Selective Syntheses of Aliphatic Ketones Using Sodium Tetracarbonylferrate(−II)

Sir:

In spite of extensive recent research few organo transition metal complexes have become important reagents in organic synthetic methodology. Side reactions, expensive reagents, and tedious work-ups account for the limited impact of this new chemistry on practical laboratory synthesis. We have found $Na_2Fe(CO)_4$ to be an inexpensive, versatile, selective reagent[1] converting alkyl bromides, iodides, and tosylates into aldehydes,[2] carboxylic acid derivatives, and ketones in high yields.[3] The use of this reagent to prepare unsymmetrical ketones is described herein.

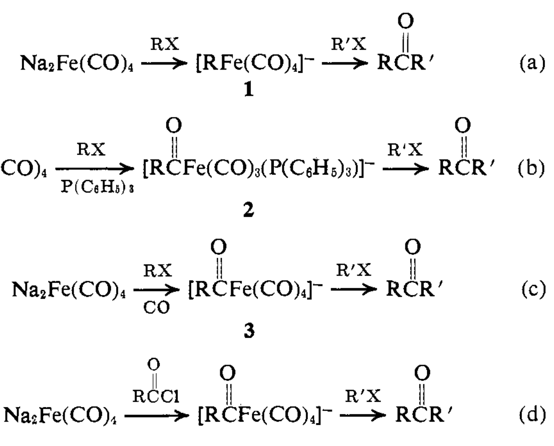
Table I

RX[a] (mmol)	R′X[a] (mmol)	Method	Ligand	Solvent[b]	Product[c]	% yield[d]
n-$C_8H_{17}Br$ (10)	C_2H_5I (30)	a		MP	*n*-$C_8H_{17}COC_2H_5$	80 (99)
n-$C_8H_{17}I$ (1)	C_2H_5I (1)	a		MP	*n*-$C_8H_{17}COC_2H_5$	(98)
C_2H_5I (10)	*n*-$C_8H_{17}I$ (60)	a		MP	*n*-$C_8H_{17}COC_2H_5$	77 (91)
n-$C_5H_{11}Br$ (1)	C_2H_5 (1)	b	$P(C_6H_5)_3$ (1.2)	MP	*n*-$C_5H_{11}COC_2H_5$	(95)
sec-$C_8H_{17}OTs$ (8.5)	CH_3I (24)	c	CO (10 psi)	THF–HMPA (2:1)	*sec*-$C_8H_{17}COCH_3$	79
n-$C_8H_{17}Br$ (4)	CH_3OCH_2Cl (4)	b	$P(C_6H_5)_3$ (5)	MP	*n*-$C_8H_{17}COCH_2OCH_3$	31
n-$C_5H_{11}COCl$ (10)	C_2H_5I (60)	d		THF–HMPA (2:1)	*n*-$C_5H_{11}COC_2H_5$	87 (99)
$Br(CH_2)_4CO_2C_2H_5$ (10)	C_2H_5I (30)	a		MP	$C_2H_5CO(CH_2)_4CO_2C_2H_5$	74 (80)

[a] In all reactions the amount of $Na_2Fe(CO)_4$ used corresponded to that of RX or to a slight excess of the former. [b] MP, *N*-methyl-2-pyrrolidone; THF in first step, HMPA added with the iodide. [c] Products were all characterized by their ir, pmr, and mass spectra and, in the case of new compounds, by elemental analyses. [d] Yields in parentheses were determined by glc analysis using internal standards. Other yields are for isolated products.

Four similar, but distinct ketone syntheses are outlined (Scheme I). Method a makes use of anionic alkyl iron intermediates whereas paths b, c, and d involve anionic acyl iron complexes.[4]

Scheme I



$$Na_2Fe(CO)_4 \xrightarrow{RX} \underset{\mathbf{1}}{[RFe(CO)_4]^-} \xrightarrow{R'X} R\overset{O}{\overset{\|}{C}}R' \qquad (a)$$

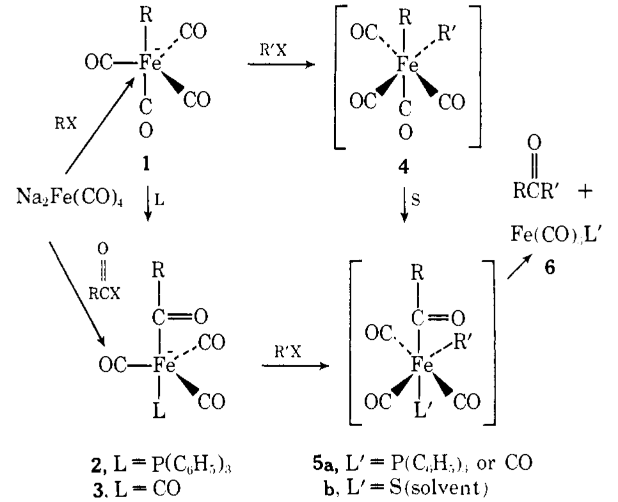
$$Na_2Fe(CO)_4 \xrightarrow[P(C_6H_5)_3]{RX} \underset{\mathbf{2}}{[R\overset{O}{\overset{\|}{C}}Fe(CO)_3(P(C_6H_5)_3)]^-} \xrightarrow{R'X} R\overset{O}{\overset{\|}{C}}R' \qquad (b)$$

$$Na_2Fe(CO)_4 \xrightarrow[CO]{RX} \underset{\mathbf{3}}{[R\overset{O}{\overset{\|}{C}}Fe(CO)_4]^-} \xrightarrow{R'X} R\overset{O}{\overset{\|}{C}}R' \qquad (c)$$

$$Na_2Fe(CO)_4 \xrightarrow{R\overset{O}{\overset{\|}{C}}Cl} [R\overset{O}{\overset{\|}{C}}Fe(CO)_4]^- \xrightarrow{R'X} R\overset{O}{\overset{\|}{C}}R' \qquad (d)$$

The experimental nuances and relative advantages of each method are better discussed in terms of the apparent mechanisms by which these reactions take place (Scheme II). Alkyl halides or tosylates react with $[Fe(CO)_4]^{2-}$ to afford anionic iron alkyls **1**, examples of which have been isolated and thoroughly characterized.[5] This reaction can be considered either an S$_N$2 attack[6] on the alkyl halide or as an oxidative addition to the d^{10} iron(−II).[7] Further reaction of **1** with another alkyl halide (method a) should lead to a yet undetected dialkyl iron complex **4** which appears to immediately decompose to the ketone, probably *via* the alkyl–acyl iron complex **5b** formed by solvent assisted migratory insertion. It is remarkable that none of the alkyl coupling products anticipated from the dialkyl **4** could be detected. The absence of these coupling products emphasizes our limited understanding of reductive elimination reactions. Methods b and c involve the generation of anionic iron acyls **2** or **3** through migratory insertion promoted by triphenylphosphine or CO. In method d the acyl complex is obtained directly from an acid chloride. Salts of **3** have also been isolated and characterized. Further alkyl-

Scheme II



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[1] We have developed a new large-scale preparation of $Na_2Fe(CO)_4$ from the reduction of $Fe(CO)_5$ with sodium dispersion in THF using benzophenone ketyl as an electron carrier. This procedure will be published separately.

[2] M. P. Cooke, *J. Amer. Chem. Soc.*, **92**, 6080 (1970).

[3] Aspects of this work were presented at the 162nd National Meeting of the American Chemical Society in Washington, D. C., Sept 13, 1971.

[4] Benzyl ketones have been prepared by related methods. See I. Rhee, M. Ryang, and S. Tsutsumi, *J. Organometal. Chem.*, **9**, 361 (1967), and Y. Sawa, M. Ryang, and S. Tsutsumi, *J. Org. Chem.*, **35**, 4183 (1970).

[5] J. P. Collman and W. O. Siegl, submitted for publication.

[6] Preliminary kinetic studies show the rate law for the formation of the iron alkyl in THF to be of the form $-d[RX]/dt = k_2[RX][Fe(CO)_4{}^{2-}]$; J. P. Collman and J. N. Cawse.

[7] J. P. Collman, *Accounts Chem. Res.*, **1**, 136 (1968).

ation of **2** and **3** probably affords the yet undetected alkyl–acyl intermediate **5a**[8] which appears to collapse by reductive elimination to the ketone and a coordinatively unsaturated iron(0) complex.[10] Protonation of the alkyl and acyl intermediates **1**, **2**, and **3** affords the corresponding alkanes and aldehydes. The latter reaction is the basis of the aldehyde synthesis which we reported earlier.[2]

Specific examples of ketone syntheses listed in Table I illustrate the following points.[11] Since both alkylations in eq a, b, and c are SN2 reactions, substrate limitations are understandable in view of the apparent order of decreasing nucleophilicity: $[Fe(CO)_4]^{2-}$ > $[RFe(CO)_4]^-$ > $[(RCO)Fe(CO)_3(P(C_6H_5)_3)]^-$ > $[(RCO)Fe(CO)_4]^-$. In the first alkylation primary bromides, iodides, and tosylates and secondary tosylates can be used, but the second stage requires more reactive alkylating agents such as primary iodides or tosylates, benzylic halides, or α-chloro ethers. To ensure maximum yields an excess of the second alkylating agent must be employed, especially for methods c and d which involve the poorest iron nucleophile. Secondary tosylates are preferred over the bromides to minimize eliminations.[12]

The most remarkable and potentially useful feature of the $[Fe(CO)_4]^{2-}$ reagent is its toleration of organic functional groups. This is illustrated (Table I) by the conversion of a 5-bromo ester into a 6-keto ester.

Method c is stereospecific, and it is likely that the other methods will also be so. (*S*)-(+)-2-Octyl tosylate ($[\alpha]^{25}D$ +7.96°, 99% ee) afforded (*R*)-(−)-3-methyl-2-nonanone ($[\alpha]^{25}D$ −12.03°, 99% ee) with overall inversion at the chiral carbon.[14] In view of the well-known inversion in SN2 reactions and the recently established retention in an alkyl–acyl insertion,[15] we suppose that **1** is formed with inversion and that the transformation to **3** takes place with retention.

Acknowledgments. We wish to acknowledge assistance from M. P. Cooke, J. N. Cawse, and L. Libit. This work was supported by a grant from the National Science Foundation (GP 20273X).

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[8] It is possible that the reaction proceeds *via* a neutral carbene complex, $(OC)_4FeC(OR')R$, but similar carbene complexes have been prepared[9] and appear to be too stable thermally to account for our mild ketone synthesis.

[9] E.O. Fischer and C. G. Kreiter, private communication.

[10] The purported intermediate in eq c, $Fe(CO)_4$, trimerizes to $Fe_3(CO)_{12}$ when free CO is not present.

[11] All reactions were conducted under a nitrogen atmosphere. In a typical preparation 2.16 g (10.3 mmol) of ethyl 5-bromovalerate was added to a solution of 2.37 g (11.1 mmol) of $Na_2Fe(CO)_4$ in 30 ml of *N*-methyl-2-pyrrolidone (distilled from CaH_2), the reaction stirred for 1 hr, and 2.4 ml (30.0 mmol) of ethyl iodide added. After 24 hr the solution was diluted with ether, washed three times with brine, dried, and filtered, and the ether was removed with a rotary evaporator. The residue was placed on a short column (130 g of silica gel) and washed free of the colored iron byproducts with hexane, and the product removed with 50% ether–hexane. Fractional distillation gave 1.41 g (74%) of ethyl 6-ketooctanoate.

[12] The basicity of $[Fe(CO)_4]^{2-}$ is estimated to be about that of $[OH^-]$ on the basis of pK_a values reported[13] for the corresponding hydrides.

[13] W. Hieber and W. Hubel, *Z. Elecktrochem.*, **57**, 235 (1953).

[14] The configuration of (*R*)-(−)-3-methyl-2-nonanone was established by Baeyer–Villiger degradation to 2-acetoxyoctane which was compared with an authentic sample prepared from (*S*)-(+)-2-octanol.

[15] G. M. Whitesides and D. J. Boschetto, *J. Amer. Chem. Soc.*, **91**, 4313 (1969).

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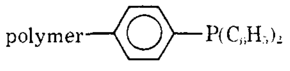
Received November 24, 1971

Resin-Bound Transition Metal Complexes

Sir:

Organic reactions in which one component is fastened to a porous solid support offer strategic synthetic advantages in the dilution[1] or isolation[2] of that component and the removal of byproducts.[3] Homogeneous transition metal catalysts bound to a resin may also exhibit properties different from those in solution. For example, a rhodium hydrogenation catalyst attached to polystyrene exhibits selectivity toward smaller olefins.[4,4a] Since the active forms of homogeneous catalysts are unsaturated,[5] immobilization on a solid support might prevent self-aggregation affording high concentrations of unsaturated complexes. As is shown below, this effect will be difficult to achieve with phosphine-substituted polystyrene because of the pronounced tendency of such polymeric ligands to chelate.

Resin-substituted triphenylphosphine **1** was prepared from cross-linked polystyrene (Biobeads SX-2, 2% crosslinking) by sequential bromination (Br_2, $FeBr_3$), lithiation (*n*-BuLi, THF), and treatment with $(C_6H_5)_2PCl$. The following experiments with **1** employed 1.2 mmol of P/g corresponding to 10% ring substitution. Treatment of **1** with the rhodium(I) or iridium(I) complexes, **2**, afforded the resin-bound complexes, **3**, releasing two $P(C_6H_5)_3$ per metal atom introduced into the polymer.[6] Similarly two $P(C_6H_5)_3$ and one $CH_2{=}CH_2$ were displaced from **4** affording the red polymeric complex **5**, an analog of the Wilkinson hydrogenation catalyst.[7] In these and similar cases, intermediate levels of coordination per metal atom in the polymer by resin-bound phosphine could not be achieved either by varying the ratio of starting complex to resin or the level of phosphine incorporated[8] in the resin. That nonstatistical functionalization



1

$MCl(CO)(P(C_6H_5)_3)_2$
2a, M = Rh
b, M = Ir

$MCl(CO)L_2$
3a, L = **1**; M = Rh
b, L = **1**; M = Ir

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[1] R. L. Letsinger, M. J. Kornet, V. Mahadevan, and D. M. Jermia, *J. Amer. Chem. Soc.*, **86**, 5163 (1964).

[2] (a) I. T. Harrison and S. Harrison, *ibid.*, **89**, 5724 (1967); (b) J. I. Crowley and H. Rapoport, *ibid.*, **92**, 6363 (1970).

[3] R. B. Merrifield, *Fed. Proc.*, **21**, 412 (1962); *J. Amer. Chem. Soc.*, **85**, 2149 (1963); **86**, 304 (1964).

[4] R. H. Grubbs and L. C. Kroll, *ibid.*, **93**, 3062 (1971).

[4a] NOTE ADDED IN PROOF. Other resin-bonded catalysts have been described: Mobil Oil, U. S. Patent 1,800,371 (1969); British Petroleum Co., Belgian Patents 739,607 and 739,609.

[5] J. P. Collman, *Accounts Chem. Res.*, **1**, 136 (1968).

[6] These quantities were determined by analysis of the filtrates from reactions using measured quantities of **1** and the homogeneous complex. A small portion of resin phosphine sites were too sterically hindered to act as ligands. Resin-bound complexes exhibited the same ν_{CO} and colors as their homogeneous counterparts.

[7] J. A. Osborn, F. H. Jardine, J. F. Young, and G. Wilkinson, *J. Chem. Soc. A*, 1711 (1966).

[8] Phosphine substitution levels down to 2% of the benzene rings in the resin were employed with similar results. Analytical errors become correspondingly larger at these low levels.