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Synthesis of Five-Membered Cyclic Ketones Using Potassium Tetracarbonylferrate(2−)

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Synopsis. Various five-membered cyclic ketones were prepared from 1,4-dihaloalkanes and potassium tetracarbonylferrate(2−) in moderate to high yields. However, the yields of six- or seven-membered cyclic ketones from the corresponding dihalides were rather low.

The alkali metal tetracarbonylferrate(2−) $M_2Fe(CO)_4$ (M=Na, K) (**1**) is one of the most characteristic reagents and is used as a stoichiometric reagent in the synthesis of carbonyl compounds including ketones, aldehydes, carboxylic esters and amides via acylcarbonylferrates.[1] On the other hand, saturated and unsaturated five-membered cyclic ketones are important compounds that are not only included in a large number of biologically active natural products as a structural feature, but also as a precursor of lactones by Baeyer–Villiger oxidation. Therefore, undiminished efforts have been devoted to the synthesis of this moiety.[2]

In this paper we wish to report on a facile synthetic method of the five-membered cyclic ketones from 1,4-dihaloalkanes using tetracarbonylferrate (**1**) as a carbonylating agent.

Experimental

The IR spectra were recorded on a Hitachi 260-10 Infrared Spectrophotometer. The NMR spectra were measured on a Hitachi R-600 FT-NMR spectrometer at 60 MHz, using tetramethylsilane (δ=0.00) as an internal standard; chemical shifts are given in ppm. The mass spectra (MS) were determined on a Hitachi RM-50 GC-MS spectrometer. Analytical gas chromatography was carried out on a Yanagimoto G-8 gas chromatograph with a column of 10% Silicone gum SE-30 on Chromosorb and a Shimadzu GC-14A instrument using a Shimadzu capillary column HiCap CBP1-W12-100. The column chromatography was performed on Nakarai silica gel 60 (230—400 mesh).

Materials. Tetrahydrofuran (THF) was dried and deoxygenated by distillation from potassium-benzophenone under argon just before use. *N*-Methyl-2-pyrrolidone (NMP) was dried by distillation at reduced pressure and stored over 3A molecular sieves. Pentacarbonyliron (Strem Chemical Co.) was used without further purification. Potassium tri-s-butylhydroborate was purchased from the Aldrich Chemical Co. as a 1.0 M (1 M=1 mol dm^{-3}) THF solution under the trade name K-Selectride. 1,4-Dibromobutane, 1,5-dibromopentane, and 1,6-dibromohexane were commercial products of the highest available purity. *cis*-1,2-Bis(bromomethyl)cyclohexane, 1,2-bis(bromomethyl)-4-methylcyclohexane, *endo-cis*-2,3-bis(bromomethyl)bicyclo[2.2.1]heptane, 1,4-dibromo-2-phenylbutane, 1-bromo-3-(bromomethyl)pentadecane, and 1,5-dibromo-3-phenylpentane were prepared from *cis*-1,2-cyclohexanedicarboxylic anhydride,[3,4] 4-methyl-*cis*-1,2-cyclohexanedicarboxylic anhydride,[3,4] *cis*-5-bicyclo[2.2.1]heptene-*endo*-2,3-dicarboxylic anhydride,[5] diethyl 2-phenylsuccinate,[3,6,7] dodecylsuccinic anhydride,[3,7] and diethyl 3-phenylglutarate,[6,8] respectively, by usual hydrogenation and the following bromination. Potassium tetracarbonylferrate (**1**) was prepared by a method mentioned in the literature.[9]

Synthesis of *cis*-Bicyclo[4.3.0]nonan-8-one. General Procedure. Reactions were conducted under an argon atmosphere. To the THF solution (13 ml) of 1.0 M potassium tri-*s*-butylhydroborate, 0.79 ml of pentacarbonyliron (6 mmol) was added, and the reaction mixture was refluxed for 4 h. After cooling, a supernatant solution was removed, and the resultant white solid was washed several times with hexane and dried by blowing argon through the flask. Then, 30 ml of NMP was injected and 1,2-bis(bromomethyl)cyolohexane (5 mmol) was added. After stirring the mixture for 24 h at room temperature, the solution was diluted with ether, washed three times with saturated brine, and the organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was separated by column chromatography (hexane : dichloromethane : diethyl ether=5 : 1 : 1) to afford bicyclo[4.3.0]nonan-8-one as oil in 61% isolated yield.[10] IR (cm^{-1}): 2935, 1743, 1163. ^{1}H NMR (CDCl$_3$) (δ): 1.18—1.78 (m, 8H), 2.03—2.58 (m, 6H). MS (*m/z*): 138 (M$^+$).

Other cyclic ketones were synthesized following the general procedure described above.[10]

***cis*-3-Methylbicyclo[4.3.0]nonan-8-one.** Yield 60%. Oil. IR (cm^{-1}): 2930, 1748, 1162. ^{1}H NMR δ=0.90 (d, 3H, *J*=4.0 Hz), 1.00—1.95 (m, 7H), 1.95—2.75 (m, 6H). MS (*m/z*): 152 (M$^+$).

***endo*-Tricyclo[3.2.1.0^{2,6}]decan-4-one.** Yield 52%. Oil. IR (cm^{-1}): 2960, 1742, 1175. ^{1}H NMR δ=1.25—1.70 (m, 6H), 2.17—2.88 (m, 8H). MS (*m/z*): 150 (M$^+$).

3-Phenylcyclopentanone. Yield 58%. Oil. IR (cm^{-1}): 2975, 1750, 1290, 760, 700. ^{1}H NMR δ=1.30 (m, 2H), 2.22—2.77 (m, 4H), 3.40 (m, 1H), 7.28 (s, 5H). MS (*m/z*): 160 (M$^+$).

3-Dodecylcyclopentanone. Yield 60%. Oil. IR (cm^{-1}): 2940, 1750, 1475, 1162. ^{1}H NMR δ=0.90 (t, 3H, *J*=4.0 Hz), 1.20—1.40 (m, 25H), 1.95—2.42 (m, 4H). MS (*m/z*): 252 (M$^+$).

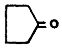
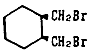
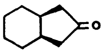
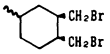
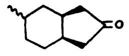
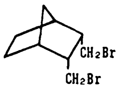
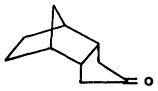
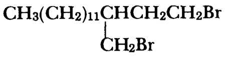
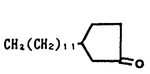
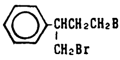
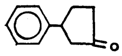
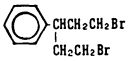
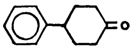
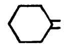
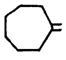
4-Phenylcyclohexanone. Yield 15%. Mp 78—80 °C. IR (cm^{-1}): 2940, 1710, 759, 699. ^{1}H NMR δ=1.80—2.30 (m, 4H), 2.38—2.75 (m, 5H), 7.28 (s, 5H). MS (*m/z*): 174 (M$^+$).

Results and Discussion

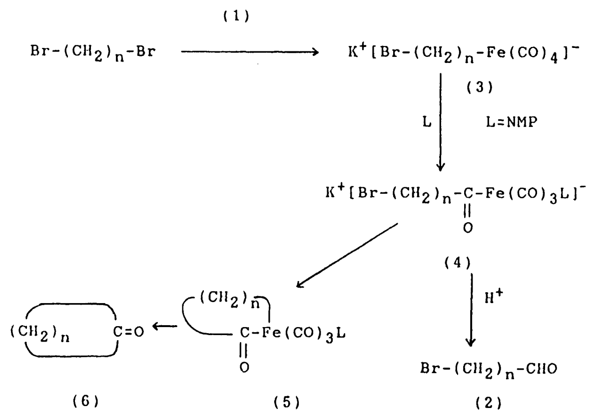
The various 1,4-dibromoalkanes reacted with potassium tetracarbonylferrate (**1**) in NMP to give the five-membered cyclic ketones in good isolated yield. The results of these reactions are listed in Table 1. However, the yields of six- or seven-membered cyclic ketones were rather low. This shows that it is difficult to cyclize intramolecularly. In fact, ω-bromo aldehydes (**2**) were obtained as by-products in these reactions.

The mechanism of these reactions is considered to be as follows (Scheme 1). First, an dibromoalkane reacts with (**1**) to afford an alkylcarbonylferrate (**4**), which transforms into an acylcarbonylferrate (**4**) with the solvent assisted migratory insertion of carbon monoxide. Intramolecular cyclization of the acylcar-

Table 1. Reaction of Dibromoalkanes with $K_2Fe(CO)_4$

Run	Dibromoalkane	Product	Yiels(%)[a]
1	$Br(CH_2)Br$		(60)[b]
2			61
3			60
4			52
5	 $\mathrm{CH_3(CH_2)_{11}\underset{CH_2Br}{\underset{\vert}{C}}HCH_2CH_2Br}$		60
6			58
7			15
8	$Br(CH_2)_5Br$		(35)[b]
9	$Br(CH_2)_6Br$		(5)[b]

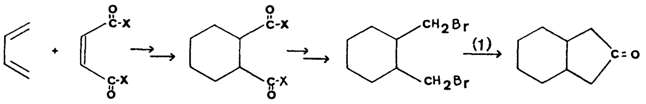
a) Isolated yields. b) Yields in parentheses are determined by GLC.



Scheme 1.

bonylferrate (**4**) leads to an acylalkyliron complex (**5**) which appears to collapse by reductive elimination to a cyclic ketone (**8**). In the reaction of (**1**) with 1,3-dibromopropane, the corresponding acylalkyliron complex (**5**) (n=3, L=triphenylphosphine) has been isolated as crystals.[11] The formation of ω-bromo aldehyde (**2**) is also considered to be derived from (**4**) by protonation in the work-up.[12]

By this method, five-membered cyclic ketones fused to the cyclohexane ring were prepared in good yields. The starting dibromoalkanes were easily prepared from the Diels-Alder adducts via hydrogenation and



bromination. Therefore, this method is considered to be useful in the synthesis of these cyclic ketone skeletons which appear widely in naturally occurring organic compounds.

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