was allowed to proceed for 1.5 hr at 4°. The reaction mixture was centrifuged, and the aqueous THF was decanted. The alumina residue was washed twice with 10 ml of ethyl acetate containing 1% acetic acid, and the washings were combined with the THF solution. The solution was acidified with acetic acid and extracted with 10 ml of saturated sodium chloride solution. Drying (Na_2SO_4) and evaporation of the solvent gave 16.1 mg of material which was almost entirely PGE_2 with some PGA_2 and starting material (no detectable epi-PGE_2).

This was dissolved in a small amount of ethyl acetate at *ca.* 40°, and hexane was added until the solution was cloudy. The solution was cooled at −20° for 2 hr, then overnight at −75° to give 11 mg (0.031 mmol, 72.5%): mp 63–66°; nmr ($CDCl_3$, 100 MHz) δ 5.65–5.48 (multiplet, 2 H, olefinic), 5.48–5.25 (multiplet, 2 H, olefinic), 5.17 (broad singlet, 3 H, CO_2H and OH), 4.23–3.83 (multiplet, 2 H, C_{11} H and C_{15} H), 2.80–0.70 (multiplet, 23 H); ir ($CHCl_3$) 3400, 1733, 1704, 967 cm^{-1}. An additional 2 mg of PGE_2 could be obtained from the mother liquor by thin layer chromatography, raising the yield to 85%.

15-Tribenzylsilyloxy-PGA_2 (1).—A mixture of 345 mg (1.03 mmol) of PGA_2 (purity 70–80%) and 1.237 g (3.67 mmol) of tribenzylsilyl chloride was slurried under argon in 5 ml of DMF. The slurry was cooled to −20°, and 113 mg (1.03 mmol) of 2,6-lutidine in 0.5 ml of DMF was added. The solution was stirred for 12 hr at −20° and then another 101 mg (0.94 mmol) of 2,6-lutidine was added and the solution was stirred for 12 hr at −20°. After another 50 mg (0.47 mmol) of 2,6-lutidine and 12 hr at −20°, the silylation was complete. The solution was diluted with 20 ml of methylene chloride and extracted twice with 20 ml of water and then 10 ml of brine. The aqueous layers were extracted with 10 ml of methylene chloride, and the combined methylene chloride solutions were dried (Na_2SO_4). Tlc shows tribenzylsilyl chloride (R_f 0.58, Et_2O) and a small amount of 15-tribenzylsilyloxy-PGB_2 (R_f 0.23, Et_2O) as impurities. Chromatography on silica gel gave 452 mg (0.71 mmol, 88–100%) of 15-tribenzylsilyl-PGA_2 as an oil: nmr ($CDCl_3$) δ 9.8 (1 H, CO_2H), 7.40–6.80 (multiplet, 16 H, ArH and C_{11} H), 6.25–6.05 (multiplet, 1 H, C_{10} H), 5.45–5.15 (multiplet, 4 H, olefinic), 4.20–3.95 (multiplet, 1 H, C_{15} H), 3.22–2.96 (multiplet, 1 H, C_{12} H), 2.50–0.85 (multiplet, 20 H); ir (neat) 2970, 1740, 1720, 1600, 1500, 1450 cm^{-1}; mass spectrum (70 eV) *m/e* 634 (M^+), 527.

10,11-Epoxy-15-tribenzylsilyloxy-PGA_2 (3) and PGE_2.—To a solution of 64 mg (0.10 mmol) in 1 in 5 ml of methanol at −17.5° was added 1 ml (*ca.* 5 mmol) of 30% H_2O_2 followed by 20 μl (0.06 mmol) of 3 *N* NaOH.[6] After 4 hr at −17.5° another 20 μl (0.06 mmol) of 3 *N* NaOH was added and the solution was stirred for 8 hr. Another 25 μl (0.075 mmol) of 3 *N* NaOH was added, and the solution was stirred for another 18 hr. Then 2 ml of saturated NH_4Cl solution was added, and the volume was reduced to *ca.* 5 ml. The residue was diluted with 10 ml of saturated NH_4Cl solution and extracted with 10 ml of CH_2Cl_2 which was washed twice with 5 ml of saturated NH_4Cl solution and then washed with 5 ml of brine. After drying (Na_2SO_4) and evaporation of the solvent, there was obtained 60.7 mg (0.094 mmol, 94%) of a mixture of epoxides: nmr ($CDCl_3$) δ 7.32–6.80 (broad doublet, 15 H, ArH), 5.60–5.10 (multiplet, 4 H, olefinic), 4.20–3.90 (multiplet, 1 H, C_{15} H), 3.56 (doublet, J = 4 Hz, 1 H, C_{10} H), 3.35 (multiplet, 1 H, C_{11} H), 2.80–0.85 (multiplet, 27 H); ir ($CHCl_3$) 3400, 2960, 1760, 1720, 1600, 1500 cm^{-1}; mass spectrum (70 eV) *m/e* 650 (M^+), 541.

Although the two epoxides were inseparable by tlc, they were easily separated by llc.[10] This showed a mixture of 84.5:15.5 with the major isomer being the desired epoxide.

When the epoxidation was carried out at −40°, the isomer ratio was 87.5:12.5 and the yield was 95%. However, epoxidation did not occur at −78° even using 90% H_2O_2 instead of 30% H_2O_2.

The conversion of **3** to PGE_2 was carried out by the same procedure described above for the synthesis of PGE_2 from **4**.

Registry No.—**1**, 41366-90-9; **2**, 41366-91-0; **3**, 41366-92-1; PGA_2, 13345-50-1; 10,11-epoxy-PGA_2, 41366-94-3; PGE_2, 363-24-6; tri-*p*-xylylsilyl chloride, 41366-95-4; tribenzylsilyl chloride, 18740-59-5; **4**, 41366-93-2.

A Study of the Scope and Mechanism of Displacement of Halogen from a Saturated Carbon by Organocadmium Reagents[1]

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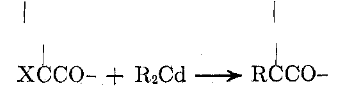
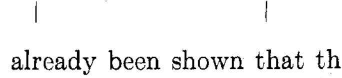
Displacement of halogen with phenylcadmium reagent has been effected in several substrates: ethyl bromoacetate, ethyl α-bromopropionate, ethyl α-bromobutyrate, 3-bromocyclohexene, allyl bromide, benzyl bromide, and chloromethyl methyl ether. Under similar reaction conditions, 1-bromobutane, ethylene bromide, bromoacetaldehyde diethyl acetal, *tert*-butyl chloride, trimethylsilyl chloride, chlorocyanomethane, and 1-chloro-1-nitroethane were unreactive. With α-halo esters, an α hydrogen, as well as halogen, seems to be a minimum requirement for displacement. A carbene intermediate ($R\ddot{C}COOR'$) seems unlikely, inasmuch as none of the expected bicyclo product was found when cyclohexene was added as a carbene trapping agent. The generation of free radicals is evident from the strong esr signal observed initially on mixing of the reactants. The intermediacy of a free-radical intermediate, either by homolysis or electron transfer, is consistent with the fact that the displacement proceeds with racemization, which was established in the formation of (±)-methyl hydratropate from (R)-(+)-bromopropionate and phenylcadmium reagent under conditions when the starting ester was optically stable. The interesting observation has been made that the displacement in 3-bromocyclohexene proceeds without the intermediacy of free radicals, as judged by esr spectroscopy.

For some time we have been investigating a fascinating reaction of promising synthetic value, namely, the displacement of substituents—often but not always halogen—in esters, lactones, and ketones with organocadmium reagents.[2] The general reaction is represented in eq 1a and 1b.



$$\mathrm{X\overset{|}{\underset{|}{C}}OCO\text{-} + R_2Cd \longrightarrow R\overset{|}{\underset{|}{C}}OCO\text{-}} \qquad (1a)$$



$$\mathrm{X\overset{|}{\underset{|}{C}}CO\text{-} + R_2Cd \longrightarrow R\overset{|}{\underset{|}{C}}CO\text{-}} \qquad (1b)$$

While it had already been shown that the displacement from a phthalide[2e] was stereoselective, no such information was at hand concerning the steric course of displacement in α-halo esters[2d] when this present work was undertaken. We found that (R)-(+)-methyl α-bromopropionate (**1**) underwent reaction with ethereal phenylcadmium reagent to afford racemic

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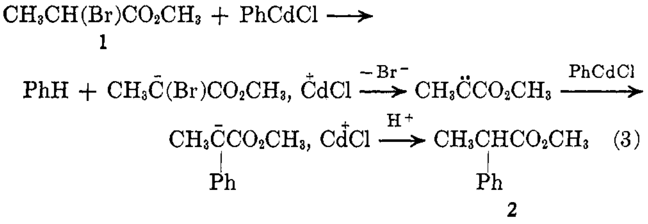
[1] (a) Taken in part from the Ph.D. thesis of S. J. C., University of New Hampshire, 1972. (b) Presented in part at the 164th National Meeting of the American Chemical Society, New York, N. Y., 1972, ORGN 169.

[2] (a) P. R. Jones and S. L. Congdon, *J. Amer. Chem. Soc.*, **81**, 4291 (1959); (b) P. R. Jones and A. A. Lavigne, *J. Org. Chem.*, **25**, 2020 (1960); (c) P. R. Jones, C. J. Jarboe, and R. Nadeau, *J. Organometal. Chem.*, **8**, 361 (1967); (d) P. R. Jones and J. R. Young, *J. Org. Chem.*, **33**, 1675 (1968); (e) P. R. Jones and C. J. Jarboe, *Tetrahedron Lett.*, 1849 (1969); (f) P. R. Jones and C. J. Jarboe, *J. Organometal. Chem.*, **24**, 555 (1970).

$$\underset{\mathbf{1}}{(R)\text{-}(+)\text{-}CH_3CH(Br)CO_2CH_3} + PhCdCl \xrightarrow[\text{ether}]{60\%} \underset{\mathbf{2}}{(\pm)\text{-}CH_3CH(Ph)CO_2CH_3} \quad (2)$$

methyl hydratropate (**2**) (eq 2). In the course of our investigation, we learned that Van Horn[3] had observed a similar behavior with "active" ethyl α-bromopropionate, which was converted to "racemic" ethyl α-(α-naphthyl)propionate with the α-naphthylcadmium reagent in ether–THF. Like Van Horn, we were able to show that racemization of the starting ester could not account for racemic displacement product; in addition, Van Horn carried out control experiments to demonstrate that optically active α-(α-napthyl)propionate was configurationally stable under the reaction conditions.

This racemization pathway for α-halo esters, in marked contrast to the behavior of phthalides, rules out certain mechanisms which otherwise would be attractive: an SN2 displacement, a concerted reaction involving either a four- or six-center transition state. While an SN1 reaction seemed unlikely, two mechanistic pathways warranted further experimental verification: substitution by way of a carbene (eq 3)



$$\underset{\mathbf{1}}{CH_3CH(Br)CO_2CH_3} + PhCdCl \longrightarrow PhH + CH_3\bar{C}(Br)CO_2CH_3,\ \overset{+}{C}dCl \xrightarrow{-Br^-} CH_3\ddot{C}CO_2CH_3 \xrightarrow{PhCdCl} CH_3\underset{Ph}{\bar{C}}CO_2CH_3,\ \overset{+}{C}dCl \xrightarrow{H^+} \underset{\mathbf{2}}{CH_3\underset{Ph}{C}HCO_2CH_3} \quad (3)$$

and a reaction involving free radicals. Evidence against the carbene mechanism is provided by the observation that none of the expected bicyclo[4.1.0] product was formed when the reaction was carried out in the presence of cyclohexene as a carbene trapping agent. This conclusion was based on the absence of any additional peaks (aside from that of cyclohexene) in the glpc, under conditions where all the components were cleanly separated, and the lack of typical cyclopropyl protons in the nmr spectrum of the reaction mixture.

Some preliminary esr experiments provided impressive evidence for the involvement of free radicals in the displacement reaction. When reactants—phenylcadmium reagent and bromopropionate ester—were placed in a reaction flask as usual, and an aliquot immediately transferred to an esr sample tube, a strong signal was observed. As the mixture was allowed to reflux, aliquots were removed every few minutes, their esr spectra being measured as quickly as possible. After 1 hr the esr signal was weak; in 24 hr it had disappeared. In parallel experiments it could be shown by glpc analysis that the amount of hydratropic ester, the displacement product, increased up to about 1 hr and then remained unchanged for periods as long as 24 hr. No such strong initial esr signal was produced by a 0.05 *M* reaction mixture to which 0.5 g of AlBN had been added; and, indeed, no hydratropic ester was formed, as shown by glpc. It should be stressed that the strong esr signal was lacking in ethereal solutions of phenylmagnesium bromide, phenylcadmium reagent, or bromopropionate alone. An aliquot from the reaction mixture of ethereal phenylcadmium reagent and acetyl chloride, under conditions leading to acetopheneone,[4] likewise gave rise to no esr signal.

It is an attractive possibility that the displacement with bromopropionate ester may involve an electron transfer, with the intermediacy of anion radicals, a pathway postulated by Kornblum[5] for the reaction of *p*-nitrocumyl chloride with sulfur, carbon, nitrogen, and oxygen nucleophiles. As outlined in eq 4–7,

$$\mathbf{1} \xrightarrow{e} \underset{\mathbf{3}}{[CH_3CH(Br)CO_2CH_3]\cdot^-} \longrightarrow \underset{\mathbf{4}}{[CH_3CHCO_2CH_3]\cdot} + Br^- \quad (4)$$

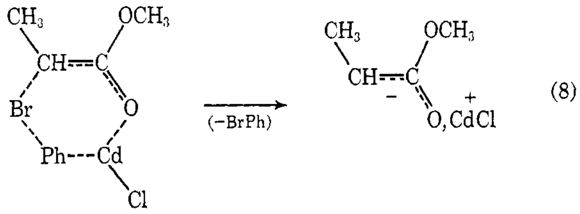
$$\mathbf{4} \xrightarrow{e} \underset{\mathbf{5}}{[CH_3CHCO_2CH_3]^-} \quad (5)$$

$$\mathbf{4} + PhCdCl \longrightarrow \underset{\mathbf{6}}{[CH_3CH(Ph)CO_2CH_3]\cdot^-} \quad (6)$$

$$\mathbf{6} + \mathbf{1} \longrightarrow \mathbf{2} + \mathbf{3} \quad (7)$$

the bromine-containing radical anion **3** may undergo bromide elimination with generation of the radical **4**, which, in turn, can be reduced through another electron transfer to the enolate **5** or be transformed to a new radical anion **6** by addition of "phenyl anion" from the cadmium reagent. The radical anion **6**, serving itself as an electron transfer agent, would react with bromopropionate, with formation of the final product **2** and regenerated **3**.

This series of steps accounts for the observation that the generation of the "dehalogenation" product, propionate ester, is not accompanied by formation of bromobenzene, as would be required by an alternate "enolization" scheme,[6] eq 8. Bromobenzene was consistently absent from the reaction mixtures. On the contrary, bromomalonate and phenylcadmium reagent exchange, very likely by the mechanism represented in eq 8, the products formed in equal amounts being malonate and bromobenzene.[2b] Cason and Fessenden[6] had proposed the dehalogenative enolization to account for the Claisen product during interaction of ethyl α-bromoisobutyrate with butylcadmium reagent.



(8)

Although we looked for Claisen products in reactions with phenylcadmium reagents, they were never detectable by glpc, ir, or nmr.

In experiments designed to define the scope of this displacement we found that ethyl esters of α-bromoacetic, -propionic, and -butyric acids afforded the expected products with the phenylcadmium reagent, whereas none was found with α-bromoisobutyrate and ethyl α-bromisovalerate. All esters underwent some

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(3) A. R. Van Horn, private communication, 1970.

(4) J. Cason, *Chem. Rev.*, **40**, 15 (1947).

(5) N. Kornblum, T. M. Davies, G. W. Earl, N. L. Holy, R. C. Kerber, M. T. Musser, and D. H. Snow, *J. Amer. Chem. Soc.*, **89**, 725 (1967).

(6) J. Cason and R. J. Fessenden, *J. Org. Chem.*, **22**, 1326 (1957).

degree of dehalogenative enolization (eq 4, 5) and the last two appeared to give coupling products, substituted succinate esters. Thus it seems that both hydrogen and halogen at the α carbon are necessary for the displacement to occur, although the steps outlined in eq 4–7 should be equally valid for α-halo esters which do not contain an α hydrogen. Reactions of ethyl- or isopropylcadmium reagents with ethyl α-bromoacetate or α-bromopropionate led to dehalogenated (enolization) ester, Claisen product, or polymeric material.

Replacement of halogen by the phenylcadmium reagent is by no means limited to esters, lactones, and ketones. We have found that allyl bromide, benzyl bromide, 3-bromocyclohexene, and chloromethyl methyl ether are all converted to their corresponding phenyl substitution products in yields of 39, 40, 81, and 34%, respectively. No attempt was made to optimize yields. Reactions proceeded readily, and glpc analysis indicated few or no side products. Unlike the reactions with esters, no strong esr signal was produced on admixture of 3-bromocyclohexene and phenylcadmium reagent, an observation which lends support for a concerted mechanism in this case. A variety of other halides failed to give any detectable amounts of displacement products: 1-bromobutane, ethylene bromide, bromoacetaldehyde diethyl acetal, *tert*-butyl chloride, trimethylsilyl chloride, chlorocyanomethane, and 1-chloro-1-nitroethane. Earlier investigators have observed the failure to effect displacement with alkylcadmium reagents at secondary,[6] tertiary,[7] and allylic[6] carbons. Our results seem to be the first instances of displacement of an allyl or benzylic halogen with a cadmium reagent, apparently by a nonradical process.

From among the displacements by organocadmium reagents with a wide variety of substrates, there must be postulated at least two distinct mechanistic pathways: a concerted, stereoselective process in the case of α′-halo lactones and a radical reaction accompanied by racemization with α-halo esters. On the basis of the preliminary esr results, the behavior of allylic halides appears to fit the former category as well, but the stereochemistry of their displacements has not yet been established.

Experimental Section

Instrumentation.—Infrared (ir) spectra were recorded as films with Perkin-Elmer Model 337 and Model 700 grating spectrophotometers. Nuclear magnetic resonance (nmr) spectra were obtained with a Varian A-60 spectrometer and recorded in parts per million downfield from tetramethylsilane used as an internal standard. Gas–liquid phase chromatography (glpc) was accomplished with a Varian Model 90-P gas chromatograph, with a recorder speed of 2.54 cm/min and helium flow rate of 50 ml/min. The columns were all 10 ft along and 0.25 in. in diameter. Peak areas were determined from the product of the height and the width at half height. Yields were calculated from glpc by the method of peak enrichment. Esr spectra were determined with a Varian Model E-4 X-band instrument. Rotations were obtained with a Zeiss polarimeter. Melting points are corrected.

Materials.—Grignard reagents were prepared under anhydrous conditions from reagent-grade magnesium turnings and the appropriate halide. The solutions were refrigerated in serum-capped bottles, and their normality was determined by titration with *sec*-butyl alcohol as titrant and 1,10-phenanthrolene as indicator.[8] Anhydrous cadmium chloride (reagent grade) was oven dried for at least 24 hr at 110°. The halo esters were obtained from Aldrich Chemical Co., Milwaukee, Wis., unless otherwise indicated.

Apparatus.—Reactions were carried out in a flame-dried, three-necked, round-bottomed flask, fitted with a mechanical stirrer, reflux condenser, and pressure-equalizing addition funnel. Grignard reagents were transferred to the flask from the serum-capped bottles with a 20-ml syringe. Nitrogen was not used as an inert atmsophere, except where noted.

Reaction of Phenylcadmium Reagent with Ethyl α-Bromopropionate.—The following is typical of displacements carried out with ethyl α-bromoacetate, -propionate, and -butyrate.

Phenylcadmium reagent (0.10 mol) in 100 ml of anhydrous ether was prepared from the Grignard reagent (22 ml, 0.10 mol) and 18.33 g (0.10 mol) of anhydrous cadmium chloride. After a negative Gilman test,[9] 6.5 ml (0.05 mol) of ethyl α-bromopropionate in 25 ml of anhydrous ether was added dropwise to the solution, and stirring at reflux was maintained for 3 hr. The mixture was then hydrolyzed with 10 ml of water, the ether layer was dried with $MgSO_4$, and the solvent was removed in a rotary evaporator. Some of the crude material was injected into a glpc column (10% Carbowax, 150°) and the peaks were collected directly onto salt plates, from which the infrared spectra were measured. The first peak (1.1 cm), too volatile to collect, was probably ether, inasmuch as an injection of pure ether emerged at this point on the chromatogram. The next peak appeared at 1.7 cm and the ir spectrum indicated it to be ethyl propionate (as shown by comparison with Sadtler[10] Spectrum No. 303) contaminated with benzene. That benzene and ethyl propionate were emerging from the column at the same place was confirmed by their identical retention times under the same column conditions in a separate experiment. The next peak at 5.5 cm was identified as ethyl α-bromopropionate by comparison with an ir spectrum of authentic material. Ethyl hydratropate at 26.4 cm was identified in a similar way. The final peak, appearing at about 56 cm on the chromatogram, was collected as a white solid, mp 68–70° [lit.[11] mp (biphenyl) 70°].

Reaction of Ethyl α-Bromoisobutyrate with Phenylcadmium Reagent.—The following description is typical of the results with ethyl α-bromoisobutyrate and -isovalerate. The crude mixture, obtained from reaction of 9.75 g (0.05 mol) of ethyl α-bromoisobutyrate and 0.10 mol of phenylcadmium reagent for 3 hr at ice-bath, room, or reflux temperature, was analyzed on an SAIB column at 170°. In addition to peaks at 5.7 (starting bromo ester and bromobenzene), 22.0 (phenol), and 46.0 cm (biphenyl, mp 69–70°), one at 30.0 cm was collected and analyzed: ν_{CO} 1730 cm^{-1}; bp (micro) 238–240° (760 mm) [lit.[12] bp (diethyl tetramethylsuccinate) 115–121° (15 mm); 238–240° (760 mm)].

Reaction of Phenylcadmium Reagent with (*R*)-(+)-Methyl α-Bromopropionate.—(*S*)-(−)-Methyl lactate, α^{26}_{578} −9.67° (neat, *l* 1 dm), obtained by esterification of (*S*)-(+)-lactic acid with diazomethane, was converted to (*R*)-(+)-methyl α-bromopionate α^{26}_{578} +66.21° (neat, *l* 1 dm), according to the method of Gerrand and Richmond.[13] To an ethereal solution of 0.04 mol of phenylcadmium reagent was added dropwise 3.34 g (0.02 mol) of the (+)-bromo ester, and then the mixture was allowed to reflux for 3 days. It was hydrolyzed with 10 ml of distilled water, and the pasty, gray-white precipitate was washed three times with 25-ml portions of anhydrous ether; the washings were combined with the original liquid layer. The solution was dried over $MgSO_4$ and the ether was removed on the rotary evaporator. The crude reaction mixture was then separated by vacuum distillation, the fraction, bp 55–60° (1 mm), being collected [lit.[14] bp 62–65° (0.5 mm)], α^{27}_{578} +0.06° (neat, *l* 0.2 dm). The ir spectrum of this product indicated that it was methyl hydratropate, but a chromatogram, (SAIB, 170°) showed that, besides the methyl hydratropate, a small amount of biphenyl was also present.

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(7) H. Gilman and J. F. Nelson, *Recl. Trav. Chim. Pays-Bas*, **55**, 518 (1936).

(8) S. C. Watson and J. F. Eastham, *J. Organometal. Chem.*, **9**, 165 (1967).

(9) H. Gilman and F. Schulze, *J. Amer. Chem. Soc.*, **47**, 2002 (1925).

(10) "The Sadtler Standard Spectra," Sadtler Research Laboratories, Philadelphia, Pa., 1965.

(11) R. C. Weast and S. M. Selby, Ed., "Handbook of Chemistry and Physics," 47th ed, The Chemical Rubber Company, Cleveland, Ohio, 1966.

(12) B. E. Hudson, Jr., and C. R. Hauser, *J. Amer. Chem. Soc.*, **63**, 3156 (1941).

(13) W. Gerrard and M. J. Richmond, *J. Chem. Soc.*, 853 (1945).

(14) S. M. McElvain and C. L. Stevens, *J. Amer. Chem. Soc.*, **69**, 2663 (1947).

The sample was further purified by preparative glpc (SAIB, 170°), α^{27}_{578} +0.02° (neat, *l* 0.1 dm). The amide of hydraptropic acid was prepared by saponification of methyl hydratropate and treatment of the intermediate acid chloride ($SOCl_2$) with concentrated ammonia, mp 91–92° (lit.[15] mp 91–92°).

Similar results were obtained when the reaction was repeated for a 3-hr reflux period with 0.05 mol of phenylcadmium reagent and 0.025 mol of bromo ester. Control experiments to determine the degree of racemization of bromo ester were carried out by measuring the optical rotation and glpc peak area before and after the addition of fresh (+)-bromo ester. It was concluded that recovered bromo ester had racemized to the extent of 9% (maximum) during the course of the reaction.

Reaction of Allyl Bromide with Phenylcadmium Reagent.—A solution of 6.05 g (0.05 mol) of allyl bromide in 10 ml of anhydrous ether was added dropwise with stirring to 0.1 mol of phenylcadmium solution diluted with 75 ml of dry ether. After spontaneous refluxing subsided (about 5 min), the mixture was heated to reflux for an additional 4 hr. It was hydrolyzed with 10 ml of water, whereupon the usual precipitate formed. The liquid was decantated from the solid, and the precipitate was washed twice with 25-ml portions of ether. The washings were combined with the decantate, dried with $MgSO_4$, and filtered, and the ether was removed. When a portion of the 2.60 ml of crude residue was injected onto a column (10% Carbowax, 130°), three major peaks besides ether were observed. The one at 2.4 cm had the same retention time as that of allyl bromide. One at 10.7 cm was isolated, and its ir spectrum was identical with that of 3-phenylpropene (Sadtler[10] Spectrum No. 13701). The ir spectrum of the large peak at 16.1 cm was identical with that of bromobenzene. The yield of 3-phenylpropene was 39%, as determined by peak enhancement.

Reaction of Benzyl Bromide with Phenylcadmium Reagent.—To 0.1 mol of phenylcadmium reagent in 75 ml of anhydrous ether, 8.55 g (0.05 mol) of benzyl bromide was added dropwise with stirring at room temperature. The mixture was maintained at reflux for 10 hr, and then hydrolyzed with 10 ml of water. A portion of the crude mixture isolated as above was injected onto the gc (Apiezon L, 150°); three peaks were observed at 1.8, 2.4, and 15.3 cm. The last exhibited an ir spectrum identical with that of diphenylmethane (Sadtler[10] Spectrum No. 3389). Its yield, as determined by the peak enhancement method, was 40%.

Reaction of Phenylcadmium Reagent with 3-Bromocyclohexene.—To 0.1 mol of phenylcadmium reagent in 75 ml of anhydrous ether, 8.05 g (0.05 mol) of 3-bromocyclohexene was added slowly with stirring. After reaction conditions and workup identical with those of allyl bromide, there was obtained 7.0 g (7.40 ml) of crude product. Glpc analysis (10% Carbowax, 150°) gave peaks for ether and starting halide and one at 23.4 cm. Its ir spectrum was that expected for 3-phenylcyclohexene: 3080, 3050 (ArH, C═CH), 1650 cm^{-1} (C═C). The yield (81%) of 3-phenylcyclohexene was established by the method of peak enhancement.

The above reaction of 3-bromocyclohexene with phenylcadmium reagent was repeated, and aliquots of the reaction mixture were removed at various time intervals, placed in a sample tube, and the esr spectrum taken. Aliquots were taken immediately after mixing of the reagents at room temperature, after 5 min of stirring at room temperature, after 0.5 hr of refluxing, and after 4 hr of refluxing. None of the spectra indicated the presence of radicals.

Reaction of Chloromethyl Methyl Ether with Phenylcadmium Reagent.—Reaction as above of a solution of 4.0 g (0.05 mol) of chloromethyl methyl ether in 10 ml of anhydrous ether and phenylcadmium reagent afforded 6.0 ml of crude product. On glpc (Apiezon L, 160°) it exhibited peaks for ether and benzene and one at 7.5 cm. The ir spectrum of the third peak was identical with that of commercial benzyl methyl ether (Sadtler[10] Spectrum No. 17013). The yield, determined by the peak enhancement method, was 34%. No starting material or other by-products were found.

Registry No.—Phenylcadmium reagent, 15924-35-3; ethyl α-bromopropionate, 535-11-5; ethyl α-bromoisobutyrate, 600-00-0; (*R*)-(+)-methyl α-bromopropionate, 20047-41-0; allyl bromide, 106-95-6; benzyl bromide, 100-39-0; 3-bromocyclohexene, 1521-51-3; chloromethyl methyl ether, 107-30-2.

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[15] H. Janssen, *Justus Liebigs Ann. Chem.*, **250**, 125 (1889).

Noble Metal Catalysis. II. Hydratocarbonylation Reaction of Olefins with Carbon Monoxide to Give Saturated Acids

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A process study of the hydratocarbonylation reaction of olefins with carbon monoxide to give saturated acids is described. The catalyst is probably a zero valent palladium–phosphine complex. Effects of changes in temperature, pressure, and concentrations of the three reactants and the complex catalyst system were studied. The rate of reaction depends approximately in a linear manner on the concentration of olefin and the pressure of carbon monoxide, while the rate reaches a maximum with a water concentration of 5–10%. The catalyst system undergoes a complex number of changes between the zero and plus two valence states, probably some involving the carbon moieties attached to the phosphine ligand.

The synthesis of saturated carboxylic acids from olefins, carbon monoxide, and water has been recently described,[1] according to eq 1 using a palladium–phosphine complex as catalyst.

$$RCH{=}CH_2 + CO + H_2O \xrightarrow{\text{cat.}} RCH_2CH_2CO_2H + CH_3CHRCO_2H \quad (1)$$

If alcohols are used in place of water, then esters are produced.[2] These palladium–phosphine catalyzed systems have advantages in rate and selectivity over the earlier palladium complexes without phosphines.[3] However, in those examples involving α olefins the branched-chain isomer was shown to be dominant.[2,4] The purpose of this paper is to describe methods for obtaining increased yields of the straight-chain acids starting from α olefins, since the straight-chain acids find greater utility as surface active agents.

Results

The following variables were studied: temperature and pressure, catalyst and solvent changes, proportions of olefin and water, and oxidation–reduction conditions.

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[1] N. von Kutepow, K. Bittler, and D. Neubauer, U. S. Patent 3,437,676 (1969), to Badische Anilin- and Soda-Fabrik.

[2] K. Bittler, N. von Kutepow, D. Neubauer, and H. Reis, *Angew. Chem., Int. Ed. Engl.*, **7**, 329 (1968).

[3] J. Tsuji, M. Morikawa, and J. Kiji, *Tetrahedron Lett.*, 1937 (1963).

[4] R. Huttel, *Synthesis*, **5**, 225 (1970).