New Applications of Crown Ethers. I. Primary Alkylamine-Water-Crown Ether System as a Hydroxide Ion Source in the Reduction with Carbonylhydridoferrate Anion

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Utility of the primary alkylamine–water–crown ether system as an effective source of hydroxide ion was studied by the reduction of benzylideneacetone with carbonylhydridoferrate anion. Excellent conversion and selectivity for the reduction were attained in a two-phase system (benzene–water) in the presence of dicyclohexano-18-crown-6, comparable to those obtained with use of potassium hydroxide in place of the amine. Effects of several alkylamines and crown ethers were presented. IR examination of pentacarbonyliron–butylamine–water in benzene with or without the crown ether showed that the presence of the crown ether markedly alters the route of formation of the reducing agent(s).

The macrocyclic polyethers (crown ethers) form stable complexes with alkali and alkaline earth metal cations as well as primary alkylammonium ions. The chemistry of the ammonium salt complexes was investigated in detail by Cram and his collaborators.[1] They utilized the nature of the complexes as a novel method for optical resolution of amino acids.[2]

Primary alkylamine in water is in equilibrium as shown by Eq. 1. When an alkylammonium hydroxide is brought into formation of a complex (**1**) with a crown ether, the equilibrium would shift to the right, and in a two phase, *e.g.* benzene and water, the resulting complex could be transferred to the organic phase to greater extent. The phenomenon can be considered to be production of an increased concentration of hydroxide ion from an alkylamine and water, especially in the organic phase.

$$RNH_2 + H_2O \rightleftharpoons R\overset{+}{N}H_3\,OH^- \qquad (1)$$

$$R\overset{+}{N}H_3\,OH^- + \text{crown ether} \rightleftharpoons [R\overset{+}{N}H_3\cdot\text{crown ether}]\,OH^- \qquad (2)$$

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The postulate led us to study the use of primary alkylamine–water–crown ether system as a source of hydroxide ion in organic reactions.

Pentacarbonyliron and its polynuclear homologs can be converted into carbonylhydridoferrate anions ($HFe(CO)_4^-$ from $Fe(CO)_5$) by the action of a strong base. The hydrido anions have been used in the selective reduction of activated double bonds.[3] This paper reports on the use of primary alkylamine–water–crown ether combination as an effective alkali in the hydrido anion reduction. Unsaturated esters (acrylates or cinnamates) could be reduced by the reduction system, but side reactions such as transamination and Michael addition as well as hydrolysis are involved, thus affording unreproducible results. Benzylideneacetone was selected as an adequate substrate, although its reduction was also accompanied by Michael addition. The present study was undertaken in order to confirm the possibility of suppression of the side reaction by a technique consisting of phase-transfer effect and enhancement of hydroxide ion activity.

Results and Discussion

Effect of Dicyclohexano-18-crown-6 (DC18C6). Benzylideneacetone (1 mmol) was allowed to react with a reduction system, butylamine(2 mmol)–water(0.5 ml)–$Fe(CO)_5$(4 mmol)–benzene(2 ml), at 25 °C under vigorous stirring for 24 h. GLC analysis of the product in the benzene layer showed a 77% consumption(conversion) of the substrate and 22% formation of 4-phenyl-2-butanone (based on benzylideneacetone reacted; selectivity). The balance represents the extent of side reaction. Two of the by-product A and B were observed in the ratio 9: 1. Treatment of benzylideneacetone with 2 molar excess of butylamine in benzene gave the main by-product which coincided with peak A and was considered to be the Michael adduct. Attempt to isolate the two peaks from the reduction mixture for structural identification by preparative GLC was unsuccessful because of decomposition of the components during the course of separation. The results of the reduction under various conditions are summarized in

TABLE 1. REDUCTION OF BENZALACETONE[a] WITH $Fe(CO)_5$–RNH_2–H_2O–CROWN ETHER–BENZENE SYSTEM

Run	CE[a]	Base[a]	Reaction time/h	Result[b] Conversion %	Selectivity %
1	DC18C6	n-C_4NH_2	24	100	88
2	DC18C6	t-C_4NH_2	24	77	95
3	DC18C6	n-C_8NH_2	24	100	65
4	DC18C6	n-C_8NH_2	5	84	83
5	DC18C6	KOH	24	93	93
6	—	n-C_4NH_2	24	76	22
7	—	t-C_4NH_2	24	38	61
8	—	n-C_8NH_2	24	84	32
9	—	KOH	24	10	100
10	DC18C6	n-C_4NH_2	9	65	86
11	18C6	n-C_4NH_2	9	51	29
12	DC18C6	K_2CO_3	24	87	92
13	DC18C6	CH_3CO_2K	24	17	88

a) Reaction conditions: benzalacetone, 1 mmol; crown ether (CE), 1 mmol; base, 2 mmol, at 25 °C. b) Determined by GLC.

Table 1. When an equimolar amount of DC18C6 was added, the reduction of benzylideneacetone proceeded to give 100% conversion and 88% selectivity. The result is nearly comparable to that obtained with $Fe(CO)_5$–KOH–DC18C6 combination (Run 5, Table 1), and evidences pronounced effect of the crown ether addition. The expected phase-transfer effect in the present system is also observed in the $Fe(CO)_5$–KOH combination. Other weak bases, K_2CO_3 and CH_3CO_2K, can also act as a hydroxide ion source in the presence of DC18C6, though less effectively in the latter. Fedoryński *et al.*[4] recently reported that a combination of K_2CO_3 and a crown ether in non-polar solvents can be used effectively for generating carbanions from active methylene compounds in a solid-liquid system.

Effect of Structures of Primary Alkylamines and Crown Ethers. The stability of primary alkylammonium ion–crown ether complexes depends on the structure of the amines, and steric bulk of the alkyl groups is an important factor.[5] The steric effect was examined with the use of *t*-butylamine in the reduction. Its use in place of butylamine gave a low conversion as expected, but selectivity for reduction was considerably high even in the absence of DC18C6. The low conversion could be much improved by the addition of the crown ether, accompanied by increase in selectivity. The high selectivity obtained with the tertiary-amine under both conditions can be interpreted by the decrease in nucleophilic function of the amine due to the bulky *t*-butyl group. Octylamine was more efficient than butylamine for the reduction probably because of an increase of its solubility and the resulting increase of hydroxide ion concentration in the benzene layer even in the absence of the crown ether. However, the increase of solubility of the amine seems to cause an increase of Michael adduct leading to a lower selectivity.

18-Crown-6(18C6) is a more favorable complexing agent to alkylammonium salts than DC18C6. However, it gave no improvement in both conversion and selectivity as compared to the latter. This might be attributed to a larger solubility of 18C6 and its ammonium ion complex in water. Benzocrown ethers, benzo-18-crown-6 and dibenzo-18-crown-6, were less efficient than 18C6. This indicates that conversion and selectivity in the present reduction depend not only on the stability of **1** but also on solubilities of **1** and free amines in the benzene layer.

Routes of the Formation of Reducing Agent. In the present reduction, reducing agents are considered to be $HFe(CO)_4^-$ and $HFe_2(CO)_8^-$ which might be formed from the mononuclear anion under the reaction conditions. Collman *et al.*[3d] reported that $Na^+HFe_2(CO)_8^-$ is more reactive (>26 times) than $Na^+HFe(CO)_4^-$ in the reduction of activated double bonds in THF. A qualitative examination for the presence of the reagents and also for the effect of DC18C6 on their formation was made by IR measurement.[6] When $Fe(CO)_5$ (1 mmol) was allowed to react with a mixture of butylamine (2 mmol) and water (0.5 ml) in benzene (4 ml) at 25 °C under vigorous stirring in the presence of the crown ether, the color of the mixture turned rapidly from yellow to deep-red. A spectrum of the benzene layer taken 2 h after mixing showed the formation of $HFe(CO)_4^-$ (ν_{CO} 1915 cm^{-1} sh), 1880 cm^{-1} (s)) and $HFe(CO)_{11}^-$ (ν_{CO} 2070 cm^{-1} (vw), 1995 cm^{-1}(s), 1978 cm^{-1} (m), 1950 cm^{-1} (sh)), and the presence of a small quantity of unreacted $Fe(CO)_5$ (ν_{CO} 2020 cm^{-1} (s), 1995 cm^{-1} (s)). On the other hand, in the absence of the crown ether the color change to deep-red proceeded slowly, the IR spectrum of the benzene layer indicating a large quantity of $Fe(CO)_5$ remaining unreacted. Hydrido anions observed in the spectrum were small amounts of $HFe_2(CO)_8^-$ (ν_{CO} 1913 cm^{-1}) and $HFe_3(CO)_{11}^-$, the absorption of $HFe(CO)_4^-$ being very weak.

The marked effect of DC18C6 in the formation of $HFe(CO)_4^-$ strongly suggests that there are two major routes for the formation of the anion, the reaction of $Fe(CO)_5$ with free amine and that with hydroxide ion in **1** derived according to Eq. 2. The reaction of $Fe(CO)_5$ with alkylamines, especially with secondary amines, was studed in detail by Edgell *et al.*[7] Application of their results to the present primary amine system gave the following results. A reaction of a primary amine with $Fe(CO)_5$ gives an equilibrium mixture of $R\overset{+}{N}H_2COFe(CO)_4^-$ (**3**) and $[R\overset{+}{N}H_3][RNHCOFe(CO)_4^-]$ (**4**); in the presence of water and excess amine they are hydrolyzed to an equimolar mixture of $[R\overset{+}{N}H_3][HFe(CO)_4^-]$ (**2**) and $[R\overset{+}{N}H_3][RNHCO_2^-]$ (**5**) (Scheme 1). Under the present conditions containing only a small quantity of water (especially in the benzene layer) hydrolysis would be sluggish and far from complete. The lower selectivity for benzylideneacetone in the absence of DC18C6 (Table 1) can be accommodated with the slow formation of the hydrido anions (HFe-

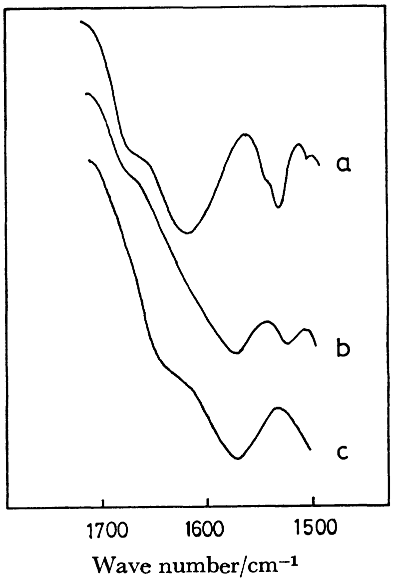

Fig. 1. IR spectra of the reaction mixture of $Fe(CO)_5$ and butylamine, and butylcarbamate solution.

a) $Fe(CO)_5$–*n*-$BuNH_2$–DC18C6–H_2O–C_6H_6.

b) $Fe(CO)_5$–*n*-$BuNH_2$–H_2O–C_6H_6.

c) $[n\text{-}Bu\overset{+}{N}H_3][n\text{-}BuNHCO_2^-]$–DC18C6–$C_6H_6$.

The crown ether was added to solubilize the salt in benzene.

$(CO)_4^-$ and $HFe_2(CO)_8^-$). The formation of butylcarbamate salt (**5**) in the reduction mixture was also confirmed by comparison of its IR spectrum with that of an authentic butylcarbamate solution (1570 cm^{-1}) (Fig. 1).

In the absence of a crown ether.

$$RNH_2 + Fe(CO)_5 \rightleftarrows \underset{\mathbf{3}}{R\overset{+}{N}H_2COFe(CO)_4^-}$$

$$\xrightleftharpoons{RNH_2} \underset{\mathbf{4}}{[R\overset{+}{N}H_3][RNHCOFe(CO)_4^-]}$$

$$\mathbf{3} \text{ and } \mathbf{4} \xrightarrow{H_2O,\ RNH_2}$$

$$\underset{\mathbf{2}}{[R\overset{+}{N}H_3][HFe(CO)_4^-]} + \underset{\mathbf{5}}{[R\overset{+}{N}H_3][RNHCO_2^-]}$$

Scheme 1.

In the presence of a crown ether (CE).

$$RNH_2 + H_2O \rightleftarrows R\overset{+}{N}H_3\,OH^-$$

$$R\overset{+}{N}H_3\,OH^- \xrightleftharpoons{CE} \underset{\mathbf{1}}{[R\overset{+}{N}H_3\cdot CE]\,OH^-}$$

$$\mathbf{1} + Fe(CO)_5 \longrightarrow \underset{\mathbf{6}}{[R\overset{+}{N}H_3\cdot CE][HFe(CO)_4^-]}$$

$$+ \underset{\mathbf{7}}{[R\overset{+}{N}H_3\cdot CE]\,HCO_3^-}$$

$$\text{and/or } \underset{\mathbf{8}}{[R\overset{+}{N}H_3\cdot CE]_2CO_3^{2-}}$$

Scheme 2.

Scheme 2 is a modification of the pathway commonly accepted for the formation of carbonylhydridoferrate anions by causic alkalis (so-called base reaction), and could be realized by complexization of the alkylammonium hydroxide with crown ether. Hydroxide ion of **1** would effectively react with $Fe(CO)_5$ to give **6** and **7** (and/or **8**). The rapid formation of $HFe(CO)_4^-$ in a large quantity and the enhanced conversion in the reduction, as high as that observed when KOH was used, could be interpreted by this route, though the extent of the participation of $HFe_2(CO)_8^-$ in the reduction is not clear. IR inspection of the reduction mixture obtained in the presence of DC18C6 indicated the presence of hydrogencarbonate and/or carbonate ions (*ca.* 1620 cm^{-1}) and a marked decrease of the butylcarbamate ion (Fig. 1). It is obvious that the increased formation of **6** (and its polynuclear homologs) as well as **7** and **8** cause a decrease of free alkylamine, especially in the benzene layer, by its conversion into the onium ion complexes. An interpretation for the increase in selectivity in the reduction effected by the addition of DC18C6 is given by Scheme 2.

It is concluded that the primary alkylamine–water–crown ether system can be used as effective hydroxide ion source especially in a two phase system.

Eoperimental

Materials. Benzylideneacetone, DC18C6,[8] and benzocrown ethers[8] were prepared by conventional methods. Commercial 18C6 (Bokusuy Brown Co.) was used. Pentacarbonyliron (Alfa Products), primary amines, water, and benzene were distilled and stored under nitrogen.

General Procedure. All reactions were carried out under nitrogen with a vessel (*ca.* 10 ml) equipped with an outer jacked for circulation of water (thermostated at 25±0.5 °C) and a serum cap for introduction of pentacarbonyliron by means of a syringe. Water (0.5 ml), alkylamine (2 mmol), benzene (2 ml) containing heptadecane as an internal standard, benzylideneacetone (1 mmol) and a crown ether (1 mmol) were placed in the vessel, and then pentacarbonyliron (4 mmol) was added. The mixture was vigorously stirred at 25 °C. After a certain time (24 h or 8 h), the reaction mixture was neutralized by addition of aq HCl, and the aqueous layer was extracted by ether twice. The products in the combined organic layer were analyzed by GLC (PEG 20M 10%-Celite 545, 3 mm×2 m, FID).

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