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The Formation of Carbon-Carbon and Carbon-Oxygen Bonds in the Oxidation of Enolizable Ketones with Iron(III) Chloride

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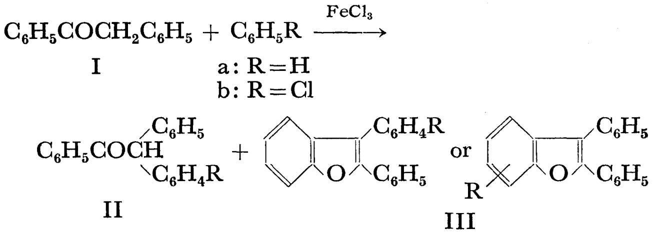
We have recently reported that the oxidation of enolizable alkyl aryl ketones with iron(III) chloride brings about carbon-carbon coupling and/or the chlorination of the α-methylene group.[1] Here we undertook the study of the heterogeneous oxidation of benzyl phenyl ketone (I) with iron(III) chloride in benzene and chlorobenzene. As a result, we found that the reaction differs from those of alkyl aryl ketones and results in the direct arylation of the α-methylene group by a two-electron oxidation. Furthermore, it was found that ring closure by carbon-oxygen coupling occurs in the oxidation of the arylation product (II) with two phenyl groups at the α-position of the carbonyl group.



When a solution of I in benzene containing dispersed iron(III) chloride was refluxed for several hours, the I was converted to 2,2-diphenylacetophenone (IIa) and 2,3-diphenylbenzofuran (IIIa) was formed. Iron(III) chloride was reduced to iron(II) chloride. The nuclear chlorination did not occur at all. The irradiation of a solution of I in benzene in the presence of iron(III) chloride also gave IIa, along with a small amount of IIIa, although I undergoes photolysis to 1,2-diphenylethane, benzaldehyde, and 1,2,3,4-tetraphenyl-1,4-butanedione in the absence of iron(III) chloride.[2] The results are shown in Table 1. The addition of a small amount of water to the reaction system did not have any significant effect on the reaction pathway.

Table 1. The oxidation of I with iron(III) chloride in benzene or chlorobenzene[a)]

Solvent	Therm. or *hν*	Reaction time hr	Yield of product, % II	Yield of product, % III	Recovery %
C_6H_6	Reflux	7	83	7	7
C_6H_6[b)]	Reflux	7	72	8	11
C_6H_6	*hν*	2.5	33	0.2	53
C_6H_5Cl	Reflux	7	60[c)]	—	19

a) The amount of $FeCl_3$: 1.02 mmol in 5 ml of the solvent. The concentration of I: 10^{-1} mol/l. The amounts of the products were determined by glc.
b) Water was added into the reaction system (the molar ratio of $H_2O/FeCl_3$: 1.3).
c) This is the yield of the *p*-isomer.

When chlorobenzene was used as the solvent, the *p*-isomer of IIb was isolated by a treatment similar to that used in the case of benzene (Table 1). However, the *o*- and *m*-isomers and IIIb could not be isolated because their yields were considerably lower than that of the *p*-isomer. The reaction of 2-chloro-2-phenylacetophenone (IV) with chlorobenzene in the presence of aluminum chloride at room temperature also gave the *p*-isomer of IIb in a 63% yield. Furthermore, the *p*-isomer has been prepared by the Friedel-Crafts reaction of benzoin with chlorobenzene in the presence of sulfuric acid.[3] These facts suggest strongly that the reaction proceeds *via* an intermediate (V) which is formed by a two-electron oxidation, followed by the reaction with the solvent, since, in the reaction of the α-keto radical formed by a one-electron oxidation, it is predicted that the yields of the *o*- and *m*-isomers will become higher. Such a process has been considered

$$\mathrm{I} \xrightarrow{FeCl_3} \underset{\mathrm{V}}{C_6H_5CO\overset{+}{C}HC_6H_5} \xrightarrow{C_6H_5R} \mathrm{II}$$

in the oxidative dimerization of phenols with a variety of oxidants.[4] In the oxidation of alkyl aryl ketones with iron (III) chloride, we have reported that the homogeneous reaction results in the coupling of the α-keto radical, while, in the heterogeneous system, α-chlorination occurs by means of a two-electron oxidation.[1] Therefore, the fact that the arylation proceeds by a two-electron oxidation may be explained as resulting from the heterogeneous oxidation by iron(III) chloride. The phenyl group at the α-position of I must be required for the reaction of V with benzene, since the oxidation of propiophenone with iron(III) chloride in benzene resulted in only chlorination, without any arylation. This result agreed with the fact that 1-bromo-1-phenyl-2-propanone undergoes Friedel-Crafts reaction, 2-bromoacetophenone showing no reaction with benzene in the presence of aluminum chloride.[5]

$$C_6H_5COCH_2CH_3 \xrightarrow[C_6H_6]{FeCl_3} C_6H_5CO\overset{Cl}{C}HCH_3$$

On the other hand, IIIa was produced consecutively

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from IIa by the oxidative ring closure with iron(III) chloride; when a solution of IIa in benzene containing iron(III) chloride was refluxed for 2 hr, IIIa was obtained in a 10% yield, with an 85% recovery of IIa, although IIIa was converted to a polymeric material in a longer reaction time. The arylation and chlorination at the α-position of the carbonyl group did not occur. The formation of IIIa indicates that the stereochemical conditions of IIa strongly favor the ring closure by carbon-oxygen coupling, as is shown in the syntheses of xanthones, which can be effected by oxidizing 2,3′-dihydroxybenzophenones with alkaline ferricyanide.[6)]

Experimental

Materials. The I was prepared by the method described in the literature.[7)] The anhydrous iron(III) chloride was prepared by the sublimation of commercial iron(III) chloride under a reduced pressure of 1 mmHg at 300 °C.

Oxidation of I with Iron(III) Chloride. A solution of 5 mmol of Ia in 30 ml of benzene or chlorobenzene containing 10.1 mmol of the dispersed anhydrous iron(III) chloride was refluxed for 7 hr, or was irradiated under stirring with a Pyrex-covered 100-W high-pressure mercury lamp at the distance of 6 cm under a nitrogen atmosphere at room temperature for 2.5 hr. Hydrogen chloride was generated during the reaction. After the reaction period, the precipitate, which contained mainly iron(II) chloride, was filtered off. The iron(II) chloride was confirmed spectrophotometrically by the *o*-phenanthroline method.[8)] The filtrate was submitted to chromatography on alumina (elution with dry benzene), leading to the separation of IIa and IIIa. After removing the benzene, the residue (IIa or IIIa) was recrystallized from ethanol. The isolation of *p*-IIb was carried out according to the method used in the case of IIa, IIa (mp 134—136 °C (lit,[9)] 136 °C)) exhibited NMR (CCl_4) signals at δ 5.87 (s, 1H, CH), and 7.16—7.98 (m, 15H, aromatic protons) and an IR (KBr plate) peak at 1675 cm^{-1} (CO). Mass *m/e*, 272 (parent peak). IIIa (mp 121—122 (lit,[10)] 123 °C)) exhibited NMR (CCl_4) signals of aromatic protons at δ 7.04—7.60. Mass *m/e*, 270 (parent peak). *p*-IIb (mp 102—104 °C (lit,[3)] 104 °C)) exhibited NMR (CCl_4) signals at δ 5.85 (s, 1H, CH) and 7.10—7.94 (m, 14H, aromatic protons) and an IR (KBr plate) peak at 1670 cm^{-1} (CO). Mass *m/e*, 305 and 306 (parent peaks).

Reaction of IV with Chlorobenzene in the Presence of Aluminum Chloride. A solution of 1.2 mmol of IV in 3 ml of chlorobenzene containing 1.4 mmol of the dispersed aluminum chloride was refluxed for 50 min. After the solution had then cooled to room temperature, *p*-IIb was isolated by a method similar to that used in the case of IIa; the amount was determined by glc.

Oxidation of Propiophenone with Iron(III) Chloride. A solution of 1.1 mmol of propiophenone in 3 ml of benzene containing 2 mmol of the dispersed anhydrous iron(III) chloride was refluxed for 22 hr. 2-Chloropropiophenone[1)] was obtained in a 40% yield, along with the recovery of propiophenone. No other products were detected by glc at all.

Oxidation of IIa with Iron(III) Chloride. A solution of 0.3 mmol of IIa in 3 ml of benzene containing 0.6 mmol of the dispersed anhydrous iron(III) chloride was refluxed for 2 hr. The reaction mixture was submitted to glc analysis. IIIa was thus obtained in a 10% yield.

Analyses. The amounts of the products in the reaction mixture were determined by means of glc using a 3 mm × 1 m column of 30% high-vacuum silicon grease on Celite 545 (80—100 mesh).

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