50	7.01	not detectable

3.2. REDUCTION OF FREE AND CYCLODEXTRIN COMPLEXED ISOMENTHONE

Since it has been known for many years that the reduction of isomenthone gives all the four possible isomeric menthols [5] we compared the ratio of isomeric alcohols in the reaction mixture of free and complexed isomenthone after the $NaBH_4$ reduction.

Surprisingly no detectable amount of isomenthol was found by gas-chromatography in either reaction mixtures. Similarly only menthol, neomenthol and neoisomenthol were formed from both the free and the complexed isomenthone. The composition of products after its reduction is shown in Table II.

Table II. Products obtained by reducing isomenthone or cyclodextrin-complexed isomenthone with $NaBH_4$

Ketone	Menthol (%)	Neomenthol (%)	Neoisomenthol (%)	Isomenthol (%)
Free isomenthone	20.41	18.16	61.42	not detectable
Iso-menthone-β-cyclodextrin	46.38	11.34	36.19[a]	not detectable
Iso-menthone-γ-cyclodextrin	50.72	12.07	36.81	not detectable

[a] Two more unidentified products detected (~3–3% of each).

The following conclusions have been drawn from the above observations:

- Both β- and γ-cyclodextrin were found to influence the ratios of isomeric menthols formed in the reduction of menthone and isomenthone.
  A remarkable increase of menthol formation took place due to the presence of cyclodextrins, while the appearance of both epimers (neomenthol and neoisomethol) was hindered.
- No significant difference between the effect of β- and γ-cyclodextrin on the reduction was observed.

As for the practical usefulness of the above results, we note that the essential oil of the Vietnamese Murraya glabra plant contains 85–95% of menthone and isomenthone. This essential oil is available in huge amounts in Vietnam and could be used as starting material for an industrial menthol production, involving the reduction of the menthones of the oil. The aim of the present work was to study the effect of cyclodextrin complexation on the selectivity of menthone and isomenthone reductions.

The remarkable enhancement of menthol formation (and the significant decrease of the formation of menthol epimers) as a result of cyclodextrin complexation may be of practical importance.

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