

O-ALKYLATION OF 4-NITROPHENOL BY 1-HYDROXYADAMANTANE

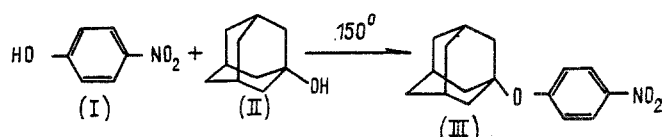
V. A. Sokolenko and S. Yu. Semenov

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1-(4-Nitrophenoxy)adamantane (III) is an intermediate in the preparation of 1-(4-amino-phenoxy)adamantane, which displays hypolipoproteinemic activity [1].

Two methods have been reported for the preparation of ether (III): 1) by the reaction of 4-nitrofluorobenzene with sodium adamantylate [1] and 2) by the reaction of 4-nitrophenol (I) with 1-bromoadamantane in the presence of silver oxide [2]. A method has also been reported for the preparation of adamantyl phenyl ethers by the reaction of 1-hydroxyadamantane (II) with phenols in the presence of dicyclohexylcarbodiimide [3].

We have shown that the reaction of phenol (I) with alcohol (II) at 150°C without catalyst gives ether (III) in 77% yield.



The mp of ether (III) was 128-130°C (lit. 129-130°C). The structure of this product was confirmed by its PMR spectrum.

Our method for the preparation of ether (III) is simple and does not require the use of alkali metals or their hydrides, noble metal compounds, or any catalyst. This is the first example of the O-alkylation of a phenol by an alcohol without the use of catalyst or a condensing agent. In previous work [4], we showed that the reaction of phenol with alcohol (II) gives C-alkylation products. Thus, the introduction of a strong electron-withdrawing group into phenol alters the direction of the reaction and leads to the exclusive formation of the O-alkylation product. This reaction apparently proceeds through the formation of an adamantyl cation, while phenol (I) acts as an acid.

LITERATURE CITED

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