change reaction between an acid chloride, ethyl chloroformate, and tetra-*n*-butylammonium chloride-^{36}Cl, an ionic chloride known to be dissociated in aqueous organic solvents.[6] This type of study has the advantage that the addition intermediate has an equal probability of partitioning between reactant and product ($k_2/k_3 = 1$). As a result, the rate of radiochloride incorporation is twice the rate of chloride addition to the carbonyl carbon (k_1). Similarly, the rate of addition of water to the carbonyl carbon may be approximated by the rate of hydrolysis of the acid chloride since acid chlorides show little or no carbonyl oxygen-18 exchange[7] ($k_2/k_3 \ll 1$). Evidence for the presence of a tetrahedral intermediate in the hydrolysis of ethyl chloroformate has been presented by Hudson and Green[5] and Kivinen.[8] Consistent with this suggestion is our observation that the hydrolysis of this acid chloride shows no electrophilic catalysis when studied in the presence of silver perchlorate. The rates of nucleophilic chloride exchange and solvolysis of ethyl chloroformate at 30° are tabulated in Table I. The ratio $2k_e/k_s$ is a measure of the rate of chloride *vs.* water addition to the carbonyl carbon to give the tetrahedral intermediate.

TABLE I

RATES OF CHLORIDE EXCHANGE AND SOLVOLYSIS FOR ETHYL CHLOROFORMATE IN WATER–ACETONITRILE MIXTURES AT 30.1°[a]

H_2O, %	$k_e \times 10^5$, M^{-1} sec^{-1}	$k_s \times 10^6$, M^{-1} sec^{-1} [b]	$2k_e/k_s$
40	12.1 ± 1.3	5.35 ± 0.12	45
60	6.32 ± 0.22	6.74 ± 0.13	19
85	6.71 ± 0.10	7.31 ± 0.10	18

[a] For these measurements, the n-$BuN_4{}^+Cl^-$ concentrations were varied from 0.021 to 0.380 *M* and the ethyl chloroformate concentrations were varied from 0.021 to 0.210 *M*. [b] Second-order rate constant for solvolysis were obtained by dividing the observed first-order rate constant by the water concentration.

These data clearly indicate that at least in this one system chloride ion in aqueous solution is a more reactive nucleophile toward the carbonyl carbon atom than is water. Its reactivity, however, appears to be somewhat less than that observed for displacement at saturated carbon.[9] These results also suggest that Hudson and Green[5] failed to observe bromide or iodide ion catalysis for ethyl chloroformate in 85% aqueous acetone because the halide ion concentrations employed in their studies were too low to permit the detection of such displacement reactions by titrimetric methods. This would be true even though bromide is normally a better nucleophile than chloride ion in aqueous solution[9] because the breakdown of the tetrahedral intermediate (eq 2) would be unfavorable ($k_2/k_3 > 1$). Bromide is a more effective leaving group than chloride ion.[10]

Experimental Section

Materials.—Eastman practical grade acetonitrile was purified by preliminary distillation from sodium hydroxide followed by distillation from phosphorus pentoxide to yield material having bp 80–81°. Matheson technical grade *n*-hexane was stirred over concentrated sulfuric acid, washed with water, dried over sodium hydride, and distilled to give material having bp 68–69°. Eastman White Label ethyl chloroformate was filtered to remove the calcium carbonate stabilizer and distilled through a short Vigreaux column to give material having bp 93.5–94.5°. Dioxane and tetrahydrofuran were purified by standard procedures.[11]

Tetra-*n*-butylammonium Chloride-^{36}Cl.—Tri-*n*-butylamine (43 g, 0.23 mole) and *n*-butyl bromide (32 g, 0.23 mole) were refluxed for 2 days in 250 ml of dry acetonitrile. The pale yellow solution was poured into 700 ml of dry ether and the resultant crystalline precipitate was filtered. The tetra-*n*-butylammonium bromide was dissolved in 100 ml of water and the solution was passed through a Dowex 1-X8 anion-exchange resin in the chloride form enriched with chlorine-36. The water was removed under reduced pressure and the viscous solution was dried in a vacuum desiccator over phosphorus pentoxide to yield 38 g of a white powder. This compound was extremely hydroscopic and had to be stored in a dry atmosphere.

Scintillation Solution.—To 750 g of dioxane and 250 g of tetrahydrofuran was added 4 g of 2,5-diphenyloxazole (PPO) and 0.2 g of 1,4-bis(4-methyl-5-phenyloxazolyl)benzene (POPOP). PPO and POPOP were obtained from Packard Instrument Co.

Exchange Measurements.—A reaction flask containing the aqueous acetonitrile solvent and the desired quantity of tetra-*n*-butylammonium chloride-^{36}Cl was allowed to reach thermal equilibrium in a constant-temperature bath maintained at 30.1 ± 0.05°. The required amount of ethyl chloroformate was added and aliquots of the reaction mixture were removed at various time intervals and extracted with *n*-hexane. Experiments indicated that equilibration of the ethyl chloroformate between the aqueous and *n*-hexane layers was rapid and required less than 2 min. The ionic chloride remained in the aqueous layer. A 1-ml sample of the *n*-hexane layer was then placed in a counting vial containing 15 ml of scintillation solution and the radiochloride concentration was determined by counting with a Nuclear Chicago Mark I liquid scintillation counter. High specific activities of tetra-*n*-butylammonium chloride were employed to increase the sensitivity of the measurements. Product studies by Hudson and Green[5] indicate that the radioactivity in the hexane layer must be due to labeled ethyl chloroformate.

Solvolytic Measurements.—For internal consistency a kinetic technique analogous to that employed for the chloride-exchange measurements was followed except unlabeled tetra-*n*-butylammonium chloride was used. Samples taken from the extracted *n*-hexane phase were analyzed for ethyl chloroformate according to the procedure of Kivinen.[8]

Kinetic Treatment.—The kinetic analysis of the solvolytic reactions has been described elsewhere[7] and was used without modification. The kinetic treatment for the chloride-exchange rates was similar to that used by McCleary and Hammett.[12]

Registry No.—Ethyl chloroformate, 541-41-3; tetra-*n*-butylammonium chloride-^{36}Cl, 13096-55-4.

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Single-Pass Zone Refining. Preparation of an Enantiomerically Pure Compound

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Multipass zone melting is now an established technique for the ultrapurification of metals, semiconductors, and some inorganic and organic compounds.[1,2] For effective ultrapurification, numerous passes are required on initially high-purity material. The achievement of ultrapurity by a single-zone pass should be possible for systems forming simple eutectics, which include most organic mixtures.[3]

Eliel[4] and Mislow[5] have discussed the problems in obtaining enantiomerically pure compounds and in measuring optical purity. Recrystallization from solutions is often the method of choice. Zone refining is generally not considered, but the *d* and *l* molecules are not identical in their behavior with respect to a crystal of *d*, for instance. A physically perfect *d* single crystal would be expected to exclude *l* molecules from its lattice, resulting in ultrapurification. The growth of enantiomerically pure single crystals (essentially a single-pass refining operation) and the measurement of their purity are reported here as an example of the effectiveness of single-crystal growth in achieving chemical ultrapurity.

Single crystals of several organic compounds have recently been obtained by the Czochralski[6] method, for purposes of purification as well as their desirable physical state.[7] The method consists of maintaining a quantity of the compound (in a protective atmosphere if needed) just above its melting point, contacting the top surface of the melt with a crystalline seed, and slowly withdrawing the seed as the crystal growth occurs.

Single-crystal seeds may be obtained by allowing polycrystalline (impure) material or even a metallic rod to contact the liquid surface; then by reorienting the growing polycrystalline mass it is possible to decrease the number of growing crystals. Under these circumstances, most compounds will soon grow as single crystals, unless the melt approaches a eutectic composition. This latter condition demands a partially purified or resolved starting material in almost all cases, although the purity need not be high. It is, of course, essential that the compound not decompose extensively at its melting point.

Triphenylene, fluoranthene, cholesterol, N,N-dimethyl-2,2-diphenylacetamide, and others have been so prepared as large single crystals. To measure the purity obtained for one such compound, ^{14}C-labeled *α-l*-propoxyphene[8] was prepared from the corresponding high optical purity carbinol and used as a measurable contaminant for its enantiomer, *α-d*-propoxyphene, in the following way.

High-purity *α-l*-carbinol was obtained as a single crystal by "pulling" it from a 95+% melt at rates 0.3–2 mm/hr. This crystal was utilized to prepare chemically radioactive *α-l*-propoxyphene by means of ^{14}C-labeled sodium propionate. Any *α-d*-carbinol remaining in the *α-l*-carbinol crystal would contribute to the radioactivity measured as *α-l*-propoxyphene in subsequent steps. From nonradioactive melts of ~93% *α-d*-propoxyphene, 6 g of single-crystal *α-d*-propoxyphene was also prepared by the Czochralski method. The products of these two steps, each enantiomerically pure to a high degree, were then combined in such a ratio as to yield ~3% radioactive *α-l*- and ~97% nonradioactive *α-d*-propoxyphenes as free bases. From a melt of this mixture single crystals (and bicrystals) of *α-d*-propoxyphene were prepared and their ^{14}C content was counted by standard methods. The radioactivity in crystalline sections submitted to such counting would be derived from at least three possible sources: (1) *α-d* contamination of the original *α-l* crystal, (2) contamination of the *α-d* crystal with *α-l*, either incorporated or on its surface, and (3) interchange of the ^{14}C-labeled propionyl group among *α-l* and *α-d* moieties at the melt temperature.

It can be shown that the fraction F of *α-l* in the sample of crystal is given by

$$F = \left[\frac{k}{M} - \frac{aR}{(1-n)S} - K\Delta t\right]\left[1 + \frac{nS}{(1-a)R}\right]$$

where k is the radioactivity of the crystalline sample in decompositions per minute per gram, a is the fraction of *α-d* in the radioactive sample of *α-l*-propoxyphene of mass R and M decompositions per minute per gram, n is the fraction of *α-l* in the nonradioactive sample of *α-d*-propoxyphene of mass S, K is a pseudo rate constant for ester interchange, and Δt is the elapsed time at the interchange temperature.

The final factor, $1 + nS/[(1 - a)R]$, is relatively constant near unity if 99+% *α-d*-propoxyphene is used with radioactive *α-l* to make up a test melt of greater than 2% *α-l*. Under these conditions, the decomposition fraction k/M represents the *maximum* impurity concentration in the crystal sample. A closer approach to the impurity level can be obtained if values are available for either the *α-d* content of the radioactive *α-l* sample or the interchange rate. Counting results indicate test-crystal purities greater than 99.7% and assuming the source *α-d* crystals are of comparable purity, the term $nS/[(1 - a)R]$ can be neglected in the results of Tables I and II.

TABLE I

PURIFICATION FROM 3.1% RADIOACTIVE *α-l*-PROPOXYPHENE

	Factor of purification[a]	Impurity content, %	Purity, %
Entire crystal 1	20	0.16	99.84
Portions of "crystal" 2			
Clear section	70	0.05	99.95
Grain boundary	24	0.13	99.87
Cloudy section	10	0.34	99.67

[a] Reciprocal of effective distribution coefficient.

Several small test *α-d*-propoxyphene crystals were prepared from a melt containing approximately 3.1% *α-l*-propoxyphene. Before sectioning the crystals with a razor blade and subjecting them to counting procedures, the surfaces were carefully scraped and washed

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TABLE II

PURIFICATION FROM MELT CONTAINING 5% α-*l* IMPURITY

Crystal fragment	Labeled impurity, %
Interior sections washed with hexane	0.21
	0.23
	0.27
Interior section obtained by cleavage only	0.18
Fragment including exterior surface	0.17
Av impurity, %	0.2
Concn of impurity in melt, %	~5
Purification factor	25

in flowing hexane. Results for the first two masses grown are shown in Table I. The data demonstrate excellent reductions in impurity levels, or factors of purification of 10–70, from relatively impure starting material. It will be noted that the optically clear region of the crystal showed the highest purity.

Another clear crystal was prepared after about half of the α-*d*-propoxyphene in the original 3% radioactive melt had been allowed to solidify or had been withdrawn by crystal growth. Relevant data for sections of this crystal and its surface shavings are found in Table II.

As an approach to ultrapurity, the purification obtained with starting material of 99+% purity was then studied, using a synthetic starting material containing 0.15% α-*l*, radioactively labeled. Two single crystals were prepared; data for these appear in Table III. The experiments show that purification factors increase with (1) increasing purity of starting material and (2) physical clarity of the crystal. They demonstrate that single-crystal growth may find application in the preparation of compounds which are chemically, including enantiomerically, ultrapure.

TABLE III

PURIFICATION FROM MELT CONTAINING 0.15% α-*l* IMPURITY

	Purification factor	Impurity content, ppm	Final purity, %
Crystal 1			
Center section	35	40	99.996
Crystal 2			
Center section	35	40	99.996
Center section	32	43	99.996
Exterior shavings	30	50	99.995

(2*R*:3*S*)-4-Dimethylamino-1,2-diphenyl-3-methyl-2-(propionoxy-1-^{14}C)butane Hydrochloride.—The radioactive α-*l*-hydrochloride was prepared by the acylation of the α-*l*-carbinol with mixed propionic-1-^{14}C–trifluoroacetic anhydride. Recrystallization from methanol-ethyl acetate, adding ether, gave product melting at 162–164°. Thin layer chromatography was carried out on a silica gel GF (E. Merck) plate using an ethyl acetate–ethanol (1:1) system. The single fluorescent spot was shown to be radiochemically pure by liquid scintillation counting of 1-cm sections of the plate.

Registry No.—(2*R*:3*S*-4-Dimethylamino-1,2-diphenyl-3-methyl-2-(propionoxy-1-^{14}C)butane hydrochloride, 13133-76-1; (2*R*:3*S*)-4-dimethylamino-1,2-diphenyl-3-methyl-2-propionoxybutane hydrochloride, 13133-77-2.

A Novel, Facile Preparation of 1,1′-Bipyrene

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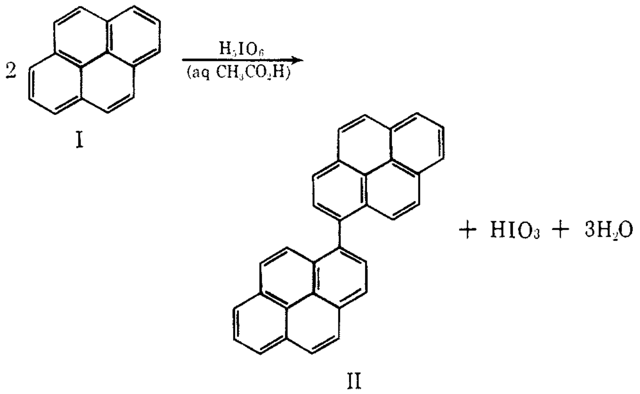
Previously, 1,1′-bipyrene (II) has been prepared in low yield (20–30%) by Ullman coupling, from iodopyrene and magnesium,[1] or bromopyrene and copper powder.[2,3] It has also been prepared[4] by shaking a mixture of pyrene (I), *p*-iodosotoluene, aqueous hydrofluoric acid, and chloroform for 3 days at 50°. The present method is the first report of a simple, one-step preparation of bipyrene by the use of a unique property of periodic acid; other important properties of this oxidant have been well reported.[5]



It has been found that treatment of a solution of pyrene (1 mole) in glacial acetic acid with an aqueous solution of periodic acid (1 mole) at 50° produces 1,1′-bipyrene in a yield of over 70%. The success of the reaction is dependent on (1) selectivity of the solvent (acetic acid) and (2) specificity of the oxidant (periodic acid). Acetic acid apparently participates in formation of solvated radicals and practically no coupling reaction is observed in *p*-dioxane, N,N-dimethylformamide, or ethanol. On the other hand, there is no coupling of pyrene when sodium periodate is used as the oxidant instead of periodic acid. This fact is consistent with the basicity of pyrene[6] and the assumption that the steps in the coupling of two pyrene molecules to give bipyrene include association with periodic acid, hydrogen abstraction, and recombination of radicals. The coupling reaction described may be specific for pyrene. Coupling products have not been obtained with 12 other polycyclic aromatic hydrocarbons examined.

Experimental Section[7]

Preparation of 1,1′-Bipyrene (II).—A solution of 12.0 g (0.053 mole) of periodic acid in 10 ml of water and 40 ml of glacial

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