CHEMISTRY LETTERS, pp. 533-536, 1980. © The Chemical Society of Japan 1980

POTASSIUM FLUORIDE ON ALUMINA AS BASE FOR CROWN ETHER SYNTHESIS

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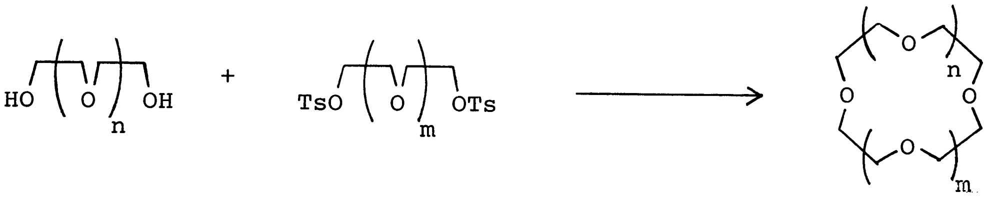
Alumina coated with potassium fluoride was found to be an effective and practical reagent for the synthesis of some simple crown ethers.

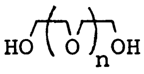
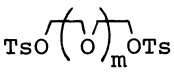
Much attention has been focused on the chemistry of crown ethers in recent years because of their ability to complex cationic species and, consequently, to enhance the nucleophilicity of anionic species.$^{1)}$ Most of them have been prepared by a modified Williamson synthesis; cyclization of a diol with a ditosylate or a dihalide catalyzed by a base, for example, alkali metal hydroxides or potassium tert-butoxide.$^{2-6)}$

In our previous papers,$^{7,8)}$ we reported that a variety of inorganic supports coated with potassium fluoride (KF-support) are effective reagents for various types of alkylations. In particular, KF-alumina is the most effective reagent to promote even O-alkylation of an aliphatic alcohol. The alumina support in this KF-alumina reagent may act as solid reaction media in which cyclization may be promoted more advantageously than in usual liquid reaction media. In this paper we describe the application of KF-alumina to the synthesis of some simple crown ethers.



The reaction of a polyethylene glycol (0.01 mol) and a polyethylene glycol ditosylate (0.01 mol) was carried out in the presence of KF-alumina$^{9)}$ (ca. 5 equiv) in 60 ml of acetonitrile. The mixture was magnetically stirred at room temperature for 72 hours. The solid material was filtered off and washed with methylene chloride, and the filtrate was evaporated. The crown ether was isolated from the crude crown ether-potassium tosylate complex by distillation under high vacuum or by column chromatography. The results obtained are summarised in Table 1.

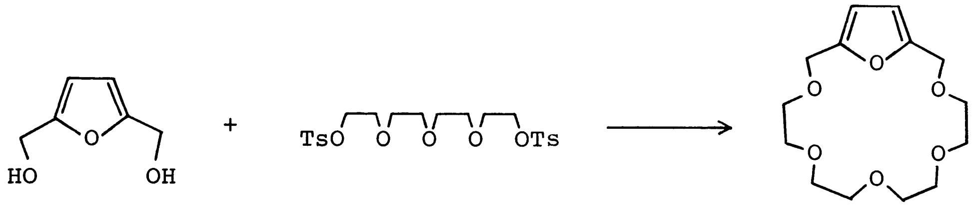
Table 1. Synthesis of crown ethers with KF-alumina

		Product	GLC Yield[a,b]	Isolated Yield[a,c]	Greene[d]	Dale and Kristiansen[e]
n=1	m=2	15-crown-5	33			
2	1	"	35	25[f]		20
2	2	18-crown-6	70	78[f]	30-60	30
3	1	"	70			
2	3	21-crown-7	50	54[g]	18[h]	26
3	2	"	51			
3	3	24-crown-8	24	27[g]	15[h]	15

a) The reaction in acetonitrile with KF-alumina at room temparature. b) Yields (%) after 24 h using internal standards. c) Yields (%) after 72 h. d) Yields (%) of the reaction in tetrahydrofuran with tert-BuOK at 35 °C for 16 h.[2]
e) Yields (%) of the reaction in benzene with tert-BuOK with heating.[3]
f) Purified by distillation under high vacuum. g) Purified by column chromatography. h) Combination of a diol and a ditosylate was not specified.

Various sizes of crown ethers were prepared in moderate to good yields under the reaction conditions not optimized. Even crown ethers with large ring sizes, namely, 21-crown-7 and 24-crown-8, were obtained in satisfactory yields. In the conventional method using a diol and a ditosylate reported by Greene,[2] and Dale and Kristiansen,[3] it is considered that the metal cation acts as a template in the cyclization and thus increases the yield. Our method shows a qualitatively similar relationship between the ring size and the yield of crown ether as that observed in the conventional method, although ours gave better yields than the old one throughout the series of crown ethers.[2,3,10] It is noteworthy in this regard that the different combinations of diols and ditosylates gave the same yields for the same size of crown ethers (Table 1).

Monofuranyl-18-crown-6 was also obtained in a 34 % yield from a diol having an unstable furan ring.[12]



In this crown ether synthesis using the solid-supported reagent, the reaction can be carried out under mild conditions with easy and non-aqueous work-up. The crown ethers thus obtained are pure enough possibly because by-products such as polymers or acyclic compounds which may be produced during the course of the reaction are adsorbed on the alumina support.

Reinhoudt et al.[13] reported that solid metal fluorides facilitate the synthesis of benzo-crown ethers from aromatic diols, for example, catechol, with polyethylene glycol ditosylates in dry acetonitrile under reflux. However, similar reactions of polyethylene glycols with ditosylates did not give crown ethers at all but only yielded the corresponding difluorides. In the latter case the fluoride anion reacted as a nucleophile rather than a base. In contrast to potassium fluoride without support, KF-alumina was effective as a base at a lower temperature in the synthesis of simple crown ethers.

From the viewpoint of the solid-liquid interfacial reaction it is interesting to compare the effectiveness of KF-alumina with that of another

Table 2. Comparison of KF-alumina and KOH-alumina as base for O-alkylation[a]

Alcohol	Alkylating Agent	T/h	KF-alumina[b]	KOH-alumina[b]
$CH_3(CH_2)_7OH$	MeI	8	69	85
HO O OH	MeI	2	73	100
HO O O OH	TsO O O OTs	24	70±2[c]	19±1[c]

[a] Reaction in acetonitrile at room temperature. [b] GLC yields (%) using internal standards. [c] Average value of triplicate runs using different batches of solid bases.

solid base. Alumina coated with potassium hydroxide (KOH-alumina) was prepared in a similar procedure as KF-alumina. As shown in Table 2, KOH-alumina was equally or even a little more effective for the methylation of 1-octanol and diethylene glycol than KF-alumina. However, the former was less effective than the latter for cyclization of a diol with a ditosylate. Although the reason of the different behavior in their reactivity is not clear, it can be concluded that KF-alumina is an effective solid base especially suitable for cyclization.

References and Notes

1) See, for example, G. W. Gokel and H. D. Durst, Synthesis, 1976, 168; R. M. Izatt and J. J. Christensen, Ed., "Synthetic Multidentate Macrocyclic Compounds," Academic Press, New York (1978).

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9) We used KF-alumina of Type B prepared as described previously.8)

10) Methods described in references 2 and 3 are not the best practical ones for the preparation of 18-crown-6 and 15-crown-5. See references 4, 5, and 11.

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(Received March 11, 1980)