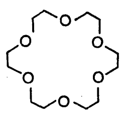
The Catalytic Effect of Crown Ethers on Benzoin Condensation

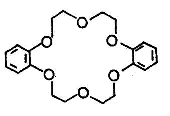
Sadatoshi Akabori,* Michiko Ohtomi, and Katsuhiko Arai
Department of Chemistry, Faculty of Science, Tōho University, Funabashi, Chiba 275

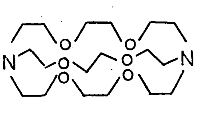
(Received August 9, 1975)

Aromatic aldehydes were treated with potassium cyanide in the presence of a crown ether in water or in aprotic solvents to give benzoins in high yields, although similar reactions in the absence of the crown ether proceeded sluggishly in general. The catalysis is believed to be due to the ability of the crown ether to bring anions into the organic phase.

In recent years there have been reported several synthetic applications of crown ethers, such as 18-crown-6 (I) and dibenzo-18-crown-6 (II), which possess the ability to form complexes with a variety of inorganic salts and also the ability to solubilize these salts in aprotic solvents. The following reactions are reported to be enhanced by the crown ether: substitution reactions,[1-6] elimination reactions,[7,8] a condensation reaction,[9] oxidation reactions,[3,10] a reduction reaction,[3] and an addition reaction.[11]


(I)

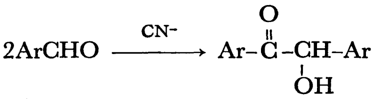

(II)


(III)

In a previous paper,[12] we have reported on the reaction of potassium alkanoate with alkyl halide in an aprotic solvent. Although the reaction of potassium alkanoate with alkyl halide does not proceed in aprotic solvents such as benzene, the reaction with the same starting materials in the presence of catalytic amounts of a bicyclopolyether such as III affords alkyl esters in high yields. As an extension of our previous work, we have been interested in seeking examples of the enhancement of the reaction by crown ethers in the field of condensation, which has been little studied.[9] Benzoin condensation was taken as our target. Generally benzoins are generated by the action of sodium cyanide or potassium cyanide on aromatic aldehydes in aqueous ethanol.[13] We now wish to report that dramatic results can be achieved by the addition of crown ethers (I and II) to benzoin condensations in water and in aprotic solvents at appropriate temperatures.

Results and Discussion

Benzoin Condensation in Water. The condensation reactions represented by Eq. 1 were run in heterogeneous systems by the use of crown ethers (I and II) as anion-transfer catalysts:



$$2\text{ArCHO} \xrightarrow{\text{CN}^-} \text{Ar-}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{-}\underset{\text{OH}}{\underset{|}{\text{CH}}}\text{-Ar} \qquad \text{Eq. (1)}$$

IV: Ar=C_6H_5-, V: Ar=p-CH_3-C_6H_4-,
VI: Ar=furyl

The reagent is prepared by dissolving potassium cyanide in water and by then adding 18-crown-6. After the mixture has been stirred for 30 min, the organic substrate is added and the resulting heterogeneous mixture is stirred for 15 min to 6 hr at appropriate temperatures. The results are shown in Table 1. The reaction conditions are relatively mild (at 25 or 60 °C), and the conversions are high at 60 °C; in the presence of *ca.* 7% of crown ether, benzoin was obtained in more than 78% yields within 15 min from benzaldehyde, *p*-toluoin (99%) in 3 hr from *p*-tolualdehyde, and furoin (66%) in 15 min from 2-furaldehyde.

Table 1. Reactions of aromatic aldehydes with potassium cyanide

Substrate	Solvent[a]	Reaction temp (°C)	Reaction time (hr)	Product[b]	Yield(%)[c] Crown ether present	Yield(%)[c] Crown ether absent
IV	H_2O	25	1.5	Benzoin	73.9	3.1
IV	H_2O	60	0.25	Benzoin	78.0	3.3
V	H_2O	25	6.0	*p*-Toluoin	44.3	0.0
V	H_2O	60	3.0	*p*-Toluoin	99.0	1.9
VI	H_2O	25	1.5	Furoin	35.6	24.4
VI	H_2O	60	0.25	Furoin	66.2	48.0
IV	CH_3CN	25	3.0	Benzoin	78.4	1.1
IV	CH_3CN	60	1.5	Benzoin	73.6	9.0
IV	C_6H_6	25	3.0	Benzoin	70.9	0.1
IV	C_6H_6	60	3.0	Benzoin	95.9	0.5
V	CH_3CN	25	6.0	*p*-Toluoin	56.4	2.7
V	CH_3CN	60	3.0	*p*-Toluoin	99.0	6.0
V	C_6H_6	25	6.0	*p*-Toluoin	29.1	0.0
V	C_6H_6	60	3.0	*p*-Toluoin	90.8	0.0
VI	CH_3CN	25	3.0	Furoin	65.0	3.7
VI	CH_3CN	60	0.25	Furoin	43.6	3.6
VI	C_6H_6	25	3.0	Furoin	52.7	0.3
VI	C_6H_6	60	3.0	Furoin	53.0	0.0

a) 2.7 ml of water or 9.0 ml of aprotic solvents were used. b) All product show the same retention time with authentic sample and mass spectra were consistent with the proposed structure. c) The values are those obtained by GLC.

In sharp contrast, benzoin and *p*-toluoin were obtained in less than 3% yields in the absence of the crown ether, although furoin was obtained in a good yield from 2-furaldehyde under similar conditions. These results can be accounted for in terms of the solubility of aldehydes in water; 2-furaldehyde is fairly soluble in water, whereas benzaldehyde and *p*-tolualdehyde are soluble in water to only a limited extent. Generally a reaction between two substrates located in different phases of a mixture is often inhibited because of the inability of reagents to come together. However, this reaction is brought about by the use of small quantities of a reagent, which transfers one reactant across the interface into the other phase. Although potassium cyanide is an excellent catalyst for benzoin condensation at 90 °C in 95% ethanol,[14] it exhibits hardly any catalytic ability in water at room temperature.[15] However, as is shown in Table 1, complexes of crown ether with potassium cyanide afford benzoin in high yields even when the reaction was run at room temperature. Thus, in the benzoin condensation of aromatic aldehydes, it is most likely that crown ethers transport cyanide into the organic phase, although the possibility of transforming the aromatic aldehyde into the aqueous phase can not be ruled out.

Benzoin Condensation in Aprotic Solvents. The crown ethers are known to form complexes with alkali and other metal salts to increase the solubility and to increase the reactivity of anions in aprotic solvents. The potassium cyanide complex of 18-crown-6 was prepared *in situ* by dissolving a catalytic amount of 18-crown-6 in *ca.* 9 ml of a dry aprotic solvent (benzene or acetonitrile) and by then adding appropriate amounts of potassium cyanide, most of which remained insoluble. After the heterogeneous system had been stirred for 30 min, the aromatic aldehyde was added at once; the resulting mixture was stirred for from 15 min to 6 hr at 25 or 60 °C. In the absence of the crown ether, potassium cyanide does not have any detectable solubility in benzene and hardly no reaction occurs; benzaldehyde gives less than a 0.5% yield of benzoin after 3 hr at 60 °C when it is treated with potassium cyanide in the absence of 18-crown-6, whereas benzoin is formed in a 95.9% yield within 3 hr when a trace amount of 18-crown-6 is present. The reaction was found to be faster in acetonitrile than benzene.

In summary, these experimental results in water indicate that crown ethers may be at least as useful as onium salts in reactions which proceed by means of phase-transfer. It has been shown that crown ether (I) effectively solubilizes potassium cyanide in aprotic solvents and that the reagent produces benzoins in high yields from a variety of organic substrates. The catalytic activity of dibenzo-18-crown-6 is almost the same as that of 18-crown-6.

Experimental

Analysis. The products were analyzed by gas chromatography. The gas chromatograms were obtained on a Hitachi 023 gas chromatograph, using 10% FFAP on Chromosorb W AW/DMCS 1 m×3 mm. The mass spectra were recorded on a Shimadzu LKB 9000 gas-chromatograph-mass-spectrometer at an ionizing voltage of 70 eV.

Materials. 18-Crown-6[16] and dibenzo-18-crown-6[17] were prepared according to the procedures described in the literature. Authentic samples (benzoin[14], *p*-toluoin[18] and furoin[19]) were also prepared according to the procedures described in the literature. Potassium cyanide of Koso Co., Ltd., and aromatic aldehydes of the Tokyo Kasei kogyo Co., Ltd., were used without further purification. The solvents used were purified by distillation.

Benzoin Condensation of Benzaldehyde in Water. The following procedure for the preparation of benzoins is representative. A mixture of potassium cyanide (20.0 mmol), 18-crowm-6 (1.22 mmol), and 2.7 ml of water was stirred for 30 min at 60 °C. Benzaldehyde (41.7 mmol) was then added at once, and the mixture was stirred for a further 15 min. A yellow precipitate, which gradually formed, was collected by filtration, and the filtrate was extracted with chloroform. The yellowish solid was dissolved in the chloroform extract, and then the solution was subjected to gas-chromatographic analysis.

Benzoin Condensation of Benzaldehyde in Aprotic Solvents. A mixture of potassium cyanide (20.7 mmol), 18-crown-6 (1.40 mmol), and *ca.* 9 ml of benzene was stirred for 30 min at 25 °C. Benzaldehyde (49.9 mmol) was then added at once, and the mixture was stirred for a further 3 hr. The work-up and analysis were performed analogously with the case cited above.

Benzoin Condensation with the Aid of Dibenzo-18-crown-6. The reaction was carried out similarly. The results were usually quite similar, although results a little inferior were sometimes obtained.

The authors wish to express their gratitude to Professor Michinori Ōki, the University of Tokyo, for his valuable discussions and suggestions.

References

1) C. L. Liotta and H. P. Harris, *J. Amer. Chem. Soc.*, **96**, 2250 (1974).

2) D. J. Sam and H. E. Simmons, *J. Amer. Chem. Soc.*, **96**, 2252 (1974).

3) D. Landini and F. Montanari, *Chem. Commun.*, **1974**, 879.

4) C. L. Liotta, H. P. Harris, M. McDermott, Tom Gonzalez, and K. Smith, *Tetrahedron Lett.*, **1974**, 2417.

5) H. D. Durst, *Tetrahedron Lett.*, **1974**, 2421.

6) F. L. Cook, C. W. Bowers, and C. L. Liotta, *J. Org. Chem.*, **30**, 3416 (1974).

7) M. Svoboda, J. Hapala, and J. Závada, *Tetrahedron Lett.*, **1972**, 265.

8) R. A. Bartsch and K. E. Wiegers, *Tetrahedron Lett.*, **1972**, 3819.

9) M. Makosza and M. Ludwikow, *Angew. Chem.*, **86**, 744 (1974).

10) D. J. Sam and H. E. Simmons, *J. Amer. Chem. Soc.*, **94**, 4024 (1972).

11) T. Mastuda and K. Koida, This Bulletin, **46**, 2259 (1973).

12) S. Akabori and M. Ohtomi, *ibid.*, **48**, 2991 (1975).

13) W. S. Ide and J. S. Buck, "Organic Reactions," Vol. IV, p. 269 (1957).

14) Adams and Marvel, "Organic Syntheses," Coll. Vol. I, p. 94 (1956).

15) J. Solodar, *Tetrahedron Lett.*, **1971**, 287.

16) G. W. Gokel, D. J. Cram, C. L. Liotta, H. P. Harris, and F. L. Cook, *J. Org. Chem.*, **39**, 2445 (1974).

17) C. J. Pedersen, *J. Amer. Chem. Soc.*, **89**, 7017 (1967).

18) M. Stirelin, *Ber.*, 380 (1889).

19) W. W. Hartman and J. B. Dickey, *J. Amer. Chem. Soc.*, **55**, 1228 (1933).