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Alkylation on graphite in the absence of Lewis acids

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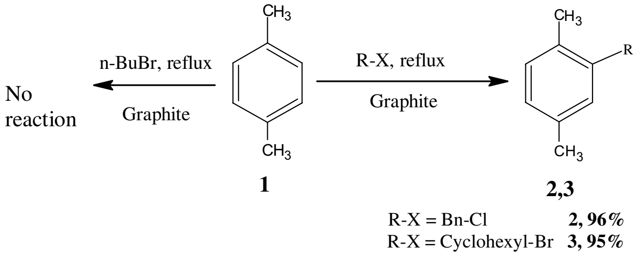
Abstract—Graphite is introduced as a convenient catalyst for alkylation of aromatic compounds and alcohols by benzyl, tertiary alkyl, and secondary alkyl halides in the absence of strong Lewis acids. Primary alkyl halides are not active under the reaction conditions.

1. Introduction

Graphite is known to catalyze Friedel–Crafts benzoylation of aromatic compounds[1] and cleavage of ethers by acyl halides.[2] Graphite-doped metal halides proved to be efficient catalysts for electrophilic alkylation of aromatic compounds.[3]

Here we are suggesting the use of graphite (particles <20 μm, Aldrich catalogue no. 28,286-3) without any strong Lewis acids as a catalyst for alkylation of aromatic compounds and alcohols by benzyl, tertiary alkyl and secondary alkyl halides. These reactions are performed by refluxing the appropriate halide and graphite in excess of the compound to be alkylated. The simple and clean workup procedure (filtration through a pad of silica gel) and reusability of the catalyst make the suggested process a good example of 'green technology'. Reaction of benzyl chloride with *para*-xylene **1** completed in 24 h and produced the hydrocarbon **2**[4] in 96% yield. Alkylation of *para*-xylene with bromocyclohexane led to the hydrocarbon **3**[5] (Scheme 1). Primary *n*-butyl bromide has not reacted under these conditions with either *p*-xylene or toluene.



R-X = Bn-Cl **2, 96%**
R-X = Cyclohexyl-Br **3, 95%**

Scheme 1.

iso-Butyl alcohol has been less reactive: its benzylation has taken 72 h and led to the ether **4**[6] in 35% yield. Benzylation of less sterically hindered *n*-butyl alcohol proceeded a little faster and produced the ether **5**[7] in 27% yield for 24 h. Tertiary *tert*-amyl alcohol did not react with benzyl chloride whereas attempt to benzylate secondary 2-butanol led to an unidentified mixture.

Benzylation of excess of phenol with benzyl chloride in chlorobenzene yielded *o*-benzylphenol **6a**[8] and *p*-benzylphenol **6b**[9] at a ratio of 1:1.2 (total yield 93%). Benzylation of phenol with an equimolar amount of benzyl chloride produced a complex mixture of mono- and polybenzylated phenols.

Toluene **7** reacted with bromocyclohexene to produce a mixture of *ortho*-, *meta*- and *para*-cyclohexylmethyl benzenes **8a–c**[5] in comparable amounts (Scheme 2).

The identity of isomers **8a**, **8b**, and **8c** as well as their relative ratio were determined on a GC/MS instrument (column temperature 100 °C). The retention times were compared with known boiling points of the isomers.[10] The **8a**:**8b**:**8c** ratio was confirmed on the basis of the integral intensities of the ^{13}C NMR signals, corresponding to the methylene groups. The influence of the NOE effect was suppressed by the use of the inverse-gated

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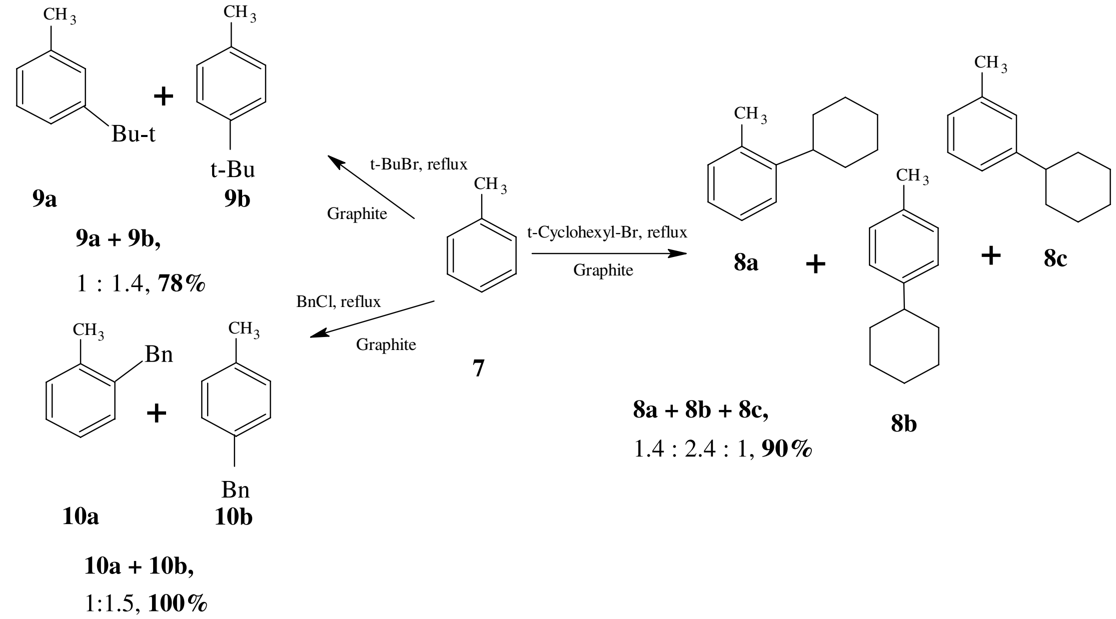

Scheme 2.

decoupling technique. The influence of the difference in relaxation times was compensated by arraying the relaxation delays until the consistent integral intensities. The integral intensities were measured at the relaxation delay of 5 s.

The ratio between the regioisomers was consistent with the known procedure of cyclohexylation of toluene with cyclohexyltosylate.[10]

tert-Butylation of toluene with *tert*-butyl bromide led to a mixture of two isomers **9a**,**b**.[11] The identity of isomers **9a** and **8b**, as well as their relative ratio were determined on a GC/MS instrument (column temperature 120 °C). The retention times were compared with those known from the literature.[11] The exact **9a**:**9b** ratio was confirmed on the basis of the integral intensities of the ^{1}H NMR signals, corresponding to the methylene groups. Lack of the *ortho*-isomer in the reaction product was consistent with the known procedure of *tert*-butylation of toluene with *tert*-butyl bromide with the use of Lewis acids as catalysts.[11] However, *tert*-butyl bromide (total yield 78%) was a little less effective alkylating agent than benzyl chloride (total yield 100%).

Benzylation of toluene led to a mixture of *ortho*- and *para*-derivatives **10a**,**b**. The identity of isomers **10a** and **10b**, as well as their relative ratio was determined by comparison of the ^{1}H NMR spectrum of the reaction product with known ^{1}H-spectra of individual isomers.[12]

We believe that the steric hindrance prevents *tert*-butylation at the *ortho*-position. Reaction of *ortho*-xylene with *tert*-butyl bromide produced 4-*tert*-butyl-1,2-dimethylbenzene **11**[13] as a single product with high yield. Unlike *o*-xylene, *p*-xylene has only *ortho*-positions available. In this case *tert*-butylation led to a complicated mixture of unidentified products.

As opposed to the common alkylation on anhydrous metal salts, graphite is less likely to cause carbon skeleton rearrangements, which would lead to undesired side-products. Lack of reactivity of primary alkyl halides brings a feature of selectivity to the reaction and widens the scope of its application. The reaction proceeds selectively for slightly activated aromatic nuclei. Benzyl chloride was not reactive toward benzene. The mechanism of the reaction is a subject of a further study. As for now, we believe that graphite acts as a Lewis base that coordinates with carbocation-like intermediates as opposed to the traditional activation of alkyl halides by the coordination of the Lewis acid catalyst with the halogen atom.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.08.026. Experimental procedures and ^{1}H and ^{13}C-DEPT NMR spectra for all synthesized compounds.

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