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Academician A. N. NESMEYANOV, V. A. SAZONOVA, and V. N. DROZD

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Abstract

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ON THE REACTIONS OF HALOGEN DERIVATIVES OF ETHYL- AND ACETYLFERROCENE

In the present work, the exchange of bromine for nucleophilic groups in the presence of copper salts has been studied in 1′-bromo-1-acetylferrocene and 1′-bromo-1-ethylferrocene. 1′-Bromo-1-acetylferrocene was obtained by acylation of bromoferrocene with acetic anhydride in the presence of phosphoric acid, analogously to the preparation of acetylferrocene ([1]), in 54% yield:

$$C_5H_5FeC_5H_4Br \xrightarrow[H_3PO_4]{(CH_3CO)_2O} CH_3COC_5H_4FeC_5H_4Br.$$

The acetyl group is located in the other cyclopentadienyl ring, which was confirmed by the absence in the IR spectrum of the 1000 and 1100 cm^{-1} frequencies characteristic of ferrocene compounds with an unsubstituted cyclopentadienyl ring.

It turned out that bromine in this compound is replaced by an acetoxy group in the presence of copper acetate much less readily than bromine in bromoferrocene ([2]); even 5-hour boiling of the reagents in aqueous alcohol does not lead to complete disappearance of the halide. To separate the reaction product from unreacted 1′-bromo-1-acetylferrocene, the reaction mixture was subjected to hydrolysis, and 1′-hydroxy-1-acetylferrocene was isolated; the latter is readily benzoylated by the Schotten–Baumann method

$$CH_3COC_5H_4FeC_5H_4Br \xrightarrow[2.\ KOH]{1.\ Cu(OCOCH_3)_2} CH_3COC_5H_4FeC_5H_4OH$$

$$CH_3COC_5H_4FeC_5H_4OH \xrightarrow{KOH,\ C_6H_5COCl} CH_3COC_5H_4FeC_5H_4OCOC_6H_5$$

If 1′-bromo-1-acetylferrocene is reduced—which is accomplished very readily (within 5 min) by the Clemmensen method—to 1′-bromo-1-ethylferrocene, then the halide in the resulting compound possesses approximately the same mobility

as bromine in bromoferrocene: it is readily replaced by acetoxy, phthalimido, and cyano groups on heating with the corresponding copper salts

$$C_2H_5C_5H_4FeC_5H_4Br \xrightarrow{Cu(OCOCH_3)_2} C_2H_5C_5H_4FeC_5H_4OCOCH_3$$

$$C_2H_5C_5H_4FeC_5H_4Br \xrightarrow{\text{phth.–Cu}} C_2H_5C_5H_4FeC_5H_4N(CO)_2C_6H_4$$

$$C_2H_5C_5H_4FeC_5H_4Br \xrightarrow{Cu_2(CN)_2} C_2H_5C_5H_4FeC_5H_4CN$$

1′-Acetoxy-1-ethylferrocene, like ferrocenyl acetate ([3]), is hydrolyzed by alkali, with formation of 1′-hydroxy-1-ethylferrocene, which is benzoylated by the Schotten–Baumann method to 1′-benzoyloxy-1-ethylferrocene. 1-Cyano-1′-ethylferrocene was hydrolyzed to 1′-ethylferrocene-1-carboxylic acid.

acid identical with the acid obtained by N. A. Nesmeyanov and O. A. Reutov [4] by reduction of 1′-acetylferrocene-1-carboxylic acid.

1′-Phthalimido-1-ethylferrocene, when heated with hydrazine hydrate, gives liquid 1′-amino-1-ethylferrocene, which was acetylated to 1′-acetamino-1-ethylferrocene.

Experimental Part

1′-Bromo-1-acetylferrocene. A mixture of 10 g of bromoferrocene, 40 ml of acetic anhydride, and 10 ml of phosphoric acid (from 2 parts of 85% H_3PO_4 and 1 part of P_2O_5) was heated on a boiling water bath with stirring for 5 min, cooled with ice, and poured into a soda solution. After neutralization the mixture was extracted with ether; the ether extract was filtered, washed with water, dried over $MgSO_4$, and the ether was distilled off. The residue was dissolved in a small amount of benzene, diluted with petroleum ether, and chromatographed on Al_2O_3. Petroleum ether elutes unreacted bromoferrocene; benzene or ether elutes 1′-bromo-1-acetylferrocene. 6.2 g of 1′-bromo-1-acetylferrocene was obtained (54% of theory), m.p. 61.5–63° (from hexane). The ketone is readily soluble in benzene, ether, and alcohol; less readily in petroleum ether.

Found, %: C 47.21; 47.22; H 3.82; 3.70; Br 25.46; 25.76; Fe 18.26; 18.15

$C_{12}H_{11}FeOBr$. Calculated, %: C 46.95; H 3.61; Br 26.03; Fe 18.20

An oxime was obtained with m.p. 109.5–111.5° (from aqueous alcohol).

Found, %: C 44.68; 44.79; H 3.78; 3.76; Br 25.02; 25.20; Fe 17.80; 17.81; N 4.07; 4.12

$C_{12}H_{12}FeOBrN$. Calculated, %: C 44.76; H 3.76; Br 24.82; Fe 17.34; N 4.35

1′-Hydroxy-1-acetylferrocene. To a boiling solution of 1.0 g of 1′-bromo-1-acetylferrocene in 20 ml of alcohol was added a hot solution of 3 g of copper acetate in 20 ml of water, and the mixture was boiled under nitrogen on a water bath for 40 min. The mixture was then diluted with water and extracted with ether; the ether was washed with a small amount of water, dried over $MgSO_4$, and distilled off. The remaining oil gives a positive test for halogen. It was hydrolyzed under nitrogen by boiling (10 min) in a solution of 5 ml of alcohol and 10 ml of 10% KOH. The alcohol was distilled off. The unreacted ketone was extracted with ether; 0.23 g of ketone was obtained. CO_2 was passed through the alkaline solution; the 1′-hydroxy-1-acetylferrocene was extracted with ether; the ether was washed with a small amount of water and distilled off under nitrogen, and the residue was recrystallized under N_2 from water. 0.21 g of 1′-hydroxy-1-acetylferrocene was obtained (26% of theory), m.p. 115.5–118.5° (under nitrogen).

Found, %: C 58.65; 58.51; H 5.02; 5.08; Fe 23.09; 23.09

$C_{12}H_{12}FeO_2$. Calculated, %: C 59.05; H 4.96; Fe 22.88

In air it is somewhat more stable than oxyferrocene; it is readily oxidized in solutions.

1′-Benzoyloxy-1-acetylferrocene. 1′-Hydroxy-1-acetylferrocene (0.21 g) was dissolved in 10 ml of 10% KOH and benzoylated by the Schotten-Baumann method with 0.5 ml of benzoyl chloride. 0.23 g of 1′-benzoyloxy-1-acetylferrocene was obtained (77% of theory), m.p. 84–85° (from a mixture of cyclohexane with hexane, 2:1).

Found, %: C 65.50; 65.74; H 4.66; 4.67; Fe 16.07; 15.83

$C_{19}H_{16}O_3Fe$. Calculated, %: C 65.54; H 4.63; Fe 16.04

1′-Bromo-1-ethylferrocene. 8 g of zinc dust was amalgamated with 0.8 g of mercuric chloride in 32 ml of dilute HCl (1 : 20). After 10 min the liquid was decanted, and a solution of 2.0 g of 1′-bromo-1-acetylferrocene in 20 ml of acetic acid and 20 ml of conc. HCl was added. The mixture was boiled under a reflux condenser for about 5 min until the dark cherry-red color of the ketone disappeared. The mixture was then cooled and filtered from zinc; the zinc was washed with ether. The filtrate was diluted with water and extracted with ether; the combined ether extracts were washed with water, 10% KOH, and water, and the ether was distilled off. The residue in *n*-hexane was chromatographed on Al_2O_3; the hexane was distilled off, and the substance was distilled in vacuo. 1.46 g (77% of theory) of 1′-bromo-1-ethylferrocene was obtained. B.p. 110–112° (1.2 mm); n_D^{20} 1.6238; d_4^{20} 1.5584.

Found, %: C 49.42; 49.35; H 4.55; 4.54; Br 27.34; 27.23; Fe 19.28; 19.58
$C_{12}H_{13}FeBr$. Calculated, %: C 49.18; H 4.47; Br 27.28; Fe 19.06

Replacement of halide in 1′-bromo-1-ethylferrocene by an oxy group. 1′-Benzoyloxy-1-ethylferrocene. To a boiling solution of 1.3 g of 1′-bromo-

1-ethylferrocene in 35 ml of alcohol was added a hot solution of 3.5 g of copper acetate in 35 ml of water, and the mixture was boiled on a water bath for 15 min. The reaction mixture was diluted with water and extracted with ether; the ether extract was washed with water, 5% KOH, and water, dried over $MgSO_4$, and the ether was distilled off. The remaining oil contains no halide. On distillation in vacuo at 1.2 mm, 1′-acetoxy-1-ethylferrocene decomposes, and therefore it was used for further work without distillation.

A solution of 0.3 g of 1′-acetoxy-1-ethylferrocene in 4 ml of alcohol and 4 ml of 10% KOH was boiled for 15 min; the alcohol was distilled off, and the solution was cooled and filtered. On passing CO_2, 1′-oxy-1-ethylferrocene separates as a liquid. It was again dissolved in alkali and benzoylated by the Schotten-Baumann method. 0.26 g (71% of theory) of 1′-benzoyloxy-1-ethylferrocene was obtained, m.p. 42.5–44.5° (from methanol on cooling with dry ice).

Found, %: C 68.33; 68.27; H 5.43; 5.44; Fe 16.75; 16.54
$C_{19}H_{18}FeO_2$. Calculated, %: C 68.28; H 5.43; Fe 16.71

1′-Phthalimido-1-ethylferrocene. A mixture of 0.5 g of 1′-bromo-1-ethylferrocene with 1.5 g of copper phthalimide was heated under nitrogen at 135–140° for 1.5 h. The mixture was then repeatedly washed with ether. The ether extract was thoroughly washed with 10% KOH and water, dried over $MgSO_4$, and the ether was distilled off. The remaining dark-red oil contains no halide; on drying in vacuo over P_2O_5 it crystallizes. 0.44 g (72% of theory) of 1′-phthalimido-1-ethylferrocene was obtained, m.p. 81.5–82.5° (from methanol).

Found, %: C 66.90; 66.72; H 4.75; 4.75; Fe 15.78; 15.67; N 4.06; 3.90
$C_{20}H_{17}FeO_2N$. Calculated, %: C 66.87; H 4.77; Fe 15.55; N 3.90

1′-Acetamino-1-ethylferrocene. 0.4 g of 1′-phthalimido-1-ethylferrocene in 6 ml of alcohol was boiled under nitrogen with 0.6 ml of hydrazine hydrate for 30 min. The mixture was diluted with water and extracted with ether; the ether was washed with 10% KOH and water; the amine was extracted with 10% HCl. On addition of alkali, 1′-amino-1-ethylferrocene separates as an oil, which was extracted with ether. After removal of the ether, 0.19 g (77% of theory) of amine was obtained, which was acylated with 0.7 ml of acetic anhydride in 1.5 ml of abs. pyridine. 0.19 g (85% of theory) of 1′-acetamino-1-ethylferrocene was obtained, m.p. 69.5–70.5° (from a 2 : 1 mixture of benzene and hexane).

Found, %: C 62.15; 62.05; H 6.37; 6.52; Fe 19.90; 19.90; N 5.48; 5.32
$C_{14}H_{17}FeNO$. Calculated, %: C 62.01; H 6.32; Fe 20.60; N 5.17

1-Cyano-1′-ethylferrocene. A mixture of 0.4 g of 1′-bromo-1-ethylferrocene with 1.5 g of cuprous cyanide was heated under nitrogen at 135–140° for 104

50 min. The reaction mixture was washed with ether, the ether was evaporated, and the residue was chromatographed on Al_2O_3. Benzene elutes 1-cyano-1′-ethylferrocene. Obtained: 0.26 g (80% of theory), m.p. 28–29° (from hexane, upon cooling with dry ice).

Found, %: C 65.25; 65.25; H 5.45; 5.76; N 5.72; Fe 23.72; 23.57
$C_{13}H_{13}FeN$. Calculated, %: C 65.30; H 5.48; N 5.86; Fe 23.36

After many hours of hydrolysis in an aqueous alcoholic solution of KOH under reflux, 1′-ethylferrocene-1-carboxylic acid is obtained, m.p. 74.5–76.5°; a mixed sample with an authentic specimen melts without depression. Literature data: m.p. 75.5–77.5° (4).

Moscow State University
named after M. V. Lomonosov

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Note: Figure translations are in progress. See original paper for figures.