same way. An analytical gas chromatogram of the resulting ester mixture showed relative peak areas of about 33 to 67. The mixture of diastereomeric esters was spearated from extraneous impurities by preparative glpc (SF-96 silicone column, 6 ft × 1/4 in. 190°, helium flow rate 100 ml/min, retention time 10 min, one peak) to give 0.37 g which was reduced with lithium aluminum hydride, hydrolyzed, and distilled to give 0.29 g of a carbinol mixture which was separated by glpc (SE-30 silicone column, 20 ft × 3/8 in. 200°, helium flow rate 75 ml/min) to give phenyltrifluoromethylcarbinol {retention time 16 min; 10 mg; $\alpha^{28}D$ −0.26 ± 0.02° (c 2.0, chloroform, l = 0.5); $[\alpha]^{28}D$ −25 ± 2° (c 2, chloroform)} and 2-methoxy-2-phenylethanol {retention time 36 min; 26 mg; $\alpha^{28}D$ −1.89 ± 0.01° (c 5.15, ethanol, l = 0.5); $[\alpha]^{28}D$ −73° (c 5.15, ethanol)}. The rotation of the volatile phenyltrifluoromethylcarbinol was determined on a very small amount of material, and the indicated racemization of 15 ± 6% may not be significant, but the latter compound is clearly racemized to the extent of approximately 35% as shown by the following experiment.

(−)-2-Methoxy-2-phenylethanol.—O-Methylmandelic acid {1.0 g; $[\alpha]^{25}D$ −144° (c 1.2, ethanol); 96% enantiomerically pure} was reduced with lithium aluminum hydride, and the (−)-2-methoxy-2-phenylethanol was isolated and purified as above to give a product with $\alpha^{27}D$ −134.78° (neat, l = 1); $\alpha^{29}D$ −8.17 ± 0.02° (c 6.425, ethanol, l = 1); $[\alpha]^{29}D$ −127.0 ± 0.4° (c 6.4, ethanol).

Partially Active (+)-Methyltrifluoromethylcarbinol.—Methyl trifluoromethyl ketone (7 g) was treated with 65 ml of a 0.93 *N* solution of the Grignard reagent from (+)-1-chloro-2-phenylbutane[5] [$\alpha^{27}D$ +5.68° (neat); 96% enantiomerically pure] in ether at 35°. The reaction mixture was processed in the usual way and distilled to give a 63% yield of (−)-methyltrifluoromethylcarbinol which upon purification by gas chromatography had $\alpha^{26}D$ −2.20° (neat, l = 0.5). A second experiment using twice these amounts gave material after purification of $\alpha^{24}D$ −2.03° (neat, l = 0.5).

Esters from (+)-, (−)-, and (±)-Methyltrifluoromethylcarbinol and (−)-O-Methylmandelic Acid.—The preparation and gas chromatography of these have been previously described.[2]

Registry No.—Phenyltrifluoromethylcarbinyl 3β-acetoxy-Δ5-etienate, 17628-68-1; (−)-IA, 10531-50-7; (+)-IA, 340-06-7; *t*-butyltrifluoromethylketimine, 17629-00-4; (+)-IB, 17628-71-6; (−)-2-methoxy-2-phenylethanol, 17628-72-7; (+)-IC, 17628-73-8.

Absolute Configuration of Substituted Trifluoromethylcarbinols[1,2]

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By application of Freudenberg's rule of rotational shifts as applied to a series of acetate, benzoate, and acid phthalate esters, the absolute *S* configuration was assigned to (+)-phenyltrifluoromethylcarbinol, (−)-methyltrifluoromethylcarbinol, and (−)-*t*-butyltrifluoromethylcarbinol. However, these correlations were not ideal, and thus the absolute configurations of the phenyl and methyl compounds were verified by synthesis of their O-methyl and O-ethyl ethers by the action of sulfur tetrafluoride on (*S*)-O-methylmandelic acid and (*S*)-O-ethyllactic acid, respectively. This process is one which does not affect the chiral center of known configuration. The absolute configurations of these trifluoromethyl compounds and their several derivatives are now established with certainty.

In order to gain additional information concerning the relative importance of steric *vs.* electronic effects in the Grignard asymmetric reduction reaction[4-8] we have been studying the asymmetric reduction of several substituted trifluoromethyl ketones. The previous paper in this series[9] describes the resolution of three such compounds: phenyltrifluoromethylcarbinol, methyltrifluoromethylcarbinol, and *t*-butyltrifluoromethylcarbinol. The present paper describes studies which establish the absolute configuration of these compounds.

We initially investigated[5] the application of Freudenberg's rule of rotational shifts[10] to a series of derivatives of these carbinols and compared the results with those from the corresponding nonfluorinated carbinols of known configuration. The results for the phenylalkylcarbinols are summarized in Table I, for the methylalkylcarbinols in Table II, and for the *t*-butylalkylcarbinols in Table III.[11]

The derivatives of (+)-phenyltrifluoromethylcarbinol exhibit rotational shifts comparable with those for the corresponding (+)-phenylalkylcarbinols if one excludes the acid phthalate of phenylmethylcarbinol from consideration.[12,13]

It is *not* possible to make a logical arrangement of the data based upon the opposite assumption that (−)-phenyltrifluoromethylcarbinol is related to the other (+)-phenylalkylcarbinols. Therefore, it seems reasonably certain, based upon these data, that (+)-phenyltrifluoromethylcarbinol is configurationally related to the (+)-phenylalkylcarbinols as represented

(1) Presented in part before the Division of Organic Chemistry at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967.

(2) We acknowledge with gratitude support for these studies from the National Science Foundation (GP 6738) and the National Institutes of Health (GM 05248).

(3) (a) Taken in part from the Ph.D. Theses of H. M. Peters, Stanford University, Oct 1966, and D. M. Feigl, Stanford University, Oct 1965. (b) Parke, Davis & Co Fellow, 1965–1966.

(4) H. S. Mosher, J. E. Stevenot, and D. O. Kimble, *J. Amer. Chem. Soc.*, **78**, 4374 (1956).

(5) D. M. Feigl, Ph.D. Thesis, Stanford University, Oct 1965.

(6) D. L. Dull, Ph.D. Thesis, Stanford University, June 1967.

(7) B. J. G. McFarland, Ph.D. Thesis, Stanford University, Nov 1965.

(8) J. S. Birtwistle, K. Lee, J. D. Morrison, W. A. Sanderson, and H. S. Mosher, *J. Org. Chem.*, **29**, 37 (1964), and references therein.

(9) D. M. Feigl and H. S. Mosher, *ibid.*, **33**, 4242 (1968).

(10) K. Freudenberg, "Stereochemie," Franz Deuticke, Leipzig, 1933, p 677.

(11) These data are presented in modified form. Derivatives actually may have been prepared from either enantiomer, but the results reported in Tables I–III have been adjusted as if compounds of only one of the two enantiomers had been used. Enantiomerically impure samples were often used in the preparation of derivatives. However, great care was taken to prevent the concentration of either enantiomer during the synthesis or purification of these derivatives, and the rotations presented in Tables I–III have been adjusted to those for enantiomerically pure derivatives using the known purity of the starting carbinols.

(12) The rotation of the acid phthalate of phenylmethylcarbinol does not fit well into this series as has been observed earlier. At one time this anomaly rendered the assignment of relative configurations of the phenylalkylcarbinols uncertain. However, (+)-phenylmethylcarbinol and (+)-phenylethylcarbinol have been interrelated by direct chemical means[13] and it is now certain that they have the same relative configuration.

(13) R. MacLeod, F. J. Welch, E. M. La Combe, and H. S. Mosher, *J. Amer. Chem. Soc.*, **82**, 876 (1960).

TABLE I
MAXIMUM MOLECULAR ROTATIONS
OF HO–C(R)(Ph)–H AND DERIVATIVES[a]

	[M]D,[a] deg				
		Carbinol		Acid	
R	Benzoate (neat)	(neat)	(in benzene)	phthalate (in $CHCl_3$)	Acetate (neat)
Methyl		+53		−45	+194
Ethyl	−41[b,c]	+39		+100	+186
n-Propyl		+44	+65	+130	+200
Isopropyl	−98[b,c]	+37		+133	
Cyclohexyl	−95[d]		+54	+178	+165
n-Butyl		+28	+52	+200	+163
Isobutyl		+40	+54	+110	
t-Butyl	−240[b,e]		+45	+86	
Trifluoromethyl	−235	+56	+26	+69	+209

[a] Except for the trifluoromethyl compounds, all rotations were taken from R. MacLeod, F. J. Welch, and H. S. Mosher, *J. Amer. Chem. Soc.*, **82**, 876 (1960), unless otherwise noted. See ref 11 in text. [b] Compound prepared for the present study.[5] [c] Value given is for MD, not [M]D. Specific rotation could not be calculated because density was not available. [d] From M. P. Balfe, G. H. Beaven, and J. Kenyon, *J. Chem. Soc.*, 1857 (1950). [e] Rotation taken in benzene.

TABLE II
MAXIMUM MOLECULAR ROTATIONS
OF H–C(CH3)(R)–OH AND DERIVATIVES[a]

	[M]D,[a] deg			
R	Carbinol (neat)	Acetate (neat)	Benzoate (neat)	Acid phthalate (in $CHCl_3$)
Trifluoromethyl	−6.3	+29	+0.3[b]	+52
Ethyl	+10.3[c]	+30[d]	+70[e]	+88[c,f]
Isopropyl	+4.3	+25	+80	+89
n-Propyl	+12.1	+22		+95
n-Butyl	+12.0	+17		+117
t-Butyl	+7.8	+26	+93	+160

[a] Except for the trifluoromethyl compounds, all rotations are from P. G. Stevens, *J. Amer. Chem. Soc.*, **55**, 4237 (1933), unless otherwise noted. See ref 11 in text. [b] Value given is MD, not [M]D. Specific rotation could not be calculated because density was not available. [c] C. E. Wood, J. E. Such, and F. Scarf, *J. Chem. Soc.*, 1935 (1926). [d] R. H. Pickard and J. Kenyon, *ibid.*, **105**, 830 (1914). [e] J. Kenyon and R. H. Pickard, *ibid.*, **107**, 115 (1915). [f] Rotation taken in ethanol.

TABLE III
MAXIMUM MOLECULAR ROTATIONS
OF H–C(R)(*t*-C4H9)–OH AND DERIVATIVES[a]

	[M]D,[a] deg			
R	Carbinol (neat)	Acetate (neat)	Benzoate (neat)	Acid phthalate (in $CHCl_3$)
Trifluoromethyl	+8.7	−50[b]	+64[b]	+148
Methyl	+7.8	+26	+93	+160
Isopropyl	−14	+3.7	−0.5	0.0
Ethyl	−39	−44	−18	+3.3
n-Propyl	−55	−59	−20	+8.4
n-Butyl	−60	−51	−40	−13
Isobutyl	−78	−66	−43	−24

[a] Except for the trifluoromethyl compounds, all rotations were taken from W. M. Foley, F. J. Welch, E. M. La Combe, and H. S. Mosher, *J. Amer. Chem. Soc.*, **81**, 2779 (1959). See ref 11 in text. [b] Value given is for MD, not [M]D. Specific rotation could not be calculated because density was not available.

in Table I. Since the absolute configuration of (+)-phenylmethylcarbinol (I) has been established unequivocally as *R*, (+)-phenyltrifluoromethylcarbinol (II) must have the absolute *S* configuration.

R-(+) I *S*-(+) II

That (*S*)-phenyltrifluoromethylcarbinol (II) is configurationally related to (*R*)-phenylmethylcarbinol (I) results from the inversion in order of precedence assigned to the trifluoromethyl group and phenyl group compared with the other alkyl groups and phenyl according to the configurational nomenclature scheme of Cahn, Ingold, and Prelog.[14]

All the derivatives of both (−)-methyltrifluoromethylcarbinol and (+)-alkylmethylcarbinols have a positive rotational shift in progressing from the carbinols to the acetates, benzoates, and acid phthalates as represented in Table II. Except for the benzoate, the magnitudes of the shifts for the trifluoromethyl compounds are comparable with those of the nonfluorinated derivatives. Although the benzoate rotation was close to zero, there is no reason to believe that preparation of the benzoate was accompanied by any racemization since the preparations of the other benzoates, including those of the other trifluoromethyl compounds, was not accompanied by racemization. Despite this one nonideal fit to the Freudenberg series, it is not logically possible to fit the (+) enantiomer of methyltrifluoromethylcarbinol and its derivatives to this series, and thus the evidence strongly supports the conclusion that (−)-methyltrifluoromethylcarbinol is configurationally related to the other (+)-methylalkylcarbinols of Table II.

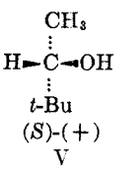
Since the absolute configuration of (+)-methylethylcarbinol (III), (+)-2-butanol, has been established as *S* with certainty,[15] (−)-methyltrifluoromethylcarbinol (IV) must have the absolute *S* configuration also.

(*S*)-(+) III (*S*)-(−) IV

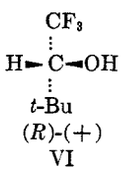
The optical rotations of the esters of (+)-*t*-butyltrifluoromethylcarbinol are compared with those of other *t*-butylalkylcarbinols in Table III. There is excellent correlation of increasing rotational shifts for these derivatives in going from the acetates to the benzoates to the acid phthalates with the exception of the isopropyl example which has already been discussed.[16] The correlations in going from the rotations of the neat carbinols to those of the acetate, however, are erratic. The rotational shift is slightly negative for the ethyl, *n*-propyl, and isobutyl compounds; slightly positive for the methyl, isopropyl, and *n*-butyl compounds; but strongly negative for the trifluoromethyl case. Never-

(14) R. S. Cahn, C. K. Ingold, and V. Prelog, *Angew. Chem. Intern. Ed. Engl.*, **5**, 385 (1966).
(15) K. Wiberg, *J. Amer. Chem. Soc.*, **74**, 3891 (1952).
(16) W. M. Foley, F. J. Welch, E. M. La Combe, and H. S. Mosher, *ibid.*, **81**, 2779 (1959).

theless it is not possible to fit the enantiomeric (−)-*t*-butyltrifluoromethylcarbinol and its derivatives logically into this series, and we are compelled to conclude that (+)-*t*-butyltrifluoromethylcarbinol is configurationally related to (+)-*t*-butylmethylcarbinol and the other (−)-*t*-butylalkylcarbinols of Table III. It is reasonably certain that the absolute configuration of (+)-*t*-butylmethylcarbinol is *S*[16,17] as represented by V and therefore the absolute configurations of the trifluoromethyl derivatives is *R* as represented in VI.



(*S*)-(+)
V



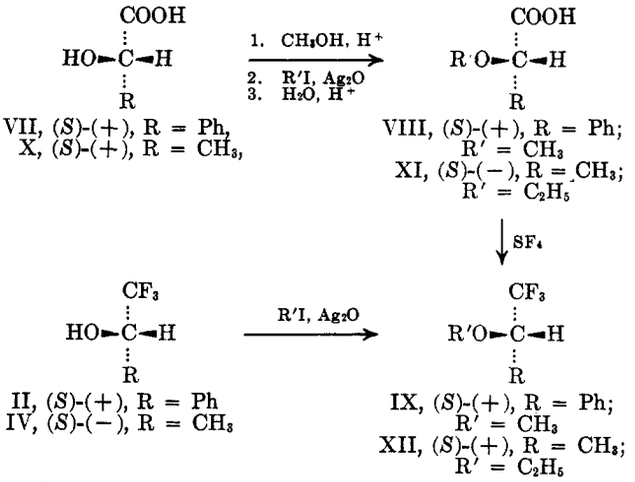
(*R*)-(+)
VI

The configurational designations for V and VI are *S* and *R*, respectively, in spite of the fact that they are configurationally related. This is a result of the fact that in the Cahn–Ingold–Prelog rotational scheme *t*-butyl take precedence over methyl, but trifluoromethyl takes precedence over *t*-butyl.

Although the results from the studies of rotational shifts appeared to establish the absolute configuration of these three trifluoromethyl-substituted carbinols with reasonable certainty, several small points such as the anomalously low rotation of methyltrifluoromethyl benzoate and *t*-butyltrifluoromethyl acetate were not completely satisfactory. Of primary concern was the fundamental assumption that a trifluoromethyl group would act normally as another alkyl group comparable with methyl or ethyl in a Freudenberg series. Since this was the first such study involving the application of Freudenberg's generalization to a series including the trifluoromethyl group, we felt that it should be subjected to further verification. Furthermore some of our asymmetric reduction results[7] were difficult to rationalize with the absolute configuration found. We therefore undertook a direct chemical correlation which would be unequivocal.

The method chosen is outlined in Scheme I. The key reaction is the conversion of a carboxyl group into a trifluoromethyl group by the use of sulfur tetrafluoride.[18,19] This method under mild conditions does not cause racemization. Martin and Kagan[20] prepared a trifluoromethyl steroid without epimerization from the corresponding acid using sulfur tetrafluoride and hydrogen fluoride at room temperature. Raasch[21] treated both L-leucine and L-glutamic acid with sulfur tetrafluoride and recovered optically active trifluoromethyl-substituted amines, although in very low yields. Cram and Wingrove[22] treated (−)-methyl-3-phenylpropanoic acid and (+)-2-phenylbutanoic acid with sulfur tetrafluoride at 35–40° and recovered the corresponding optically active trifluoromethyl products in

SCHEME I[a]



[a] In actual practice the (*R*)-(+) enantiomer of IV was employed, and it gave the (*R*)-(−) enantiomer of XII. However, it is represented here as shown for the sake of clarity. The Experimental Section describes the actual isomer employed.

moderate yields. Furthermore it was determined that deuterium was not lost during the reaction from the α-deuterio derivative of 2-phenylbutanoic acid, confirming that racemization did not occur by this pathway. Finally it has been found by Della[23] that sulfur tetrafluoride at 70° converted *cis*- and *trans*-4-methyl- or 4-*t*-butyl-cyclohexanecarboxylic acids into the corresponding 1-trifluoromethyl-4-alkylcyclohexane without isomerization, although at 130° isomerization did occur.

Thus there is ample precedence for the use of this reaction for correlations of configurations as shown in Scheme I starting with mandelic acid (VII) or lactic acid (X). Because the alcoholic hydroxyl group is converted into the fluoro group by this reagent, it was necessary to protect it by conversion into the methyl or ethyl ether.

The preparation of (*S*)-(+)-O-methylmandelic acid (VIII) has been reported.[24] Upon treatment with sulfur tetrafluoride at 30° for 2 days a 10% yield of the desired trifluoromethyl derivative IX, $[\alpha]^{26}D$ +91.5° (neat), was obtained.[25] (+)-Phenyltrifluoromethylcarbinol (II), available from an asymmetric Grignard reduction,[4,5] was converted into the same dextrorotatory methyl ether (IX), without change in sign of rotation, upon treatment with methyl iodide in the presence of silver oxide. Thus, (+)-phenyltrifluoromethylcarbinol must have the same relative configuration as (+)-mandelic acid with a CF_3 group replacing the COOH group. Since the absolute configuration of (+)-mandelic acid is known with certainty to be *S*,[26] that for (+)-phenyltrifluoromethylcarbinol (II) must also be *S*.

When corrections are made for the known purity of the two starting materials VII and II, the rotation of the resultant ether, IX, obtained by the two different

(17) In spite of the doubt raised by H. C. Brown and D. B. Bigley, *J. Amer. Chem. Soc.*, **83**, 3166 (1961), concerning the absolute configurational assignment for *t*-butylmethylcarbinol this correlation appears well founded[16] although not absolute.

(18) W. R. Hasek, W. C. Smith, and V. A. Engelhardt, *ibid.*, **82**, 543 (1960).

(19) We wish to thank Dr. W. C. Smith, Marshall Laboratory, E. I. du Pont de Nemours and Co., and Dr. E. R. Larsen, Halogens Research Laboratory, The Dow Chemical Co., for helpful discussions concerning this reaction.

(20) D. J. Martin and F. Kagan, *J. Org. Chem.*, **27**, 1406 (1962).

(21) M. Raasch, *ibid.*, **27**, 1406 (1962).

(22) D. J. Cram and A. S. Wingrove, *J. Amer. Chem. Soc.*, **86**, 5490 (1964).

(23) E. W. Della, *Tetrahedron Lett.*, 3347 (1966).

(24) W. A. Bonner, *J. Amer. Chem. Soc.*, **73**, 3126 (1951).

(25) There was also collected a 10% yield of α,α-difluorotoluene and a 50% yield of benzaldehyde. These by-products can be readily rationalized by assuming that the initially formed acid fluoride undergoes internal decomposition to give carbon monoxide, methyl fluoride, and benzaldehyde. Benzaldehyde is known to be converted into α,α′-difluorotoluene upon treatment with sulfur tetrafluoride.[18]

(26) K. Mislow, *ibid.*, **73**, 3954 (1951).

methods, was approximately the same, namely $[\alpha]^{26}D$ +91.5° (neat) from (*S*)-O-methylmandelic acid and $[\alpha]^{26}D$ +95.4° (neat) from phenyltrifluoromethylcarbinol. Since no racemization would be expected in proceeding from II to IX it is reasonable to conclude that the sulfur tetrafluoride reaction proceeded with a maximum of 4% racemization. (*S*)-(−)-O-Ethyllactic acid[27] (XI) was converted into the corresponding dextrorotatory ether XII in 6% yield upon treatment with sulfur tetrafluoride for 4 days at 30°.[28] Levorotatory methyltrifluoromethylcarbinol IV[19] was converted with change in sign of rotation into the dextrorotatory ether XII by treatment with sodium and ethyl bromide.[29] It is, therefore, demonstrated that (−)-methyltrifluoromethylcarbinol (IV) has the same relative configuration as (+)-lactic acid (X) with a CF_3 group replacing the COOH group. Since the absolute configuration of (+)-lactic acid is known to be *S*, that of (−)-methyltrifluoromethylcarbinol must also be *S*.

When corrections are made for the enantiomeric purity of the starting materials, the specific rotations of the ethyl methyltrifluoromethylcarbinyl ether (XII) produced from lactic acid was $[\alpha]^{25}D$ +0.90° (neat), while that obtained from the methyltrifluoromethylcarbinol by the method of Henne and coworkers[29] was $[\alpha]^{25}D$ +0.68° (neat).[19] The preparation of ether XII from carbinol IV did not go to completion and unreacted carbinol which showed 19% racemization was recovered. If one assumes that all of the carbinol which was converted into the ether was racemized to this same extent, then the fully corrected rotation for XII made by this route would be $[\alpha]^{25}D$ +0.83 ± 0.05° (neat) which is just within experimental error of the $[\alpha]^{25}D$ +0.90 ± 0.02° (neat) value found for the derivative made from mandelic acid.

These direct chemical interconversions have established unequivocally the absolute configuration of methyltrifluoromethylcarbinol and phenyltrifluoromethylcarbinol. The configurational assignments in these two cases were the same as those arrived at by application of Freudenberg's rule of rotational shifts. The success of the Freudenberg rule in these two cases increases the confidence with which it can be applied to other cases involving the trifluoromethyl group. Specifically we can conclude that the configurational assignment for *t*-butyltrifluoromethylcarbinol (VI) based upon the Freudenberg correlation is secure.

Experimental Section

Melting points were determined in capillary tubes and are uncorrected. The analyses were performed by Messrs. E. Meir and J. Consul of the Stanford University Microanalytical Laboratory. The ir spectra were taken on a Perkin-Elmer 237B grating spectrophotometer. The nmr spectra were obtained on a Varian Associates A-60 spectrometer in deuteriochloroform solvent under the direction of Dr. L. J. Durham. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane as zero. The optical rotations were determined on a Carl–Zeiss half-shadow polarimeter. Solution rotations were always taken in a center-filled polarimeter tube with zero correction for the empty tube with end plates in place. Neat rotations with limited samples were taken of necessity in non-center-filled, micropolarimeter tubes.

Acetate, Benzoate, and Acid Phthalate Derivatives for Evaluation of Rotational Shifts.—These derivatives were prepared and purified by the usual procedures. A single example is described in detail for the synthesis of phenyltrifluoromethylcarbinyl acetate. Essentially this same procedure was employed for all the other derivatives by the substitution of benzoyl chloride or phthalic anhydride for the acetyl chloride and the appropriate carbinol for the phenyltrifluoromethylcarbinol. These esters were usually prepared from enantiomerically impure carbinols obtained from asymmetric Grignard reductions[4,5] or incompletely resolved fractions from the resolution studies.[9] Care was taken to ensure that one enantiomer of the derivative was not concentrated by selective crystallization during the preparation and purification procedures. Each derivative was therefore presumed to have the same enantiomeric purity as the alcohol from which it was prepared. The rotation of the enantiomerically pure carbinol was calculated by dividing the observed rotation of the derivative by the per cent enantiomeric purity of the starting carbinol and multiplying by 100.

Phenyltrifluoromethylcarbinyl Acetate.—A mixture of phenyl trifluoromethylcarbinol [3.0 g (17 mmol); $\alpha^{24}D$ +8.96° (neat, l = 1); $[\alpha]^{24}D$ +6.95° (neat); enantiomeric purity[9] 21.8%], acetyl chloride (1.5 g, 19 mmol, distilled prior to use), anhydrous pyridine (2 ml), and dry ether (15 ml) was heated under gentle reflux for 2 hr. Water (20 ml) was added to the reaction mixture, and the ether layer was separated and washed successively with dilute hydrochloric acid, sodium bicarbonate solution, and water, and finally dried ($MgSO_4$). After the ether was removed on a rotary evaporator, the residue (3.4 g, 92% crude yield) was distilled, and a portion of the fraction, bp 40–44° (0.7 mm), was preparatively chromatographed (6 ft × 1/2 in. WS-30 column at 200° and 60-ml/min He flow), and the purity of this final sample was confirmed by analytical vapor phase chromotography (vpc): $\alpha^{26}D$ +25.83° (neat, l = 1); corrected for enantiomeric purity of starting material, $[\alpha]^{26}D$ +96.0°; $[M]^{26}D$ +209° (neat); $n^{23}D$ 1.4424; d_4^{23} 1.230.

Anal. Calcd for $C_{10}H_9F_3O_2$: C, 55.05; H, 4.13. Found: C, 55.26; H, 4.22.

Phenyltrifluoromethylcarbinyl Benzoate.—By the above procedure the same sample of carbinol gave the benzoate in 94% crude yield: bp 110–114° (0.7 mm); $\alpha^{24}D$ −23.01° (neat); corrected for enantiomeric purity of starting material, $[\alpha]^{24}D$ −84°; $[M]^{24}D$ −235° (neat); $n^{25}D$ 1.5120; d^{24} 1.261.

Anal. Calcd for $C_{15}H_{11}F_3O_2$: C, 64.29; H, 3.93. Found: C, 64.50; H, 4.01.

Phenyltrifluoromethylcarbinyl Hydrogen Phthalate.—The classical procedure was employed[30] but without crystallization of the product. Using the same sample of carbinol as above, a 75% yield of white solid was obtained upon evaporation of the chloroform solution to dryness: mp 130–134°; $[\alpha]^{27}D$ +4.6° (*c* 8.1, $CHCl_3$); corrected to 100% enantiomeric purity, $[\alpha]^{27}D$ +21°; $[M]^{27}D$ +69° (*c* 8.1, $CHCl_3$). The ir spectrum of this material matched that of an analytical sample of inactive phenyltrifluoromethylcarbinyl hydrogen phthalate, mp 134–135°, prepared by Stevenot.[4]

***t*-Butyltrifluoromethylcarbinyl Acetate.**—*t*-Butyltrifluoromethylcarbinol [2.0 g, $\alpha^{28}D$ −3.74° (neat, l = 1), enantiomeric purity 60.3%] was converted into the acetate in the usual way but in low yield: $\alpha^{28}D$ +7.53° (neat, l = 0.5); corrected to 100% enantiomeric purity, $\alpha^{28}D$ +25°; $M^{28}D$ +50° (neat, not enough sample was available for density measurement); $n^{28}D$ 1.3608.

Anal. Calcd for $C_8H_{13}F_3O_2$: C, 48.48; H, 6.56. Found: C, 48.20; H, 6.49.

***t*-Butyltrifluoromethylcarbinyl Benzoate.**—Starting with the same sample of carbinol the benzoate was prepared: bp 94–96° (4 mm); $n^{28}D$ 1.5430; $\alpha^{27}D$ −7.47° (neat, l = 0.5); corrected to 100% enantiomeric purity, $\alpha^{27}D$ −24.8°; $M^{27}D$ −64° (neat, the density was not available).

***t*-Butyltrifluoromethylcarbinyl Hydrogen Phthalate.**—Using the same carbinol sample, a 67% yield of unrecrystallized hydrogen phthalate was obtained: mp 95–105°; $\alpha^{26}D$ −2.66° (*c* 4.555, $CHCl_3$, l = 2); corrected to 100% optical purity, $[\alpha]^{26}D$ −48.4°; $[M]^{26}D$ −148° (*c* 4.5, $CHCl_3$).

Anal. Calcd for $C_{14}H_{15}F_3O_4$: C, 55.26; H, 4.93. Found: C, 55.12; H, 5.22.

(27) T. Purdie and J. Irvine, *J. Chem. Soc.*, **75**, 483 (1899).

(28) Presumably the low yield was caused by the formation of side products corresponding to those observed in the mandelic acid case.[25] In this case, however, these would be gases and no attempt was made to recover them.

(29) A. L. Henne, M. A. Smook, and R. L. Pelley, *J. Amer. Chem. Soc.*, **72**, 4756 (1950).

(30) A. W. Ingersoll, *Org. Reactions*, **2**, 376 (1944).

Methyltrifluoromethylcarbinyl Acetate.—Methyltrifluoromethylcarbinol [2.4 g, $\alpha^{24}D$ −4.06° (neat, l = 1), enantiomeric purity 57%] was converted into the acetate in 76% distilled yield, bp 83–85°. Preparative gas chromatography (6 ft × 1/2 in. Carbowax 20M, 140°, 110-ml/min He flow rate) gave a sample: $n^{23}D$ 1.3295; $\alpha^{23}D$ +6.32° (neat, l = 0.5); corrected to 100% enantiomeric purity, $[\alpha]^{23}D$ +18.7°; $[M]^{23}D$ +29°.

Anal. Calcd for $C_5H_7F_3O_2$: C, 38.46; H, 4.49. Found: C, 38.46; H, 4.38.

The properties reported[31] for the racemic compound are bp 85.6°, $n^{15}D$ 1.3314, d^{15}_4 1.1823.

Methyltrifluoromethylcarbinyl Benzoate.—The benzoate was prepared from the same sample of carbinol in 68% distilled yield, bp 94–96° (14 mm). Preparative gas chromatography (6 ft × 1/2 in. Carbowax 20M, 200°, 86-ml/min He flow rate) gave a sample: $n^{21}D$ 1.4468; $\alpha^{21}D$ + 0.04 +0.01 (neat, l = 0.5); corrected to 100% enantiomeric purity, $\alpha^{21}D$ +0.14 ± 0.04° (neat, l = 1); $M^{21}D$ +0.3 ± 0.1° (neat).

Anal. Calcd for $C_{10}H_9F_3O_2$: C, 55.05; H, 4.13. Found: C, 55.00; He, 4.36.

Methyltrifluoromethylcarbinyl Hydrogen Phthalate.—The unrecrystallized hydrogen phthalate was prepared in 66% yield from the same sample of carbinol as used for the acetate and benzoate: mp 95–99°; $\alpha^{22}D$ +1.15° (c 5.081, $CHCl_3$, l = 2); corrected to 100% enantiomeric purity, $[\alpha]^{22}D$ +19.8°; $[M]^{22}D$ +52° (c 5, $CHCl_3$).

Anal. Calcd for $C_{11}H_9F_3O_4$: C, 50.38; H, 3.44. Found: C, 50.16; H, 3.64.

Ethylphenylcarbinyl Benzoate.—A sample of ethylphenylcarbinol,[8] $[\alpha]^{25}D$ −10.74° (neat, enantiomeric purity 36.9%), was converted into the benzoate, distilled, and purified by vpc (6 ft × 1/2 in. SE-30 silicon oil column, 250°, He flow rate 60 ml/min): $\alpha^{25}D$ +3.18° (neat, l = 0.5); corrected to 100% enantiomeric purity, $\alpha^{25}D$ +17.3°; $M^{25}D$ +41° (neat, density not available). This compound was not obtained analytically pure.

Isopropylphenylcarbinyl Benzoate.—A sample of isopropylphenylcarbinol,[8] $[\alpha]^{26}D$ −27.7° (c 4.3, ether, enantiomeric purity 58.1%), was converted into the benzoate in 98% crude yield, distilled, bp 132–134° (0.7 mm), and purified by vpc (6 ft × 1/2 in. SE-30 silicone oil column, 250°, He flow rate 84 ml/min): $\alpha^{26}D$ +11.20° (neat, l = 0.5); corrected to 100% enantiomeric purity, $\alpha^{26}D$ +38.6°; $M^{26}D$ +98° (neat, density not available).

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.31; H, 7.09. Found: C, 80.02; H, 7.21.

***t*-Butylphenylcarbinyl Benzoate.**—A sample of *t*-butylphenylcarbinol,[8] $[\alpha]^{26}D$ +4.15 (c 4.8, ether, enantiomeric purity 11.5%), was converted into the distilled benzoate in 85% yield: mp 65–69°; $\alpha^{25}D$ −2.80° (c 13.6, benzene, l = 2); corrected to 100% enantiomeric purity $[\alpha]^{25}D$ −89.6°; $[M]^{25}D$ −240° (c 13.6, benzene).

(*S*)-(+)-Methyl Mandelate.—Mandelic acid {27 g, 180 mmol, $[\alpha]^{26}D$ +150.5° (c 1, water)}, which was 95% optically pure based on the maximum literature value[32] of $[\alpha]^{14}D$ −158° (c 1.6, water), was esterified using methanol and dry hydrogen chloride according to the method of Fischer and Speier[33] to give 21.9 g (74% yield) of (+)-methyl mandelate: bp 100–105° (1–5.1 mm); $[\alpha]^{25}D$ +172.9° (c 1, $CHCl_3$). On the basis of the maximum rotation in the literature[22] of $[\alpha]^{25}D$ +173.5° (c 1, $CHCl_3$) this ester was 99.6% optically pure.

(*S*)-(+)-O-Methylmandelic Acid[24] (VIII).—Methyl mandelate {21.0 g, 127 mmol, $[\alpha]^{25}D$ +172.9° (c 1, $CHCl_3$)} was refluxed for 24 hr with methyl iodide (460 g), silver oxide (30 g), and anhydrous calcium sulfate (40 g) to give 20 g (88% yield), $[\alpha]^{85}D$ +87.0° (c 1.182, acetone), of methyl O-methylmandelate. On the basis of the maximum reported rotation[22] of $[\alpha]^{24}D$ −89.1° (c 1.111, acetone) the product was 97.5% enantiomerically pure. This product, 20 g (110 mmol), $[\alpha]^{26}D$ +87.0° (c 1.182, acetone), was hydrolyzed with hot, dilute sulfuric acid. The product was recovered in two fractions from petroleum ether (bp 55–85°) as long white needles {fraction 1, 10 g, mp 64–66°, $[\alpha]^{25}D$ +150.1° (c 1.057, ethanol); and fraction 2, 4 g, mp 64–66 $[\alpha]^{23}D$ +135° (c 1.71, ethanol)}. On the basis of the maximum reported rotation[34] of $[\alpha]^{17}D$ −150° (ethanol), the acid in fraction 1 was 100% enantiomerically pure.

(*S*)-(+)-Methyl Phenyltrifluoromethylcarbinyl Ether (IX).—The above sample of (+)-O-Methylmandelic acid {5 g, 30 mmol, $[\alpha]^{26}D$ +150.1° (c 1.171, ethanol)} was treated with sulfur tetrafluoride (34 g, 310 mmol) at 30° for 2 days in a 300-ml stainless steel rocking autoclave.

The low-boiling gases were vented through dilute sodium hydroxide, and the reaction mixture was poured into pentane containing sodium fluoride. The pentane was filtered, dried (Na_2SO_4), and fractionally distilled. The first fraction [bp 30–60° (5–6 mm), 2.86 g] was subjected to preparative vpc separation (Carbowax 20M, 10 ft × 1/4 in., 130°, He flow rate 55 ml/min) to give four components with retention times of 11, 19, 43, and 55 min, respectively.

The most volatile component under these conditions (10% yield, retention time 11 min) was identified as α,α-difluorotoluene by the following properties: $n^{20}D$ 1.4570 (lit.[35] $n^{20}D$ 1.4577); nmr signal for aromatic proton at δ 7.44 (5 H, singlet) and benzylic proton 6.57 ppm (1 H, triplet, J = 56 cps); ir ν^{film}_{max} 3030, 2940, 1620, 1460, 1380, 1220, 1120–1000 (multiplet) 925, 850, 770, 700, and 660 cm^{-1}.

Anal. Calcd for $C_7H_6F_2$: C, 65.62; H, 4.73. Found: C, 65.88; H, 4.54.

The properties of the second fraction, 10% yield, with retention time of 19 min, corresponded to the desired methyl phenyltrifluoromethylcarbinyl ether (IX): $n^{25}D$ 1.4382; $\alpha^{26}D$ +56.95° (neat, l = 0.5); $[\alpha]^{26}D$ +91.5° (neat); nmr aromatic signal at δ 7.35 (5 H, singlet), methyl signal at 3.40 (3 H, singlet), methine signal centered at 4.40 ppm (1 H, quartet, J = 7 cps).

Anal. Calcd for $C_9H_9OF_3$: C, 56.84; H, 4.77. Found: C, 56.93; H, 4.82.

The rich ir spectrum of this sample [ν^{film}_{max} 2940, 1460, 1370, 1200–1100 (multiplet), 985, 760, and 710 cm^{-1}] was identical with that of the same ether made as described below from phenyltrifluoromethylcarbinol.

The third component, retention time 43 min, 50% yield, was identified as benzaldehyde, and the fourth component with the following properties has not been identified and may not be homogeneous: $n^{22}D$ 1.4490; nmr δ 3.55 (3 H, singlet), 7.43 (5 H, singlet), centered at 4.70 (1/2 H, triplet, J = 3 cps), and centered at 5.78 ppm (1/2 H, triplet, J = 3 cps) [the triplets were coupled (J = 64 cps) as determined at 100 Mc]; ir ν^{film}_{max} 2950, 1450, 1380, 1300, 1275, 1225, 1060, 980, 825, 760, 730, and 680 cm^{-1}.

Anal. Found: C, 57.72; H, 4.48.

(*S*)-(+)-Methyl Phenyltrifluoromethylcarbinyl Ether (IX).—(+)-Phenyltrifluoromethylcarbinol [1.2 g, 6.6 mmol, $\alpha^{25}D$ +7.70° (neat, l = 1)], which was 18.7% enantiomerically pure based on the maximum rotation[5,9] of $\alpha^{25}D$ +41.18° (neat, l = 1), was refluxed for 36 hr with methyl iodide (23 g), silver oxide (3 g), and anhydrous calcium sulfate, (3 g). The product was diluted with ether (25 ml), and the solid cake extracted with five 20-ml portions of ether. The combined ether extracts were dried (Na_2SO_4); the solvent was evaporated; and the residue was distilled to give 1.0 g (83% yield), bp 68–72° (15 mm). This product was purified by preparative vpc and showed a single peak upon reinjection (Carbowax 20M 10 ft × 1/4 in., 125°, He flow rate 55 ml/min, retention time 21 min): $n^{25}D$ 1.4381, d^{20}_4 1.243. The ir and nmr spectra of this sample were identical with those of the ether obtained by the sulfur tetrafluoride treatment of VIII. The observed rotation of this sample was $\alpha^{26}D$ +11.08° (neat, l = 0.5); the rotation corrected to 100% enantiomorphic purity was $[\alpha]^{26}D$ +95.3° (neat).

Anal. Calcd for $C_9H_9OF_3$: C, 56.84; H, 4.77. Found: C, 56.90; H, 4.73.

(*S*)-(−)-O-Ethyllactic Acid (XI).—(*S*)-(−)-Sodium lactate (40% solution Nutritional Biochemicals, Inc.) was converted according to the procedure of Purdie and Irvine[27] into (*S*)-(−)-ethyl O-ethyllactate, bp 150–155°, $n^{20}D$ 1.4005, $\alpha^{23}D$ −32.38° (neat, l = 0.5), $[\alpha]^{23}D$ −69.3° (neat), which was 87% enantiomerically pure based upon the maximum literature value $[\alpha]^{20}D$ −79.69° (neat).[27] This product (8.0 g, 55 mmol) was hydrolyzed with hot sulfuric acid according to the procedure of Purdie and Irvine[27] to give (*S*)-(−)-O-ethyllactic acid (XI): 5.92 g (92% yield); bp 114–116° (20 mm); $n^{20}D$ 1.4143; $\alpha^{23}D$ −57.58° (neat); $[\alpha]^{23}D$ −55.3° (neat). A portion of this material was purified by preparative vpc (Apiezon L, 5 ft × 1/4 in., 130°, He flow rate 25 ml/min, retention time 13 min): $n^{20}D$ 1.4163; $\alpha^{23}D$ −30.21° (neat, l = 0.5); $[\alpha]^{23}D$ −58.3° (neat). Based on the maximum literature value,[27] $[\alpha]^{20}D$ −66.36°, this material is 88% enantiomerically pure.

(31) F. Swartz, *Bull. Soc. Chim. Belges*, **38**, 99 (1929).
(32) G. W. Clough, *J. Chem. Soc.*, **127**, 2808 (1935).
(33) E. Fischer and A. Speier, *Ber.*, **28**, 3252 (1895).
(34) A. McKenzie and H. Wren, *J. Chem. Soc.*, **115**, 611 (1919).
(35) F. Swartz, *J. Chem. Phys.*, **20**, 65 (1922).

(*S*)-(+)-**Ethyl Methyltrifluoromethylcarbinyl Ether (XII).**—The above sample of (−)-O-ethyllactic acid (5.1 g, 43 mmol was treated with sulfur tetrafluoride (20 g, 186 mmol) for 4 days at 30° in a 300-ml stainless steel rocking autoclave. The product was processed as before and the fraction bp 30–90°, 700 mg) was purified by preparative vpc (Apiezon L, 5 ft × 1/4 in. column, 60°, He flow rate 25 ml/min, retention time 3 min) to give 340 mg (6% yield) of the desired ether (XII) as shown by the following properties: $n^{25}D$ 1.3195, d^{20}_4 1.042 (lit.[29] $n^{25}D$ 1.3219; d^{20}_4 1.062);[36] ν^{film}_{max} 3000, 2900, 1275, 1200–1100 (multiplet), and 1010 cm^{-1}; nmr spectrum centered at about δ 1.20 (6 H, unsymmetrical triplet, J = 7 cps) and centered at about 3.62 (3 H, poorly resolved multiplet, J = 7 cps); $\alpha^{25}D$ +0.41° (neat, l = 0.5), corrected to 100% enantiomeric purity, $[\alpha]^{25}D$ +0.90° (neat).

Anal. Calcd for $C_5H_9OF_3$: C, 42.25; H, 6.39. Found: C, 42.21; H, 6.45.

(*R*)-(−)-**Ethyl Methyltrifluoromethylcarbinyl Ether.**—According to the procedure described for the racemic compound[29] a sample of (+)-methyltrifluoromethylcarbinol [2.0 g, 17 mmol, $\alpha^{25}D$ 1.61° (neat, l = 0.5, 45% enantiomeric purity)], prepared by an asymmetric reduction[3,5,37] procedure, was treated first with sodium (0.4 g, 17 g-atoms) in dibutyl ether solvent (10 g) under nitrogen and then with ethyl bromide (10 g, 93 mmol) in a 300-ml stainless steel rocking autoclave at 30° for 12 hr, then at 100° for 6 hr. The autoclave was cooled, and the reaction mixture was poured from the autoclave which was rinsed out with butyl ether (two 5-ml portions) and ethyl bromide (two 5-ml portions). The reaction mixture was centrifuged to remove sodium bromide and the supernatant fractionated to give 600 mg (33% yield as calculated from the vpc analysis of this material). A portion of this product was purified by preparative vpc (Carbowax 20M, 10 ft × 1/4 in. column, 90°, He flow rate 40 ml/min) to give material, having ir and nmr spectra identical with those of the sample prepared from (−)-O-ethyllactic acid by the action of sulfur tetrafluoride. The rotation, however, was $\alpha^{25}D$ −0.16 ± 0.01° (neat, l = 0.5) which corresponds to $[\alpha]^{25}D$ −0.68 ± 0.05° (neat) when corrected for the 45% enantiomeric purity of the starting methyltrifluoromethylcarbinol.

Anal. Calcd for $C_5H_9OF_3$: C, 42.25; H, 6.39. Found: C, 41.95; H, 6.01.

Unreacted methyltrifluoromethylcarbinol, 0.27 g (13.5% recovery) was also isolated in the preparative vpc process. The ir spectrum of this carbinol was identical with that of the starting material, but the rotation was now $\alpha^{25}D$ −1.30° (neat, l = 0.5, 37% enantiomerically pure) indicating about 19% racemization. Racemization of a secondary alcohol would not be unexpected in the presence of any ketone or a trace of oxygen.[38] If one assumes that all of the carbinol which was converted into the ether was racemized to this same extent, then the corrected rotation for the (*R*)-(−)-ethyl methyltrifluoromethylcarbinyl ether prepared by this route would be $[\alpha]^{25}D$ −0.83 ± 0.05° (neat) which is not far from the rotation $[\alpha]^{25}D$ +0.90° (neat) observed for the enantiomer made *via* the sulfur tetrafluoride reaction on XII.

Registry No.—Phenyltrifluoromethylcarbinyl acetate, 17659-26-6; phenyltrifluoromethylcarbinyl benzoate, 17659-27-7; *t*-butyltrifluoromethylcarbinyl acetate, 17659-28-8; *t*-butyltrifluoromethylcarbinyl benzoate, 17659-29-9; *t*-butyltrifluoromethylcarbinyl hydrogen phthalate, 17659-30-2; methyltrifluoromethylcarbinyl acetate, 17659-31-3; methyltrifluoromethylcarbinyl benzoate, 17659-32-4; methyltrifluoromethylcarbinyl hydrogen phthalate, 17659-33-5; isopropylphenylcarbinyl benzoate, 17659-34-6; *t*-butylphenylcarbinyl benzoate, 17659-35-7; α,α-difluorotoluene, 2155-31-2; IX, 17659-36-8; XI, 17659-37-9; (*S*)-(+) XII, 17659-38-0; (*R*)-(−) XII, 17659-39-1.

(36) Our observed refractive index and density are significantly lower than the literature values. Since our product showed no impurities by vpc analysis, we assume that the material described in the literature was contaminated with some higher density, higher refractive index material, probably ethyl bromide.

(37) D. M. Feigl and H. S. Mosher, *Chem. Commun.*, 615 (1965).

(38) W. von E. Doering and T. C. Aschner, *J. Amer. Chem. Soc.*, **71**, 838 (1949).