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USE OF PHASE-TRANSFER CATALYSIS IN ORGANOMETALLIC REACTIONS: A CONVENIENT SYNTHESIS OF KETONES FROM ALKYL HALIDES AND IRON PENTACARBONYL

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The $Fe(CO)_5$-aqueous NaOH reagent system in benzene in the presence of a phase-transfer catalyst reacts efficiently with alkyl halides to afford symmetrical and unsymmetrical ketones, depending on the structure of alkyl halides and procedures employed. The features of this reaction are discussed.

Disodium tetracarbonylferrate, $Na_2Fe(CO)_4$, has been shown to be a useful reagent for organic synthesis.[1)] However, the tedious preparation and handling of this reagent prevent its practical applications in laboratory synthesis: $Na_2Fe(CO)_4$ has been prepared from $Fe(CO)_5$ and Na-Hg amalgam[2)] or metallic sodium[3)] in non-aqueous media under unaerobic conditions. On the other hand, phase-transfer catalysis has been developed as a powerful and convenient tool for organic synthesis, although this technique has little been applied to organometallic chemistry.[4)]

We now wish to report a simple and convenient method for the synthesis of ketones starting from alkyl halides. The method involves the generation of a ferrate ion, $Fe(CO)_4^{2-}$, from $Fe(CO)_5$ and aqueous sodium hydroxide in an organic solvent in the presence of phase-transfer catalyst. The ferrate ion thus produced reacts efficiently with alkyl halides to give symmetrical and unsymmetrical ketones, depending on the structure of alkyl halides and procedures employed. These reactions can be carried out in a single flask.

$$\underset{[1]}{RX} \xrightarrow[Bu_4NBr]{Fe(CO)_5\ ,\ NaOH} \underset{[2]}{RCOR}$$

a: R= $C_6H_5CH_2$, X= Br
b: R= p-$ClC_6H_4CH_2$, X= Br
c: R= p-$CH_3C_6H_4CH_2$, X= Br
d: R= n-C_8H_{17} , X= I
e: R= n-C_8H_{17} , X= Br

A mixture of benzyl bromide [1a] (1.5 mmol), $Fe(CO)_5$ (1.5 mmol), 33% aqueous NaOH (4 ml), and tetrabutylammonium bromide [Bu_4NBr] (0.18 mmol) in 4 ml of benzene was stirred for 3 h at room temperature under N_2. The resulting mixture was poured onto I_2-benzene solution and stirred for 0.5 h. The mixture was washed successively with aqueous $Na_2S_2O_3$, 10% HCl, and water. The benzene solution was dried (Na_2SO_4) and evaporated, and the residue was submitted to TLC (silicagel-benzene)

Table 1 Preparation of symmetrical ketones[a)]

Halide	Reaction time, h	Product	Yield, %[b)]
Benzyl bromide [1a]	3	Dibenzyl ketone [2a]	94 (83)
Benzyl chloride	13	[2a]	3
p-Chlorobenzyl bromide [1b]	3	Bis(p-chlorobenzyl) ketone [2b]	88 (70)
p-Methylbenzyl bromide [1c]	3	Bis(p-methylbenzyl) ketone [2c]	98 (77)
1-Iodooctane [1d]	30	9-Heptadecanone [2d]	91
1-Bromooctane [1e]	30	[2d]	trace

a) The reactions were conducted in the same manner as described in the text.

b) Yields were determined by GLC analysis, and those in parentheses are for isolated products.

to give 0.26g (83%) of dibenzyl ketone [2a]. Similarly, substituted benzyl bromides were converted into the corresponding dibenzyl ketones. An alkyl iodide gave the corresponding dialkyl ketone in high yield. In all cases, no ketones were obtained when the reactions were carried out in the absence of Bu_4NBr. The results are summarized in Table 1.

By this procedure, 1-bromooctane [1e] failed to give 9-heptadecanone [2d], in spite of its disappearance during the reaction. From this result, it was suspected that [1e] forms an alkyl-iron complex by the reaction with the ferrate ion produced during the reaction, and the complex may be converted into unsymmetrical ketones by treating with other reactive alkyl halides.

$$RBr \xrightarrow[Bu_4NBr]{Fe(CO)_5\ ,\ NaOH} [R\text{-}Fe(CO)_4]^- \xrightarrow{R'I} RCOR'$$

[4] a: $R = n\text{-}C_8H_{17}$, $R' = C_2H_5$

Thus, [1e] (less reactive halide) was at first treated with a mixture of $Fe(CO)_5$ and aqueous NaOH in benzene in the presence of Bu_4NBr, and then ethyl iodide (more reactive halide) was added to the resulting mixture. Work-up of the reaction mixture gave the unsymmetrical ketone, 3-undecanone [4a].[5)] Similarly, several unsymmetrical ketones were synthesized. The results are given in Table 2.

Table 2 Preparation of unsymmetrical ketones[a)]

RX	R'X	Product (%)[b)]
$C_8H_{17}Br$	C_2H_5I	$C_8H_{17}COC_2H_5$ (45)
$C_{16}H_{33}Br$	C_2H_5I	$C_{16}H_{33}COC_2H_5$ (60)
C_6H_5COCl[c)]	C_2H_5I	$C_6H_5COC_2H_5$ (15)

a) A mixture of RX(1.5 mmol), $Fe(CO)_5$ (1.5 mmol), 33% NaOH(4 ml), Bu_4NBr (0.5 mmol) in benzene(4 ml) was stirred for 12 h at room temperature under N_2, and then R'X(4.5 mmol) was added into the mixture. The resulting mixture was further stirred for 5 h. b) Yields are for isolated products. c) Benzoyl chloride was used as a starting compound.

Further, the following features were observed from preliminary mechanistic investigations.

1) In the synthesis of symmetrical ketones, alkyl halides reacted with $Fe(CO)_5$ in a molar ratio of 4:1. For example, [1a] reacted with $Fe(CO)_5$ in a molar ratio of 4:1 to produce two molar amounts of [2a], which corresponds to a 200% yield based on $Fe(CO)_5$ used (Fig. 1). This is in sharp contrast with the case of $Na_2Fe(CO)_4$ in that [1a] reacted with $Na_2Fe(CO)_4$ in THF in a molar ratio of 2:1 to produce one molar amount of [2a].

2) The addition of potassium bromide into the reaction system hindered the formation of ketones. This result suggests that the anion exchange reaction between Bu_4NBr and NaOH (see reaction (a) in Scheme I) participates in this ketone synthesis.

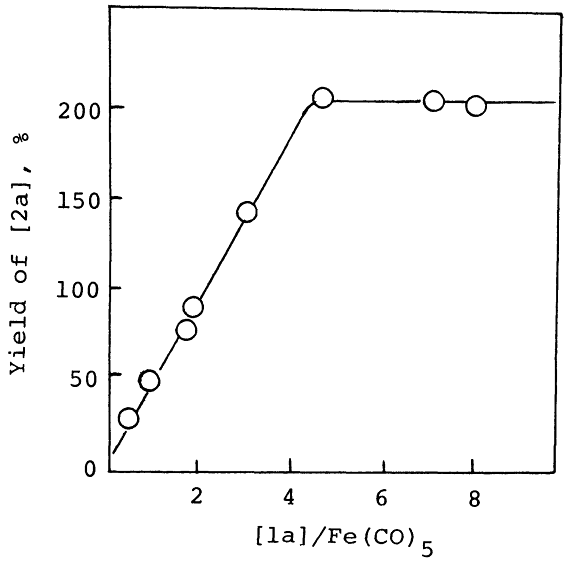
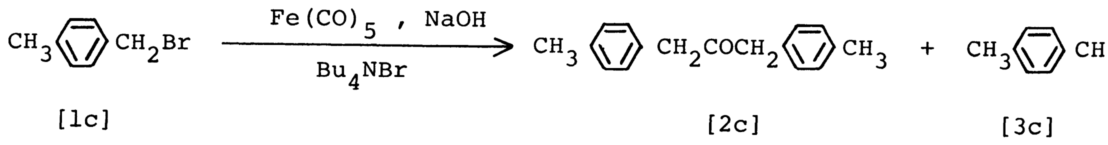


Fig. 1 Change of yields of [2a] with variation of the ratio of $[1a]/Fe(CO)_5$: $Fe(CO)_5$ (0.75 mmol), Bu_4NBr (0.09 mmol), 33% NaOH (2 ml), C_6H_6 (2 ml). Yields based on $Fe(CO)_5$ used.

Table 3 Dependence of the product distributions on the concentrations of NaOH in the reaction of [1c] with $Fe(CO)_5$

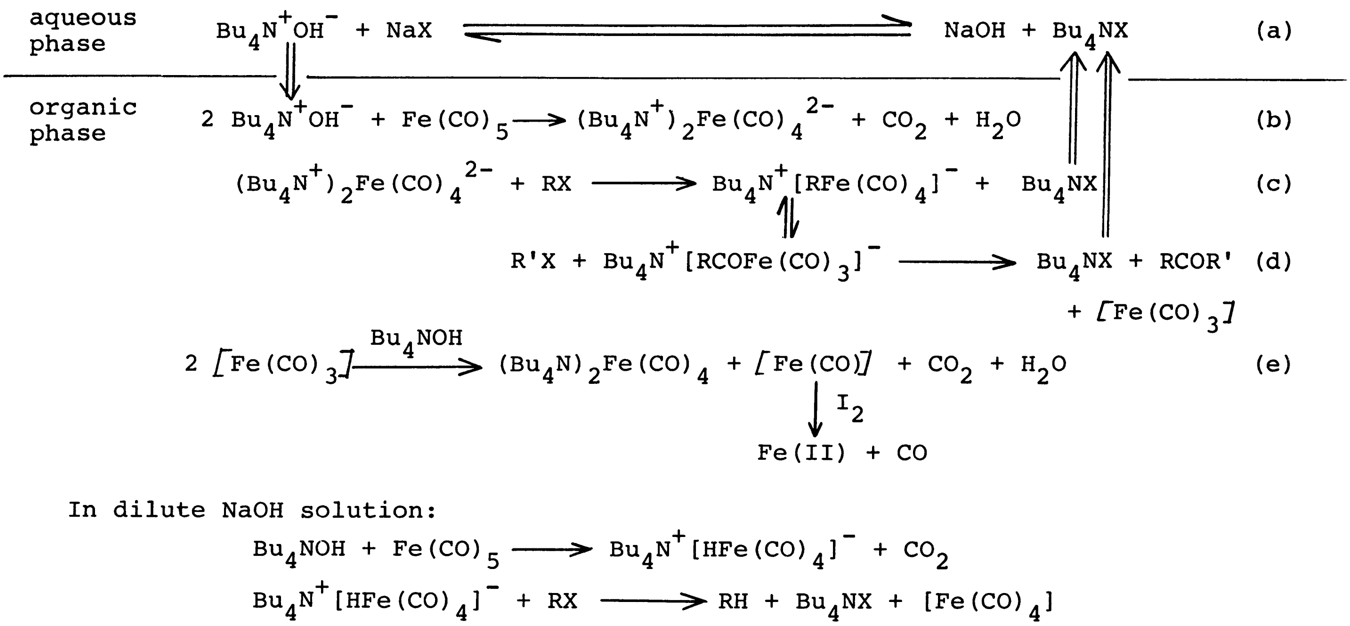
Concn of NaOH (%)	Product distribution (%)	
	[2c]	[3c]
0.4	30	70
2.0	33	67
3.8	50	50
16.6	85	15
28.7	84	16
33.0	95	5
50.0	97	3

3) Concentration of added NaOH affected the sort and distribution of products. The reaction of [1c] with $Fe(CO)_5$ at various concentrations of NaOH gave [2c] and [3c], and their proportion depended upon the concentration of NaOH (Table 3). The proportion of the reduction product [3c] increased with decreasing the concentration of NaOH. This result suggests that a hydrido complex $HFe(CO)_4^-$ is produced in a dilute NaOH solution.$^{6)}$



These results can be explained in terms of mechanistic pathways illustrated in Scheme I. In the ketone synthesis, the ferrate ion $(Bu_4N)_2Fe(CO)_4$ participates as a key reactive intermediate. A striking feature of this phase-transfer-catalyzed reaction is that the ferrate ion is regenerated from a reaction product such as $[Fe(CO)_3]$ speciés, although the regeneration process has not yet been clarified: the regeneration of one mole of the ferrate ion from two moles of $Fe(CO)_5$ accounts for the results illustrated in Fig. 1.[7)]

Detailed mechanism and scope of the reactions are now under investigation.



Scheme I

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References and Notes

1) J. P. Collman, Acc. Chem. Res., 8, 342 (1975) and references cited therein.

2) M. P. Cooke, J. Am. Chem. Soc., 92, 6080 (1970).

3) J. P. Collman, R. G. Finke, J. N. Cawse, and J. I. Brauman, J. Am. Chem. Soc., 99, 2515 (1977).

4) E. V. Dehmlow, Angew. Chem. Int. Ed. Engl., 13, 170 (1974); ibid, 16, 493 (1977).

5) The reactivity of alkyl halides in the reaction with $Na_2Fe(CO)_4$ decreases in the order: RI > RBr > RCl.[1)]

6) Takegami and his coworkers have proposed that $HFe(CO)_4^-$ is mainly produced from $Fe(CO)_5$ and ethanolic KOH when a dilute KOH solution was used: Y. Takegami, Y. Watanabe, H. Masada, and I. Kanaya, Bull. Chem. Soc. Jpn., 40, 1456 (1967).

7) Quantitative analysis of the evolved gas in the reaction of [1a] with $Fe(CO)_5$ indicated that one mole of CO evolved from one mole of $Fe(CO)_5$ consumed when the analysis was carried out after the reaction was completed and then the resulting mixture was treated with I_2.

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