chloronortricyclene (**13x**) (31%) and *exo,endo*-3-methoxy-5-chloronortricyclene (**13n**) (18%), respectively, by nmr comparison with authentic samples.[16] A third nonester product was assigned the structure *exo,endo*-3,5-dimethoxynortricyclene (**14**) (5%): nmr ($CDCl_3$) δ 3.97 (bs, 1), 3.52 (t, 1), 3.30 (s, 6), and 2.2–1.2 ppm (6); mass spectrum (70 eV) *m/e* 154 (M^+). The major ester product was indentified as *exo,exo*-3-methoxy-5-carbomethoxynortricyclene (**11**) (34%) by vpc and nmr comparison with an authentic sample.[7] The minor ester product was identified as methoxycarbomethoxynortricyclene (**12**) (10%): nmr ($CDCl_3$) δ 6.10 (dd, 1, J = 6.1 Hz, 3.8 Hz), 5.88 (dd, 1, J = 6.1 Hz, 3.0 Hz), 3.62 (s, 3) 3.25 (s, 3), 3.3–2.6 (4), 1.87 (drn, 1, J = 12.5 Hz), and 1.44 ppm (dd, 1, J = 12.5 Hz, 3.8 Hz); mass spectrum (70 eV) *m/e* 183 (M^+).

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Registry No.—**1**, 5274-83-9; **2**, 32737-75-0; **3**, 53494-63-6; **4**, 13640-66-9; **5**, 53418-54-5; **6**, 53418-37-4; **8**, 53418-55-6; **9**, 53494-62-5; **10**, 53494-64-7; **12**, 53418-38-5; **14**, 53418-56-7; dichloro(norbornadiene)palladium(II), 12317-46-3; silver acetate, 563-63-3.

References and Notes

(1) G. W. Parshall and J. J. Mrowca, *Advan. Organometal. Chem.*, **7**, 157 (1968).
(2) R. F. Heck, *J. Amer. Chem. Soc.*, **90**, 5518 (1968).
(3) R. F. Heck, *J. Amer. Chem. Soc.*, **91**, 6707 (1969).
(4) R. F. Heck, *J. Amer. Chem. Soc.*, **93**, 6896 (1971).
(5) R. F. Heck, *J. Amer. Chem. Soc.*, **94**, 2712 (1972).
(6) W. Kitching, *Organometal. Chem. Rev.*, **3**, 61 (1968).
(7) L. F. Hines and J. K. Stille, *J. Amer. Chem. Soc.*, **94**, 485 (1972).
(8) S. Wolfe and P. G. C. Campbell, *Can. J. Chem.*, **43**, 1184 (1965).
(9) E. Vedejs and M. F. Salomon, *J. Org. Chem.*, **37**, 2075 (1972).
(10) R. A. Alexander, N. C. Baenziger, C. Carpenter, and J. R. Doyle, *J. Amer. Chem. Soc.*, **82**, 535 (1960).
(11) D. R. Coulson, *J. Amer. Chem. Soc.*, **91**, 200 (1969).
(12) J. K. Stille and R. A. Morgan, *J. Amer. Chem. Soc.*, **88**, 5135 (1966).
(13) M. Green and R. I. Hancock, *J. Chem. Soc. A*, 2054 (1967).
(14) W. A. Whitla, H. M. Powell, and L. M. Venanzi, *Chem. Commun.*, 310 (1966).
(15) C. Panattoni, G. Bombieri, E. Forsellini, B. Crociani, and U. Belluco, *Chem. Commun.*, 187 (1969).
(16) P. K. Wong and J. K. Stille, *J. Organometal. Chem.*, **70**, 121 (1974).
(17) G. A. Gray and W. R. Jackson, *J. Amer. Chem. Soc.*, **91**, 6205 (1969).
(18) F. R. Jensen and B. Rickborn, "Electrophillic Substitution of Organomercurials," McGraw-Hill, New York, N.Y., 1968.
(19) G. M. Intille and M. J. Braithwaite, *J. Chem. Soc., Dalton Trans.*, 645 (1972).
(20) M. S. Silver, P. R. Shafer, J. E. Nordlander, C. Ruchardt, and J. D. Roberts, *J. Amer. Chem. Soc.*, **82**, 2646 (1960).
(21) F. J. McQuillin and K. G. Powell, *J. Chem. Soc., Dalton Trans.*, 2123 (1972).
(22) L. M. Jackman and S. Sternhell, "Applications of NMR Spectroscopy in Organic Chemistry," Pergamon Press, New York, N.Y., 1969, p 230.
(23) E. I. Snyder and B. Franzus, *J. Amer. Chem. Soc.*, **86**, 1166 (1964).
(24) P. Laszlo and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **86**, 1171 (1964).
(25) C. B. Anderson and B. J. Burresson, *J. Organometal Chem.*, **7**, 181 (1967).
(26) D. Drew and J. R. Doyle, *Inorg. Syn.*, **13**, 47 (1972).

A Stereochemical Study of the Mechanism of the Conversion of Phenyl(trichloromethyl)carbinol to α-Methoxyphenylacetic Acid[1]

Wilkins Reeve,* Robert J. Bianchi, and James R. McKee

Chemistry Department, University of Maryland, College Park, Maryland 20742

Received March 25, 1974

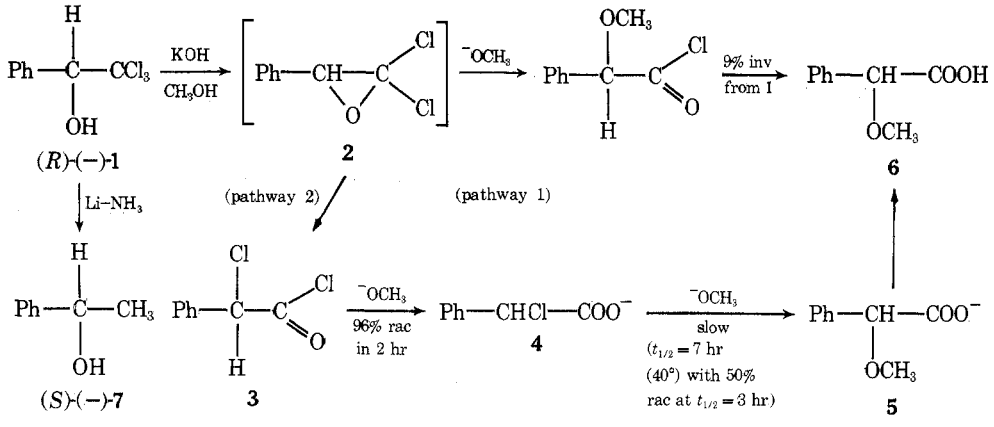
Two reaction pathways are considered for the reaction of phenyl(trichloromethyl)carbinol (**1**) with sodium methoxide to α-methoxyphenylacetic acid in methanol. Pathway 1 involves the conversion of the carbinol to a dichloro epoxide (**2**), followed by an SN2 attack of the methoxide nucleophile to give α-methoxyphenylacetic acid; this pathway involves one stereochemical inversion. The second pathway involves initial formation of the dichloro epoxide **2** followed by an intramolecular rearrangement to α-chlorophenylacetate anion and a subsequent attack of the methoxide nucleophile on this anion. This second pathway involves almost complete racemization during the 2-hr reaction period used; one step alone (**3** going to **4**) involves 96% racemization, and, in the next step, racemization of **4** occurs twice as fast as the conversion of **4** to **5**. The second pathway is proven to account for the formation of approximately 23% of the final product by the detection of the presence of 20% α-chlorophenylacetic acid in the crude α-methoxyphenylacetic acid and by measuring the kinetics of the reaction of the α-chloro acid with methoxide anion. The balance of the reaction proceeds by pathway 1 and this reaction pathway accounts for the stereochemistry experimentally observed. Nine per cent inversion of configuration occurs with the balance racemization. Control experiments show that the large amount of racemization is due to the ease with which α-methoxyphenylacetate anion racemizes in the methanolic potassium hydroxide reaction medium.

Phenyl(trichloromethyl)carbinol (**1**) reacts with a wide variety of nucleophiles at 50° in methanolic potassium hydroxide to form α-substituted phenylacetyl chlorides. These are not isolated but usually react with the basic solution to form α-substituted phenylacetate anions. Examples include reaction of the carbinol with methoxide to give α-methoxyphenylacetic acid[2] and with potassium amide in liquid ammonia to form α-aminophenylacetic acid.[3] With some nucleophiles ring closure occurs; thiourea forms 2-imino-5-phenyl-4-thiazolidinone,[4] and cyanamide forms alkyl 5-aryl-2-imino-4-oxo-1-imidazolidinecarboximidates.[5] All of these reactions occur in yields of 45–80% of the theoretical.

These reactions have been postulated to proceed through a dichloro epoxide (**2**) followed by an SN2 attack of the nucleophile on this epoxide. This seems inherently reasonable because it is necessary to rationalize somehow the facile substitution of the α-hydroxyl group of the starting carbinol by the new nucleophile, and it is well-known that hydroxyl groups themselves are very poor leaving groups in SN2 reactions. The hydroxyl group of phenyl(trichloromethyl)carbinol is even more inert than the hydroxyl group of a typical secondary alcohol; it does not react with Lucas reagent (concentrated hydrochloric acid containing zinc chloride), either under the usual room-temperature conditions or after standing at steam bath temperature for 90 min.

An alternative mechanism involves the dichloro epoxide intermediate first rearranging to the α-chlorophenylacetyl chloride, which then hydrolyzes and reacts with the nucleophile. Phenyl(trichloromethyl)carbinol is known to be slowly converted to α-chlorophenylacetic acid in 27% yield by 10% aqueous potassium hydroxide at 0°.[6] We have found the half-life for this reaction to be 16 hr at 0° under heterogeneous, aqueous reaction conditions. These experimental conditions are quite different from those employed

Scheme I



in carrying out the reactions with the other nucleophiles first discussed. Those reactions are carried out in alcohol solution at 50° (except the reaction using potassium amide in liquid ammonia) and are virtually complete in 2–3 hr. In contrast, the reaction of the carbinol 1 with hydroxide ion at 0° is slower, and if the reaction is carried out under homogeneous conditions in 80% ethanol–20% water at 0°, the half-life is nearly 600 hr (as measured by titration of aliquots of the base during the reaction).

We have determined the mechanisms by which phenyl(trichloromethyl)carbinol reacts with methoxide anion in methanol solution at 40°. This reaction was chosen for study because it is typical of the reactions of strong nucleophiles with (trichloromethyl)carbinols in alcoholic potassium hydroxide solutions at 50°. The 40° temperature and the shortened reaction time of 2 hr was chosen to minimize racemization reactions. The α-methoxyphenylacetic acid is formed in 75% yield when the reaction is carried out at 50° for 3–5 hr; the methoxy acid is easily isolated and purified; and the stereochemistry of the reaction can be studied and used to help elucidate the mechanism. The configurations are known of the optical isomers of the product, α-methoxyphenylacetic acid, and of the possible intermediate, α-chlorophenylacetic acid.

Pathway 1 (Scheme I) clearly involves one inversion of configuration at the α carbon whereas the second pathway should require two or three inversions depending on whether or not an α-lactone was involved in the replacement of chlorine by methoxide. The first inversion in pathway 2 would result from the opening of the epoxide ring by the attack of the migrating chlorine on the α carbon from the side opposite the departing epoxide oxygen. This step cannot be studied by itself in methanolic potassium hydroxide at 40°; however step **3**–**4** can be studied in methanolic potassium hydroxide at 40°, and 96% racemization occurs in a 2-hr period. This racemization is several times more rapid than the racemization of α-chlorophenylacetate anion itself under the same conditions and suggests the possibility of a ketene intermediate in going from **3** to **4** under basic reaction conditions.

Step **4**–**5** also can be studied by itself. This is a surprisingly slow reaction ($t_{1/2}$ = 7 hr) which follows first-order kinetics to at least 75% completion. This strongly indicates that the rate-controlling step must be α-lactone formation,[7] and in theory there must be two inversions in going from **4** to **5**. In reality, 96% of the material reacting by pathway 2 has been racemized by the time **4** has been formed, and **4** is racemized under the reaction conditions twice as fast as it reacts with methoxide (k_1 for racemization is 0.0038 min^{-1} and k_1 for **4** → **5** is 0.0017 min^{-1}, both at 40° in methanolic potassium hydroxide). Only 3% of the product **6**, isolated from the 2-hr reaction at 40°, is formed by pathway 2 (*vide infra*), and this combined with the successive partial racemizations listed above reduces to 1% the contribution pathway 2 makes to the final observed optical activity of **6**.

Pathway 2 is demonstrated to account for approximately 23% of the product by the detection of 20% of α-chlorophenylacetic acid in the crude α-methoxyphenylacetic acid when the reaction is carried out for 2 hr at 40°. A kinetic study of the displacement of chlorine by methoxide (**4** → **5**) at 40° shows the reaction to be sufficiently slow so that the formation of 23% of **4** would give rise to the observed 20% of **4** with 3% being converted to **5**. (However, at 50° for 15 hr, almost all of **4** is converted to **5**.)

Accordingly, under the above 40° reaction conditions, **1** must be converted into products (**4** + **6**) approximately 23% by pathway 2 with the balance going by pathway 1. As discussed above, most of that going by pathway 2 is trapped as **4**, and successive partial racemizations along this pathway cause the small amount of **6** formed to be almost completely racemized.

Experimentally, the final methoxy acid **6** is obtained with 9% inversion (91% racemization) and 99% of this optical activity must be assigned to pathway 1. The conversion of the carbinol **1** to **6** with inversion is consistent with pathway 1. The 91% racemization is attributed to the base-catalyzed racemization of intermediate methyl α-methoxyphenylacetate or α-methoxyphenylacetate anion. Control experiments with methyl (*R*)-(−)-α-methoxyphenylacetate confirm this.

Phenyl(trichloromethyl)carbinol was resolved by preparing phenyl(trichloromethyl)carbinyl hydrogen succinate and resolving this with quinine. The resolved quinine salt was converted back to the hydrogen succinate ester, and the optically active carbinol was obtained by acid-catalyzed hydrolysis of the succinate acid ester. The optically pure carbinol ($[\alpha]^{25}D$ +38°) was shown to have the *S* configuration by converting it in 9% yield to (*R*)-(+)-α-methylbenzyl alcohol (**7**) ($[\alpha]^{25}D$ +18.6°) of 37% optical purity by treatment with lithium and liquid ammonia.[8] The rotations[9] and configurations[10] of the α-methylbenzyl alcohols are well-known. Reduction of the levorotatory isomer of phenyl(trichloromethyl)carbinol, having an optical purity of 54%, gave (*S*)-**7** with an optical purity of 18% under the same reaction conditions. The crude **7** as isolated from the reduction consisted of 85% α-methylbenzyl alcohol, 11% β-phenethyl alcohol (*via* styrene oxide), and 4% acetophenone. The side reactions can cause no inversions of configuration and so the *S* configuration can be assigned with confidence to the dextrorotatory phenyl(trichloromethyl)carbinol. The large loss in optical purity during the reduction

is due to part of the carbinol being reduced to acetophenone. This occurs by an initial dehydrohalogenation of one of the chloro carbinols to a chloroacetophenone and the subsequent reduction of this to inactive α-methylbenzyl alcohol.

Experimental Section

Melting points and boiling points are corrected. The infrared spectra were recorded on a Beckman IR-8 infrared grating spectrophotometer and the nmr spectra on a Varian A-60A spectrometer. Chemical shift values are expressed as δ values (ppm) downfield from tetramethylsilane as internal standard. Rotations were measured on a Franz, Schmidt, and Haensch (Berlin S) polarimeter with a sodium lamp as a light source. Polarimeter tubes of 2-dm length were used; concentration terms are grams of solute per 100 ml of solution. Elemental microanalyses were performed by Dr. Franz J. Kasler and Mrs. Shelesa L. A. Brew.

Phenyl(trichloromethyl)carbinyl Hydrogen Succinate. Phenyl(trichloromethyl)carbinol[3] (226 g, 1.0 mol), 120 g (1.2 mol) of freshly distilled succinic anhydride, and 160 g (2.0 mol) of pyridine were heated on a steam bath for 24 hr and the hot solution was poured into 1 l. of benzene and allowed to cool. The benzene solution was washed with 3 *N* hydrochloric acid to remove the pyridine and then extracted with 5% sodium carbonate solution. The sodium carbonate extracts were concentrated on a "Roto-Vac" to remove the emulsified benzene and the clear solution was acidified with 6 *N* hydrochloric acid to yield 374 g of crude phenyl(trichloromethyl)carbinyl hydrogen succinate. After recrystallization from 2700 ml of cyclohexane, there was obtained 256 g of the pure material: mp 108–109°; ir (KBr) 3300–2600 (COOH), 1745 (C=O), 1708 (C=O), 1440, 1400, 1370, 1345, 1260, 1228, 1185, 1155, 1005, 930–900, 860, 790, 775, 740, 695, 670, 625, and 610 cm^{-1}; nmr (CH_2Cl_2) δ 11.2 (s, 1, COOH), 7.4 (m, 5, C_6H_5), 6.3 (s, 1, $CH(CCl_3)$), 2.7 (s, 4, $-CH_2CH_2-$).

Anal. Calcd for $C_{12}H_{11}O_4Cl_3$: C, 44.26; H, 3.41; Cl, 32.67. Found: C, 44.31; H, 3.50; Cl, 32.40.

Resolution of Phenyl(trichloromethyl)carbinyl Hydrogen Succinate. Phenyl(trichloromethyl)carbinyl hydrogen succinate (125 g, 0.38 mol), 125 g (0.30 mol) of quinine (N.F.), mp 162–166°, and 1300 ml of ethyl acetate were heated on a steam bath until nearly complete solution had taken place and then filtered to remove insoluble particles. After standing for 2 days at room temperature the crude phenyl(trichloromethyl)carbinyl hydrogen succinate quinine salt [122 g, mp 149–152°, $[\alpha]^{25}D$ −82° (*c* 1.06, EtOH)] was filtered and the last traces of ethyl acetate were pressed out with a rubber dam. The quinine salt was dissolved in 3.5 l. of ethyl acetate; after standing for 1 day at room temperature, 71 g of the crystalline quinine salt was obtained: mp 155–156°; $[\alpha]^{26}D$ −66° (*c* 1.01, EtOH). The 3.5 l. of the ethyl acetate mother liquor was placed in a cold room overnight and an additional 18 g of crude quinine salt ($[\alpha]^{26}D$ −72°) was obtained. Three further recrystallizations of a 5-g sample of the quinine salt with an $[\alpha]^{25}D$ of −66° from ethyl acetate gave products with rotations of −63.7, −64.0, and −63.7°, respectively.

The ethyl acetate mother liquor from the precipitation of the levorotatory quinine salt of phenyl(trichloromethyl)carbinyl hydrogen succinate was reduced in volume from 1300 to 400 ml, cooled to 0° overnight, filtered to remove a slight precipitate, and then evaporated to dryness on a steam bath. The residue, which contained the other diastereoisomer, was a dark brown, tacky material which could not be induced to crystallize but was satisfactory for the preparation of *l*-phenyl(trichloromethyl)carbinyl hydrogen succinate having an optical purity of 53%.

The phenyl(trichloromethyl)carbinyl hydrogen succinate quinine salt ($[\alpha]^{26}D$ −66°) was converted to (*S*)-(+)-phenyl(trichloromethyl)carbinyl hydrogen succinate by dissolving 79 g (0.12 mol) in 300 ml of hot ethanol and slowly adding this solution with stirring to 300 ml of 1 *N* hydrochloric acid and an equal amount of ice. A white solid formed which made stirring difficult. The solid was removed by decantation and dissolved in benzene. The aqueous solution was extracted twice with 500-ml portions of benzene and the combined benzene solutions were washed with water, dried ($MgSO_4$), and concentrated to a clear, glassy material (36 g, 90%). A small portion was recrystallized from cyclohexane to give **(*S*)-(+)-phenyl(trichloromethyl)carbinyl hydrogen succinate:** mp 66–68°; $[\alpha]^{25}D$ +62° (*c* 2.1, EtOH). The ir and nmr spectra were the same as for the racemic compound.

(*S*)-(+)-Phenyl(trichloromethyl)carbinol. To 36 g (0.11 mol) of (*S*)-(+)-phenyl(trichloromethyl)carbinyl hydrogen succinate dissolved in 120 ml of glacial acetic acid was added 100 ml of water and 16 ml of concentrated hydrochloric acid. The mixture was refluxed in an oil bath for 6 hr and cooled, an equal amount of water was added, and the resultant solution was extracted with two 500-ml portions of carbon tetrachloride. The combined carbon tetrachloride extracts were washed twice with sodium bicarbonate solution and twice with water, dried ($MgSO_4$), and concentrated to yield 17.1 g (69% yield from the acid ester, 15% from the racemic carbinol) of (*S*)-(+)-phenyl(trichloromethyl)carbinol: bp 149–151° (14 mm); $[\alpha]^{25}D$ +38° (*c* 5.0, EtOH). The ir and nmr spectra were the same as for the racemic compound.

In the same manner the impure quinine salt of the (*R*)-(−)-phenyl(trichloromethyl)carbinyl hydrogen succinate was converted to 20 g of (*R*)-(−)-phenyl(trichloromethyl)carbinol: $[\alpha]^{25}D$ −20.6° (*c* 10.1, EtOH); this rotation corresponds to an optical purity of 53%.

Reduction of (*S*)-(+)-Phenyl(trichloromethyl)carbinol to (*R*)-(+)-α-Methylbenzyl Alcohol. To a stirred solution of 5 g (0.022 mol) of (*S*)-(+)-phenyl(trichloromethyl)carbinol ($[\alpha]^{25}D$ +38°) in 1500 ml of liquid ammonia was added 1 g (0.14 g-atom) of lithium metal that had been cut into small pieces. After about 1.5 min the blue color appeared, and 24 g (0.3 mol) of ammonium nitrate dissolved in 200 ml of liquid ammonia was added to destroy any unreacted lithium metal and also to destroy the lithium amide formed during the reaction. The liquid ammonia was allowed to evaporate and to the dark residue was added 200 ml of 2 *N* hydrochloric acid. The acid solution was extracted with two 100-ml portions of ether; the combined extracts were washed with three portions of water, dried ($MgSO_4$), and distilled to give 0.25 g (9% yield) of (*R*)-(+)-α-methylbenzyl alcohol: bp 84–85° (8 mm); $[\alpha]^{25}D$ +18.6° (*c* 5.0, toluene). The literature value[11] for (*S*)-(−)-α-methylbenzyl alcohol is $[\alpha]^{27}D$ −50.6° (*c* 3, toluene). The nmr spectrum showed the product to consist of 85% α-methylbenzyl alcohol, 11% β-phenethyl alcohol (*via* styrene oxide), and 4% acetophenone.

Conversion of (*S*)-(+)-Phenyl(trichloromethyl)carbinol to (*R*)-(−)-α-Methoxyphenylacetic Acid. Over a 90-min period, 4.9 g (0.088 mol) of potassium hydroxide dissolved in 100 ml of methanol was added to a stirred solution of 5 g (0.022 mol) of (*S*)-(+)-phenyl(trichloromethyl)carbinol ($[\alpha]^{25}D$ +38°) in 35 ml of methanol. The temperature was maintained at 40–42°. After the addition was complete, the reaction mixture was stirred for an additional 30 min. The solution was then cooled, the precipitated potassium chloride filtered off, and the alkaline methanol solution diluted with an equal volume of water and extracted with three 100-ml portions of ether. The combined ether extracts were dried ($MgSO_4$), concentrated, and distilled to yield 2.63 g (53% recovery) of (*S*)-(+)-phenyl(trichloromethyl)carbinol having the same rotation as the starting material. The aqueous alkaline solution was acidified to pH 1 with dilute hydrochloric acid, extracted with three 100-ml portions of ether, and dried ($MgSO_4$); the ether was evaporated to give a residue of 0.6 g. This was dissolved in 20 ml of chloroform and extracted with three 10-ml portions of water to remove mandelic acid. The chloroform solution was dried ($MgSO_4$) and evaporated to give 0.51 g (13.5% yield, or 29% allowing for recovered carbinol) of α-methoxyphenylacetic acid. This was recrystallized (decolorizing carbon) from 15 ml of cyclohexane. There was obtained 0.21 g of (*R*)-(−)-α-methoxyphenylacetic acid: mp 67–68° [lit. 65–66° for *R*-(−),[12] 71–72° for *RS*[13]]; $[\alpha]^{25}D$ −13.1° (*c* 4.1, EtOH) [lit.[12] $[\alpha]^{20}D$ −150.7° (*c* 0.57, EtOH)]. The $[\alpha]^{25}D$ of −13.1° is equal to an optical purity of 8.7%. The nmr and ir spectra were identical with spectra of authentic α-methoxyphenylacetic acid.

In the same manner, 5 g of (*R*)-(−)-phenyl(trichloromethyl)carbinol ($[\alpha]^{25}D$ −20.6°) was converted to 0.22 g of (*S*)-(+)-α-methoxyphenylacetic acid, mp 64–65°, with an $[\alpha]^{25}D$ of +18° (*c* 4.0, 20% ethanol).

In another experiment 5 g of racemic phenyl(trichloromethyl)carbinol was allowed to react with methanolic potassium hydroxide as above, but the crude acid fraction (1.3 g) was studied by nmr to determine the amount of α-chlorophenylacetic acid present. The α-CH signals (CCl_4) for the α-chloro acid, mandelic acid, and the α-methoxy acid occur at δ 5.27, 5.13, and 4.65, respectively, and the observed area ratios are 20:12:68.

In another experiment, 5 g of racemic phenyl(trichloromethyl)carbinol was allowed to react with stronger methanolic potassium hydroxide (containing 6.6 g of base, 0.1 mol) as above except at 50°. The reaction mixture was stirred at this temperature for 3 hr after the addition of base was completed and was then allowed to stand overnight at 50°. Under these conditions all of intermediate

chloro acid was converted to the methoxy acid. The crude acid was obtained as an oil which set up to a crystalline solid, mp 53–58° (3.35 g, theory 3.65 g), and its nmr spectrum was that of the pure α-methoxy acid. The α-CH nmr signal was at δ 4.65, and the α-CH signals of the mandelic acid (δ 5.13) and of the α-chloro acid (δ 5.27) were too small to be measured.

Racemization of Methyl (*R*)-(−)-α-Methoxyphenylacetate. A methanolic solution of potassium hydroxide was prepared by dissolving 6.7 g (0.12 mol) of potassium hydroxide in 200 ml of methanol. To this stirred solution at 40° was added, dropwise over a period of 1.3 hr, 1 g (0.0055 mol) of methyl (*R*)-(−)-α-methoxyphenylacetate in 70 ml of methanol. The ester had an $[\alpha]^{25}D$ of −88.5° (*c* 2.5, acetone) and was prepared by methylating (*R*)-(−)-mandelic acid with methyl iodide and silver oxide.[14] The literature value for this ester is $[\alpha]^{24}D$ −89.1° (*c* 1.11, acetone).[15] The mixture was stirred an additional 30 min at 40° and was then cooled and diluted with an equal volume of water. The solution was saturated with potassium chloride and extracted with two 100-ml portions on ether to remove any unreacted ester. The aqueous solution was acidified with dilute hydrochloric acid to pH 1 and extracted with three 100-ml portions of ether; the combined ether extracts were dried ($MgSO_4$) and evaporated to give 0.81 g of residue (89% yield). This α-methoxyphenylacetic acid was dissolved in cyclohexane, treated with decolorizing carbon, and chilled overnight near 0°. There was obtained 0.34 g of α-methoxyphenylacetic acid: mp 65–66°; $[\alpha]^{25}D$ −25.6° (*c* 4.0, EtOH). This represented a 17% retention of optical activity.[12] The nmr and ir spectra were identical with spectra of the authentic α-methoxyphenylacetic acid.

(*R*)-(−)-α-Chlorophenylacetyl Chloride. The following new preparation of the chloro acid chloride is a modification of Coll's procedure[16] for preparing the chloro acid from mandelic acid. Thionyl chloride (44 g, 0.374 mol) was dissolved in 200 ml of carbon tetrachloride, the solution was cooled to 5°, and 27 g (0.374 mol) of dimethylformamide was added over a 10-min period so the temperature did not exceed 7°. After stirring for 30 min in an ice bath, 20 g (0.135 mol) of (*S*)-(+)-mandelic acid [$[\alpha]^{27}D$ +152.9° (*c* 19.7, EtOH); mp 126–133°] was added at such a rate that the temperature did not exceed 7°; the reaction mixture was stirred at 4–7° for 1 hr and then allowed to warm up to room temperature during the next 2 hr. The resultant solution was poured over 200 ml of ice and quickly shaken. The carbon tetrachloride layer was separated, washed a second time with 200 ml of ice water, dried ($MgSO_4$), concentrated, and distilled to give 17 g (77% of theory) of (*R*)-(−)-chlorophenylacetyl chloride: bp 85–88° (2 mm); $[\alpha]^{31}D$ −160° (*c* 20.4, CCl_4) [lit.[17] bp 120° (23 mm); lit.[17] $[\alpha]^{17}D$ +158° (*c* 6, CS_2) for dextrorotatory isomer].

The $[\alpha]^{31}D$ rotation of −160° corresponds to an optical purity of 65% as determined by adding a 5-g sample to 50 ml of cold water and allowing the solution to stand overnight at room temperature. The (*R*)-(−)-α-chlorophenylacetic acid obtained had an $[\alpha]^{30}D$ of −122.3° (*c* 14.3, EtOH) and a melting point of 58–60° [lit.[18] mp 60–61°; lit.[18] $[\alpha]^{12}D$ −191° (*c* 3.35, benzene)]. The chloro acid chloride gave the following spectral data: ir (neat) 3070, 3040, 2980, 1810, (C=O), 1780, 1500, 1460, 1180, 1045, 1005, 980, 840, 790, 760, and 700 cm^{-1}; nmr (CCl_4) δ 7.35 (s, 5, Ph), 5.56 (s, 1, α-CH).

Reaction of (*R*)-(−)-α-Chlorophenylacetyl Chloride with Methanolic Potassium Hydroxide. A 5-g (0.026-mol) sample of the chloro acid chloride ($[\alpha]^{31}D$ −159°, 65% optical purity) was added dropwise over a period of 90 min to methanolic potassium hydroxide prepared by dissolving 6 g (0.106 mol) of potassium hydroxide in 100 ml of methanol. The temperature was maintained at 40°. After the addition was completed, the reaction mixture was stirred for an additional 30 min. The solution was then cooled with ice, diluted with an equal volume of water, acidified to pH 1 with dilute hydrochloric acid, and extracted with three 100-ml portions of ether. The ether was dried ($MgSO_4$) and evaporated to give a residual oil (4.3 g) which solidified on standing to give crystals, mp 65–75°. This was shown to be 95% α-chlorophenylacetic acid and 5% α-methoxyphenylacetic acid by comparing the nmr signals ($DCCl_3$) at δ 5.35 (–CHCl–) and 4.71 (–C*H*OCH_3–). The $[\alpha]^{33}D$ of the mixture was −4.1° (*c* 14.4, EtOH) [lit.[18] −191° (*c* 3.35, benzene)] corresponding to over 96% racemization.

Anal. Calcd for $C_8H_7O_2Cl$: C, 56.3; H, 4.1; Cl, 20.8. Calcd for $C_8H_7O_2(OCH_3)$: C, 65.0; H, 6.03. Found: C, 56.39; H, 4.38; Cl, 19.98.

Racemization of (*S*)-(+)-α-Chlorophenylacetic Acid. The acid [1.1 g, $[\alpha]^{31}D$ +37.5° (20% optically pure)][19] was dissolved in 25 ml of methanol containing 1 g of potassium hydroxide and thermostated at 40° for 3 hr. The acid mixture was isolated as before by acidification and extraction with ether. The oily acid was dissolved in chloroform and washed with water to remove mandelic acid. There was obtained 1 g of recovered acid analyzing (nmr) for 84% α-chloro acid and 16% α-methoxy acid, $[\alpha]^{32}D$ +18.5°. This corresponds to 50% racemization at 40° in 3 hr, equal to a first-order *k* of 3.8×10^{-3} min^{-1}.

Kinetic Measurements with α-Chlorophenylacetic Acid. Ten 2-ml aliquots from a solution of 2.14 g of α-chlorophenylacetic acid and 1.85 g of potassium hydroxide in 50 ml of methanol, thermostated at 40°, were titrated with 0.1 *N* hydrochloric acid over a 13-hr period. The log of the fraction of unreacted chloro acid was plotted against time. A linear plot was obtained with $t_{1/2}$ equal to 7 hr and a first-order *k* of 1.7×10^{-3} min^{-1}. From this the calculated values for the extent of the reaction at various times are 12% in 75 min and 19% in 2 hr. Seventy-five minutes is the average time of reaction for α-chlorophenylacetic acid formed from the carbinol in the 2-hr reaction described above consisting of 90-min addition time followed by 30-min additional reaction time.

Methyl phenyl(trichloromethyl)carbinyl ether was prepared by allowing 30 g (0.13 mol) of racemic phenyl(trichloromethyl)carbinol to react with 60 g (0.42 mol) of methyl iodide in 100 ml of anhydrous ether and 36 g (0.16 mol) of silver oxide for 12 hr with stirring at room temperature. There was obtained 19 g (80% yield) of methyl phenyl(trichloromethyl)carbinyl ether: mp 54–55° [lit.[20] mp 58°]; nmr (CCl_4) δ 7.48 (m, 5, C_6H_5), 4.60 (s, 1, >CH–), and 3.38 (s, 3, $-OCH_3$).

Registry No.—(*S*)-(+)-**1**, 53432-38-5; (*S*)-(+)-**1** hydrogen succinate, 53432-41-0; (*S*)-(+)-**1** hydrogen succinate quinine salt, 53432-42-1; (*R*)-(−)-**1**, 53432-39-6; (*R*)-(−)-1 hydrogen succinate, 53432-43-2; (*R*)-(−)-1 hydrogen succinate quinine salt, 53432-44-3; (±)-**1**, 53495-27-5; (*R*)-(−)-**3**, 53432-40-9; (*R*)-(−)-**6**, 3966-32-3; (*S*)-(+)-**6**, 26164-26-1; (*R*)-(−)-**6** Me ester, 32174-46-2; (*R*)-(+)-**7**, 1517-69-7; succinic anhydride, 108-30-5; quinine, 130-95-0; (*R*)-(−)-mandelic acid, 611-71-2; (*S*)-(+)-mandelic acid, 17199-29-0; (*R*)-(−)-α-chlorophenylacetic acid, 43195-94-4; (*S*)-(+)-α-chlorophenylacetic acid, 29125-24-4; racemic α-chlorophenylacetic acid, 39266-56-3.

References and Notes

(1) Taken in part from the doctoral theses of R. J. Bianchi (1967) and J. R. McKee (1974).
(2) Consult W. Reeve and C. W. Woods, *J. Amer. Chem. Soc.*, **82**, 4026 (1960), for leading references.
(3) W. Reeve and L. W. Fine, *J. Org. Chem.*, **29**, 1148 (1964).
(4) W. Reeve and M. Nees, *J. Amer. Chem. Soc.*, **89**, 647 (1967).
(5) W. Reeve and E. Barron, *J. Org. Chem.*, **34**, 1005 (1969).
(6) Zh. Jocicz, *Zh. Russ. Fiz.-Khim. Obshchest.*, **29**, 97 (1897).
(7) E. S. Gould, "Mechanism and Structure in Organic Chemistry," H. Holt and Co., New York, N.Y., 1959, p 270.
(8) Before choosing the lithium–liquid ammonia procedure for reducing the trichloromethyl group to methyl, the usefulness of potassium, sodium, zinc, Raney nickel, and catalytic methods was studied in an effort to accomplish this conversion more efficiently. Catalytic hydrogenation over platinum oxide, 5% palladium on carbon, or 20% palladium on carbon failed. Reduction proceeded to the dichlorocarbinol stage and then stopped. A fourfold excess of Raney nickel was refluxed with a methanolic solution of phenyl(trichloromethyl)carbinol but only (dichloromethyl)phenylcarbinol could be detected. Zinc and acetic acid, or a zinc–copper couple in ethanol, gave (dichloromethyl)phenylcarbinol, β,β-dichlorostyrene, and β-chlorostyrene. Potassium and liquid ammonia gave primarily acetophenone. With sodium and liquid ammonia a mixture of α-methylbenzyl alcohol and acetophenone was formed. After dissolving sodium in liquid ammonia to give the characteristic blue solution and then adding phenyl(trichloromethyl)carbinol, only acetophenone was formed. The above results indicate that the reduction is occurring with the carbinol adsorbed on the surface of the alkali metal, and the slower disolving lithium metal gives better results because the adsorbed (trichloromethyl)carbinol is present on the metallic surface for a longer time. The reduction of the methyl ether of **1** using the above reagents was also studied, but without success.
(9) R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **99**, 71 (1914); E. Downer and J. Kenyon, *ibid.*, 1156 (1939).
(10) The configurational relationships were summarized by E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N.Y., 1962, p 99.
(11) W. E. Doering and T. C. Aschner, *J. Amer. Chem. Soc.*, **71**, 838 (1949).
(12) D. Neilson and D. Peters, *J. Chem. Soc.*, 1519 (1962).
(13) R. Meyer and H. Boner, *Justus Liebigs Ann. Chem.*, **220**, 44 (1883).
(14) K. Freudenberg, J. Todd, and R. Seidler, *Justus Liebigs Ann. Chem.*, **501**, 212 (1933).
(15) W. A. Bonner, *J. Amer. Chem. Soc.*, **73**, 3126 (1951).
(16) A. I. P. Coll, German Offen. 1,963,645 (July 9, 1970); *Chem. Abstr.*, **73**, 120615 (1970).
(17) P. Walden, *Ber. Deut. Chem. Ges.*, **28**, 1295 (1895).
(18) A. McKenzie and G. W. Clough, *J. Chem. Soc.*, **93**, 818 (1908).
(19) E. L. Eliel, M. T. Fisk, and T. Prosser, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 169.
(20) Sh. Mamedov, G. Ya. Lerner, and D. N. Khydyrov, *Zh. Obshch. Khim.*, **34**, 53 (1964); *Chem. Abstr.*, **60**, 13172 (1964).