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Acetylation of B15C5 Crown Ether on Cu Modified Clay Catalysts

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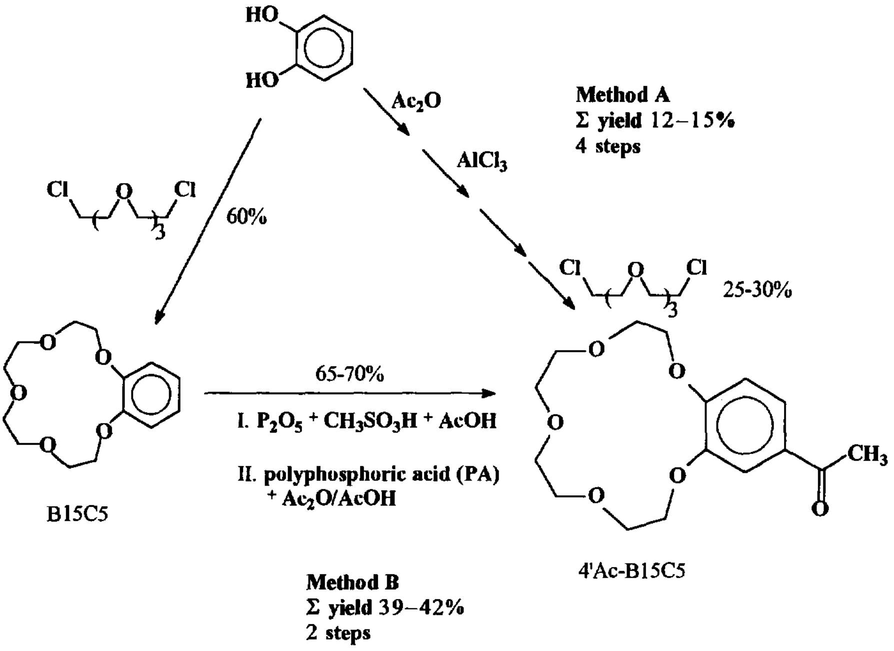
Abstract: *With different copper-clay based catalysts, in the presence of AcCl as acetylation agent, B15C5 crown ether is acetylated in a convenient heterogeneous catalytic procedure. We show here the first heterogeneous catalytic method for crown ether acylation, where the Cu exchanged clay gives the best results using really catalytic amount of catalyst.*

Crown ethers are well known for their ability to form strong complexes with alkali metal and organic cations. Introduction of lipophilic substituents into crown ethers is very important for their application as electroactive substances in ion-selective membrane electrodes[1]. 4'-Acetyl-benzo-15-crown-5 is a key intermediate in the synthesis of many analogous ionophores[2,3]. For the preparation of 4'-acetyl-benzo-15-crown-5 on catechol basis there are two main possibilities showed on the Scheme below.



In the **Method A** the acetyl substitution is realized first, and the 4 steps procedure results in a very low final chemical yield (12-15 %)[3]. The **Method B** seems to be more interesting, where the crown ring was prepared first and then acetylated with a final yield of 39-42 %[4]. Using **Method B** the key step for a better final yield could be the acetylation of benzo-15-crown-5 to 4'-acetyl-benzo-15-crown-5.

In the recent studies homogeneous systems were applied for this acetylation using liquid mineral acids[4,5] or aluminium chloride[6,7] as usual catalyst. Wada et al. established the existence of a stable $AlCl_3$-crown ether complex using $AlCl_3$ as traditional Friedel-Crafts catalyst[6] and there was no reaction at the usual 1-2 mol $AlCl_3$/mol B15C5 ratio. Because of this complexation problem Szabó[7] used a large excess of $AlCl_3$ (370-450 %) for this type of acetylation, but obtained only 30-35 % chemical yield.

Solid acids offer many advantages by their nature over soluble counterparts such as aluminium chloride or other liquid mineral acids. The substitution of liquid acids by solids as catalysts for organic synthesis is attractive for the protection of environment. Recently we have proposed clays as good catalysts for this purpose[8-10]. In our previous publications the results obtained in the alkylation of anisole[8], as well as in benzylation of aromatics[9] with K10 exchanged with different cations and on alkylation of aromatics with acid treated clays[10] were reported. In these Friedel-Crafts type alkylations the clay based catalysts showed good activities and we obtained high selectivities[9,10], and with a good choice and convenient pretreatment of the catalysts we can eliminate the harmful secondary reactions[8]. These mesoporous solids offer a good possibility for the transformation of large molecules, and their high acidity can also be advantageous for Friedel-Crafts acylation.

It was then interesting to investigate these clay based catalysts in the Friedel-Crafts acetylation of B15C5 crown ether. The aim of this work was to elaborate a simple heterogeneous method for acylation process of benzo crown ethers with solid catalysts.

RESULTS AND DISCUSSION

For the catalytic acylation reactions different clay based catalysts were chosen, which have several successful Friedel-Crafts type application also in industrial scale[9,11,12].

K10[13] clay has a high specific surface area (229 m^2/g)[14], a mesoporous pore system (average pore diameter: 56 Å)[14] and important Broensted acidity[15].

$CuCl_2$/K10. K10 supported $CuCl_2$ contains 0.8 mmol $CuCl_2$/g K10. The catalyst was prepared by evaporating to dryness a suspension of K10 in methanolic $CuCl_2$ solution[16], the solid was then dried at 120 °C and ground.

Cu^{2+}-K10. Cation exchange was performed[9] by gradually adding the K10 clay (10 g) to a 1 M/l stirred solution of the $CuCl_2$ (125 ml) at room temperature and stirring the suspension for 24 hours. After exchange, suspension was filtered and washed with deionised water. The resulting solid was dried on a thin bed at 473 K and ground. Cu^{2+}-K10 has a specific surface area of 236 m^2/g. The exchanged charge was 0.39 meq/g solid with a Cu contents of 1.24 wt %[17]. The cation exchange increases Lewis acidity at the expense of Broensted acidity[9,15].

General reaction conditions: Using a batch reactor, 0.027 g (0.1 mmol) B15C5 crown ether was acetylated with 0.15 cm^3 (2 mmol) acetyl chloride in 15 cm^3 1,2-dichloroethane as solvent at a temperature of 83.7 °C (boiling point of the solvent). The reactions were monitored by HPLC (C_{18} reversed phase column, methanol/water = 60/40 (v/v) as eluent).

The results obtained without catalyst, with $CuCl_2$ and with different Cu-K10 based catalysts are reported on the Figure 1. The yields are expressed in 4'-acetyl-benzo-15-crown-5 %.

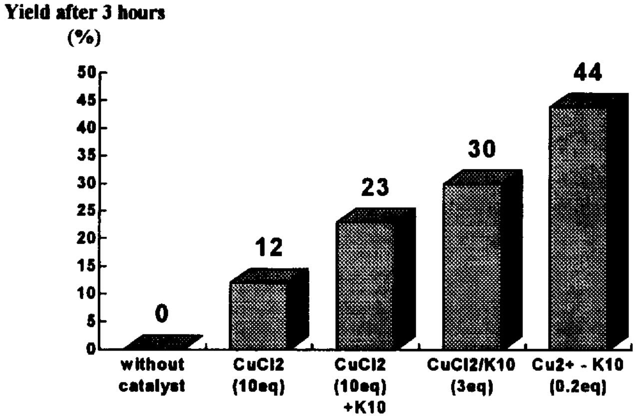


Figure 1. Comparison of different Cu-K10 based catalysts in benzo-15-crown-5 acetylation.

Without catalyst there was no reaction. The final yield on $CuCl_2$ is relatively low even at a large excess of $CuCl_2$, probably due to formation of $CuCl_2$-crown ether complex as supposed earlier[6] for $AlCl_3$. Using the same amount of $CuCl_2$ with K10 for in situ preparation (simple addition in the reaction mixture) a better yield was obtained because of advantageous support effect of K10. The K10 supported $CuCl_2$ (prepared by impregnation) gives relatively good results due to the well dispersed $CuCl_2$ on the surface of K10. In the case of $CuCl_2$ based catalysts a large amount of acetylated crown ether could be complexed on the catalyst surface, consequently this part of crown ether can not be detected during the monitoring of reaction. The Cu^{2+} exchanged K10 gives the best result. In that case a really catalytic amount of catalyst can be used (Cu^{2+}/B15C5 molar ratio is 0.2). In Table 1 the results of a more detailed investigation on this Cu^{2+}-K10 catalyst are expressed. The catalyst was pretreated at 200 °C and the Cu^{2+}/B15C5 molar ratio was 0.2 as best values from the preliminary experiments.

Table 1. 4'-Acetyl-benzo-15-crown-5 Yields (%) on Cu^{2+}-K10 Catalyst.

Reaction temperature °C	AcCl/B15C5 molar ratio	*Reaction time*	
		1h	*3h*
83.7	10	7	10
83.7	14	15	21
83.7	20	28	42
83.7	30	34	41
52	2000 (without 1,2-dichloroethane)	47	48

Pure AcCl was used as solvent in the last experiment to eliminate the separation problems, in that case higher yield was observed also at lower reaction temperature.

The chemical yields are not exceeding 40-50 % level, the reason of this fact is under investigation.

The pattern marked reaction was scaled-up by a factor of 100, and the yield of the isolated 4'-acetyl-benzo-15-crown-5 (purified by column chromatography) was 32 %. The product was identified by different methods (m.p., IR, TLC, NMR).

Final conclusion: the acetylation of B15C5 crown ether can be realized by heterogeneous process using really catalytic amount of catalyst. This new method - not yet optimized - is competitive to classical known acylating methods in homogeneous phase (yield, protection of environment, economy).

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13. K10 clay is manufactured by high temperature acidic treatment from a Bavarian bentonite and was purchased from Süd-Chemie, München. The high temperature acidic treatment destroyes the originally layered structure of bentonite clay and results in a loss of crystallinity with a mesoporous pore system[10].
14. Specific surface areas were calculated by the BET equation, from nitrogen isotherms determined at 77 K (Micromeritics ASAP 2000) on samples degassed at 523 K for 12 h before the experiment. The pore size distribution was calculated from nitrogen adsorption-desorption by the BJH method.
15. Mesured by IR spectroscopy of pyridine adsorption (Nicolet 320 FTIR).
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