2,3-Dimethoxy-5-methylpropiophenone (XIX). To a solution of ethyl zinc iodide (prepared according to Mauthner[13] from 35 g. of copper-zinc couple, 73 g. of ethyl iodide, 36.5 g. of toluene, and 18.5 g. of ethyl acetate in presence of a few milligrams of iodine), cooled at 0°, a solution of 30 g. of 2,3-dimethoxy-5-methylbenzoyl chloride (XVIII) in 200 ml. of toluene was added dropwise with stirring. The reaction mixture was left to stand at room temperature for 2 hr., transferred in a separatory funnel, and vigorously shaken with water and with dilute hydrochloric acid. The aqueous layer was extracted twice with ether and the ethereal extracts were added to the toluene layer. After washing with sodium bicarbonate solution, with sodium thiosulfate solution and finally with water, the toluene layer was dried over anhydrous sodium sulfate. Removal of the solvent left an oil which was distilled in vacuum. The fraction boiling at 104–105°/0.2–0.3 mm. was collected. It weighed 20.5 g.

(13) J. Mauthner, *J. prakt. Chem.* (*2*), **103**, 393 (1922).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.18; H, 7.74. Found: C, 69.10; H, 7.70. This product gave the same dinitrophenylhydrazone of XI. A mixture melting point of these derivatives was not depressed.

2,3-Dihydroxy-5-methylpropiophenone. Seven grams of 2,3-dimethoxy-5-methylpropiophenone (XIX) and 21 g. of pyridinium chloride were refluxed for 30 min. By pouring the reaction mixture in water, the demethylated product was isolated. On crystallizing from ligroin, 3.1 g. of 2,3-dihydroxy derivative, m.p. 84–85°, was obtained.

A mixture melting point with a sample of VII was not depressed.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.40; H, 6.74.

Ultraviolet spectrum of 8-hydroxy-2,3-dimethylchromone in ethanol 95°: λ_{max} 235 and 310 mμ.

MILANO, ITALY

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

The Fries Reaction of 2,4-Dichloro-5-methylphenyl Acetate[1]

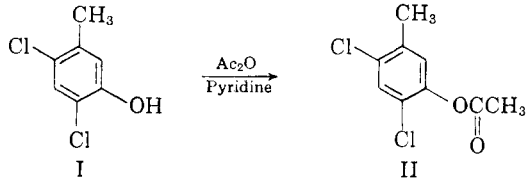
S. E. CREMER[2] AND D. S. TARBELL

Received March 28, 1961

Treatment of 2,4-dichloro-5-methylphenyl acetate (II) with aluminum chloride at 135° gave 3,5-dichloro-2-hydroxy-6-methylacetophenone (III) as the major product and a small amount of 6,8-dichloro-2,5-dimethylchromone (IV). The structure of the former compound was substantiated by converting it to the hydrazone of 2-hydroxy-6-methylacetophenone which was synthesized by an independent method.

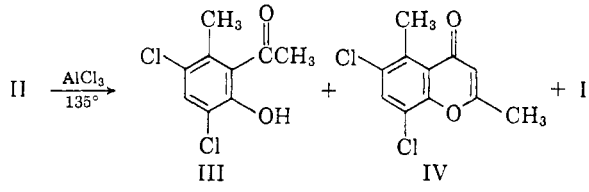
During the synthesis of 2-isoamyl-3,4-dimethylbenzofuran,[3] a degradation product of the antibiotic fumagillin,[4] 2 - hydroxy - 6 - methylacetophenone (XVIII) was considered as a possible starting material. The present paper describes a study of the Fries reaction on 2,4-dichloro-5-methylphenyl acetate (II), and shows that one of the products is 3,5-dichloro-2-hydroxy-6-methylacetophenone (III) by relating it to the hydrazone of 2-hydroxy-6-methylacetophenone, which has been prepared by an unambiguous method.

Acetylation of 2,4-dichloro-5-methylphenol (I) with acetic anhydride–pyridine gave a high yield of the acetate II.



I II

Treatment of the acetate II with aluminum chloride at 135° produced three compounds: the desired 3,5-dichloro-2-hydroxy-6-methylacetophenone (III), 6,8-dichloro-2,5-dimethylchromone (IV), and deacetylated material I.



III IV

The infrared spectrum of IV indicated the presence of a conjugated carbonyl function (1653 cm.$^{-1}$) consistent[5] with the chromone structure (as opposed to a coumarin structure). Moreover, the ultraviolet spectrum (see experimental) was similar to 2-hydroxymethylchromone and 2-methylchromone.[6]

When subjected to basic hydrolysis, IV was converted back to the acetophenone III; no 3,5-dichloro-2-hydroxy-6-methylbenzoic acid was formed—an observation which is characteristic of 5-substituted chromones.[7]

(1) Supported in part by Grant E-1138 of the U. S. Public Health Service.

(2) Abbott Laboratories Fellow, 1960–1961.

(3) D. S. Tarbell, R. M. Carman, D. D. Chapman, K. R. Huffman, and N. J. McCorkindale, *J. Am. Chem. Soc.*, 82, 1005 (1960).

(4) D. D. Chapman, S. E. Cremer, R. M. Carman, M. Kuntsmann, J. G. McNally, Jr., A. Rosowsky, and D. S. Tarbell, *J. Am. Chem. Soc.*, 82, 1009 (1960).

(5) M. S. Newman and S. Schiff, *J. Am. Chem. Soc.*, 81, 2266 (1959); Coumarins absorb in the 1754–1695 cm.$^{-1}$ region, whereas chromones absorb at 1667–1639 cm.$^{-1}$

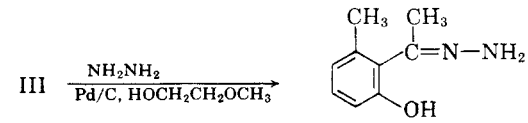
(6) T. A. Geissman and J. W. Bolger, *J. Am. Chem. Soc.*, 73, 5875 (1951).

(7) R. C. Elderfield, *Heterocyclic Compounds*, Vol. 2, Wiley, New York, 1951, pp. 258–259.

Treatment of the acetophenone III with sodium and ethyl acetate, a standard procedure for the formation of chromones,[8] produced a crystalline substance which was identical to IV.

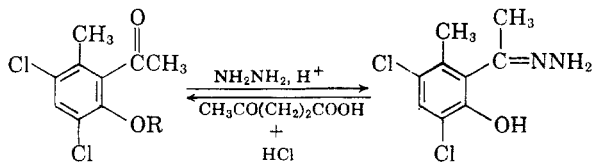
The possibility of rearrangement during the Fries reaction required proof for the structure of III. The synthesis of the chromone IV from III provided supporting evidence for the *ortho* relationship of the hydroxyl and acetyl groups.

Treatment of III with hydrazine and palladium on carbon in refluxing Methyl Cellosolve, a procedure used for removing aromatic halogens,[9] gave the hydrazone of 2-hydroxy-6-methylacetophenone (V).



V

Indeed, conversion of III to the corresponding hydrazone VI proceeded readily at room temperature and in the presence of a trace of acetic acid. Regeneration of III was accomplished, although in poor yield, by heating the hydrazone with a mixture of levulinic and hydrochloric acids.[10]



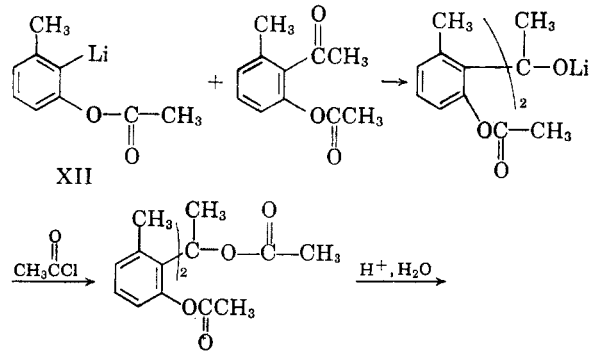
III. R = H
VII. R = CH_3

VI

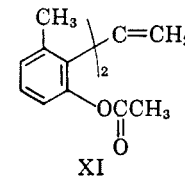
On the other hand, the methyl ether VII did not form a hydrazone at room temperature; at higher temperatures (120–125°) hydrazone formation did occur, but ether cleavage also took place to produce compound VI.

In an attempt to protect the ketone function, the crystalline ketal of III was made (ethylene glycol and *p*-toluenesulfonic acid), from which the parent ketone could be regenerated on treatment with aqueous acid. Efforts to remove the chlorine atoms from the ketal (VIII) were unsuccessful.

In order to prove the 1,2,3-substitution pattern in the hydrazone V, an independent synthesis of this compound was carried out. 2-Bromo-3-methylphenol[11] (IX) was treated with *n*-butyllithium, followed by the addition of acetyl chloride, to produce 3-methylphenyl acetate (X) and 1,1-bis(2-acetoxy-6-methylphenyl)ethylene (XI). The structure of the latter compound was substantiated by its infrared and NMR spectra (see Experimental), as well as by a satisfactory elemental analysis. It probably arose from the reaction of 2-acetoxy-6-methylphenyllithium (XII) with the desired product, 2-acetoxy-6-methylacetophenone, followed by elimination to form the double bond during the workup.

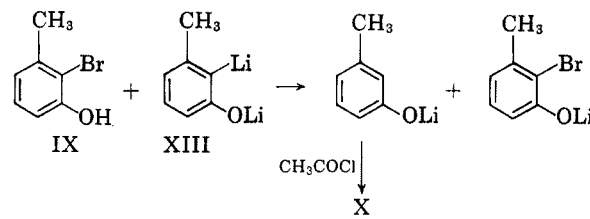


XII



XI

The 3-methylphenyl acetate (X) probably arose from the protonation of the lithium salt XIII by the phenol IX. An analogous reaction has been described by Gilman.[12]



IX XIII X

In view of the previous results, the phenol IX was converted to its methyl ether XIV which was treated with *n*-butyllithium followed by carbonation to produce 2-methoxy-6-methylbenzoic acid (XV). The acid was converted to the acid chloride XVI, which was treated with dimethylcadmium to give 2-methoxy-6-methylacetophenone (XVII).

To serve as a model for the ether cleavage, 3,5-dichloro-2-methoxy-6-methylacetophenone (VII) was treated with pyridine hydrochloride at 210° to produce the hydroxyacetophenone III; conversion of XVII to 2-hydroxy-6-methylacetophenone (XVIII) was achieved by this same method.[13]

(8)(a) R. Mozingo, *Org. Syntheses*, **Coll. Vol. III,** 387 (1941); (b) G. Wittig, *Ber.*, **57,** 88 (1924).

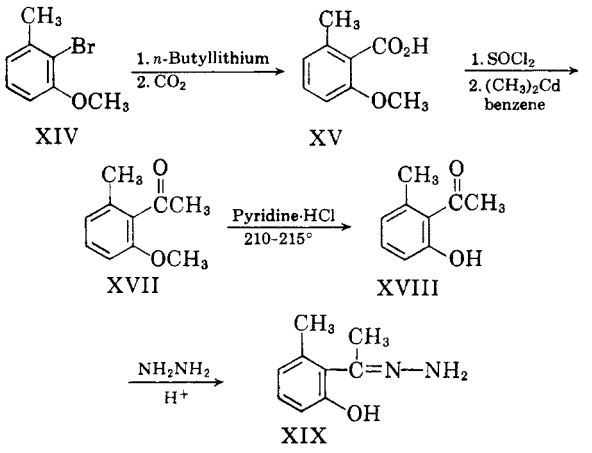
(9) W. L. Mosby, *Chem. & Ind.*, 1348 (1959).

(10) C. H. DePuy and B. W. Ponder, *J. Am. Chem. Soc.*, **81,** 4629 (1959).

(11) R. A. Benkeser and W. E. Buting, *J. Am. Chem. Soc.*, **74,** 3012 (1952); *cf.* E. L. Eliel, D. E. Rivard, and A. W. Burgstahler, *J. Org. Chem.*, **18,** 1679 (1953).

(12) H. Gilman and C. E. Arntzen, *J. Am. Chem. Soc.*, **69,** 1537 (1947).

(13)(a) A. L. Wilds and W. B. McCormack, *J. Am. Chem. Soc.*, **70,** 4127 (1948); (b) V. Prey, *Ber.*, **75,** 445 (1942); (c) The referee has pointed out that although such halogen migrations are known, they require distinctly more vigorous conditions [*cf. inter alia*, A. A. Spryskov and I. G. Erykalov, *J. Gen. Chem.*, **29,** 2798 (1959) (Consultants Bureau trans. p. 2862) + papers cited].



Transformation of XVIII to the hydrazone XIX was accomplished with hydrazine and a trace of acid in refluxing ethanol. The crystalline hydrazone XIX was identical (mixed melting point and infrared spectrum) to the hydrazone V produced from the Fries reaction. Hence, the position of three of the substituents in III was confirmed; moreover, it was likely (although not substantiated) that the halogens retained their original *meta* relationship during the conversion of II to III by the Fries reaction.[13c]

EXPERIMENTAL[14]

2,4-Dichloro-5-methylphenyl acetate (II). A mixture of 35.4 g. (0.20 mole) of 2,4-dichloro-5-methylphenol (I)[15] and 40.8 g. (0.40 mole) of acetic anhydride in 21 ml. of pyridine was heated and stirred on a steam bath for 4 hr. (the reaction was initially exothermic). The solution was cooled and poured over 300 g. of ice; after stirring for several minutes, a solid precipitate formed. Recrystallization from ice cold petroleum ether (b.p. 30–60°) gave 41.8 g. (95% yield) of white needles, m.p. 35–38°. For analysis the compound was sublimed at room temperature and 0.1 mm. pressure; the m.p. was 39.5–40.5°.

Anal. Calcd. for $C_9H_8O_2Cl_2$: C, 49.80; H, 3.68. Found: C, 49.72; H, 3.32.

Formation of 3,5-dichloro-2-hydroxy-6-methylacetophenone (III) *and 6,8-dichloro-2,5-dimethylchromone* (IV) *from the Fries reaction.* A mixture of 39.6 g. (0.181 mole) of the acetate II and 32 g. of anhydrous aluminum chloride was heated and stirred on an oil bath; the reaction turned green and hydrogen chloride gas was liberated at 105–115°. After 10–20 min. at 135° the color was brown. The reaction was heated and stirred for a total of 1 hr. and 20 min. at 135°, was cooled in an ice bath, and was decomposed with 150 g. of ice. After thoroughly extracting the aqueous solution with several portions of ether, the ether extracts were combined and extracted with 10–15% sodium hydroxide solution.

The ether phase was dried and evaporated to an oil which was dissolved in ethanol-water. Upon cooling a crude solid precipitated. The solid was taken up in petroleum ether (not all the material went into solution), and the solution was filtered to afford 1 g. of residue, m.p. 125–135°. The filtrate was cooled to produce 3.4 g. of starting material, II. The residue was crystallized from absolute ethanol to yield 200 mg. of needles of the chromone IV, m.p. 154–156.5°, whose infrared spectrum indicated the presence of a conjugated carbonyl at 1653 cm.$^{-1}$ The ultraviolet spectrum (95% ethanol) exhibited absorption: λ 315 (log ε 3.77); λ 250 (log ε 3.92; inflection); λ 230 (log ε 4.41).

Anal. Calcd. for $C_{11}H_8O_2Cl_2$: C, 54.35; H, 3.32; Cl, 29.17. Found: C, 54.27; H, 3.56; Cl, 29.28.

The original sodium hydroxide solution was neutralized with cold, 6*N* hydrochloric acid, and the solution was extracted with ether. The ether was dried (magnesium sulfate) and evaporated to an oil, which was dissolved in 150–200 ml. of petroleum ether. On standing at room temperature, grainy crystals of the Fries product III (only sparingly soluble in petroleum ether) came out of solution. Slow recrystallization of III from alcohol-water afforded 8.2 g. of chunky crystals (rapid recrystallization produced needles), m.p. 104–105.5°.

Anal. Calcd. for $C_9H_8O_2Cl_2$: C, 49.80; H, 3.68; Found: C, 49.48; H, 3.67.

Cooling and concentration of the petroleum ether mother liquor from III gave 9.3 g. of a mixture of crystals. Repeated fractional recrystallization from petroleum ether gave 1.3 g. of 2,4-dichloro-5-methylphenol; the residual 8 g. consisted of III, IV, and I, but no further effort was made to separate this mixture.

Basic hydrolysis of 6,8-dichloro-2,5-dimethylchromone (IV) *to form* III. A mixture of 1.5 g. of IV, 50 ml. of 5% sodium hydroxide, and 100 ml. of methanol was allowed to reflux for 12 hr. Evaporation of the solvent left a residue which was dissolved in ether. Extraction of the ether with sodium hydroxide and neutralization of the basic extract with hydrochloric acid did not produce any acidic material. Distillation of the ether afforded a product which was recrystallized from ethanol. This material was identical to the acetophenone III (melting point and mixed melting point).

6,8-Dichloro-2,5-dimethylchromone (IV) *from* III. To 1.6 g. (0.07 g.-atom) of sodium (cut into small pieces) suspended in 20 ml. of ethyl acetate, 5 g. (0.02 mole) of 3,5-dichloro-2-hydroxy-6-methylacetophenone (dissolved in ethyl acetate) was added slowly to maintain gentle refluxing. After the exothermic reaction had subsided, the mixture was heated on a steam bath for 1 hr. The ethyl acetate was evaporated, and the residue was treated with dilute acetic acid. The aqueous layer was extracted with ether, and the ether was evaporated to a viscous oil, which was allowed to reflux in concentrated hydrochloric acid and glacial acetic acid (1:5) for 30 min. Evaporation of the acid under reduced pressure afforded a compound which was recrystallized from ethanol (together with decolorizing carbon) to yield 3.3 g. of product. Further recrystallization gave a compound identical to the chromone from the Fries reaction (melting point and mixed melting point; infrared spectrum).

2-Hydroxy-6-methylacetophenone hydrazone (V) *from* III. A mixture of 5 g. of III, 3 g. of 5% palladium on carbon, 150 ml. of Methyl Cellosolve, and 17 ml. of hydrazine (95+%) was brought to reflux. Additional 5-and 10-ml. portions of hydrazine were added after 5- and 20-hr. periods, respectively. After 48 hr. at reflux temperature, the solvent and catalyst were removed, 20 ml. of water was added, and the mixture was extracted with ether. The ether was dried and evaporated to 3.2 g. of viscous oil. In an attempt to distill the product, white crystals formed on the cold finger. Recrystallization from heptane gave needles, m.p. 138.5–139.3°.

Anal. Calcd. for $C_9H_{12}N_2O$: C, 65.83; H, 7.37; N, 17.06. Found: C, 66.23; H, 7.51; N, 16.93.

3,5-Dichloro-2-hydroxy-6-methylacetophenone hydrazone (VI) *and regeneration of* III. To 1.75 g. of III dissolved in ethanol, water was added until the solution was turbid. After the addition of 2 drops of acetic acid and 2 g. of hydrazine (95+%), the mixture was heated on a steam bath

(14) All melting points and boiling points are uncorrected. Analyses were carried out by Micro-Tech Laboratories, Skokie, Ill. The infrared spectra were taken as Nujol mulls or on the liquid film. The solvents were generally removed at steam bath temperatures with the aid of a rotating film evaporator.

(15) Aldrich Chemical Co., m.p. 71–73°; R. C. Huston and P. S. Chen, *J. Am. Chem. Soc.*, **55**, 4214 (1933).

for 10 min. On standing a precipitate formed, which was recrystallized from ethanol-water to give white needles (450 mg.), m.p. 155–156°.

Anal. Calcd. for $C_9H_{10}N_2OCl_2$: C, 46.37; H, 4.32; N, 12.02. Found: C, 46.40; H, 4.54; N, 12.14.

To 140 mg. of the hydrazone VI, 2 ml. of a solution of levulinic and 1*N* hydrochloric acid (9:1) was added. After heating on the steam bath for 3 hr., the mixture was cooled, neutralized with sodium carbonate, and extracted with ether. Evaporation of the ether gave a semisolid residue which was sublimed *in vacuo* to give 20 mg. of crystalline product identical to the acetophenone III.

3,5-Dichloro-2-methoxy-6-methylacetophenone (VII). To 0.6 g. of sodium dissolved in 100 ml. of absolute alcohol, 5.1 g. (0.023 mole) of III was added, followed by 8.5 g. of methyl iodide. After 3 to 4 hr. at reflux temperature, the mixture was neutral to moist litmus paper. The ethanol was distilled, ether was added, and the precipitated sodium iodide was filtered. The ether solution was passed over a column of alumina (neutral, grade I), and the column was eluted with ether to give 4.85 g. of a colorless liquid. The infrared spectrum showed the absence of O—H stretching and the presence of a carbonyl function (1695 cm.$^{-1}$).

The analytical sample was prepared by rechromatography and subsequent evaporative distillation.

Anal. Calcd. for $C_{10}H_{10}O_2Cl_2$: C, 51.52; H, 4.32. Found: C, 52.00; H, 4.57.

3,5-Dichloro-2-hydroxy-6-methylacetophenone hydrazone (VI) *from* VII. To 500 mg. of VII in 15 ml. of Methyl Cellosolve, water was added until the mixture was turbid; 2 ml. of hydrazine (95+%) and 2 drops of glacial acetic acid were added, and the mixture was allowed to reflux for 44 hr. Evaporation of the solvent (*in vacuo*) left a viscous oil which was dissolved in ethanol. Water was added to produce a solid precipitate. The product, 150 mg., was identical (mixed melting point and infrared spectrum) to VI.

2-(3,5-Dichloro-2-hydroxy-6-methylphenyl)-1,3-dioxolane (VIII). A solution of 2 g. (0.01 mole) of III, 0.1 g. of *p*-toluenesulfonic acid, 5 g. of ethylene glycol, and 30 ml. of benzene was allowed to reflux under a water separator for 50 hr. The cooled benzene solution was washed with sodium bicarbonate solution, dried (magnesium sulfate), and evaporated to produce 2.15 g. of solid, m.p. 93–97.5°; further recrystallization from ethanol-water raised the melting point to 97.5–99°. The infrared spectrum confirmed the absence of a carbonyl function. Regeneration of III from the ketal was accomplished (88% yield) by aqueous acid hydrolysis.

Anal. Calcd. for $C_{11}H_{12}O_3Cl_2$: C, 50.21; H, 4.60. Found: C, 50.18; H, 4.73.

1,1-Bis(2-methyl-6-acetoxyphenyl)ethylene (XI) *and 3-methylphenyl acetate* (X) *from 2-bromo-3-methylphenol* (IX). A solution of *n*-butyllithium[16] in ether was prepared from 34 g. (0.25 mole) of *n*-butyl bromide and 3.5 g. (0.50 g.-atom) of lithium wire. A solution of 18.6 g. (0.1 mole) of IX in 50 ml. of ether was added dropwise to the *n*-butyllithium solution (the temperature was maintained below 10°). After stirring for 2 hr. at room temperature, 19.6 g. of acetyl chloride in 30 ml. of ether was added to the mixture (maintained at −10°). The reaction was warmed to room temperature and then allowed to reflux for 30 min. The mixture was cooled to 0°, and water was added until two liquid phases appeared. The ether layer was extracted with sodium hydroxide, dried, and evaporated to an oil. Distillation gave 7.4 g. of a mobile liquid X (b.p. 94–100° at 10 mm.), which showed a band at 1754 cm.$^{-1}$ in the infrared. Saponification in methanolic sodium hydroxide afforded *m*-cresol (characterized in the infrared and by a tribromo derivative). The residue from the distillation was dissolved in 30 ml. of ether. On standing a precipitate (XI) formed, which was recrystallized from ethanol to give 1.5 g. of white flakes, m.p. 129–130°. The infrared spectrum showed peaks at 1754 cm.$^{-1}$, 1626 cm.$^{-1}$, and 897–902 cm.$^{-1}$ An NMR spectrum showed two unsplit vinyl protons (τ 4.48), six aromatic protons (centered at τ 2.90), and six aromatic methyl or acetyl protons (τ 7.68). The remaining six protons were masked by the acetone signal (acetone was used as a solvent).

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.06; H, 6.22. Found: C, 73.96; H, 6.22.

2-Bromo-3-methylanisole (XIV). To 9.36 g. (0.05 mole) of 2-bromo-3-methylphenol[11] (m.p. 61–63°, reported[11] m.p. 61.5–62°) in absolute alcohol containing sodium ethoxide (0.05 mole), 7.1 g. of methyl iodide was added and the solution stirred for 1 hr. Another portion of methyl iodide (14.2 g.) was added and the solution was allowed to reflux for 5 hr. Evaporation of the ethanol was followed by ether addition and filtration of the sodium iodide. The ether was evaporated to an orange-red oil, which was crystallized from ethanol-water (sodium thiosulfate was added to discharge the iodine color) to give 7 g. (70% yield) of white needles. Another run (0.1*M* scale) gave 87% of the desired product, m.p. 41–43° (reported[11] m.p. 41.5–42°).

2-Methoxy-6-methylbenzoic acid (XV). A solution of *n*-butyllithium[16] in ether was prepared from 22 g. (0.16 mole) of *n*-butyl bromide and 2.22 g. (0.32 g.-atom) of lithium wire. A solution of 17.3 g. (0.086 mole) of XIV dissolved in ether was added to the *n*-butyllithium solution (maintained at 10°). The reaction was warmed to room temperature and stirred for 50 min. The mixture was cooled to −10° and dropped in a thin stream with stirring onto powdered Dry Ice. The mixture was decomposed with water followed by dilute hydrochloric acid. The aqueous solution was extracted with ether and the ether was subsequently extracted with dilute sodium carbonate solution. Acidification of the basic extract gave 11.4 g. of crude product. Recrystallization from alcohol-water produced 8.65 g. (60% yield) of XV, m.p. 138–141°. Recrystallization from water afforded the analytical sample, m.p. 139–141° (reported[17] m.p. 141–142°).

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.29; H, 6.11.

2-Methoxy-6-methylbenzoyl chloride (XVI). To 8.65 g. (0.052 mole) of XV, 25 g. of thionyl chloride was added, and the mixture was allowed to stand for 1 hr. at room temperature. The reaction was then heated at reflux for 90 min. After the excess thionyl chloride had been removed, the residue was distilled (b.p. 94° at 1.0 mm.). The clear, colorless distillate, 8.08 g. (84% yield) showed a band at 1776 cm.$^{-1}$ in the infrared.

The acid chloride XVI was characterized as the amide derivative, m.p. 159–160° (reported[18] m.p. 157°).

Anal. Calcd. for $C_9H_{11}NO_2$: C, 65.44; H, 6.71. Found: C, 65.45; H, 6.63.

2-Methoxy-6-methylacetophenone (XVII). A mixture containing dimethylcadmium in benzene was prepared[19] from methylmagnesium bromide (0.064 mole) and cadmium chloride (0.032 mole). To this mixture (cooled in an ice bath), 8.08 g. (0.044 mole) of XVI (in benzene) was added over 2 min. The reaction was stirred at 50° for 1 hr. and then at reflux for 2 hr. Decomposition of the cooled reaction with water, followed by dilute hydrochloric acid, afforded two phases. The organic layer was separated and the aqueous phase was extracted with ether. The combined organic and ether extract was washed with sodium bicarbonate solution and dried. Distillation gave a colorless liquid (b.p. 91–94° at 0.5 mm.) which showed strong carbonyl absorption at 1686 cm.$^{-1}$ and a weak band at 1773 cm.$^{-1}$ (approximately 5% of unchanged XVI). Chromatography over neutral alumina (grade I) and elution with ether gave 2.4 g. (33% yield) of the pure acetophenone XVII.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37 Found: C, 72.67; H, 7.38.

Formation of III *from 3,5-dichloro-2-methoxy-6-methylacetophenone* (VII). A mixture of 500 mg. of VII and 3 g.

(16) H. Gilman *et al.*, *J. Am. Chem. Soc.*, **71**, 1499 (1949).
(17) D. Peltier, *Compt. rend.*, **236**, 1972 (1953).
(18) G. P. Gibson, *J. Chem. Soc.*, 1274 (1923).
(19) J. Cason, *J. Am. Chem. Soc.*, **68**, 2078 (1946).

of pyridine hydrochloride was heated at 210° for 2 hr. The reaction was cooled and poured onto ice water to produce a crude precipitate. After several recrystallizations of the solid from alcohol-water, 100 mg. of crystalline material was obtained, which was identical to III (melting point and mixed melting point).

2-Hydroxy-6-methylacetophenone (XVIII) *and the corresponding hydrazone* (XIX). A mixture of 1 g. of 2-methoxy-6-methylacetophenone (XVII) and 7 g. of pyridine hydrochloride was heated under nitrogen at 210–215° for 90 min. The deep red mixture was cooled and water was added. The aqueous solution was extracted with ether and the ether layer was extracted with 1N sodium hydroxide solution. The basic extract was acidified and extracted with ether. Distillation of the ether gave 400 mg. of XVIII, which showed hydroxyl and carbonyl (1667 cm.$^{-1}$) absorption in the infrared.

To 300 mg. of XVIII dissolved in ethanol, 2 ml. of hydrazine (95+%) and a drop of glacial acetic acid were added. After 3 hr. at reflux temperature, the solvent and excess hydrazine were removed to give a residue, which was dissolved in 100 ml. of boiling *n*-heptane. Upon cooling 120 mg. of white needles, m.p. 139–141° were obtained. A mixture melting point with V from the Fries reaction showed no depression; the infrared spectra of V and XIX were identical.

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Thermal Isomerization of Hydroborated Olefins

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The effects of chain length and hydroxyl substituents on the extent and direction of boron migration along a hydrocarbon chain were studied by thermal isomerization, oxidation, and hydrolysis of hydroborated 11-tricosene and oleyl alcohol. Boron migration along the long chains in the trialkylborane derived from the unsubstituted 11-tricosene is complete, and oxidation gives good yields of 1-tricosanol. Migration along the long chains in the trialkylborane derived from the terminally substituted oleyl alcohol proceeds in both directions. Migration in one direction gives, after oxidation and hydrolysis, 1,18-octadecanediol, while migration in the other direction, toward the original hydroxyl group, does not go beyond the 4- position, possibly due to coordination with the oxygen atom in a 6-membered ring. Oxygenated functional groups, such as in free alcohols and ketones, appear to be capable of inhibiting boron migration.

Brown and Subba Rao discovered that, in the presence of ethers, olefins of wide structural variety react with diborane at room temperature to yield trialkylboranes.[1] Products thus formed from terminal olefins may be oxidized and hydrolyzed to primary alcohols, providing a convenient anti-Markownikoff hydration. Trialkylboranes from internal olefins may be thermally isomerized to the corresponding 1-alkylboranes,[2] which then yield primary alcohols on oxidation.

In the present study, the effect of a hydroxyl substituent, and of the chain length on the extent and direction of boron atom migration along a hydrocarbon chain was investigated.

Hydroxy-substituted olefin. A recent publication by Fore and Bickford[3] described the successive hydroboration, attempted isomerization, and oxidation of methyl oleate. They found that oxidation of heat-treated and nonheat-treated boranes of methyl oleate yielded the same products, namely 1 : 1 mixtures of 9- and 10-hydroxystearic acids (after saponification of the ester).

An unsaturated alcohol was used for the present study because the alcohol group undergoes no net change in the procedures employed. Oleyl alcohol was chosen to ascertain the direction and extent of boron migration in terminally hydroxy-substituted long-chain compounds.

Oleyl alcohol was hydroborated and esterified by diborane to give a cross-linked, polymeric tris(tristearylborane) borate. Oxidation and hydrolysis gave a mixture of the isomeric 1,9- and 1,10-octadecanediols identical to that produced by epoxidation and reduction of oleyl acetate. Working with methyl oleate, Fore and Bickford[3] had already demonstrated that the hydroboration was nonselective as to the 9- and 10- positions.

Thermal isomerization (four hours at 160°) before oxidation and hydrolysis of hydroborated oleyl alcohol led to 10–13% yields of the 1,18-isomer in the octadecanediol product. This isomer was isolated by urea adduction of the isomeric diacetates and identified by elemental analyses, hydroxyl value, and infrared analysis, the last showing no secondary alcohol absorption.

The diols from the unadducted fraction of the diacetates did not contain 1,2-diols (negative periodate tests) and were different, on the basis of mixed melting point determinations, from the previously mentioned mixture of 1,9- and 1,10-diols and also the 1,6- and 1,7-diol mixture obtained

(1) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, 22, 1136 (1957).

(2) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, 22, 1137 (1957).

(3) S. P. Fore and W. G. Bickford, *J. Org. Chem.*, 24, 920 (1959).