The Reaction of Carbon Monoxide with Organometallic Compounds. VIII. The Synthesis of Aromatic Aldehydes by the Reaction of Iron Pentacarbonyl with Aryllithiums*

By Membo RYANG, Ilsong RHEE and Shigeru TSUTSUMI

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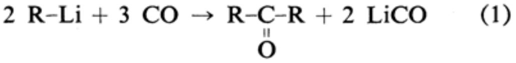
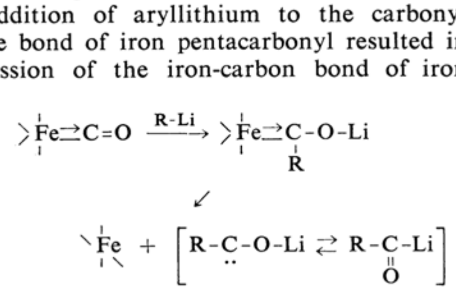
In a previous paper[1] of this series, it was reported that carbon monoxide reacted with organolithium compounds in an ether solution at -70°C to give the corresponding symmetrical ketones in good yields. In these reactions, it was assumed that carbon monoxide attacked organolithium compounds and abstracted the lithium as lithium carbonyl, producing symmetrical ketones (Eq. 1).



$$2\ \mathrm{R{-}Li} + 3\ \mathrm{CO} \rightarrow \mathrm{R{-}}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}\mathrm{{-}R} + 2\ \mathrm{LiCO} \qquad (1)$$

On the other hand, iron pentacarbonyl reacted with organolithium compounds in an ethereal solution at -50°C, giving various reaction products.[2] For example, the aryllithium yielded the corresponding aromatic aldehydes, benzhydrol derivatives and benzoin derivatives by the reaction with iron pentacarbonyl, but the alkyllithium and *p*-tolyllithium yielded symmetrical ketones. The formation of aldehydes, benzhydrol derivatives and benzoin derivatives can be interpreted in terms of an ionic reaction sequence judging from the results of the reaction of carbon monoxide with organomagnesium halides[3]. Therefore, the following reaction scheme was assumed: the addition of aryllithium to the carbonyl double bond of iron pentacarbonyl resulted in the fission of the iron-carbon bond of iron pentacarbonyl, producing the unstable intermediate I (aroyllithium). (Fig. 1)

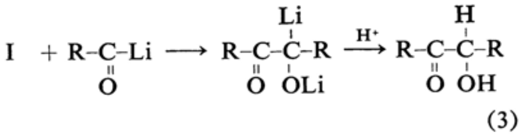


(I)

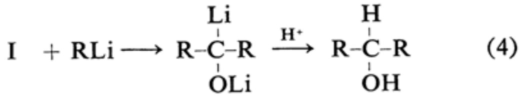
Fig. 1

This intermediate I is assumed to give aldehydes by hydrolysis (Eq. 2), benzoin derivatives by dimerization (Eq. 3), and benzhydrol derivatives by further reaction with aryllithium (Eq. 4).

$$\mathrm{I} \xrightarrow{\mathrm{H^+}} \mathrm{RCHO} \qquad (2)$$



$$\mathrm{I} + \mathrm{R{-}}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}\mathrm{{-}Li} \longrightarrow \mathrm{R{-}}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}\mathrm{{-}}\overset{\mathrm{Li}}{\underset{\mathrm{OLi}}{\mathrm{C}}}\mathrm{{-}R} \xrightarrow{\mathrm{H^+}} \mathrm{R{-}}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}\mathrm{{-}}\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}R} \qquad (3)$$



$$\mathrm{I} + \mathrm{RLi} \longrightarrow \mathrm{R{-}}\overset{\mathrm{Li}}{\underset{\mathrm{OLi}}{\mathrm{C}}}\mathrm{{-}R} \xrightarrow{\mathrm{H^+}} \mathrm{R{-}}\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}R} \qquad (4)$$

The aroyllithium in the above reaction scheme was considered to have characteristics analogous to the aroylmetallic compounds (metal: magnesium,[3] sodium[4] and cobalt[5]), as has previously been proposed by the present authors. Hence, it was expected that the stabilization of the above intermediate I would lead to the formation of aromatic aldehydes in high yields.

In order to stabilize the unstable aroyllithium, it was necessary to suppress the dimerization reaction of aroyllithium (Eq. 3) and the reaction of aryllithium with aroyllithium (Eq. 4.) by dilution with a solvent and by the rapid addition of iron pentacarbonyl, which would react with aryllithium and decrease the concentration of free aryllithium. Therefore, iron pentacarbonyl was added rapidly (within two minutes) to the diluted solution of aryllithium in diethyl ether at -60°C and then allowed to react at $-50^\circ\mathrm{C}\sim-60^\circ$C for 2 hr.

The results of the synthesis of various aromatic aldehydes according to our new method are summarized in Table I.

The isolation and identification of aromatic aldehydes were carried out by the ordinary

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* Part VII: *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zasshi*), **66**, 1086 (1963).

[1] M. Ryang and S. Tsutsumi, This Bulletin, **35**, 1121 (1962).

[2] M. Ryang, Y. Sawa, H. Masada and S. Tsutsumi, *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zasshi*), **66**, 1086 (1963).

[3] M. Ryang and S. Tsutsumi, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **82**, 880 (1961).

[4] M. Ryang, H. Miyamoto and S. Tsutsumi, ibid., **82**, 1276 (1961).

[5] M. Ryang and S. Tsutsumi, This Bulletin, **34**, 1341 (1961).

TABLE I

Starting material	Aromatic aldehyde	Yield,* %
2, 6-Dimethylbromobenzene	2, 6-Dimethylbenzaldehyde	36.4
2, 4-Dimethylbromobenzene	2, 4-Dimethylbenzaldehyde	65.4
p-Bromo-*t*-butylbenzene	*p*-*t*-Butylbenzaldehyde	47.0
o-Bromo-*t*-butylbenzene	*o*-*t*-Butylbenzaldehyde	54.3
p-Bromoanisole	*p*-Methoxybenzaldehyde	24.2
Bromomesitylene	2, 4, 6-Trimethylbenzaldehyde	60.5

* The calculations of yields are based on the number of organic halides used.

methods: elementary analysis, mixed melting point measurements of their semicarbazone derivatives, and infrared absorption spectra measurements.

Thus various aromatic aldehydes were synthesized in a good yield, and we have found that this new method is simple and can be extended to the synthesis of other aromatic aldehydes, the preparation of which by earlier methods was not satisfactory in yield and involved complicated starting materials. Of course, the exclusive formation of aldehydes in good yields in these reactions, even though various products were obtained from the reaction in the previous report,[2] is not due only to the reaction conditions (dilution with the solvent and the rapid addition of iron pentacarbonyl). It also seemed to be connected with the structural factor of organolithium compounds; for example, *m*-tolylaldehyde was isolated as a main product from the reaction of *m*-tolyllithium with iron pentacarbonyl under the conditions described in our previous report.

Details of the studies of the mechanism of the above reactions will be published elsewhere in the near future.

Experimental

Materials. — Several bromobenzene derivatives were prepared by the Sandmeyer reaction of the corresponding aniline derivatives: 2, 6-dimethylbromobenzene (b. p. 97°C/26 mmHg, $n_D^{15.5}$ 1.5573), 2, 4-dimethylbromobenzene (b. p. 95~97°C/22 mmHg), *o*-*t*-butylbromobenzene (b. p. 115°C/22 mmHg, n_D^{15} 1.5285), and *p*-*t*-butylbromobenzene (b. p. 114°C/20 mmHg, n_D^{15} 1.5377).

p-Methoxybromobenzene.—Commercial *p*-methoxybromobenzene was purified by fractional distillation; b. p. 95°C/15 mmHg, n_D^{15} 1.5641. Bromomesitylene was prepared by the action of bromine on mesitylene:[6] b.p. 105~107°C/17 mmHg. Iron pentacarbonyl was prepared by the reaction of fine iron poweder with carbon monoxide at 200°C under 300 CO atm. and was purified by distillation; b. p. 102°C, n_D^{15} 1.5202.

n-Butyllithium.—A commercial heptane solution of *n*-butyllithium (21.4 wt.%) was used.

The Synthesis of Aromatic Aldehydes.—*2, 6-Dimethylbenzaldehyde.*—Into a 500 ml., four-necked flask equipped with a mechanical stirrer, a low temperature thermometer, a reflux condenser protected from moisture, a gas bubbler and a dropping funnel, 40 ml. of anhydrous ether (dried over sodium) were placed and, after sweeping the apparatus with dry oxygen-free nitrogen, 1.4 g. (0.2 g. atom.) of lithium in the form of small pieces of thin coil. A solution of 14.8 g. (0.08 mol.) of 2, 6-dimethylbromobenzene in 20 ml. of anhydrous ether was stirred in via the dropping funnel over a period of 2 hr., while the internal temperature was maintained at 35°C.

After the addition had been completed, the stirring was continued for a further 2 hr., after which the reaction mixture was cooled to −60°C with a dry ice-methanol bath kept at −65°C. 3.2 g. (0.016 g. atom) of iron pentacarbonyl in 40 ml. anhydrous ether were next introduced via the dropping funnel over a period of 2 min. Then, with the internal temperature maintained at −50°C, the stirring was continued for a further 2 hr. The reaction mixture was decomposed with 20 ml. of 95% ethanol and, further, with 40 ml. of 4 N hydrochloric acid. The separated organic layer was treated with three succesive 50 ml. portions of saturated aqueous potassium carbonate and then with three succesive 50 ml. portions of aqueous sodium hydroxide and divided into (1) the organic layer, (2) a potassium carbonate solution and (3) a sodium hydroxide solution. The organic layer containing neutral compounds was washed with water and dried over sodium sulfate. The brownish residual oil obtained after removal of the solvent was distilled under reduced pressure to give the following fractions: (1) b. p. 30~40°C/18 mmHg (0.8 g.), (2) b. p. 40~60°C/18 mmHg (1.1 g.), (3) b. p. 100~110°C/18 mmHg (3.9 g.), and a dark orange residue. Fraction 3 was identified as 2, 6-dimethylbenzaldehyde from the results of infrared absorption spectra measurement and a mixed melting point test of its semicarbazone (m. p. 176~177°C, recrystallized from benzene). Also, the results of gas chromatographic analysis showed that fraction 3 was mainly 2, 6-dimethylbenzaldehyde (theoretical yield: 36.4 %).

Found: C, 62.76; H, 6.92. Calcd. for $C_{10}H_{13}ON_3$: C, 62.80; H, 6.85%.

The other fractions have not yet been examined. The acidic and phenolic compounds which were involved in the potassium carbonate solution and the sodium hydroxide solution respectively were confirmed to be the same as those of a previous report.[1]

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[6] "Organic Syntheses," Coll. Vol. II (1948), p. 95.

2, 4-Dimethylbenzaldehde. — The procedure employed here was identical with that described above. 3.92 g. of iron pentacarbonyl were added to the ethereal solution of 2,4-dimethylphenyllithium, which had been prepared by using 18.5 g. of 2, 4-dimethylbromobenzene and 1.75 g. of lithium. The neutral part was distilled under reduced pressure to give the following fractions: (1) b. p. 110~137°C/13 mmHg (8.7 g.), and (2) b. p. 160~163°C/4 mmHg (0.3 g.). Fraction 1 gave a positive result with the Brady's reagent and was identified as 2, 4-dimethylbenzaldehyde by the elementary analysis of its semicarbazone derivative (m. p. 222°C, recrystallized from ethanol) (theoretical yield: 65.4 %).

Found: C, 62.50; H, 6.93. Calcd. for $C_{10}H_{13}\cdot ON_3$: C, 62.82; H, 6.85%.

Fraction 2 was recrystallized from petroleum ether to give yellow crystals (m. p. 137°C). The infrared spectrum of this crystal showed the presence of the conjugated carbonyl group (1650 cm^{-1}), and the elementary analysis of the above crystal is correct for $C_{18}H_{18}O_2$. From the above results, fraction 2 was confirmed to be 2, 2′, 4, 4′-tetramethylbenzil.

Found: C, 81.08; H, 6.93. Calcd. for $C_{18}H_{18}O_2$: C, 81.20; H, 6.78%.

p-t-Butylbenzaldehyde.—2.5 g. of pure iron pentacarbonyl were allowed to react with *p-t*-butylphenyllithium prepared from 10.7 g. of *p-t*-butylbromobenzene and 1 g. of lithium. The neutral part was distilled under reduced pressure to give the following fractions: (1) b. p. 100~115°C/11 mmHg (2.8 g.), (2) b. p. 130~133°C/3 mmHg (0.3 g.), and (3) b. p. 160~185°C/3mmHg. (2.3 g).

The infrared spectrum of fraction 1 showed the presences of a carbonyl group conjugated with an aromatic ring (1680 cm^{-1}) and a 1, 4-disubstituted aromatic ring (820 cm^{-1}, 1210 cm^{-1}, 1090 cm^{-1} and 1070 cm^{-1}). Fraction 1 was confirmed to be *p-t*-butylbenzaldehyde from the results of the mixed melting point measurement of its semicarbazone derivative. Fraction 3 was recystallized from ethanol to give colorless crystals (m.p. 131°C). This compound was assumed to be 1, 4-disubstituted aromatic hydrocarbon from the results of the infrared spectrum and was confirmed to be *p, p′*-di-*t*-butyl-diphenyl.

Found: C, 89.50; H, 10.06. Calcd. for $C_{20}H_{26}$: C, 90.16; H, 9.84%.

o-t-Butylbenzaldehyde.—2.5 g. of iron pentacarbonyl were added to an ether solution of *o-t*-butylphenyllithium prepared by using 10.7 g. of *o*-bromo-*t*-butylbenzene and 1.0 g. of lithium. The distillation of the neutral part gave the following fractions: (1) b. p. 50~55°C/10 mmHg (0.6 g.), (2) b. p. 80~90°C/3 mmHg (4.4 g.), and (3) b. p. 100 ~160°C/3 mmHg (0.3 g.). Fraction 2 gave a positive result to Brady's reagent and was identified as *o-t*-butylbenzaldehyde by the mixed melting point measurement of its 2, 4-dinitrophenylhydrazone (m. p. 256°C, recrystallized from ethylacetate) and of its semicarbazone (m. p. 210~211°C, recrystallized from ethanol) (theoretical yield: 54.3%). The elementary analysis of semicarbazone is correct for $C_{12}H_{18}ON_3$:

Found: C, 65.68; H, 7.93. Calcd. for $C_{12}H_{18}\cdot ON_3$: C, 65.72; H, 7.81%.

p-Methoxybenzaldehyde.—A solution of 18.7 g. of *p*-bromoanisol in 40 ml. of anhydrous ether was stirred in via the dropping funnel, over a period of 2 hr., to 30 g. of a solution of *n*-butyllithium (*n*-heptane solution, 21.4 wt. %), while the internal temperature was maintained at −10°C. After the addition had been completed, the stirring was continued for a further 8 hr., after which the reaction mixture was cooled to −65°C and allowed to react with 5 g. of iron pentacarbonyl. The neutral part was distilled under reduced pressure to give the following fractions: (1) b. p. 20~27°C/22 mmHg (2.4 g.), (2) b. p. 80~118°C/15 mmHg (3.3 g.), and (3) b. p. 105~140°C/5 mmHg (1.6 g.). Fraction 2 gave a positive result to Brady's reagent and was confirmed to be *p*-methoxybenzaldehyde from the results of the elemental analysis of its semicarbazone (m. p. 211~212°C, recrystallized from ethanol) (theoretical yield: 24.2%).

Found: C, 56.19; H, 5.80. Calcd. for $C_9H_{11}O_2\cdot N_3$: C, 55.95; H, 5.69%.

Fraction 3 was recrystallized from ethanol to give colorless crystals (m. p. 185°C), which were assumed to be *p, p′*-dimethoxy-diphenyl.

2, 4, 6-Trimethylbenzaldehyde.—2.5 g. of iron pentacarbonyl were added to a solution, cooled to −65°C, of 2, 3, 6-trimethylphenyllithium prepared from 10 g. of bromomesitylene and 15 g. of a heptane solution of *n*-buthyllithinum (21.4 wt. %). The neutral part was distilled under reduced pressure to give the following: (1) b. p. ~115°C/10 mmHg (2.3 g.), (2) b. p. 105~110°C/10mmHg (5.0 g.), and (3) b. p. 160~170°C/2.5 mmHg (1.4 g.).

Fraction 2 gave a positive result to Brady's reagent and was assumed to be 2, 4, 6-trimethylbenzaldehyde (theoretical yield: 60.5%), and its 2, 4-dinitrophenylhydrazone was recrystallized from ethylacetate to give reddish-yellow crystals (m. p. 227~228°C).

Summary

The reaction of iron pentacarbonyl with aryllithiums at −50~−60°C has yielded the corresponding aromatic aldehydes in good yields. 2, 6-Dimethylbenzaldehyde (36.4%), 2, 4-dimethylbenzaldehyde (65.4%), *p-t*-butylbenzaldehyde (47.0%), *o-t*-butylbenzaldehyde (54.3%), *p*-methoxybenzaldehyde (24.2%) and 2, 4, 6-trimethylbenzaldehyde (60.5%) have been prepared by this method.

A reaction process for this reaction has been discussed.

Department of Chemical Technology
Faculty of Engineering
Osaka University
Miyakojima-ku, Osaka