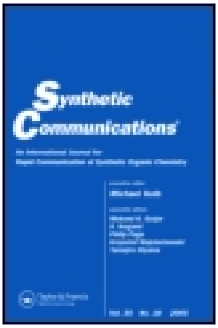

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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To cite this article: Katalin Bir , Sndor Bkssy , Bla gai & Franois Figueras (2000) Heterogeneous Catalytic Acylation of Benzo Crown Ether Using Acetic Anhydride, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 30:22, 4159-4165, DOI: 10.1080/00397910008087032

To link to this article: http://dx.doi.org/10.1080/00397910008087032

SYNTHETIC COMMUNICATIONS, 30(22), 4159–4165 (2000)

HETEROGENEOUS CATALYTIC ACYLATION OF BENZO CROWN ETHER USING ACETIC ANHYDRIDE

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Abstract: Benzo-15-crown-5 macrocycle has been acetylated using acetic anhydride and a series of cation exchanged clays. This acetylating method has great advantages such as the significant reduction of the formation of by-products, lower price and the possibility of environmental friendly process. Yields as high as 80% for the acetylated compound are reached in short times.

In a previous paper[1] we reported a novel method for acetylating benzo-crown ethers by acetyl chloride, based on a Friedel-Crafts reaction catalysed heterogeneously with ion-exchanged clay catalysts[2].

In the latter case very good yields could be achieved, but the reaction leads to the formation of one mol of HCl per one mol of acetyl chloride. To eliminate the formation of HCl which is well known by its corrosive and environment polluting properties, we tried to carry out the acetylation with acetic anhydride (Ac_2O) instead of acetyl chloride.

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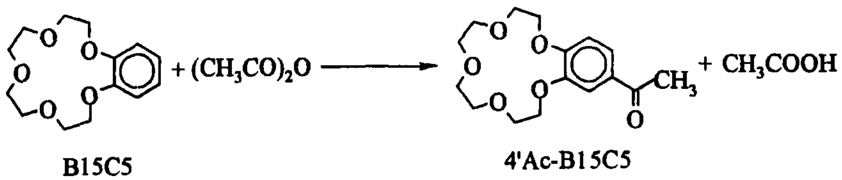
In this paper we demonstrate that acetic anhydride is as much an efficient reagent as acetyl chloride.



Experimental

Preparation of the catalysts: K10 clay (manufactured by high temperature acidic treatment of bavarian montmorillonite) was purchased from Süd Chemie (Germany) and used as received. Cation exchange was performed with the method of Rhodes et al.[3] by gradually adding 10 g of K10 clay to a stirred solution of $CuCl_2$, $FeCl_3$, $ZnCl_2$ or $SnCl_2$ (125 cm^3, 1 mol dm^{-3}) at room temperature and stirring the suspension for 24 hours. The catalysts were filtered off, washed with deionised water, dried and calcined at 120°C, 250°C or 500°C. The ion-exchanged catalysts so obtained were designated as Me^{n+}-K10 and have been characterised as reported in an earlier paper[4].

General procedure: The reactions were carried out in a three neck glass reactor, in which 0.54 g of benzo-15-crown-5 (B15C5), 1 cm^3 of acetic anhydride ($n_{Ac2O}/n_{B15C5} = 5$), 1 g of catalyst and in some cases 15 cm^3 of 1,2-dichloroethane as a solvent were introduced. The reaction mixture was refluxed either at the boiling temperature of 1,2-dichloroethane (83°C) or at that of acetic anhydride

(139°C). The reaction was monitored by HPLC (C18 reversed phase column, methanol/water = 60/40 (v/v) as eluent, UV-detection at 254 nm).

Preparation of 4'-acetyl-benzo-15-crown-5 (4'Ac-B15C5): The reaction mixture was filtered and the filtrate was treated with methanol at 60°C for 2 hours to destroy the unreacted acetic anhydride, than the volatile components were removed under reduced pressure. The dark, thick residual oil was repeatedly extracted with hot n-heptane. Crystals of 4'Ac-B15C5 were obtained by cooling the hot solution.

Results and discussion

Determination of the suitable reaction conditions

In Fig. 1, the overall yields of 4'Ac-B15C5 using different catalysts (in 15 cm^3 of 1,2-dichloroethane at 83°C) are presented as the function of molar ratios n_{Ac2O}/n_{B15C5}. With a ratio of $n_{Ac2O}/n_{B15C5} = 5$ quite poor yields could be obtained (no reaction for Fe^{3+}-K10 and Zn^{2+}-K10). Increasing the relative amount of the acetylating agent to $n_{Ac2O}/n_{B15C5} = 10$ the reaction reached its maximum yield. A further increase of n_{Ac2O}/n_{B15C5} up to 20 had no more effect into the overall yield.

The influence of the solvent and the concentration was also investigated: decreasing gradually the amount of 1,2-dichloroethane we observed that the overall yield increased systematically. For example, by adding 15, 6 or 0 cm^3 of 1,2-dichloroethane, the yields after 120 min were 53%, 56% and 74%, respectively (the amounts of other ingredients were: 0.54 g of B15C5, 2 cm^3 of acetic anhydride and 1 g of Sn^{2+}-K10 catalyst, at 83°C).

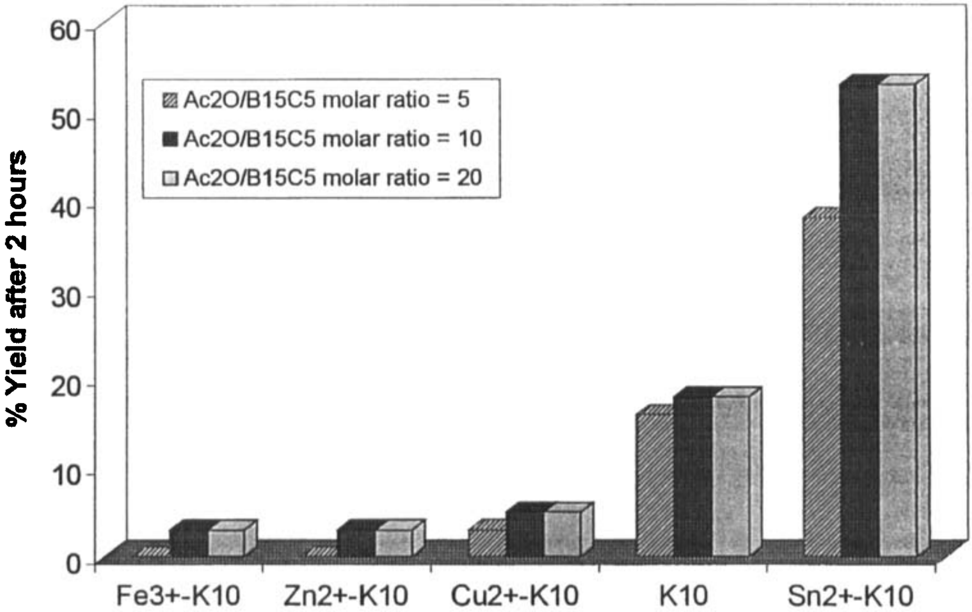


FIG. 1
Efficiency (expressed in yield % of 4'Ac-B15C5) of different ion-exchanged catalysts and the effect of the excess of acetic anhydride in reactions carried out in 1,2-dichloroethane as a solvent

On the basis of these results we can see that the best molar ratio for the reaction is n_{Ac2O}/n_{B15C5} = 10 and the reaction proceeded more efficiently in the absence of the solvent 1,2-dichloroethane, in pure acetic anhydride.

Comparison of different catalysts

It can be stated that using acetic anhydride as an acetylating agent, the initiating step of the reaction is the protonation of the anhydride, followed by formation of the appropriate acylium cation as an electrophile:

$$(CH_3\text{-}CO)_2O + H^+ \rightarrow CH_3\text{-}CO^+ + CH_3\text{-}COOH$$

It is thus evident than the catalytic activity of the catalyst should depend on

Table 1. Yields (%) of 4'Ac-B15C5 obtained with different catalysts for acetylation in pure acetic anhydride (139°C, $n_{Ac2O}/n_{B15C5} = 10$) as a function of the temperature of the heat treatment

			Reaction time	
			0.5h	2h
K10	treated at	120°C	70	74
		250°C	63	65
		500°C	32	37
Fe^{3+}-K10	treated at	120°C	36	47
		250°C	26	32
		500°C	20	27
Sn^{2+}-K10	treated at	120°C	78	79
		250°C	70	74
		500°C	35	39
Cu^{2+}-K10	treated at	120°C	59	70
		250°C	53	61
		500°C	22	26
Zn^{2+}-K10	treated at	120°C	16	40
		250°C	10	30
		500°C	6	18

its acidity. Since the Brönsted acidity of the ion-exchanged clay catalyst depends on the degree of hydroxylation of the surface, which can be altered by treatment at increasing temperature, the influence of this pretreatment was investigated.

The results are summarized in the Table 1. As expected, the catalysts pretreated at higher temperatures resulted in the poorer yields of the acetylated product.

The highest yields could be obtained using Sn^{2+}-K10. This catalyst, dried at 120 °C, gave 4'Ac-B15C5 with 57% preparative yield.

Sn^{2+}-K10 catalyst is also the most effective one in the acetylation reaction with acetyl chloride, but the activity pattern changes when different acylating agents are used. With acetic anhydride the decreasing order is Sn>K10>Cu>Fe>Zn, while with acetyl chloride the order is Sn>Fe>Cu>Zn>K10, thus here the catalysts having reducible metals are the best. In the case of acetic anhydride Sn^{2+}-K10 does not produce much higher yield than K10, but the amount of Sn^{2+}-K10 can be reduced by 50% and this reduced amount of Sn^{2+}-K10 still produces the same yield in an equally fast reaction, which is not the case regarding the K10 catalyst. Thus introducing Sn^{2+}-ions into K10 is much worth than using K10 as catalyst.

The regeneration of K10 catalyst is partially possible (washing it with methanol and drying at 120 °C for 1 hour): the HPLC yields were 76, 56 and 41% in 3-3 hours repeated reactions.

A major advantage in the reactions with acetic anhydride is the decrease of formation of by-products compared to the reaction with acetyl chloride, thus the selectivity is higher. In the present case the splitting of the crown ring does not occure and no triacetyl-derivative[2] is formed.

In **conclusion** we would like to emphasize that the heterogeneous catalytic acetylation of B15C5 can be carried out in good yields using neat acetic anhydride. An advantage of this method is that the liquid phase has only one component, therefore the excess of acetic anhydride can be easily recovered from a larger reaction mixture. The activity of the catalysts is essentially determined by their Brönsted acidity when using acetic anhydride.

Acknowledgements: K. Biró thanks the Foundation Varga József of the Technical University of Budapest and the French Government for a grant. The financial supports of OTKA (T-015677, T-029193) and the Ministry of Education and Culture (FKFP 0402/1997) are also gratefully acknowledged.

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Received in the UK 21 October 1999