gem-Diferrocenylalkane Derivatives. Acid-Catalyzed Condensation of Ferrocene with Methyl Levulinate and 5-Hydroxy-2-pentanone

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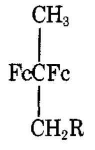
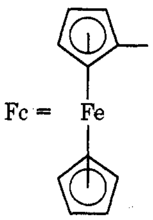
Ferrocene has been condensed with methyl levulinate in polyphosphoric acid to yield 4,4-diferrocenylpentanoate (**3**, 67% on reacted ferrocene), methyl 4-ferrocenylpentanoate (**5**, 1%) and 1,1′-bis[2-(2-ferrocenyl-4-carbomethoxy)butyl]ferrocene (**6**, 2%). Ferrocene condensed with 5-hydroxy-2-pentanone with trifluoroacetic acid catalyst to yield 4,4-diferrocenyl-1-pentanol (**6**, 70%), also prepared by lithium aluminum hydride reduction of ester **3**. Several 1-substituted 3,3-diferrocenylbutanes were synthesized in high yield including 4,4-diferrocenylpentanoic acid and 3,3-diferrocenylbutyl isocyanate. Proton and ^{13}C nuclear magnetic resonance spectra of new compounds are discussed in relation to structure.

The acid-catalyzed condensation of ferrocene with aldehydes and ketones is complex and leads to several types of compounds.[1–10] In the present study a convenient synthesis was sought for diferrocenylmethane derivatives **1**, in which R contains a reactive functional group. The acid-catalyzed ferrocene–ketone condensation, although presenting a potentially simple route to **1**, suffers the major disadvantage of providing very low yields under known reaction conditions. A major side reaction defeating the synthesis of **1** is the aldol self-condensation of reactant ketone, particularly under more vigorous conditions. The only reported synthesis of this type is the condensation of ferrocene with acetone (boron trifluoride, 25°) to produce 2,2-diferrocenylpropane (9% conversion, 31% yield based on reacted ferrocene).[1] Other ketones studied failed to produce diferrocenylmethane derivatives under a variety of conditions.[1,8,9]



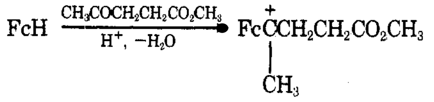
$$\mathrm{Fc\underset{CH_2R}{\overset{CH_3}{C}}Fc}$$

1



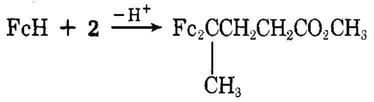
This report describes reaction conditions for the acid-catalyzed condensation of ferrocene with methyl levulinate[11] and 5-hydroxy-2-pentanone providing good yields of the desired diferrocenylmethane derivatives. Few alternate methods of synthesis of *gem*-diferrocenylalkanes are available. No other synthetic routes are known leading to alkanes with *gem*-diferrocenyl substitution on quaternary carbon. 1,1-Diferrocenylethane is formed by reaction of ferrocene with 1,2-dichloroethane (aluminum chloride catalyst).[12]

A study was made of the condensation of ferrocene with levulinic acid and methyl levulinate employing polyphosphoric, phosphoric, sulfuric, and trifluoroacetic acid catalysts. Slow addition of an excess of methyl levulinate to ferrocene and polyphosphoric acid at temperatures below 80° favors a high conversion of ferrocene to methyl 4,4-diferrocenylpentanoate (**3**, 40% conversion, 67% yield based on reacted ferrocene). Methanol and cyclohexane in the reaction mixture speed the reaction and increase the yield of **3**.



$$\mathrm{FcH}\xrightarrow[\mathrm{H^+,\ -H_2O}]{\mathrm{CH_3COCH_2CH_2CO_2CH_3}}\mathrm{Fc\underset{CH_3}{\overset{+}{C}}CH_2CH_2CO_2CH_3}$$

2

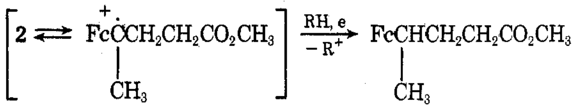


$$\mathrm{FcH} + \mathbf{2} \xrightarrow{-\mathrm{H^+}} \mathrm{Fc_2\underset{CH_3}{C}CH_2CH_2CO_2CH_3}$$

3

Substitution of sulfuric for polyphosphoric acid catalyst resulted in good yields of **3** but some ferrocene oxidation and much tar formation resulted. Trifluoroacetic acid alone failed to effect condensation of ferrocene with methyl levulinate or levulinic acid. Phosphoric, polyphosphoric, and trifluoroacetic acids have not been employed previously as catalysts in ferrocene–ketone or aldehyde condensations.[1–10]

In addition to ester **3**, the condensation of ferrocene with methyl levulinate produced other esters. Two of these were isolated in a pure state. Liquid methyl 4-ferrocenylpentanoate (**5**) was obtained by distillation under reduced pressure (ca. 1% yield).

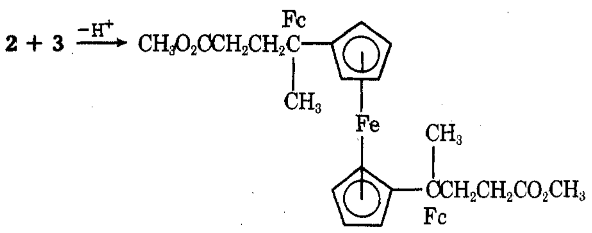


$$\left[\mathbf{2} \rightleftharpoons \mathrm{Fc\underset{CH_3}{\overset{+\cdot}{C}}CH_2CH_2CO_2CH_3}\right] \xrightarrow[-\mathrm{R^+}]{\mathrm{RH,\ e}} \mathrm{Fc\underset{CH_3}{C}HCH_2CH_2CO_2CH_3}$$

4 **5**

This 1:1 condensation product is believed to arise from **2** or a radical cation intermediate (**4**) by hydride transfer.[4,13] The identity of the reducing agent RH is unknown. The formation of **5** is favored by use of a large excess of methyl levulinate and its slow addition to the reaction mixture.

Separation of the ferrocene–methyl levulinate condensation products by dry-column chromatography permitted isolation of higher molecular weight esters. One of these (**6**) was obtained in crystalline form (mp 140–142°, 2% yield).

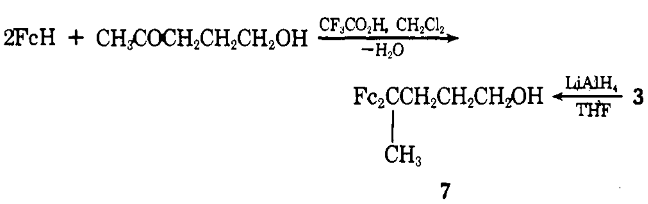


6

The formation of **6** is favored by use of a 1:1 molar ratio of ferrocene to methyl levulinate and by rapid addition of the methyl levulinate to the reaction mixture. Molecular formula and spectral data support the structure 1,1′-bis[2-ferrocenyl-4-carbomethoxy)butyl]ferrocene. The ^{13}C NMR spectrum reveals two narrowly separated ferrocenyl-substituted C-1 carbon signals (δ 99.69, 99.35) in agreement with a 1,1′-disubstituted ferrocene structure. The splitting

(0.3–0.4 ppm) of the ^{13}C NMR signals of the α (C-2 and C-5) carbon atoms of the cyclopentadienyl rings which are attached to chiral substituents is in agreement with observations of other workers.[14,15] Unresolved mixtures of oligomers related to 6 ($CH_2CH_2CO_2CH_3$ = CH_3; 1–7 monomer units) have been prepared from ferrocene and acetone (aluminum chloride catalyst).[9]

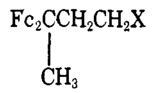
The condensation of ferrocene with 5-hydroxy-2-pentanone was effected in methylene chloride solvent with trifluoroacetic acid catalyst at ambient temperature to afford 4,4-diferrocenyl-1-pentanol (7, 44% conversion, 70% yield based on reacted ferrocene). As noted above, this procedure failed to produce ester 3 by condensation of methyl levulinate or levulinic acid with ferrocene under the same conditions. Alcohol 7 was also prepared by lithium aluminum hydride reduction of ester 3 in tetrahydrofuran solvent (94% yield).



$$2\mathrm{FcH} + \mathrm{CH_3COCH_2CH_2CH_2OH} \xrightarrow[-\mathrm{H_2O}]{\mathrm{CF_3CO_2H,\ CH_2Cl_2}} \mathrm{Fc_2}\underset{\mathrm{CH_3}}{\mathrm{C}}\mathrm{CH_2CH_2CH_2OH} \xleftarrow[\mathrm{THF}]{\mathrm{LiAlH_4}} 3$$

7

4,4-*Diferrocenylbutyl isocyanate and other derivatives of* methyl 4,4-diferrocenylpentanoate (3) were prepared (8–12). Two methods of synthesis of isocyanate 11 were investigated. The best one proceeds from 4,4-diferrocenylpentanoic acid (8) in three steps (75–80% overall yield from ester 3).

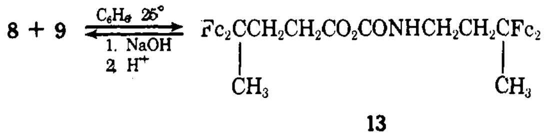


$$\mathrm{Fc_2}\underset{\mathrm{CH_3}}{\mathrm{C}}\mathrm{CH_2CH_2X}$$

8, X = CO_2H; 9, COCl; 10, CON_3; 11, NCO; 12, $CONHNH_2$

Saponification of ester 3 gave 4,4-diferrocenylpentanoic acid (8) in quantitative yield. Acid chloride 9 (prepared in 97% yield) is unstable to heat and rapidly polymerizes, exothermically, with evolution of hydrogen chloride at 100–130°.[16] Its reaction with sodium azide occurs rapidly in aqueous tetrahydrofuran at 0–5° leading to acyl azide 10. In contrast to ferrocenoyl azide, acyl azide 10 is rather unstable.[17] In benzene solution azide 10 has a half-life of ca. 14 h at 25°. This stability is sufficient to permit rapid extraction of the crude azide with aqueous base to remove any 4,4-diferrocenylpentanoic acid impurity. The pure acyl azide 10 is converted in 90–98% yield into 3,3-diferrocenylbutyl isocyanate (11).

Carboxylic acids react with isocyanates to form relatively unstable carboxylic carbamic acid anhydrides.[18–21] Failure to remove 4,4-diferrocenylpentanoic acid from the reaction mixture after formation of the acyl azide results in reaction with isocyanate 11 as it forms to produce anhydride 13, characterized by a strong carbonyl doublet at 1770, 1740 cm^{-1}. The anhydride is cleaved rapidly by reaction with aqueous sodium hydroxide solution at 25°, regenerating the acid (after acidification of the salt) and the isocyanate.



$$8 + 9 \underset{1.\ \mathrm{NaOH}\ \ 2.\ \mathrm{H^+}}{\overset{\mathrm{C_6H_6}\ 25°}{\rightleftarrows}} \mathrm{Fc_2}\underset{\mathrm{CH_3}}{\mathrm{C}}\mathrm{CH_2CH_2CO_2CONHCH_2CH_2}\underset{\mathrm{CH_3}}{\mathrm{C}}\mathrm{Fc_2}$$

13

A second route to 3,3-diferrocenylbutyl isocyanate (11) was investigated departing from 4,4-diferrocenylpentanohydrazide (12). Treatment of hydrazide 12 with nitrous acid in acidified aqueous tetrahydrofuran leads to acyl azide 10 (not isolated), which rearranges to the isocyanate in benzene solution. 3,3-Diferrocenylbutyl isocyanate reacts with water to produce *N,N′*-bis(3,3-diferrocenylbutyl)urea, with aniline to form *N*-(3,3-diferrocenylbutyl)-*N′*-phenylurea, and with methanol to form its methyl urethan derivative.

Experimental Section

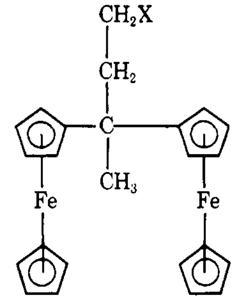
Infrared spectra were determined on a Perkin-Elmer Model 137, ^{1}H NMR spectra on a Varian A-60 or XL-100, and ^{13}C NMR spectra on a Varian XL-100 spectrometer with Transform Technology TT-100 pulsed Fourier transform system. ^{1}H and ^{13}C chemical shift measurements were determined at ca. 30° and are referenced to tetramethylsilane internal standard. Melting points were determined on a Kofler hot stage and are corrected. Elemental analyses and molecular weights were determined by Galbraith Laboratories, Knoxville, Tenn.

Methyl 4,4-Diferrocenylpentanoate (3). Polyphosphoric acid was prepared by slowly adding phosphoric anhydride (125 g) to 85% phosphoric acid (125 g), followed by warming on the steam bath, with stirring, to obtain a solution. Methanol (140 ml) was added dropwise, with stirring, to the cooled acid and 150 ml of cyclohexane contained in a three-necked flask equipped with a constant-rate addition funnel, condenser, stirrer, thermometer, and nitrogen inlet, keeping the temperature below 60°. Ferrocene (93.0 g, 0.5 mol) was introduced into the flask all at once and the stirred mixture heated in an oil bath maintained at 98–100° throughout the reaction. Methyl levulinate[22,23] (97.5 g, 0.75 mol) was added dropwise with vigorous stirring during 24 h; ca. 0.2 mol was added during the first 2 h and the remainder at a constant rate until all added; temperature 76–78° within the mixture throughout the reaction. After cooling to 25°, the mixture was stirred with 100 ml each of water and benzene. The deep-orange upper layer was separated from the dark-green lower layer which was extracted twice with benzene. The combined organic solutions were washed successively with water, 10% aqueous sodium hydroxide solution, and water and dried. Concentration under reduced pressure on the steam bath gave 119.1 g of a mixture of oil and crystals. The mixture was heated in an oil bath for 2 h (bath temperature 115–130°, 1 mm) in a rotary evaporator provided with a 20 × 3 cm collection trap. The sublimate was washed thoroughly with water to yield recovered ferrocene (37.6 g, 40.5% recovery). The residue, a red grease (69.4 g), was distilled under nitrogen through a short stillhead (Woods metal bath held at 250–260°) as rapidly as possible to yield at ca. 0.1 mm fractions (1) bp 130–200°, 2.2 g, mainly methyl 4-ferrocenylpentanoate (ca. 1% yield); (2) bp 225–236°, 48.4 g (40% conversion, 67% yield based on reacted ferrocene) of methyl 4,4-diferrocenylpentanoate which crystallized on standing, mp 104–107°; and (3) 16.8 g of black, brittle solid residue. (A parallel run of doubled scale gave comparable results.) Crystallization of fraction 2 from hexane gave orange-yellow needles, mp 107–108° (ca. 80% recovery): ir (KBr) 1725 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ 4.08 (s, 18, Fc), 3.63 (s, 3, CH_3O), 2.22 (s, 4, CH_2CH_2), 1.62 (s, 3, CH_3C); ^{13}C NMR ($CDCl_3$) δ 174.5 (C=O), 99.5 (substituted ferrocenyl C-1), 68.5 (unsubstituted cyclopentadiene rings), 66.8, 66.2 (substituted ferrocenyl C-2, C-5), 66.8 (substituted ferrocenyl C-3, C-4), 51.5 (CH_3O), 38.4 (pentanoyl C-2, CH_2), 35.9 (pentanoyl C-4 quaternary), 30.1 (pentanoyl C-3, CH_2), 24.3 (pentanoyl C-5, CH_3); see Table I. Undistilled crude product ester crystallized with great difficulty and in poor yield from hexane or other solvents; it could be purified by dry-column chromatography on alumina (elution with benzene) after which it could be crystallized from hexane in high purity and yield. Small amounts of impurities in ester 3, as well as in the other ferrocene compounds encountered in the present work, vitiate purification by crystallization.

To maximize the conversion of ferrocene to product ester it was found desirable to employ a large excess of methyl levulinate; lower keto ester/ferrocene ratios gave much lower conversions. Slow addition of levulinate to the ferrocene also minimizes side reactions. It was found that concentrated sulfuric acid could be substituted for 100% phosphoric acid, but much tar formation resulted, the yield was lower, and the product was more difficult to purify. More dilute (85%) phosphoric acid gave lower yields. Levulinic acid substituted for its methyl ester also gave lower yields. To increase the reaction rate, cyclohexane was introduced as a cosolvent. Heptane and benzene were much less effective cosolvents for this purpose—both gave lower yields and benzene addition produced much tar. Maintenance of a reaction temperature below 80° within the reaction vessel (oil bath temperature below 100°) decreases tar formation. Small amounts of ferrocene (0.1–4%) could be recovered from the dark-green aqueous acid solutions remain-

Table I

1-Substituted 3,3-Diferrocenylbutanes



Registry no.	Compd	X	Mp, °C	Molecular formula[a]
56386-19-7	3	CO_2CH_3	107–108	$C_{26}H_{28}Fe_2O_2$
56386-21-1	8	CO_2H	195–199	$C_{25}H_{26}Fe_2O_2$
57458-81-8		$CONH_2$	149–150	$C_{25}H_{27}Fe_2NO$
57458-82-9	12	$CONHNH_2$	168–171	$C_{25}H_{28}Fe_2N_2O$
56386-20-0	7	CH_2OH	115–116	$C_{25}H_{28}Fe_2O$
56386-24-4	11	NCO	135–137	$C_{25}H_{25}Fe_2NO$
57458-83-0		$NHCO_2CH_3$	130–131	$C_{26}H_{29}Fe_2NO_2$
57458-84-1		NHCONH-C_6H_5	182–183[b]	$C_{31}H_{32}Fe_2N_2O$

[a] Satisfactory analytical data (±0.3% for C, H, Fe, and N) and molecular weight data (±4%, by vapor osmometry in chloroform) for all compounds were submitted for review. [b] Previous melting at 124–129° (polymorph).

ing after removal of the water-insoluble organic products by addition of sodium sulfite or ascorbic acid. Methyl levulinate could be recovered (ca. 10–20%) from the volatile components distilled from the reaction mixture during work-up.

Methyl 4-Ferrocenylpentanoate (5). Fraction 1 in the above preparation of ester 3 was redistilled to yield a mobile red oil: bp 128° (0.05 mm); $n^{25}D$ 1.5693; ir (film) 1725 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 4.05 (s, 5, unsubstituted cyclopentadienyl), 3.98 (s, 4, substituted cyclopentadienyl), 3.59 (s, 3, CH_3O), 2.1–2.7 (m, 1, CH), 1.5–2.7 (m, 4, CH_2CH_2), 1.22 (d, 3, J = 6.5 Hz, CH_3C).

Anal. Calcd for $C_{16}H_{20}FeO_2$: C, 64.02; H, 6.72; Fe, 18.60; mol wt, 300.2. Found: C, 64.30; H, 6.66; Fe, 18.40; mol wt, 296 ($CHCl_3$).

1,1′-Bis[2-ferrocenyl-4-carbomethoxy)butyl]ferrocene (6). Polyphosphoric acid was prepared by mixing 85% phosphoric acid (22.5 g) and phosphorus pentoxide (27.5 g). Methanol (25 ml), cyclohexane (30 ml), ferrocene (18.6 g, 0.1 mol), and methyl levulinate (13.0 g, 0.1 mol) were added to the acid all at once and the mixture stirred for 16 h while heating in an oil bath (bath temperature 95–98°, pot temperature 80–82°). The mixture was worked up as described above in the preparation of ester 3 to yield 2.5 g (13%) of recovered ferrocene and 18.6 g of product mixture not subliming at 130° (1 mm). The product mixture was fractionated by dry-column chromatography on alumina (elution with benzene) to yield as principal fractions 8.3 g (34% conversion, 41% yield) of methyl 4,4-diferrocenylpentanoate (3) and 2.2 g of a more slowly eluted fraction isolated as a dark red gum; crystallization of this material from hexane gave 0.53 g (2%) of diester 6 as orange crystals, mp 132–138°. Two recrystallizations from hexane gave flat, orange, hexagonal prisms: mp 140–142°; ir (KBr) 1730 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 3.8–4.2 (m, principal peak at δ 4.04, 26, Fc), 3.60 (s, 6, CH_3O), 2.14 (s, 8, CH_2CH_2), 1.53 (s, 6, CH_3C); ^{13}C NMR ($CDCl_3$) δ 174.7 (C=O), 99.7, 99.3 (substituted ferrocenyl C-1), 68.6 (unsubstituted cyclopentadienyl rings), 68.0, 67.6 (outer substituted ferrocenyl C-2, C-5), 67.1, 66.8 (inner substituted ferrocenyl C-2, C-5), 66.8 (outer substituted ferrocenyl C-3, C-4), 66.4 (inner substituted C-3, C-4), 51.5 (CH_3O), 38.7 (pentanoyl C-2, CH_2), 36.0 (pentanoyl C-4, quaternary), 30.1 (pentanoyl C-3, CH_2), 24.1 (pentanoyl C-5, CH_3).

Anal. Calcd for $C_{42}H_{46}Fe_3O_4$: C, 64.48; H, 5.92; Fe, 21.41; mol wt, 782.4. Found: C, 64.34; H, 5.88; Fe, 21.58; mol wt, 777 ($CHCl_3$).

4,4-Diferrocenyl-1-pentanol (7). A. From Methyl 4,4-Diferrocenylpentanoate (5). A solution of methyl 4,4-diferrocenylpentanoate (3.4 g, 7.0 mmol) in 15 ml of dry tetrahydrofuran was added dropwise with stirring during 15 min to a solution of 0.27 g (7.0 mmol) of lithium aluminum hydride in 25 ml of ether. The mixture was heated under reflux with stirring for 80 min. The mixture was chilled in an ice bath and stirred with an excess of 1 N hydrochloric acid until all aluminum salts were dissolved. The ether layer was separated, washed with water, and dried with magnesium sulfate. Concentration under reduced pressure gave 3.0 g (94% yield) of the alcohol, mp 104–111°; recrystallization from cyclohexane gave small prisms, 2.8 g, mp 110–111°. Recrystallization from benzene gave chunky prisms: mp 115–116°; ir (KBr) 3350 cm^{-1} (OH), carbonyl bands absent; ^1H NMR ($CDCl_3$) δ 4.12 (s, 18, Fc), 3.3–3.8 (m, 2, CH_2O), 1.2–2.2 (m, 4, CH_2CH_2), 1.65 (s, 3, CH_2); ^{13}C NMR ($CDCl_3$) δ 95.7 (substituted ferrocenyl C-1), 70.2 (unsubstituted cyclopentadienyl rings), 68.8 (substituted ferrocenyl C-2, C-5), 68.6 (substituted ferrocenyl C-3, C-4), 65.9 (CH_2OH), 47.1 (pentanol C-2, CH_2), 43.1 (pentanol C-4, quaternary), 37.8 (pentanol C-3, CH_2), 24.9 (pentanol C-5, CH_3); see Table I.

B. From Ferrocene and 5-Hydroxy-2-pentanone. Ferrocene (10.0 g, 0.054 mol) and 5-hydroxy-2-pentanone (1.02 g, 0.01 mol, from Aldrich Chemical Co.) were dissolved in 40 ml of methylene chloride. Trifluoroacetic acid (10 ml) was then added with stirring, causing the reaction mixture to darken and become slightly warm. The mixture was allowed to stand at ambient temperature for 2.3 h; water (50 ml) was then added with stirring. A blue color which had appeared in the aqueous phase was discharged with a small amount of ascorbic acid. The methylene chloride phase was separated and poured onto an activated alumina column (5 × 25 cm). Unreacted ferrocene (7.6 g, 76%) was eluted with methylene chloride. The next band appearing on the column was removed mechanically and the mixture of alumina and product was extracted with methanol. Removal of methanol from the extract gave 2.8 g of 4,4-diferrocenyl-1-pentanol; recrystallization from cyclohexane gave 2.0 g of pure product, red-brown crystals, mp 112–113° (44% conversion, 70% yield based on reacted ferrocene). The above procedure failed to effect condensation of ferrocene with methyl levulinate or levulinic acid; reactants were recovered.

4,4-Diferrocenylpentanoic Acid (8). A mixture of methyl 4,4-diferrocenylpentanoate (24.2 g, 0.05 mol) and potassium hydroxide (15 g, 85% assay) dissolved in a solution of 50 ml each of water, ethanol, and dioxane was heated on the steam bath (nitrogen atmosphere) for 3 h. The solution was concentrated to remove solvents; 50 ml of water and 100 ml of dioxane were added and the mixture warmed to dissolve the product. The cooled solution was acidified to pH 1 by addition of concentrated hydrochloric acid; the mixture was then warmed on the steam bath to dissolve all organic material. The solution was concentrated under reduced pressure on the steam bath to remove solvents and the residue treated with 500 ml of water; the solid was filtered and washed thoroughly with water. The dried solid was heated in boiling benzene (300 ml) to dissolve organic material and filtered hot to remove insoluble matter. The filtrate was concentrated to dryness and finally heated on the steam bath at 0.1 mm for 2 h to yield 23.3 g (99%) of the acid, mp 192–199°. Recrystallization from cyclohexane gave prisms: mp 195–199°; it is necessary to heat at 100° (0.1 mm) for 2 h to remove all cyclohexane solvent; ir (KBr) 1685 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 3.98 (s, 18, Fc), 2.20 (s, 4, CH_2CH_2), 1.55 (s, 3, CH_3); see Table I.

4,4-Diferrocenylpentanohydrazide (12). A solution of methyl 4,4-diferrocenylpentanoate (2.42 g, 0.005 mol) and hydrazine hydrate (1.5 g, 0.015 mol) in 1-butanol (10 ml) was heated under reflux (nitrogen atmosphere) for 20 h. Concentration of the deep-red solution to dryness under reduced pressure gave 2.38 g (99%) of the hydrazide, mp 168–171°; recrystallization from 95% ethanol did not change the melting point; ir (KBr) 3200 (NH), 1640, 1620 cm^{-1} (C=O); see Table I.

4,4-Diferrocenylpentanoyl Chloride (9). 4,4-Diferrocenylpentanoic acid (23.5 g, 0.05 mol) dissolved in 500 ml of dry benzene containing pyridine (4.8 g, 0.06 mol) was treated with phosphorus trichloride (8.2 g, 0.06 mol). The mixture was heated in a nitrogen atmosphere on the steam bath from 25° to reflux during 15 min and at reflux for 30 min. The mixture was cooled to room temperature and the supernatant solution filtered by suction to separate it from insoluble material adhering to the flask; the solid residue was rinsed twice with dry benzene. The combined benzene solutions were concentrated under reduced pressure, *care being taken not to heat the flask contents above 25°. (Caution! The acid chloride decomposes rapidly, evolving hydrogen chloride when heated at 80–100°.)* The crude oily acid chloride revealed a strong carbonyl band at 1795 cm^{-1} and no other carbonyl absorption bands, yield 23.7 g (97%). The crude acid chloride was used immediately, without further treatment, for conversion to the acyl azide.

Prolonging the reaction time in refluxing benzene beyond 45 min to 2–6 h resulted in lowered yields of the acid chloride and formation of much benzene-insoluble material, as well as a carbonyl-containing impurity in the product (ν 1670 cm^{-1}). Heating the crude, neat acid chloride on the steam bath for a few minutes resulted in rapid evolution of hydrogen chloride and formation of a black brittle solid having no acid chloride carbonyl absorption at 1795 cm^{-1} (hydroxyl absorption absent). Attempts to purify the crude acid chloride in benzene solution by washing with cold saturated sodium bicarbonate solution caused partial hydrolysis to the acid salt; severe emulsification resulted, making the extraction quite difficult.

4,4-Diferrocenylpentanoamide. A solution of 4,4-diferrocenylpentanoyl chloride (1.0 g, 2.04 mmol) in 5 ml of dry tetrahydrofuran was treated with 15 ml of a 3% ammonia solution in dry tetrahydrofuran. After standing protected from moisture for 4 days at ambient temperature the mixture, which contained a precipitate, was concentrated to dryness under reduced pressure. The residue was diluted with water and the mixture filtered and washed with water to yield 0.94 g (98%) of the amide, mp 148–150°; recrystallization from cyclohexane gave prisms, mp 149–150°; see Table I.

4,4-Diferrocenylpentanoyl Azide (10). 4,4-Diferrocenylpentanoyl chloride (24.4 g, ca. 0.05 mol of material prepared as described above) was dissolved in 100 ml of tetrahydrofuran and added dropwise with stirring to a solution of sodium azide (4.55 g, 0.07 mol) in 15 ml of water chilled to 3° in an ice bath, keeping the temperature below 5° during the addition (nitrogen atmosphere). Stirring was continued for 30 min at 3–4°. The infrared spectrum of an aliquot sample showed strong bands at 1710 (C=O) and 2130 cm^{-1} (N_3) characteristic of the acyl azide, and virtually no other components as indicated by the absence of other infrared bands, including those of the acid chloride or carboxylic acid. A trace of isocyanate was indicated by extremely weak absorption at 2270 cm^{-1}. *The following operations were performed as rapidly as possible owing to the short half-life of the acyl azide.* The mixture was concentrated under reduced pressure at 25° to remove tetrahydrofuran and the gummy residue diluted with 30 ml of cold water. Benzene (500 ml) was added and the mixture shaken vigorously to dissolve most of the residue; an emulsion results and some gummy solid remains undissolved in either the benzene or the water phase. The mixture was transferred to a separatory funnel and the aqueous layer (an emulsion containing some benzene and other material) drawn off and mixed with Celite and filtered; the filtrate (now a clear mixture of aqueous and benzene layers) was separated and the benzene layer added to the principal benzene extract. The combined benzene solutions were extracted twice with cold water and twice with cold 10% aqueous sodium hydroxide solution. As a result of these operations more insoluble gummy material precipitated. The combined aqueous layers (again an emulsion containing some benzene and other material, including the precipitate) were mixed with Celite and the mixture filtered through a Büchner funnel with suction. The clear filtrate (again a mixture of aqueous and benzene layers) was separated and the benzene layer combined with the principal benzene extract. The combined benzene solutions were washed twice with cold water and dried at 25° with anhydrous magnesium sulfate for ca. 1 h. The solution was filtered and concentrated under reduced pressure at 25° to remove benzene, leaving the crude acyl azide as a gummy solid, 19.8 g (85%), ir (film) 1710 (C=O), 2130 cm^{-1} (N_3). The crude azide was employed immediately for conversion into the corresponding isocyanate.

3,3-Diferrocenylbutyl Isocyanate (11). A. From 4,4-Diferrocenylpentanoyl Azide (10). The crude acyl azide (10) prepared above (19.8 g) was dissolved in 400 ml of dry benzene and stored over molecular sieves for 16 h at 25° in a flask having a calcium chloride tube attached. Nitrogen gas evolved slowly during this time; the reaction was completed by heating the solution under gentle reflux for 0.5 h. The benzene was removed under reduced pressure at 25° to yield 19.1 g of crude isocyanate as orange crystals, mp 132–135°; extraction with 500 ml of dry, refluxing cyclohexane, followed by cooling, filtration of insoluble material, and concentration of the filtrate, gave the pure isocyanate as orange crystals: 17.0 g (74% from ester 3), mp 135–137°; ir (KBr) 2270 cm^{-1} (NCO); ^{1}H NMR ($CDCl_3$) δ 3.92 (s, 18, Fc), 1.8–3.3 (complex A_2B_2 multiplet centered at 2.1 and 3.1, 4, CH_2CH_2), 1.54 (s, 3, CH_3); see Table I. The isocyanate is very sensitive to moisture and must be stored in a moisture-proof container in a dry atmosphere.

B. From 4,4-Diferrocenylpentanohydrazide (12). 4,4-Diferrocenylpentanohydrazide (0.97 g, 2.0 mmol) was dissolved by warming in 20 ml of tetrahydrofuran containing 0.40 ml of concentrated hydrochloric acid. The solution was cooled to 0–5° in an ice bath and treated with a solution of sodium nitrate (0.26 g, 0.0026 mol) in 0.5 ml of water. The solution was stirred at 0–5° for 45 min, then concentrated to near dryness at ambient temperature. The residue was extracted with benzene and the benzene extracts washed with 10% aqueous sodium hydroxide solution and water and dried; the infrared spectrum of an aliquot sample revealed a strong azide band at 2180 cm^{-1}. The dried extracts were concentrated after standing at 25° for 2 days to yield 0.38 g of a gummy product, a mixture by ir assay of ca. 1:1 3,3-diferrocenylbutyl isocyanate (21% yield, ν 2270 cm^{-1}) and unreacted hydrazide (ν 1670 cm^{-1}). Insoluble material remaining after the benzene extraction (0.35 g) was insoluble in water; it showed strong infrared bands at 3400 and 1640 cm^{-1} (mp above 230°).

***N*-(3,3-Diferrocenylbutyl)carbamic 4,4-Diferrocenylpentanoic Anhydride (13).** 3,3-Diferrocenylbutyl isocyanate and 4,4-diferrocenylpentanoic acid (0.47 g, 0.001 mol of each) were added to 15 ml of dry benzene and stored at 25° over molecular sieves. The insoluble acid dissolved after shaking for a few minutes and the isocyanate band at 2270 cm^{-1} and carboxyl band at 1690 cm^{-1} nearly disappeared (aliquot sample); there appeared a characteristic anhydride doublet at 1770, 1740 cm^{-1} and carbamoyl NH at 3400 cm^{-1}. Concentration under reduced pressure at 25° gave the crude anhydride **13** as an amorphous gum. The infrared spectrum of the material was virtually unchanged by heating in refluxing dry benzene for 1 h.

A benzene solution of the anhydride was extracted with 10% aqueous sodium hydroxide solution; sodium 4,4-diferrocenylpentanoate precipitated. The benzene solution was washed with water, dried, and concentrated to yield recovered 3,3-diferrocenylbutyl isocyanate (ν 2270 cm^{-1}). The sodium 4,4-diferrocenylpentanoate was separated and converted into 4,4-diferrocenylpentanoic acid by treatment with aqueous hydrochloric acid, mp 191–199°.

***N*-(3,3-Diferrocenylbutyl)-*N'*-phenylurea.** A solution of aniline (0.25 g, 2.7 mmol) and 3,3-diferrocenylbutyl isocyanate (0.85 g, 1.8 mmol) in 15 ml of dry benzene was heated under reflux for 45 min. Cooling deposited crystals of the urea derivative, 0.56 g, mp 118–125°. Recrystallization from benzene gave flat yellow prisms (0.46 g, 46%), mp 125–129°, changing on melting to small rectangular prisms, mp 182–183°; ir (KBr) 3300 (NH), 1630 cm^{-1} (C=O); see Table I.

Methyl 3,3-Diferrocenylbutyl Carbamate. To a solution of 3,3-diferrocenylbutyl isocyanate (0.23 g, 0.49 mmol) in 10 ml of dry tetrahydrofuran was added 1 ml of methanol. The mixture was heated under reflux on the steam bath for 16 h. Concentration of the solution to dryness gave 0.25 g (100%) of the urethane derivative, mp 128–131°; recrystallization from cyclohexane gave flat hexagonal prisms, mp 130–131°; see Table I.

***N,N'*-Bis(3,3-diferrocenylbutyl)urea.** A solution of 3,3-diferrocenylbutyl isocyanate (0.65 g, 1.4 mmol) in 25 ml of benzene and 0.1 ml of water was heated under reflux for 15 min. Cooling gave 0.48 g (74%) of the urea derivative as yellow prisms, mp 233–236°. Recrystallization from benzene gave needles: mp 240–241°; ir (KBr) 3400 (NH), 1620 cm^{-1} (C=O).

Anal. Calcd for $C_{49}H_{52}Fe_4N_2O$: C, 64.79; H, 5.77; N, 3.08; Fe, 24.59; mol wt, 908.4. Found: C, 64.71; H, 5.73; N, 3.15; Fe, 24.31; mol wt, 890 (osmometry, $CHCl_3$).

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Registry No.—**5**, 56411-04-2; **6**, 57458-85-2; **9**, 56386-22-2; **10**, 56386-23-3; **13**, 57458-86-3; ferrocene, 102-54-5; methyl levulinate, 624-45-3; 5-hydroxy-2-pentanone, 1071-73-4; *N,N'*-bis(3,3-diferrocenylbutyl)urea, 57484-07-8.

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Alkylations and Competing Rearrangements in the Aluminum Chloride Catalyzed Reactions of Secondary Alkyl Chlorides with Arenes[1]

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Aluminum chloride catalyzed alkylations of benzene and *p*-xylene by 2- and 3-chloropentane and 2- and 3-chlorohexane have been studied. The alkylations are accompanied by simultaneous isomerization of the chloroalkanes and rearrangement of the product arylalkanes. At 25°, rearrangement of the arylalkanes to an equilibrium composition is the dominant product-determining factor. At −20°, this rearrangement is minimized and product composition is determined by isomerization of the chloroalkanes and competitive alkylation by the isomeric chloroalkanes. The order of mixing the reactants affects the product composition at 0 and −20°. Rough kinetic analysis of alkylations of benzene and *p*-xylene by 2- and 3-chlorohexane indicates that the rates of isomerization and alkylation of the chloroalkanes are of the same order of magnitude. The rate of alkylation by 2-chlorohexane is estimated to be about 2–3 times the rate of alkylation by 3-chlorohexane. Alkylations with $AlCl_3 \cdot CH_3NO_2$ catalyst at 25° took place without product isomerization; rates of alkylation were reduced more than rates of chloroalkane isomerization. Comparison is made of the present results from chloroalkane alkylations and isomerizations with analogous reactions of alkenes.

There have been numerous reports of alkylations of arenes with secondary alkylating agents. However, because of the analytical methods employed in some of the older work, the analysis of isomeric phenylalkanes has led to some questionable and contradictory results.

Ipatieff, Pines, and Schmerling[2] alkylated benzene with both 1-pentene and 1-pentanol using 80% sulfuric acid as a catalyst. Their report of a 60% 2-phenylpentane and 40% 3-phenylpentane product was the first report of such a reaction mixture from this type of alkylation. Pines, Huntsman, and Ipatieff[3] reported 76% 2-phenylpentane and 24% 3-phenylpentane from the reaction of 3-pentanol and benzene in the presence of $AlCl_3$ at 25–35°. 2-Pentanol was reported to yield 60% 2-phenylpentane and 40% 3-phenylpentane. Streitweiser, Stevenson, and Schaeffer[4] studied the alkylations of benzene with isomeric pentanols using BF_3 catalyst. Both 2- and 3-pentanol gave identical product mixtures containing 65% 2-phenylpentane, 25% 3-phenylpentane, and 10% 2-methyl-2-phenylbutane. These workers suggested a carbonium ion type alkylating species and stated that the 2- and 3-phenylpentane ratio was probably determined by the rearrangement of the carbonium ion prior to alkylation.

Ipatieff, Pines, and Schmerling[2] reported a mixture containing 60% 2-phenylpentane and 40% 3-phenylpentane from the alkylation of benzene with 1-pentene and sulfuric acid. However, Axe[5] and Simons and Archer[6] reported 2-phenylpentane as the only reaction product from 2-pentene and BF_3 or HF. Olson[7] found 37% 2-phenylhexane and 63% 3-phenylhexane from benzene and 1-hexene with sulfuric acid, a complete reversal from the results from 1-pentene reported by Ipatieff et al.[2] Alul has studied the alkylation of benzene by 1-dodecene, *trans*-6-dodecene,[8,9] and 8-methyl-1-nonene[10] with various catalysts, and has discussed the influence of catalyst type and medium polarity on the distribution of products. A comparison of the alkene reactions with those of the chloroalkanes in this work will be given later.

Rearrangements of *sec*-phenylalkanes have also been previously investigated. Burwell and Shields[11] found that $AlCl_3$ caused complete racemization of optically active 2-phenylpentane after only 10 min at room temperature. No 3-phenylpentane was detected in the reaction mixture. They postulated that the racemization occurred via a rapid hydride ion transfer. The interconversion of 2- and 3-phenylpentane occurred more slowly and was ascribed to disproportionation to dipentylbenzene and benzene followed by the reverse of this reaction. However, Roberts and co-workers[12,13] have suggested that the rearrangements of 2- and 3-phenylpentane as well as the isotopic scrambling of 2-phenyl-2-^{14}C-butane occur via an intermediate phenylalkyl cation produced after hydride abstraction.

This paper is concerned with alkylations by 2- and 3-chloropentanes and 2- and 3-chlorohexanes and the relationship of the concomitant isomerizations of the chloroalkanes and the *sec*-phenylalkanes to the observed final compositions of the product mixtures.

Discussion

Alkylations of Benzene with 2- and 3-Chloropentane. Both 2- and 3-chloropentane isomerized rapidly in the presence of $AlCl_3$ at temperatures from −20 to 25° to a 64:36 equilibrium ratio (Table I). This 64:36 ratio very nearly represents a statistical distribution, since the chloropentanes have two carbon atoms to which chlorine may bond in the 2 position and one such carbon atom in the 3 position. When benzene was added to an isomerized chloropentane mixture at −20°, a very similar 66:34 distribution of 2-:3-phenylpentane resulted (run 6, Table II). The procedure of isomerizing a chloroalkane with $AlCl_3$, followed by addition of the arene, will be referred to as alkylation method B. When the order of addition of reactants was