

sumption of cyclooctene. The reaction was terminated at this point with 1 ml of methanol. The resulting mixture was concentrated on a roto-evaporator under aspirator vacuum to remove benzene, hexene, and cyclooctene prior to fractionation by preparative glc.

Analytical Procedures. Analysis by glc was routinely performed on a Hewlett-Packard 7620A Model gas chromatograph using a 6 ft \times 1/8 in. 10% UC-W98 on 80–100 mesh Diatoport S column, programmed from 80 to 270° in 20 min.

As stated earlier, a typical metathesis product was concentrated by the removal of benzene, hexene, and cyclooctene. The concentrate was fractionated by means of a Hewlett-Packard preparative gas chromatograph unit and seven fractions were isolated. They were analyzed by nmr, ir, and mass spectrum.

Nmr analyses were carried out on a Varian A60 spectrometer and ir spectra recorded on a Perkin-Elmer Model 21 spectrophotometer. High resolution mass spectrum measurements were made on a Du Pont Model 21-110C mass spectrometer using perfluorokerosene as the reference compound.

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Registry No.—1-Hexene, 592-41-6; cyclooctene, 931-88-4; WCl_6 , 13283-01-7; EtOH/EtAlCl_2 , 53777-80-3; $\text{CF}_3\text{CH}_2\text{OH/Et-AlCl}_2$, 53777-81-4; $2\text{Et}_2\text{O/Bu}_4\text{Sn}$, 53777-82-5; $2\text{Et}_2\text{O/Bu}_3\text{SnCl}$, 53777-83-6; $2\text{Et}_2\text{O/Bu}_2\text{SnCl}_2$, 53777-84-7; $2\text{Et}_2\text{O}/(\text{C}_6\text{H}_5)_4\text{Sn}$, 53777-85-8; $2\text{Et}_2\text{O}/(\text{C}_6\text{H}_5)_3\text{SnCl}$, 53777-86-9.

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Synthesis of Fatty Acids Using Organocopper(I) Ate Complexes Derived from Grignard Reagents¹

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Fatty acid esters have been synthesized in good yield by reaction between copper(I) ate complexes formed from methylcopper(I) and primary or secondary Grignard reagents and esters of primary iodoalkylcarboxylic acids. The synthetic method is illustrated with procedures for $\text{CH}_2=\text{CH}(\text{CH}_2)_{19}\text{CO}_2\text{C}_2\text{H}_5$, $\text{C}_6\text{H}_5\text{CH}_2\text{O}(\text{CH}_2)_{16}\text{CO}_2\text{C}_2\text{H}_5$, $\text{CH}_3(\text{CH}_2)_{25}\text{CO}_2\text{C}_2\text{H}_5$, $\text{CH}_3\text{O}_2\text{C}(\text{CH}_2)_{22}\text{CO}_2\text{CH}_3$, $\text{C}_2\text{H}_5\text{O}_2\text{C}(\text{CH}_2)_{32}\text{CO}_2\text{C}_2\text{H}_5$, and $\text{CH}_3(\text{CH}_2)_4\text{CH}(\text{CH}_3)(\text{CH}_2)_{10}\text{CO}_2\text{CH}_3$. The reaction sequence uses starting Grignard reagent with high efficiency, provides product mixtures that are conveniently worked up, and tolerates a variety of functional groups. It provides the most direct route presently available to a variety of representative classes of simple fatty acids.

A number of procedures for the synthesis of fatty acids are available.³ Those most commonly used for fatty acids not containing extensive unsaturation include the reaction of carbonyl compounds with alkylidene phosphoranes,⁴ the Kolbe anodic coupling of half esters of dicarboxylic acids,⁵ and the acylation of enamines with acid chlorides followed by hydrolysis of the resulting β -diketones and Wolff–Kishner reduction of the product keto acid.⁶

The reaction of carbonyl compounds with alkylidene phosphoranes is particularly useful for the preparation of diastereomerically pure unsaturated fatty acids, and has also been used in the preparation of branched-chain fatty acids. Its deficiencies are that it often involves multiple steps of only moderate yields and requires a difficult separation of products from triphenylphosphine oxide. Kolbe electrolysis of half esters of dicarboxylic acids is a useful route to symmetrical long-chain dicarboxylic acid esters, but is not applicable to the preparation of unsymmetrical compounds. The procedure developed by Hünig and co-workers is applicable to the synthesis of asymmetrically di-

substituted fatty acids, symmetrically disubstituted fatty acids, and both straight- and branched-chain fatty acids. Although versatile, it is lengthy.

We have developed an efficient alternative to these procedures based on carbon–carbon bond formation by selective coupling between one alkyl group of a “mixed” copper(I) ate complex and primary iodoalkyl carboxylic esters.⁷ This procedure is compatible with a number of functional groups, yields products cleanly and in high yield, and is applicable to a number of representative classes of fatty acids.

Results

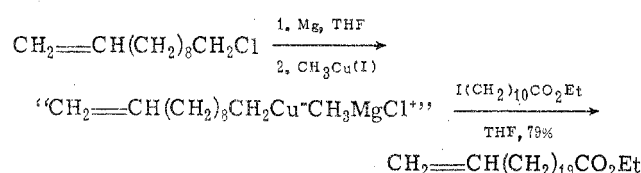
Both primary and secondary Grignard reagents react with methylcopper(I) and form copper(I) ate complexes that selectively transfer the alkyl group originally bonded to magnesium in high yield in alkylation reactions. By using the readily available methyl or ethyl 11-iodoundecanoate in this reaction, it is possible to synthesize a variety of fatty acids. A typical procedure—that for ethyl 21-do-

Table I
Fatty Acid Esters Synthesized from Grignard Reagents Using Organocopper(I) Ate Complexes "R₁CH₃CuMgX"
and Esters of 11-Iodoundecanoic Acid

Grignard reagent (R ₁)	Registry no.	Scale, mmol	Product	Isolated yield, % ^a
CH ₂ =CH(CH ₂) ₉ MgCl	53808-81-4	100	CH ₂ =CH(CH ₂) ₁₉ CO ₂ C ₂ H ₅	79
C ₆ H ₅ CH ₂ O(CH ₂) ₈ MgCl	53835-11-3	200	C ₆ H ₅ CH ₂ O(CH ₂) ₁₈ CO ₂ C ₂ H ₅	64
CH ₃ (CH ₂) ₁₅ MgBr	53808-83-6	50	CH ₃ (CH ₂) ₂₅ CO ₂ C ₂ H ₅	87
BrMg(CH ₂) ₁₂ MgBr	53862-77-4	25	H ₅ C ₂ O ₂ C(CH ₂) ₃₂ CO ₂ C ₂ H ₅	85
BrMg(CH ₂) ₁₂ MgBr		50	CH ₃ O ₂ C(CH ₂) ₂₂ CO ₂ CH ₃ ^b	72
CH ₃ (CH ₂) ₄ CH(CH ₃)MgBr	53808-85-8	100	CH ₃ (CH ₂) ₄ CH(CH ₃)(CH ₂) ₁₀ CO ₂ CH ₃	54

^a These yields are based on the Grignard reagent. A 20% excess of the 11-iodoundecanoic acid ester was used. ^b Methyl 6-iodohexanoate was used as alkylating agent.

Scheme I
Reaction of Methyl (10-Undecenyl)cuprate with Ethyl 11-Iodoundecanoate to Yield Ethyl 21-Docosenoate



cosenoate—is outlined in Scheme I. Reaction of undec-10-enylmagnesium chloride with methylcopper(I) generated a mixed copper(I) ate complex. This complex in turn reacted with ethyl 11-iodoundecanoate (0.12 mol) selectively by transfer of the undec-10-enyl moiety; ethyl 21-docosenoate was isolated in 79% yield.

This procedure is generally applicable (Table I): either primary or secondary Grignard reagents can be used; the starting Grignard reagent may contain certain functional groups (ethers or olefins); the alkylating agent may incorporate the full range of functional groups stable in cuprate coupling reactions (ethers, olefins, esters, ketones); α,ω -di-Grignard reagents⁸ can be used to prepare esters of long-chain dicarboxylic acids.

This method for the preparation of fatty acid esters has a number of advantages over previously described methods: the reaction involves only one coupling step and is shorter than the enamine method developed by Hünig and coworkers; products are obtained in high yield and can be isolated easily; starting materials are in general readily available; specialized electrochemical apparatus is unnecessary.

We have briefly investigated mixed alkyl(alkynyl)cuprates in these coupling reactions and found them to be unsatisfactory (Table II). Alkyl(alkynyl)cuprates prepared from organolithium reagents have been effectively used in the selective transfer of an alkyl group in alkylation reactions;^{7,9} however, these procedures apparently do not work well with Grignard reagent derived cuprates. Table II also indicates that although alkyl bromides do give acceptable yields, alkyl iodides are significantly better substrates. Mixed ate complexes containing copper(I) derivatives of mercaptans¹⁰ and alkyl tosylates¹¹ have both proved useful in carbon-carbon bond-forming reactions based on organolithium reagents; we have not explored either in these organomagnesium-based reactions. The basis for the selectivity in the transfer of the Grignard reagent derived alkyl group in these procedures is not well understood. Indeed, the basis for selectivity in transfer of alkyl groups from mixed diorganocuprates is in general only qualitatively understood.^{7,9,10} Regardless of the origin of the selectivity for transfer of the larger alkyl group in these cuprates, this se-

Table II
Yields in Selective Transfer of Grignard Reagent Derived Alkyl Groups from Copper(I) Ate Complexes "R₁R₂CuMgCl" in Alkylations with Alkyl Halides

R ₁ ^a	R ₂ ^b	RX	Yield, % R ₁ R
CH ₂ =CH(CH ₂) ₆ CH ₂ -	(CH ₃) ₃ CC≡C-	C ₅ H ₁₁ Br	23 (15) ^c
	(CH ₃) ₃ CC≡C-	C ₅ H ₁₁ I ^d	55
	(CH ₃) ₃ CC≡C-	C ₅ H ₁₁ I ^e	60
	Me	C ₅ H ₁₁ Br	71 ^f
	Me	C ₅ H ₁₁ I	92

^a This alkyl group was derived from an alkylmagnesium chloride. ^b This alkyl group was derived from an alkyl lithium reagent. ^c Lower yields resulted when the alkylcopper was prepared first and then allowed to react with 2,2-dimethylbutynyllithium. ^d A 50% excess of pentyl iodide was used. ^e A 500% excess of pentyl iodide was used. ^f This yield was obtained after stirring the reaction mixture for 3 hr at room temperature (see Experimental Section). Yields obtained just after the reaction mixture had warmed to room temperature were 5–10% lower.

lectivity serves usefully to permit efficient use of the alkyl groups originally present in the Grignard component of the reaction mixture.

Conclusion

The alkylation of alkyl(methyl)copper(I) ate complexes, in which the alkyl group is derived from a Grignard reagent, with iodo-substituted carboxylic acid esters forms the basis for a facile synthesis of a variety of substituted and unsubstituted fatty acids. This reaction proceeds with high selectivity in transfer of the alkyl group and gives products that can be conveniently isolated in high yield by recrystallization. This reaction is particularly well suited for the synthesis of α,ω -disubstituted fatty acid esters. It also affords a convenient route to branched- and straight-chain fatty acid esters. Further, these procedures illustrate a procedure by which the alkyl group of a Grignard reagent can be selectively and efficiently transferred from mixed diorganocuprates in alkylation reactions.

Experimental Section

General Methods. All reactions of air- and water-sensitive organometallics were carried out in flame-dried glassware under purified nitrogen using standard techniques.¹² Diethyl ether was distilled from calcium hydride under nitrogen; tetrahydrofuran and other ethereal and hydrocarbon solvents were distilled from a purple solution or suspension of disodium benzophenone dianion prior to use. Melting points were obtained on a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were recorded on a Varian T-60 spectrometer. Infrared spectra were taken in sodium chloride cavity cells using a Perkin-Elmer Model 337 grating spectrometer. F & M Model gas chromatographs were used for GLC analyses. Mass spectra were taken on a RMU-6E Hitachi Perkin-Elmer mass spectrometer. Lithium re-

agents were purchased from the Foote Mineral Co. or Alfa Inorganics, Inc. Lithium reagents were analyzed by the Gilman double titration method.¹³ 1-Chloro-6-hydroxyhexane, 3,3-dimethylbutene, 1,12-dibromododecane, 11-bromoundecanoic acid, and 10-undecenoic acid were obtained from the Aldrich Chemical Co. Less expensive technical grade 11-bromoundecanoic acid can also be used after distillation or purification by recrystallization from methanol or petroleum ether. 10-Undecenol and 10-undecenal were obtained from either International Flavors and Fragrances, Inc., Givaudan Corp., or California Aromatics and Flavors Inc. 1-Bromohexadecane was obtained from Air Products and Chemicals.

11-Chloroundecene. Following the procedure of Hooz and Gilani,¹⁴ 10-undecenol (128 g, 0.75 mol) was allowed to react with tri-*n*-butylphosphine (152 g, 0.75 mol) in 500 ml of carbon tetrachloride to give 130 g (92%) of 11-chloroundecene: bp 78–79° (0.9 Torr) [lit.¹⁵ bp 111–111.3° (10 Torr)]; ir (CCl₄) 1639 cm⁻¹; NMR (CDCl₃) δ 5.5–6.2 (m, 1 H), 4.75–5.2 (m, 2 H), 3.47 (t, 2 H), and 1.1–2.2 (m, 16 H). This reaction can be conveniently monitored by watching the disappearance of the hydroxyl peak in the ir. If necessary, the addition of more tri-*n*-butylphosphine will drive the reaction to completion after heating to reflux.

Ethyl 11-Iodoundecanoate. To an acetone solution of 11-bromoundecanoic acid (100 g, 377 mmol) was added sodium iodide (130 g, 872 mmol). This reaction mixture was then refluxed for 12 hr. After cooling to room temperature, the reaction mixture was poured into 3 l. of water. A solid formed which was separated by filtration and recrystallized from 500 ml of absolute methanol to give 114 g of pure 11-iodoundecanoic acid, mp 64–65° (lit.¹⁶ mp 64–65°). Esterification with 200 ml of absolute ethanol in 200 ml of toluene containing 2 ml of sulfuric acid according to literature procedures¹⁷ yielded ethyl 11-iodoundecanoate (88%): bp 149–151° (1 Torr) [lit.¹⁸ bp 110–112° (0.15 Torr)]; ir (neat) 1740 cm⁻¹; NMR (neat) δ 4.07 (q, 2 H), 3.18 (t, 2 H), 2.2 (t, 2 H), 2.0–1.0 (m, 19 H). The methyl ester of 11-iodoundecanoic acid could also be prepared using a literature procedure with absolute methanol and sulfuric acid.¹⁹ Methyl 11-iodoundecanoate thus prepared (78% yield) had bp 98–102° (0.15 Torr); ir (CCl₄) 1741 cm⁻¹; nmr (CCl₄) δ 3.62 (s, 3 H), 3.15 (t, 2 H), 2.2 (t, 2 H), 2.0–1.0 (m, 19 H).

Methyl 6-iodohexanoate, prepared in 87% yield from 6-bromohexanoic acid using obvious modifications of the procedure described above, had bp 75–78° (0.2 Torr) [lit.²⁰ bp 83–87° (0.8 Torr)]; ir (CCl₄) 1741 cm⁻¹; nmr (CCl₄) δ 3.60 (s, 3 H), 3.18 (t, 2 H), 2.27 (t, 2 H), 2.0–1.2 (m, 6 H).

6-Benzoyl-1-chlorohexane. 1-Chloro-6-hydroxyhexane (100 g, 0.73 mol) was dissolved in 400 ml of THF in a three-necked, 1-l. round-bottomed flask equipped with a magnetic stirring bar. Benzyl chloride (126.6 g, 1.0 mol) was added to the flask. Sodium hydride (20 g, 0.83 mol) was added in portions to this reaction mixture. Hydrogen was evolved during the sodium hydride addition. After the sodium hydride had been added, the reaction mixture was refluxed for 12 hr. At this point, TLC (CH₂Cl₂, silica gel) showed the reaction to be complete, and the reaction mixture was cooled to room temperature and quenched by cautiously pouring it into 1 l. of saturated aqueous ammonium chloride solution. The organic layer was separated and combined with two 200-ml ether washes of the aqueous layer. The organic layer was washed with 100 ml of saturated sodium chloride, dried (MgSO₄), and concentrated to an oil with a rotary evaporator. Distillation of this oil yielded 100.6 g (61%) of 1-benzoyl-6-chlorohexane: bp 110–112° (0.15 Torr) [lit.²¹ bp 136–141° (1 Torr)]; ir (neat) 3085, 3062, 3030, 1100 cm⁻¹; NMR (neat) δ 7.15 (m, 5 H), 4.33 (s, 2 H), 3.3 (m, 4 H), 1.0–1.9 (m, 8 H).

2,2-Dimethylbutyne was prepared in 82% yield according to the procedure of Collier and Macomber.²²

Ethyl 21-Docosenoate. 11-Undecenylmagnesium chloride was prepared from 11-chloroundecene and magnesium turnings in THF using standard procedures (ca. 97% yield). Cuprous iodide (19 g, 100 mmol), purified as described previously,²³ was placed in a flame-dried, 1-l. round-bottomed flask equipped with a magnetic stirring bar. Addition of 200 ml of THF gave a suspension which was cooled to -78°. A 2.2 M ether solution of methylolithium (45 ml, 99 mmol) was added to this suspension with a syringe. The reaction mixture was stirred for 1 hr at -78°. The resulting light yellow suspension was allowed to warm gradually to 0° with stirring. The resulting suspension of methylcopper was cooled to -78° and 71 ml of a 1.4 M THF solution of 11-undecenylmagnesium chloride (99 mmol) was added with a syringe. The reaction mixture was allowed to stir at -78° for another hour and warmed until a solution formed. The resulting purple solution was immediately cooled to -78°, during which time some white solid formed. Ethyl

11-iodoundecanoate (41 g, 120 mmol) was added with a syringe. The resulting suspension was stirred with an overhead stirrer for 1 hr at -78°, after which time it was allowed to come to room temperature. The reaction mixture was stirred for 2 hr at room temperature before it was quenched by pouring into a saturated aqueous ammonium chloride solution. The ethereal solution was separated and the aqueous phase was extracted with three 250-ml portions of ether. The combined organic fractions were washed once with 200 ml of saturated sodium chloride and dried (Na₂SO₄). The product, ethyl 21-docosenoate (28.5 g, 79%), was isolated by removing the ether with a rotary evaporator and recrystallizing the resulting oil from ethanol. The product was greater than 99% pure by GLC and had ir (CCl₄) 1734 and 1639 cm⁻¹; NMR (CDCl₃) δ 5.4–6.3 (m, 1 H), 4.8–5.2 (m, 2 H), 4.15 (q, 2 H), 1.0–2.6 (m, 41 H); mass spectrum (70 eV) parent peak *m/e* 366. For characterization, this material was hydrolyzed to 21-docosenoic acid (20% refluxing aqueous sodium hydroxide solution, 24 hr). After recrystallization from methanol, the acid had mp 69–70° (lit.²⁴ mp 62–63°); ir (CCl₄) 1710 cm⁻¹; NMR (CDCl₃) δ 8.6 (br, 1 H), 5.5–6.2 (m, 1 H), 4.8–5.2 (m, 2 H), 1.0–2.5 (m, 38 H); mass spectrum (70 eV) parent peak *m/e* 338.

Anal. Calcd for C₂₂H₄₂O₂: C, 78.04; H, 12.50. Found: C, 77.82; H, 12.28.

Ethyl 17-Benzoxiheptadecanoate. Using the procedure described for ethyl 21-docosenoate, 6-benzoxihexylmagnesium chloride was prepared from 6-benzoyl-1-chlorohexane and allowed to react with methylcopper and ethyl 11-iodoundecanoate to give ethyl 17-benzoxiheptadecanoate in 64% yield on a 200-mmol scale. The product ester was recrystallized from ethanol and had mp 34.5–35°; ir (CCl₄) 1740, 1180, 1103, 720, and 693 cm⁻¹; NMR (CCl₄) δ 7.2 (s, 5 H), 4.4 (s, 2 H), 4.03 (m, 2 H), 3.37 (t, 2 H), 2.2 (t, 2 H), 1.1–1.9 (broad s, 31 H).

Anal. Calcd for C₂₆H₄₄O₃: C, 77.18; H, 10.96. Found: C, 76.91; H, 10.89.

Ethyl Heptacosanoate. A copper(I) ate complex was prepared from 50 mmol of methylcopper(I) and 68 ml of 0.75 M hexadecylmagnesium bromide in THF using the procedures described above for 10-undecenylmagnesium chloride. In this case, an overhead stirrer was used to facilitate stirring of the reaction mixture. This ate complex was alkylated with ethyl 11-iodoundecanoate and worked up as described above by hydrolysis with saturated aqueous ammonium chloride and extraction with three 300-ml portions of benzene. After recrystallization from ethanol, the product ethyl heptacosanoate (18.5 g, 87% yield) had mp 61.5–62° (lit.²⁵ mp 62.5–62.6°), ir (CCl₄) 1740 cm⁻¹.

Diethyl tetratriacontanedioate was prepared on a 25-mmol scale from 1,12-dodecylid(magnesium bromide) and ethyl 11-iodoundecanoate according to the procedures described above. The product diester (12.7 g, 85% yield) was isolated by recrystallization from ethanol and had mp 76–77.5°, nmr (CCl₄) δ 4.07 (m), 2.25 (t), 1.8–1.0 (m), 1.25 (br s).

Anal. Calcd for C₃₈H₇₄O₄: C, 76.71; H, 12.54. Found: C, 77.07; H, 12.27.

Dimethyl tetracosanedioate was prepared from 1,12-didodecylmagnesium bromide and methyl 6-iodohexanoate on a 50-mmol scale according to the procedures described above. The product diester was isolated in 72% yield by recrystallization from methanol and had mp 69–71° (lit.²⁶ mp 69–70°), ir (CCl₄) 1741 cm⁻¹.

Methyl 12-Methylheptadecanoate. A 100-mmol aliquot of 2-heptylmagnesium bromide was allowed to react with methylcopper(I) (100 mmol) in the manner described above to give a copper(I) ate complex. During this procedure, care was taken to avoid allowing the ate complex to decompose by cooling the solution of the ate complex to -78° as soon as a distinct purple color appeared in the reaction mixture (ca. 10°). Alkylation with methyl 11-iodoundecanoate (110 mmol) and subsequent work-up yielded an oil which was distilled. The product, methyl 12-methylheptadecanoate, had bp 135–140° (0.2 Torr) and was isolated in 54% yield (16.1 g). A small forerun contained an additional amount of product according to TLC (~3 g), but this forerun was not redistilled. Methyl 12-methylheptadecanoate thus obtained had ir (CCl₄) 1740 cm⁻¹ and mass spectrum (70 eV) parent peak *m/e* 298.

Anal. Calcd for C₁₉H₃₈O₂: C, 76.45; H, 12.83. Found: C, 76.11; H, 12.60.

Use of 2,2-Dimethylbutynylcopper(I) in Selective Copper(I) Ate Complex Alkylations. A red-orange ether solution of 2,2-dimethylbutynylcopper was prepared from 2,2-dimethylbutynyllithium and copper(I) iodide according to the procedure of House and Umen.²⁷ Cooling this solution of copper(I) acetylide to -78° gave a yellow solution. This color change was reversible. Ad-

dition of 0.7 ml of a 1.5 M THF solution of 10-undecenylmagnesium chloride (1 mmol) to 1 mmol of this copper acetylide at -78° gave a red-orange solution of a copper ate complex. Warming this solution to room temperature resulted in no color changes other than some slight darkening. In alkylation reactions, the alkyl halide was added by syringe at -78 to this copper ate complex. After stirring at -78° for 0.5 hr, these solutions were allowed to gradually warm to room temperature. The reactions were hydrolyzed with 0.1 ml of hydrochloric acid after 2–3 hr of stirring at room temperature and analyzed by GLC on an 8-ft, SE-30 column.

Registry No.—11-Chloroundecene, 872-17-3; 10-undecenol, 112-43-6; carbon tetrachloride, 56-23-5; ethyl 11-iodoundecanoate, 53821-20-8; 11-bromoundecanoic acid, 2834-05-1; methyl 11-iodoundecanoate, 929-33-9; methyl 6-iodohexanoate, 14273-91-7; 6-bromohexanoic acid, 4224-70-8; 6-benzoxo-1-chlorohexane, 53821-21-9; 1-chloro-6-hydroxyhexane, 2009-83-8; benzyl chloride, 100-44-7; ethyl 21-docosenoate, 53821-22-0; 21-docosenoic acid, 53821-23-1; ethyl 17-benzoxoheptadecanoate, 53821-24-2; ethyl heptacosanoate, 53821-25-3; methylcopper(I), 1184-53-8; diethyl tetratriacontanedioate, 53821-26-4; dimethyl tetracosanedioate, 26134-71-4; methyl 12-methylheptadecanoate, 2490-24-6; 2,2-dimethylbutynylcopper(I), 53821-27-5.

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The Mechanism of the Reaction of Alkyl Bromides and Iodides with Mercury(II) and Silver(I) Fluorides¹

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The conversion of representative alkyl bromides and iodides to alkyl fluorides by mercury(II) and silver(I) fluoride has been shown to involve generation of intermediate alkyl carbonium ions by comparison of the product distributions obtained on conversion with those observed on solvolysis of related alkyl derivatives. Treatment of *exo*-2-bromo-*endo*-2-chloronorborene (1) and *endo*-2-bromo-*exo*-2-chloronorborene (2) with either mercury(II) or silver(I) fluoride yields *endo*-2-chloro-*exo*-2-fluoronorborene (8) as the only fluorine-containing epimer. The extensive elimination observed in the reaction of *cis*- and *trans*-4-*tert*-butylcyclohexyl bromide (3 and 4) with both mercury(II) and silver(I) fluoride, as well as the substantial fraction of *cis*- and *trans*-3-*tert*-butylcyclohexyl fluorides produced, parallels the related product ratios observed from the solvolysis of *cis*- and *trans*-4-*tert*-butylcyclohexyl arenesulfonates. Treatment of 1-iodo-2-phenylethane-2,2-*d*₂ (5) with mercury(II) or silver(I) fluoride produces a 1:1 mixture of 1-fluoro-2-phenylethane-2,2-*d*₂ and 1-fluoro-2-phenylethane-1,1-*d*₂. Similar treatment of 1-iodo- or 1-bromooctane produces a mixture of 1- and 2-fluorooctane while conversion of 2-iodo- or 2-bromooctane yields 2-fluorooctane, exclusively. The C–F bond-forming step in these reactions is suggested as proceeding by the intermolecular transfer of fluoride from a halometallo-ate complex to a carbonium ion center.

The biological activity² of organic compounds containing isolated fluorine atoms and the utility of the ¹⁹F nucleus as a probe of molecular structure³ are in large part responsible for the continuing interest in monofluoro-substituted organic compounds. The introduction of a single fluorine atom into an organic molecule is, therefore, a reaction of some importance and a variety of reagents are useful for this purpose.^{4,5} For complex molecules, however, the direct replacement of an isolated halogen atom, particularly bromine or iodine, by reaction with mercury(II) or silver(I) fluoride has frequently proven the procedure of choice for such syntheses, since these reactions proceed under mild conditions.⁵

The major fraction of evidence pertinent to the mechanism of the reaction of halocarbons with mercury(II) or silver(I) fluoride is stereochemical in nature. Conversion of 16 β -bromo-17 α ,20:20,21-bis(methylenedioxy)- Δ^4 -pregnen-3-one into 16 β -fluoro-17 α ,20:20,21-bis(methylenedioxy)- Δ^4 -pregnen-3-one and of α -1-bromo-2,3,4,6-tetraacetyl-D-galactose into β -1-fluoro-2,3,4,6-tetraacetyl-D-galactose by silver(I) fluoride are reported to proceed, respectively, with predominant retention⁶ and inversion⁷ of configuration. A concerted reaction⁸ might be expected to lead to products with retained or inverted stereochemistry while a nonconcerted process might be expected to yield, in general, products with loss of stereochemistry. Without complementary