TABLE I
CATALYTIC DECOMPOSITION OF I

No.	Compd	Temperature of initial reaction, °C	Time to completion, hr	Yield of PFBA, %	Comments
1	$(C_6H_5)_3P$	25	1.0	~90	Smooth reaction
2	NH_4OH	25		0	Solids formed
3	$(CH_3)_3CNH_2$	25		0	Solids formed
4	$(C_4H_9)_3N$	40	1.25	~90	Smooth reaction
5	$(CH_2)_4CONCH_3$	40	Not determined	~80	Smooth reaction
6	$(C_6H_5O)_3P$	40	Not determined	~90	Smooth reaction
7	C_5H_5N	42	2.0	~90	Smooth reaction
8	$HOCH_2CH_2NH_2$	50		0	Brown tarry material formed
9	p-$HOC_6H_4NH_2$	150	Slow reaction	~30	Some solids forming
10	$(CH_3)_2SO$	150	No reaction	0	
11	$C_3H_7CONH_2$	150	No reaction	0	
12	NH_4Cl	150	No reaction	0	

made to separate these at this point. The yield of PFBA hydrate was 78% as determined by formation of 2,3-bis(trifluoromethyl)-quinoxaline, mp 118°, from a weighed portion and excess *o*-phenylenediamine.[1]

The reaction was repeated with 8 g of dimethylformamide (DMF) in place of the DMSO and it was noted that some yellow color developed when the DMF came in contact with I even at 25°, but with water present the color disappeared rapidly. The second phase had disappeared in only 0.25 hr and extraction, followed by stripping of the ether, gave 25 g of PFBA hydrate and DMF. The yield of PFBA hydrate was 73%, determined as above.

Dehydration of PFBA Hydrate.—The two portions above were combined and 9 g of the mixture was heated with 40 g of 20% fuming sulfuric acid to 70° for 2.5 hr. Yellow vapors evolved and were trapped in a Dry Ice cooled trap. The melting point, −20°, and boiling point, 20°, indicated that this was nearly pure PFBA. The overall yield was about 75% based on I.

The dehydration was repeated but using 10 g of P_2O_5 in place of the fuming sulfuric acid. Evolution of yellow vapors had stopped after 1.25 hr and the yield was 2 g (39%).

Reaction of I with Excess Dimethylformamide.—A mixture of 43 g of I and 19.7 g of DMF was heated in a 150-cc flask from 30 to 145° over 1.25 hr. There was an immediate reaction and the product, 27 g, which collected in Dry Ice cooled traps, was found to be nearly pure PFBA. The yield was quantitative.

The mixture in the kettle was not identified, but there was no evidence for either SO_2 or Cl_2 evolution. The residue dissolved in water and gave strong sulfate and chloride tests.

Catalytic Preparation of PFBA from I.—DMF (1 g) and 33 g of I were stirred together in a 200-cc flask. Evolution of a yellow vapor was immediately evident and continued as the temperature was raised over 6 hr to 158°. At the end of this time the reaction kettle contained two layers of 1 g each. One was a water soluble material, apparently unreacted DMF, and the other was I.

Distillation of the material collected in a Dry Ice cooled trap gave 5 g of Cl_2, 3 g of SO_2, and 18 g of PFBA. The distillation residue, 4 g, contained 43% of sulfuryl chloride and the remainder was starting material.

Catalyst Screening.—Several compounds were examined as possible catalysts by adding 0.1 g of each to 5 g of I and then heating the mixture to 70° till the reaction was complete. The results are summarized in Table I, no. 1, 4, and 7.

Similarly, several other compounds were evaluated on a smaller scale by mixing 0.01–0.05 g of the test compound with 0.5 g of I and then, when necessary, heating either till a smooth reaction proceeded or to a maximum of 150°. The results of these experiments are summarized in Table I, no. 2, 3, 5, 6, and 8–11. In each case the volatile PFBA was collected in a Dry Ice cooled trap and identified by comparison to known material.[1]

Heptafluoroisopropyl Acrylate. Preparation in Diglyme.—To 300 ml of diethylene glycol dimethyl ether, diglyme, in a 500-cc flask was added 19.2 g of anhydrous KF; the mixture was cooled to −20° with vigorous stirring. Hexafluoroacetone, 54 g, was then added and the suspended salt dissolved. This mixture was allowed to warm to 20–23° and 29 g of acrylyl chloride was added slowly to maintain the temperature. A precipitate formed as the acrylyl chloride was added which was shown to be KCl. The mixture was then stripped to a kettle temperature of 50° (20 mm) to give 56 g of colorless liquid. Distillation separated 40 g of crude product and fractionation gave 25 g (33%) of heptafluoroisopropyl acrylate, bp 85°, $n^{20}D$ 1.3128.[2] In an earlier run, some difficulty had been encountered from polymerization so that the distillation was carried out using a slow purge of air to the kettle and hydroquinone was added to the kettle and the receiver. With these precautions no polymerization was observed.

Heptafluoroisopropyl Acrylate. Preparation in Dimethylformamide.—The above procedure was followed but with the use of DMF in place of the diglyme. The reaction appeared to proceed identically in all respects until the distillation. When the material which had been stripped off was heated to distil the final product, a low boiling material was stripped out which was identified as hexafluoroacetone and then acrylyl fluoride was distilled, bp 32.5°, $n^{20}D$ 1.3465. The acrylyl fluoride structure was confirmed by its mass spectrum and the formation of an anilide derivative, mp 103–104°.[3]

This reaction was repeated using half the quantities used above but a water wash was used to remove DMF from the crude product. Distillation gave 7 g (18%) of heptafluoroisopropyl acrylate.

Registry No.—I, 722-89-4.

(3) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd ed, Wiley, New York, N. Y., 1948, p 222.

Improved Procedure for Oxidations with the Chromium Trioxide–Pyridine Complex

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In 1948, Sisler, Bush, and Accountius reported the isolation of a brick-red complex, with the empirical composition $CrO_3 \cdot 2C_5H_5N$, from the reaction of anhydrous chromium trioxide with pyridine.[2] Poos,

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(2) H. H. Sisler, J. D. Bush, and O. E. Accountius, *J. Amer. Chem. Soc.*, **70**, 3827 (1948).

Arth, Beyler, and Sarett found that the complex, in pyridine solution, is an effective reagent for the oxidation of primary and secondary alcohols to aldehydes and ketones.[3] The reagent found wide adoption as a method of accomplishing such oxidations under nonacidic conditions. Holum reported a series of oxidations with $CrO_3 \cdot 2C_5H_5N$ dispersed in pyridine or in acetone.[4]

In 1968, Collins, Hess, and Frank found that the anhydrous complex is moderately soluble in polar chlorocarbons.[5] The solvent of choice was found to be methylene chloride, in which the complex is soluble to the extent of 12.5 g/100 ml. By this modification, primary and secondary alcohols were oxidized to aldehydes and ketones in yields of 87–98%. Subsequently, Dauben, Lorber, and Fullerton showed that methylene chloride solutions of the complex are also useful for accomplishing allylic oxidations.[6]

Our own experience with the chromium trioxide–pyridine complex has convinced us that it is the reagent of choice in almost all situations calling for the oxidation of an alcohol. The chief drawbacks are the nuisance involved in preparing the pure complex, its hygroscopic nature, and its great propensity to enflame during preparation.[2,3] We have found that these complications may be avoided by simply preparing methylene chloride solutions of the complex directly (see Experimental Section).

Oxidation of 2-octanol for 15 min with 5% solutions containing 2:1, 3:1, 4:1, and 6:1 mol ratios of complex (prepared *in situ*) to alcohol gave conversions to 2-octanone of 33, 51, 65, and 97%, respectively. When 2-octanol was treated with a 3:1 mol ratio of complex (prepared *in situ*) to alcohol for prolonged periods, conversions to 2-octanone of 54, 73, 89, and 100% were obtained after 1, 26, 50, and 97 hr, respectively. It is clear from the data that 6 mol equiv of oxidant are required for rapid, complete conversion to ketone. With less than the 6:1 mol ratio, a second, extremely slow oxidation step occurs.

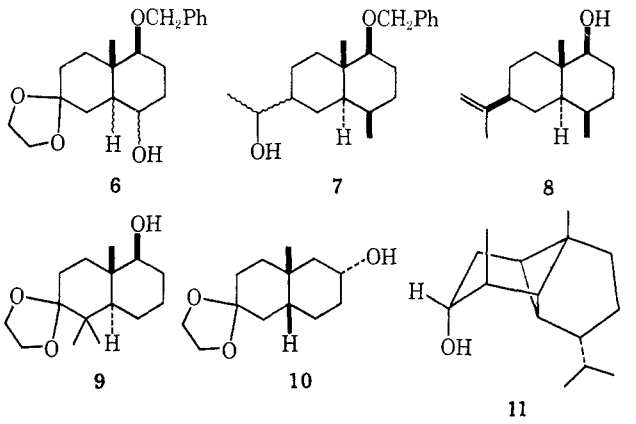
In Table I we list several alcohols which have been oxidized in our laboratories by methylene chloride solutions of the complex, prepared by the *in situ* method. In all cases, the oxidation was done at room temperature for 15 min with a molar ratio of complex to alcohol of 6:1, and the product was the corresponding aldehyde or ketone.

TABLE I

OXIDATION OF ALCOHOLS WITH CHROMIUM TRIOXIDE–PYRIDINE IN METHYLENE CHLORIDE (PREPARED *in situ*)

Alcohol	Mmol alcohol oxidized	% yield of aldehyde or ketone
1 (2-octanol)	5.0	97
2 (1-octanol)	5.0	90
3 (benzyl alcohol)	5.0	89
4 (borneol)	5.0	84
5 (cinnamyl alcohol)	5.0	96
6	137.0	94
7	26.4	99
8	1.4	95
9	42.6	85[a]
10	11.5	90[b]
11	1.3	80[b]

[a] Experiment carried out by Dr. James Macmillan. [b] Experiment carried out by Mr. Bruce Ratcliffe.



In separate experiments, we have tested the stability of the complex by allowing 5% methylene chloride solutions to stand at room temperature, under nitrogen, for periods of 7 and 28 days. In each case, a tarry, black deposit appeared after several days. However, after the specified period, the mixture smoothly oxidized $^1/_6$ mol of 2-octanol in 15 min at room temperature.

Experimental Section

Reagents.—Chromium trioxide (Mallinckrodt analytical reagent) was stored in a vacuum desiccator over phosphorus pentoxide prior to use. Anhydrous pyridine was prepared by distillation of reagent grade material from barium oxide and storing over 4A molecular sieves. Commercial methylene chloride was purified by shaking with concentrated sulfuric acid, washing with water and saturated brine, drying with calcium chloride, distilling, and storing over 4A molecular sieves. Alcohols **1–5** were obtained from commercial sources and used without further purification.

General Oxidation Procedure.—Chromium trioxide, 6.00 g (60 mmol), was added to a magnetically stirred[7] solution of 9.49 g (120 mmol) of pyridine in 150 ml of methylene chloride. The flask was stoppered with a drying tube containing drierite, and the deep burgandy solution was stirred for 15 min at room temperature. At the end of this period, a solution of the alcohol (10 mmol) in a small volume of methylene chloride was added in one portion. A tarry, black deposit separated immediately. After stirring an additional 15 min at room temperature, the solution was decanted from the residue, which was washed with 200 ml of ether. The combined organic solutions were washed with three 100-ml portions of 5% aqueous sodium hydroxide solution, 100 ml of 5% aqueous hydrochloric acid, 100 ml of 5% aqueous sodium bicarbonate solution, 100 ml of saturated aqueous sodium chloride solution, and were dried over anhydrous magnesium sulfate. Alternatively, the decanted methylene chloride solution was condensed *in vacuo* and the residue then taken up in ether, filtered to remove insoluble chromium salts, washed with dilute aqueous base and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent at reduced pressure afforded the crude aldehyde or ketone product. The described procedure has been conveniently scaled to the oxidation of various quantities of alcohol ranging from 137 mmol of compound **6** to 1.3 mmol of compound **11**.

Registry No.—**1**, 123-96-6; **2**, 111-87-5; **3**, 100-51-6; **4**, 507-70-0; **5**, 104-54-1; **6**, 25826-83-9; **7**, 25826-84-0;

(3) G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Amer. Chem. Soc.*, **75**, 422 (1953).

(4) J. R. Holum, *J. Org. Chem.*, **26**, 4814 (1961).

(5) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).

(6) W. G. Dauben, M. Lorber, and D. S. Fullerton, *J. Org. Chem.*, **34**, 3587 (1969).

(7) For large scale oxidations, ice-bath cooling during the chromium trioxide addition and a mechanical stirrer are recommended.

8, 25826-85-1; 9, 25826-86-2; 10, 25826-87-3; 11, 25877-02-5; chromium trioxide, 1333-82-0; pyridine, 110-86-1.

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Enantiomeric Purity of Phenylethylene Glycol and Reliability of Phenylglyoxylate Asymmetric Reductions in Configurational Assignments[1]

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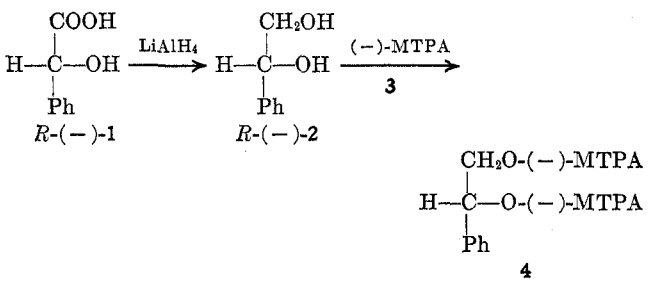
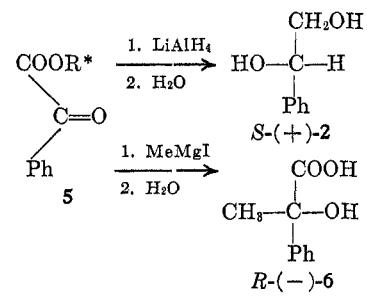
There exists a conflict in the literature concerning the maximum rotation of phenylethylene glycol.[2-6] Since this poses a crucial problem in the study of the asymmetric reduction of chiral phenylglyoxylic ester,[2] it became necessary to resolve this difficulty before we could undertake related studies.[7]

We have made use of the reagent (*S*)-(−)-α-methoxy-α-trifluoromethylphenylacetic acid (**3**, MTPA)[8] to determine the enantiomeric purity of phenylethylene glycol, and thereby to establish unequivocally its maximum rotation. The di-MTPA ester prepared

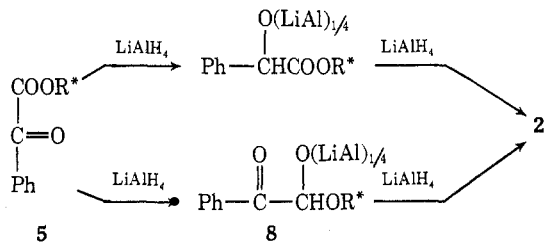


from racemic phenylethylene glycol and enantiomerically pure (*S*)-(−)-MTPA (**3**) exhibited distinct ^{19}F nmr signals for the CF_3 groups of the two diastereomers (**4** and its epimer). The signals from the CF_3 groups, belonging to the MTPA ester of the secondary alcohol function for each of the epimers, were well resolved at δ 5.10 and 4.82 (ppm downfield from the signal for trifluoroacetic acid, TFA, internal, in CCl_4 solvent, 94.1 MHz). Therefore these signals could be used for the quantitative analysis of these diastereomers in a given mixture. A sublimed sample of (*R*)-(−)-phenylethylene glycol (**2**), $[\alpha]^{25}D$ −39.7° (*c* 4.33, 95% EtOH), $[\alpha]^{25}D$ −63.7° (*c* 5.5, $CDCl_3$), prepared by lithium aluminum hydride reduction of (*R*)-(−)-mandelic acid (**1**), $[\alpha]^{24}D$ −152.3° (*c* 3.27, H_2O), gave the di-(−)-MPTA derivative **4**, the ^{19}F nmr analysis of which showed that it was 98 ± 2% stereochemically pure. Since the starting mandelic acid was 98 ± 1% enantiomerically pure, we conclude that no appreciable racemization occurs during the $LiAlH_4$ reduction of mandelic acid to phenylethylene glycol, contrary to one report[2] but in accord with previous work.[3,4,6] This finding has been independently confirmed.[9] Therefore the previously determined values for the asymmetric syntheses involving the $LiAlH_4$ reductions of chiral phenylglyoxylate esters[3-5] *need not be corrected* as suggested.[2]

Berson and Greenbaum[2] have found that the stereochemical course of the $LiAlH_4$ reduction of the phenylglyoxylate ester of phenyldihydrothebaine (**5**, R* = phenyldihydrothebainyl) giving (*S*)-(+)-phenylethylene glycol (*S*-**2**) in excess was "opposite" to that encountered for the addition of methylmagnesium iodide to the same ester giving (*R*)-(−)-atrolactic acid (*R*-**6**) in excess. This unexpected finding indicated



the need for further study of asymmetric reductions of chiral phenylglyoxylate esters before these reactions can be used with any confidence for stereochemical correlations. It was theorized[2] that the opposite stereochemical courses of these two reactions were a result of the initial reduction of the ester carbonyl group in **5**, before the keto carbonyl group, to give the keto hemiacetal derivative **8** instead of the expected mandelic ester derivative **7**. The newly created chiral center in **8** would have a different and unpredictable influence on the steric course of the further $LiAlH_4$ reduction to **2**. Thus the assumption that the



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(1) We gratefully acknowledge support of this research from the National Science Foundation, NSF GP 9432.

(2) J. A. Berson and M. A. Greenbaum, *J. Amer. Chem. Soc.*, **81**, 6456 (1959).

(3) V. Prelog, M. Wilhelm, and D. B. Bright, *Helv. Chim. Acta*, **37**, 221 (1954).

(4) S. P. Bakshi and E. E. Turner, *J. Chem. Soc.*, 168 (1961).

(5) I. Tömösközi, *Tetrahedron*, **19**, 1969 (1963).

(6) E. L. Eliel and D. Delmonte, *J. Org. Chem.*, **21**, 596 (1956).

(7) J. A. Dale, Ph.D. Thesis, Stanford University, 1970.

(8) J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, **34**, 2543 (1970).

(9) (a) J. D. Morrison and J. E. Tomaszewski, private communication. (b) The maximum rotation of phenylethylene glycol is also supported by a series of reactions in which it is related to phenylglycerol: M. H. Denton and G. U. Yuen, *J. Org. Chem.*, **33**, 2473 (1968). (c) This conclusion is consistent with our finding that (−)-menthyl phenylglyoxylate, when treated with excess $LiAlH_4$, gives phenylethylene glycol, $[\alpha]^{19}D$ −6.5 ± 0.1° (*c* 11.2, $CDCl_3$), which calculates to be 10 ± 0.4% enantiomerically pure based upon the maximum rotation of $[\alpha]^{23}D$ −63.8° (*c* 9.5, $CDCl_3$). Horeau, Kagan, and Vigneron, *Bull. Soc. Chim. Fr.*, 3795 (1968), have reported a 10% asymmetric reduction of (−)-menthyl phenylglyoxylate with 1 equiv of $LiAlH_4$ to give (−)-menthyl mandelate whose maximum rotation is well documented. Thus the extent of asymmetric synthesis as measured by either of these methods is the same, as indeed it should be.