PATENT SPECIFICATION (11) 1 565 235

1 565 235

(21) Application No. 43221/76 (22) Filed 18 Oct. 1976
(31) Convention Application No. 50/127 787
(32) Filed 23 Oct. 1975
(31) Convention Application No. 51/091 523
(32) Filed 31 July 1976 in
(33) Japan (JP)
(44) Complete Specification published 16 April 1980
(51) INT CL³ C07C 57/30; (C07C 57/30, 11/04, 25/18, 33/14)
(52) Index at acceptance
C2C 1220 1228 1675 200 213 220 226 227 22X 22Y 237 246 247 253 25Y 304 30Y 311 313 314 31Y 338 339 351 355 35X 360 362 364 366 367 368 36Y 37X 386 387 38Y 402 408 40Y 440 441 446 468 469 47X 490 491 507 50Y 561 562 56Y 623 624 625 628 652 658 65X 662 665 693 697 699 73Y 776 778 802 AA BU HK UN UR WP WR

(72) Inventors MAKOTO TAKEDA, MASAYUKI UCHIDE and HIROSHI IWANE

(54) PROCESS FOR PRODUCTION OF α -ARYL PROPIONIC ACIDS

(71) We, MITSUBISHI PETROCHEMICAL COMPANY LIMITED, a company organized and existing under the laws of Japan, of 5—2, Marunouchi 2-Chome, Chiyoda-Ku, Tokyo-To, Japan, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to a process for producing α-aryl-propionic acids which have an anti-inflammatory, analgesic or antipyretic effect, or any combination of these effects, and to precursors of the above propionic acids, namely, esters of α-aryl-propionic acids. The term "aryl" as used herein is defined below.

Various processes have been proposed in the literature for the synthesis of α-aryl-propionic acids.

The following are examples of such proposals: (i) the synthesis of Fenoprofen [α-(3-phenoxyphenyl)propionic acid] described in French Patent No. 2,015,728, and Japanese Laid-open Patent Publication Nos. 4136/1976, 16636/1976, 23235/1976; (ii) the synthesis of Ketoprofen [α-(3-benzoylphenyl)propionic acid] described in Japanese Patent publications Nos. 19287/1970, 7024/1972 and 37028/1973, French Patent No. 2,163,875 and Japanese Laid-open Patent Publication No. 16636/1976; (iii) the synthesis of Flurbiprofen [α-(2-fluoro-4-biphenyl)propionic acid] described in Japanese Patent Publications Nos. 1,545,270 and Japanese Laid-open Patent Publication Nos. 4136/1976 and 16636/1976, German Laid-open Patent Publication No. 2,341,507 and Dutch Laid-open Patent No. 7406897; (iv) the synthesis of Naproxen [α-(6-methoxy-2-naphthyl)propionic acid] described in Japanese Patent Publications Nos. 7021/1973 and 20545/1973, U.S. Patent Nos. 3,562,336, No. 3,652,683, No. 3,651,148, No. 3,651,149, No. 3,658,863, No. 3,658,858, No. 3,651,106, No. 3,720,708 and No. 3,681,432 and Japanese Laid-open Patent Publication Nos. 4136/1976, 16636/1976 and 23249/1976; and (v) the synthesis of Ibuprofen [α-(4-isobutylphenyl)propionic acid] described in Japanese Patent Publication No. 7491/1965, Japanese Laid-open Patent Publication Nos. 95931/1974, 95937/1974, 95938/1974, 108040/1974, 133351/1974, 4040/1975, 39050/1974, 4136/1976, 29466/1976, 54527/1976, 56428/1976, 16636/1976, 36432/1976, 5431/1976 and 86441/1976, Japanese Patent Publication Nos. 18105/1972 and 24550/1972, and British Patent No. 971700.

Most of these processes comprise multistage steps and are complicated. Among these known processes, however, the following processes comprise comparatively short steps:

(1) a process which comprises hydrolysis of α-aryl propionitriles,
(2) a process which comprises reduction of α-aryl acrylic acids, and

(3) a process which comprises oxidation of α-aryl propionaldehydes or β-methyl-β-aryl pyruvic acids.

Even in these processes, however, it is still rather difficult to synthesize the corresponding starting materials. Moreover, in process (3), various by-products may be formed according to the degree of oxidation.

We have sought to provide a process for preparing an α-aryl propionic acid or an ester thereof, which comprises carbonylation with carbon monoxide of the corresponding aryl ethylene, and in which the disadvantages inherent in the above-mentioned processes have been reduced or eliminated.

Other and further features and advantages of the present invention will appear fully from the following description.

The invention provides a process for the preparation of an α-aryl propionic acid and/or an ester thereof represented by the general formula (A):

$$\begin{array}{l} R^1\text{—}CH\text{—}CH_3 \\ \quad\quad | \\ \quad COOR^2 \end{array} \qquad (A)$$

wherein R^1 stands for an isobutylphenyl, a phenoxyphenyl, a benzoylphenyl, a mono- or dihalo biphenylyl, a xanthenyl, a fluorenyl or a biphenylenyl radical, and R^2 stands for hydrogen or a C_1—C_4 alkyl,
which comprises reacting an aryl ethylene represented by the general formula (C):

$$R^1\text{—}CH{=}CH_2$$

wherein R^1 is as defined above,
with carbon monoxide under pressure in the presence of a carbonylation catalyst and in the presence of water and/or a lower alcohol of the formula: R^2OH, where R^2 is a C_1—C_4 alkyl, thereby to carbonylate the aryl ethylene into the α-aryl propionic acid and/or ester thereof.

The starting materials, aryl ethylenes, can be readily prepared, for example, by dehydration of α- or β-aryl ethyl alcohols or by dehydrohalogenation of α- or β-aryl ethyl halides which are represented by the general formula (B):

$$\begin{array}{l} R^1\text{—}CH\text{—}CH_2 \\ \quad\quad | \quad\ | \\ \quad\ X \quad Y \end{array} \qquad (B)$$

wherein R^1 has the same meaning as that defined above, and one of X and Y stands for hydrogen and the other for hydroxyl or a halogen atom.

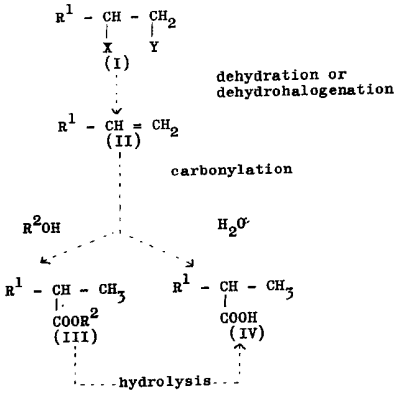
According to a preferred embodiment of the present invention, α- or β-aryl ethyl alcohols or α- or β-aryl ethyl halides are employed as starting materials and the α-aryl propionic acids are prepared by a dehydration or dehydrohalogenation process and a subsequent carbonylation process.

The process of the present invention is more effective than the conventional processes in that in general it uses starting materials which can generally be prepared with ease, it can be completed in fewer steps, its by-products are formed in smaller amounts since the compounds which take part in the present process are simple and stable, and its operation is easier.

DETAILED DESCRIPTION OF THE INVENTION.

1. *Flow Sheet.*

The process of the present invention in which an aryl ethyl alcohol or halide is preferably employed as the starting material is illustrated by the following reaction formulae:



wherein R^1, R^2, X and Y are the same as defined above.

2. *Aryl ethyl alcohols or halides.*

The compounds represented by the general formula (I), which are suitable for the starting material for preparation of the aryl ethylenes, are α-aryl ethyl alcohols, β-aryl ethyl alcohols, α-aryl ethyl halides, and β-aryl ethyl halides. In the formula (I), the halogen atoms represented by X and Y are chlorine, bromine and iodine, and the substituents in the aryl group R^1 are not especially limited to their position for substitution as long as they are within the theoretical possibility. When R^1 of the formula (I) is a halogenated biphenylyl, its halogen atom or atoms are preferably fluorine or chlorine.

The compounds represented by the general formula (I) can readily be prepared by processes known for the preparation of aralkyl alcohols and aralkyl halides.

For example, an α-aryl ethyl alcohol is prepared by reduction of the corresponding aryl methyl ketone, or by reaction of the corresponding aryl magnesium bromide with paraldehyde; and a β-aryl ethyl alcohol is prepared by reduction of the corresponding aryl acetic acid or an ester thereof, or by β-hydroxyethylation of the corresponding aromatic compound with ethylene oxide *via* a Friedel-Crafts reaction.

An α- or β-aryl ethyl halide is prepared, for example, by halogenation of the corresponding aryl alcohol or aryl ethane with a halogenating agent, or by chloroethylation of the corresponding aromatic compound with paraldehyde and hydrogen chloride.

Examples of the α- or β-aryl ethyl alcohols or halides suitable for use in the present invention include: α- or β-(2,2'-difluoro-4-biphenylyl)ethyl alcohol, α- or β-(3'-fluoro-4-biphenylyl)ethyl alcohol, α- or β-(4'-fluoro-4-biphenylyl)ethyl alcohol, α- or β-(4-phenoxyphenyl)ethyl alcohol, α- or β-(3-fluoro-4-biphenylyl)ethyl alcohol, α- or β-(2'-fluoro-4-biphenylyl)ethyl alcohol, α- or β-(3-phenoxyphenyl)-ethyl alcohol, α- or β-(4-isobutylphenyl)ethyl alcohol, α- or β-(2-fluoro-4-biphenyl)-ethyl alcohol, α- or β-(4-benzoylphenyl)ethyl alcohol, α- or β-(3-benzoylphenyl)-ethyl alcohol, α- or β-(2-xanthenyl)ethyl alcohol, α- or β-(2-fluorenyl)ethyl alcohol, α- or β-(2-biphenylenyl)ethyl alcohol, α- or β-(4-benzoylphenyl)ethyl chloride, α- or β-(2-fluoro-4-biphenylyl)ethyl bromide, α- or β-(2-chloro-4-biphenylyl)ethyl chloride, α- or β-(2-xanthenyl)ethyl bromide, α- or β-(3-benzoylphenyl)ethyl chloride, α- or β-(2-fluorenyl)ethyl bromide, α- or β-(4-isobutylphenyl)ethyl chloride, α- or β-(4-isobutylphenyl)ethyl bromide, α- or β-(4'-fluoro-4-biphenylyl)-ethyl chloride, α- or β-(3'-fluoro-4-biphenylyl)ethyl chloride, α- or β-(2'-fluoro-4-biphenylyl)ethyl chloride, α- or β-(2,2'-difluoro-4-biphenylyl)ethyl chloride, α- or β-(4-phenoxyphenyl)ethyl chloride, α- or β-(3-phenoxyphenyl)ethyl chloride, α- or β-(2-biphenylenyl)ethyl chloride.

3. *Dehydration or dehydrohalogenation step.*

The step of dehydration or dehydrohalogenation of the compounds represented by the general formula (I) to obtain the aryl ethylenes (II) can be carried out in accordance with the known methods for dehydration of aryl ethyl alcohols or for dehydrohalogenation of aryl ethyl halides.

Some methods therefor are explained in the following.

These reactions proceed in a good yield and with little formation of by-products. The resulting aryl ethylenes are stable compounds, and can generally be purified by means of a single distillation or re-crystlalization to obtain the products with a sufficiently high purity to be used as the starting material for the subsquent carbonylation step.

1) Dehydration of α- or β-aryl ethyl alcohols.

2) Liquid-phase heating under atmospheric pressure.

An α- or β-aryl ethyl alcohol and 1 to 20 moles, preferably 3 to 10 moles of dimethyl sulfoxide per mole of the alcohol are heated under atmospheric pressure at a temperature of 100° to 250°C, preferably 130° to 190°C, in the presence of 0.1—30% by weight, preferably 1—15% by weight, of the alcohol, and of a polymerization inhibitor.

The polymerization inhibitors to be used are exemplified by hydroquinone, *m*-dinitrobenzene, N-nitrosodiphenylamine, picric acid and sodium sulfite, quinhydrone.

b) Liquid-phase heating under reduced pressure

Heating is generally carried out in the presence of a sulfate compound used as a dehydration accelerator.

As the sulfate compounds there may be employed sodium hydrogensulfate, potassium hydrogensulfate or potassium pyrosulfate.

As polymerization inhibitors the same ones as in the above-mentioned step a) are used.

The alcohol is mixed with 0.01 to 10%, preferably 0.1 to 5% by weight of a sulfate compound and 0.1 to 30%, preferably 1 to 15%, by weight of a polymerization inhibitor. The mixture is heated at a temperature of 100° to 280°C, preferably 195° to 250°C under reduced pressure of 10 to 600 mmHg, preferably 20 to 400 mmHg.

c) Gas-phase heating.

Reaction is carried out in gaseous phase by contacting under heating the alcohol with activated alumina or a caustic alkali.

Into a heated bed of activated alumina or of a caustic alkali such as sodium hydroxide or potassium hydroxide, is introduced the alcohol under reduced pressure, or in the presence of a diluent gas such as nitrogen or carbon dioxide, or together with a volatile solvent such as an aromatic hydrocarbon or an ether, e.g. benzene, toluene, xylene or dioxane.

When activated alumina is employed, it is suitable to heat the reaction system to 120° to 400°C, preferably 150° to 350°C, under a reduced pressure of 10 to 600 mmHg, preferably 20 to 400 mmHg, or in the presence of 1 to 40 moles, and preferably 5 to 20 moles, of a diluent gas such as nitrogen or carbon dioxide per mole of the alcohol or, when the alcohol is a solid, in the presence of 0.01 to 10 moles, preferably 0.1 to 5 moles, of a volatile solvent such as an aromatic hydrocarbon or an ether, e.g. benzene, toluene, xylene or dioxane, per mole of the alcohol. When a caustic alkali is used, it is suitable to heat the reaction system to 100° to 250°C, preferably 120° to 200°C, under a reduced pressure of 2 to 200 mmHg, preferably 5 to 100 mmHg, or in the presence of 1 to 40 moles, preferably 5 to 20 moles, of a diluent gas such as nitrogen or carbon dioxide per mole of the alcohol or, when the alcohol is a solid, in the presence of 0.01 to 10 moles, preferably 0.1 to 5 moles, of a volatile solvent such as an aromatic hydrocarbon or an ether, e.g. benzene, toluene, xylene or dioxane per mole of the alcohol.

2) Dehydrohalogenation of α- or β-(substituted aryl)-ethyl halides.

a) Heating together with a base.

The bases to be used are exmplified by organic bases such as pyridine, quinoline, piperidine, piperazine, aniline and N,N-dimethylaniline, and inorganic bases such as sodium hydroxide and potassium hydroxide.

The reaction is preferably carried out by heating a mixture of the halide with 0.8 to 30 moles, preferably 1 to 15 moles, of the base per mole of the halide generally at a temperature of 0° to 260°C, preferably 20° to 220°C.

b) Heating with an amine hydrochloride under reduced pressure.

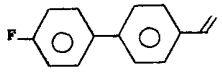
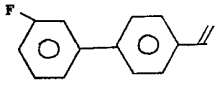
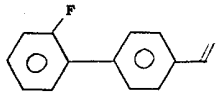
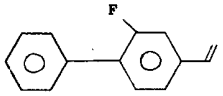
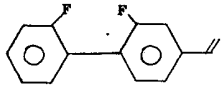
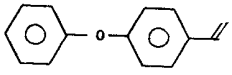
The amine hydrochloride to be used is a hydrochloride of a secondary or tertiary amine such as diamylamine hydrochloride, triamylamine hydrochloride, dihexylamine hydrochloride, and trihexylamine hydrochloride.

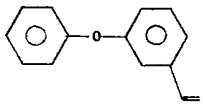
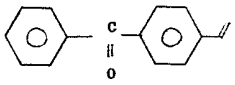
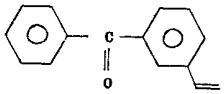
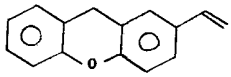
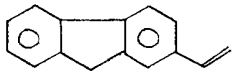
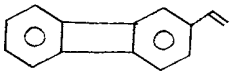
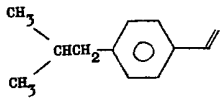
The reaction is carried out in gaseous phase by passing the halide through a molten amine hydrochloride heated at 150° to 300°C and preferably 170° to 270°C, at a reduced pressure of 20 to 760 mmHg, preferably 50 to 200 mmHg, or in the presence of 1 to 40 moles, preferably 5 to 20 moles, of a diluent gas such as nitrogen or carbon dioxide per mole of the halide or, when the halide is a solid, in the presence of 0.01 to 10 moles, preferably 0.1 to 5 moles, of a volatile solvent such as an aromatic hydrocarbon or an ether, e.g. benzene, toluene, xylene or dioxane, per mole of the halide.

4. *Aryl ethylenes.*

The aryl ethylenes thus obtained are the compounds represented by the foregoing general formula (II).

Some compounds thereof are illustrated in the following table, in which the compounds for which no literature references are given are believed to be novel. The names of α-aryl propionic acids obtained by carbonylation of the aryl ethylenes are also shown in the table.

Aryl ethylenes	Corresponding α-aryl propionic acids
(1) 4′-fluoro-4-vinylbiphenyl  (*1)	α-(4′-fluoro-4-biphenylyl) propionic acid
(2) 3′-fluoro-4-vinylbiphenyl 	α-(3′-fluoro-4-biphenylyl) propionic acid
(3) 2′-fluoro-4-vinylbiphenyl  (*7)	α-(2′-fluoro-4-biphenylyl) propionic acid
(4) 2-fluoro-4-vinylbiphenyl 	α-(2-fluoro-4-biphenylyl) propionic acid
(5) 2,2′-difluoro-4-vinylbiphenyl 	α-(2,2′-difluoro-4-biphenylyl) propionic acid
(6) 4-phenoxystyrene  (*2)	α-(4-phenoxyphenyl) propionic acid

Aryl ethylenes	Corresponding α-aryl propionic acids
(7) 3-phenoxystyrene 	α-(3-phenoxyphenyl) propionic acid
(8) 4-vinylbenzophenone  (*3)	α-(4-benzoylphenyl) propionic acid
(9) 3-vinylbenzophenone 	α-(3-benzoylphenyl) propionic acid
(10) 2-vinylxanthene  (*4)	α-(2-xanthenyl) propionic acid
(11) 2-vinylfluorene  (*5)	α-(2-fluoroenyl)-propionic acid
(12) 2-vinylbiphenylene  (*6)	α-(2-biphenylenyl)-propionic acid
(13) 4-isobutylstyrene 	α-(4-isobutylphenyl)-propionic acid

Literature
*1 Zh. Obsh. Khim., *39* 977 (1964)
*2 J. Am. Chem. Soc., *68* 1105 (1946)
*3 Makromol. Chem., *53* 219 (1962)
*4 German Laid-open Patent Publication No. 2,304,763
*5 Chem. Abst., 67 32956 r ; ibid. *66* 29 2962
*6 J. Chem. Soc., (C), 2500 (1970)
*7 J. Am. Chem. Soc., *68* 1159 (1946)

5. *Carbonylation step.*

1) Materials and reaction condition.

The process for carbonylation of the aryl ethylenes to prepare α-aryl propionates (III) or α-aryl propionic acids (IV) is carried out by subjecting the aryl ethylenes to reaction with carbon monoxide and an alcohol and/or water in the presence of a carbonylation catalyst, usually a palladium catalyst. A polymerization initiator as used in dehydration or dehydrohalogenation step may be added to the reaction system.

A palladium complex is suitable as the palladium catalyst to be used; the effective catalyst contains zero- to bi-valent palladium. Examples of a ligand of the complex include a halogen atom, a trivalent phosphorus compound, a π-allyl group, an amine, a nitrile, an oxime, an olefin, or carbon monoxide. Examples of halogen atoms include chlorine, bromine and iodine; examples of the trivalent phosphorus compounds include phosphines and phosphites having an aliphatic or aromatic hydrocarbon radical of 3 to 24 carbon atoms; examples of π-allyl groups include those of 3 to 20 carbon atoms; examples of amines include aliphatic and aromatic mono- and diamines of 1 to 20 carbon atoms; examples of nitriles include aliphatic and aromatic nitriles of 2 to 20 carbon atoms; examples of oximes include aliphatic and aromatic oximes of 3 to 20 carbon atoms; and examples of olefin include olefins of 2 to 20 carbon atoms having 1 to 4 double bonds.

The preferred catalysts have the formula:

$$PdZ_2L_2$$

wherein Z is a halogen atom, L is a ligand other than a halogen atom such as given above, such as those having, as Z, chlorine, bromine or iodine and, as L, a phosphorus compound having aromatic hydrocarbon radical of C_6 to C_{12} or an aliphatic hydrocarbon radical of C_3 to C_{10} such as a phosphine. This type of catalysts is disclosed in Japanese Patent Publication No. 21722/1968.

Examples of preferred palladium catalysts include: bis(triphenylphosphine)-dichloropalladium, bis(tributylphosphine)dichloropalladium, bis(tricyclohexylphosphine)dichloropalladium, π-allyltriphenylphosphinechloropalladium, triphenylphosphine piperidine dichloropalladium, bis(benzonitrile)dichloropalladium, bis(cyclohexyloxime)dichloropalladium, 1,5,9-cyclododecatriene dichloropalladium, bis(triphenylphosphine)dicarbonylpalladium, bis(triphenylphosphine)-palladium acetate, bis(triphenylphosphine)palladium nitrate, bis(triphenylphosphine)palladium sulfate and tetrakis(triphenylphosphine)palladium. The most preferable palladium catalysts among these are bis(phosphine having hydrocarbon radicals) dihalopalladium where the hydrocarbon radical is preferably phenyl, a linear alkyl of C_3 to C_6 or cyclohexyl, and the halo is preferably chloro, bromo or iodo.

The palladium complex catalyst is usually put into the reaction system as such, but the complex can be prepared *in situ* in the reaction system. Accordingly, the compounds which can form the above-mentioned palladium complex in the reaction system can also be employed as the catalyst. For example, a palladium salt such as palladium oxide, palladium sulfate or palladium chloride, and a ligand compound such as a phosphine, a nitrile, an allyl compound, an amine, an oxime, an olefin or carbon monoxide are caused to be present at the same time in the reaction system. These ligand compounds can be selected from those listed hereinabove and are exemplified by a phosphine such as triphenylphosphine, tritolylphosphine, tributylphosphine, tricyclohexylphosphine and triethylphosphine; a nitrile such as benzonitrile, acrylonitrile, propionitrile and benzylnitrile; an allyl compound such as allyl chloride and allyl alcohol; an amine such as benzylamine, pyridine, piperazine and tri-n-butylamine; an oxime such as cyclohexyloxime, acetoxime and benzaldoxime; and an olefin such as 1,5-cyclooctadiene and 1,5,9-cyclododecatriene.

The alcohol to be used is a lower aliphatic alcohol of the formula: R^2OH where R^2 is a lower alkyl having 1—4 carbon atoms, i.e. methanol, ethanol, *n*- or *i*-propanol and *n*-, *i*-, sec and *t*-butanol.

Hydrogen chloride and boron trifluoride (as it is or as its etherate) can be added to the reaction system in order to suppress side reactions and to maintain the life time of the palladium catalyst, and moreover for the purpose of increasing reaction velocity.

The amount of the palladium complex or palladium compound as a precursor for the complex to be used is 0.0001 to 0.5 mole, preferably 0.001 to 0.1 mole, per

mole of the substituted aryl ethylene. When the precursor palladium compound is used, the amount of the ligand compound to be added is 0.8 to 10 moles, preferably 1 to 5 moles, per mole of the palladium compound.

The alcohol and water used as starting materials may also act as solvents. The amount to be used is generally 0.5 to 50 parts, preferably 1 to 20 parts, by weight based on the substituted aryl ethylene. The alcohol and water can mainly be used as reaction material and another liquid material employed as a solvent in the reaction system. In this case, a mixture of the alcohol or water and an organic solvent miscible therewith (such as an aromatic or aliphatic hydrocarbon, e.g. benzene, toluene or hexane) can be employed.

A suitable amount of hydrogen chloride which may be used is 1 to 20%, preferably 2 to 15%, by weight based on the alcohol or water. A suitable amount of boron trifluoride which may be used is 0.8 to 15 moles, preferably 1 to 7 moles, per mole of the palladium complex or the precursor palladium compound.

Carbon monoxide is used in the carbonylation reaction preferably in excess to the amount of the aryl ethylene, which may be varied according to the size and shape of a reactor.

(2) Carbonylation reaction

The carbonylation reaction may be carried out in the following way.

(1) When an alcohol is employed.

When hydrogen chloride is added to the reaction system, it is suitable to carry out the reaction at a temperature of 40 to 150°C, preferably 60 to 140°C, and under a carbon monoxide pressure of 100 to 800 atmospheres, preferably 100 to 600 atmospheres. When boron trifluoride is added to the reaction system, it is suitable to carry out the reaction at a temperature of 40 to 120°C, preferably 50 to 100°C, and under a carbon monoxide pressure of 10 to 150 atmospheres, preferably 20 to 100 atmospheres. When no hydrogen chloride or borontrifluoride is used, the reaction temperature is usually 100 to 250°C, preferably 120 to 210°C, and the carbon monoxide pressure is usually 90 to 800 atmospheres, preferably 100 to 650 atmospheres.

(2) When water is employed.

Addition of hydrogen chloride is preferred, since boron trifluoride decomposes upon contact with water. Reaction is carried out in the same way as in the reaction condition (1) in which hydrogen chloride is used.

Thus, the ester (III) is obtained by the above-mentioned step (1), and the acid (IV) by the step (2). When a mixture of the alcohol and water is employed, a mixture of the ester and the acid is obtained.

When an aryl ethylene of high purity which has been obtained according to the preceding step, viz. dehydration step or dehydrohalogenation step, is employed as reaction material in carbonylation step, the above-mentioned carbonylation can proceed quantitatively to yield an α-aryl propionate or an α-aryl propionic acid with good selectivity and in high purity. The propionate can readily be purified by means of a single distillation or recrystallization since it is a stable substance.

3) Conversion of the product.

The esters of α-aryl propionic acid obtained by carbonylation in the alcohol can readily be converted to α-aryl propionic acids, according to a conventional process for hydrolysis of esters. For example, the propionate is refluxed with an aqueous sodium hydroxide solution, the resulting salt is acidified, and precipitated acid is separated, followed by recrystallization from petroleum ether. The α-aryl propionic acids thus obtained are of very high purity.

The following Examples are exemplary and non-limitative of the process of the present invention.

Examples 1 and 2.

1) The compounds and reaction temperatures used are shown in Table 1. Into an autoclave 100 ml. in capacity were charged aryl ethylene, alcohol, bistriphenylphosphine dichloropalladium, boron trifluoride etherate complex and 3 mg of N-nitrosodiphenylamine as a polymerization inhibitor. Carbon monoxide was introduced into the autoclave at room temperature until the pressure therein reached 85 kg/cm^2. Reaction was carried out at the reaction temperature indicated until no absorption of carbon monoxide was observed. After cooling, the reaction liquor was washed with water, and dried with magnesium sulfate. The solvent was then distilled off under reduced pressure. The resultant precipitate was recrystallized from hexane to obtain the indicated ester.

2) To 100 ml. of 30% aqueous solution of NaOH was added the ester obtained above, and the mixture was refluxed for 3 hours. After cooling, the resultant aqueous layer was acidified with hydrochloric acid. Then the precipitate thus obtained was subjected to extraction with ether. The resultant ether layer was washed with water, and dried with magnesium sulfate. The ether in the layer was then distilled off under reduced pressure, and the resultant residue was recrystallized from n-hexane to give the indicated acid.

The yields and physical properties are shown in Table 1.

TABLE 1

		Example 1	Example 2
Aryl ethylene (starting material)		4-phenoxystyrene 8.6 g	4'-fluoro-4-vinylbiphenyl 4.0 g
Alcohol		ethyl alcohol 20 ml.	ethyl alcohol 40 ml
Catalyst		bistriphenylphosphine-dichloropalladium 0.4 g	bistriphenylphosphine-dichloropalladium 0.4 g
Additive		boron trifluoride etherate 0.4 g	boron trifluoride etherate 0.4 g
Reaction temperature		80°C	84°C
Ester	Compound	ethyl α-(4-phenoxyphenyl)-propionate	ethyl α-(4'-fluoro-4-biphenylyl)propionate
	Yield (mole %) physical property	6.3 g (67%) N_D^{23} 1.5441	4.0 g (84%) –
Acid	Compound	α-(4-phenoxyphenyl)-propionic acid	α-(4'-fluoro-4-biphenyl) propionic acid
	Yield (mole %) physical property	40 g (83%) m.p. 69 – 70°C	3.8 g (92%) m.p. 151 – 153°C

Examples 3 to 12.

The compounds and reaction conditions are indicated in Table 2.

Into an autoclave 100 ml. in capacity were charged aryl ethylene, 10% aqueous solution of hydrochloric acid, catalyst solvent and polymerization inhibitor. Carbon monoxide was introduced into the autoclave at room temperature until the pressure therein reached the indicated value. Reaction was carried out at the indicated temperature until no absorption of carbon monoxide was observed. After cooling the reaction system to room temperature, the solvent layer was separated and subjected to extraction with 20% aqueous solution of NaOH. The extract was acidified with hydrochloric acid, and the resultant precipitate was extracted with ether. The ether layer thus obtained was washed with water, and dried with magnesium sulfate, followed by distilling off the ether under reduced pressure. The resultant residue was recrystallized from hexane to give the indicated compound.

The results are shown in Table 2.

TABLE 2

		Example 3	Example 4
Aryl ethylene (g)		3′-fluoro-4-vinylbiphenyl 3.3	2′-fluoro-4-vinylbiphenyl 2.5
10% aqueous hydrochloric acid (ml.)		10	10
Catalyst (g)		bis(tributylphosphine)-dichloropalladium 0.2	bis(triphenylphosphine)-dibromopalladium 0.3
Solvent (ml.)		benzene 20	toluene 15
Polymerization inhibitor (mg)		quinhydrone 15	m-dinitrobenzene 50
Pressure of carbon monoxide (kg/cm^2)		180	200
Reaction temperature (°C)		120	110
Acid	Compound	α-(3′-fluoro-4-biphenylyl)propionic acid	α-(2′-fluoro-4-biphenylyl)propionic acid
	Yield (g)	3.2	2.4
	Yield (mole %)	79	78
	Physical property	m.p. 107 – 110°C	m.p. 95 – 97°C

TABLE 2 (continued)

Example 5	Example 6	Example 7	Example 8
2-fluoro-4-vinylbiphenyl 3.5	2,2′-difluoro-4-vinylbiphenyl 3.2	3-phenoxystyrene 4.0	4-vinylbenzophenone 2.0
20	15	15	10
bistriphenylphosphine dichloropalladium 0.2	bis(tricyclohexylphosphine)-dichloropalladium 0.4	bis(triphenylphosphine)-dichloropalladium 30	bis(triphenylphosphine)-dichloropalladium 0.3
benzene 20	benzene 15	benzene 20	benzene 10
N-nitrosodiphenylamine	hydroquinone 70	m-dinitrobenzene 30	m-dinitrobenzene 300
150	150	150	200
120	120	120	120
α-(2-fluoro-4-biphenylyl)propionic acid	α-(2,2′-difluoro-4-biphenylyl)propionic acid	α-(3-phenoxyphenyl)-propionic acid	α-(4-benzoylphenyl)-propionic acid
3.5	3.1	3.1	1.9
81	72	63	78
m.p. 110 – 111°C	m.p. 120.5 – 123°C	b.p. 168 – 171°C (0.11 mmHg)	m.p. 112 – 114°C

TABLE 2 (continued)

Example 9	Example 10	Example 11	Example 12
3-vinylbenzophenone 4.2	2-vinylxanthene 2.3	2-vinylfluorene 4.1	2-vinylbiphenylene 2.1
15	15	15	10
bis(triphenylphosphine)-dichloropalladium 0.3	palladium chloride 0.075 triphenylphosphine 0.3	bis(triphenylphosphine)-dichloropalladium 0.3	bis(triphenylphosphine)-dichloropalladium 0.3
benzene 15	benzene 20	benzene 20	benzene 15
N-nitrosodiphenylamine 3	hydroquinone 400	N-nitrosodiphenylamine 3	N-nitrosodiphenylamine 3
250	200	300	200
130	140	100	100
α-(3-benzoylphenyl)-propionic acid	α-(2-xanthenyl)propionic acid	α-(2-fluorenyl)-propionic acid	α-(2-biphenylenyl)-propionic acid
4.0	1.7	4.3	1.8
78	61	85	68
m.p. 85.5 – 86°C	m.p. 190 – 191°C	m.p. 183 – 184°C	m.p. 135 – 138°C

Example 13.

1) Into a 500 ml flask were charged 0.47 g lithium aluminium hydride and 50 ml. of absolute ether. Then to the system was added dropwise 7.0 g of 4-acetyl-3'-fluorobiphenyl dissolved in 150 ml. of absolute ether at such a rate as to cause mild refluxing. After the addition was complete, the reaction mixture was further refluxed on a warm bath for one hour. After cooling, to the reaction mixture were added dropwise 30 ml. of water and then 5 ml. of 2% sulfuric acid. The ether layer thus produced was separated, washed with water, and then dried over magnesium sulfate. The ether in the layer was distilled off under reduced pressure. The resultant precipitate was recrystallized from hexane to give 6.1 g of α-(3'-fluoro-4-biphenylyl)ethyl alcohol. The product is a novel compound which has not been found in literature.

Yield: 84 mole %, m.p.: 62—62.5°C

Nuclear magnetic resonance spectrum ($CDCl_3$) δ (ppm)

1.67	(3H, d)	
2.63	(1H, s)	
4.92	(1H, q)	
6.76—7.88	(8H, m)	

2) In 50 ml. of dimethyl sulfoxide were dissolved 5.0 g of α-(3'-fluoro-4-biphenylyl) ethyl alcohol and 20 mg of N-nitrosodiphenylamine as a polymerization inhibitor, and the resultant solution was heated at 150°C for 16 hours. After cooling, 30 ml. of ethyl acetate was added to the reaction system. The dimethyl sulfoxide was then removed from the system by washing with water. The resultant ethyl acetate layer was separated, and dried over magnesium sulfate. Then the ethyl acetate was distilled off under reduced pressure, and the resultant residue was subjected to column chromatography. From hexane/benzene (1:1) eluate was obtained 3.3 g of 3'-fluoro-4-vinyl-biphenyl.

Yield: 72 mole %, m.p. 81—81.5°C

Nuclear magnetic resonance spectrum ($CDCl_3$) δ ppm

5.28	(1H, dd)	
5.77	(1H, dd)	
6.78	(1H, dd)	
6.91—7.82	(8H, m)	

The product of this example was used as the starting material of Example 3.

Example 14.

In 750 ml. of carbon tetrachloride was dissolved 10 g of 2-fluoro-4-ethylbiphenyl. Then to the solution were added 10 g of N-bromosuccinimide and 0.1 g of benzoyl peroxide. After cooling, a solid substance was filtered off, and from the filtrate containing α-(2-fluoro-4-biphenylyl)ethyl bromide was distilled off the carbon tetrachloride. The residue thus obtained was dissolved in 500 ml. of ethyl alcohol, and then 17 g of potassium hydroxide were added. The resultant mixture was refluxed under heating for 1 hour. After cooling, the reaction mixture was poured into 2.5 l. of water, and then subjected to extraction with benzene. The benzene layer was washed with water, and dried over magnesium sulfate. The benzene was distilled off, and the resulting residue was subjected to column chromatography, whereupon 5.5 g of 2-fluoro-4-vinylbiphenyl were obtained.

Yield: 56 mole %, refractive index $n_D^{25.5}$: 1.6119

Nuclear magnetic resonance spectrum (CCl_4) δ ppm.

5.29	(1H, dd)	
5.73	(1H, dd)	
6.72	(1H, dd)	

7.07—7.70 (8H, m)

The product of this example was used as the starting material of Example 5.

Example 15.

In 80 ml. of dimethyl sulfoxide were dissolved 3.7 g of α-(2'-fluoro-4-biphenylyl) ethyl alcohol and 70 mg of quinhydrone as a polymerization inhibitor. The resultant solution was heated at 170°C for 13 hours. After cooling, the reaction mixture was mixed with 20 ml. of ethyl acetate, and washed with 300 ml. of water. The resultant ethyl acetate layer was separated after the removal of dimethyl sulfoxide, and dried over magnesium sulfate. Then ethyl acetate was distilled off under reduced pressure, and the resultant residue was subjected to column chromatography, whereupon 2.5 g of 2'-fluoro-4-vinylbiphenyl were obtained.

Yield: 74 mole %, m.p.: 37.5—38°C

Nuclear magnetic resonance spectrum ($CDCl_3$) δ ppm

5.29 (1H, dd)

5.79 (1H, dd)

6.81 (1H, dd)

7.01—7.76 (8H, m)

The product of this example was used as the starting material of Example 4.

Example 16.

In 250 ml. of dimethyl sulfoxide were dissolved 7.0 g of α-(3-phenoxyphenyl)-ethyl alcohol and 0.5 g of m-dinitrobenzene as a polymerization inhibitor. The solution was heated at 160°C for 10 hours. After cooling, the reaction mixture was mixed with 250 ml. of dichloromethane, and washed with 600 ml. of water. The resultant dichloromethane layer was separated after removal of the dimethyl sulfoxide, and dried over magnesium sulfate. Then the dichloromethane was distilled off under reduced pressure, and the resultant residue was subjected to column chromatography, whereupon 4.75 g of 3-phenoxystyrene were obtained.

Yield: 75 mole %, n_D^{24}: 1.5980

Nuclear magnetic resonance spectrum ($CDCl_3$) δ ppm

5.26 (1H, dd)

5.72 (1H, dd)

6.67 (1H, dd)

6.75—7.52 (9H, m)

The product of this example was used as the starting material of Example 7.

Example 17.

1) To 6 g of α-(4-isobutylphenyl)ethyl alcohol were added 12 g of dimethyl sulfoxide and 0.1 g of m-dinitrobenzene as a polymerization inhibitor. The mixture was stirred at 160°C for 8 hours. The resultant reaction liquor was cooled, diluted with water and then subjected to extraction with benzene. After the resulting organic layer was dried over magnesium sulfate, the solvent was distilled off. The residue thus obtained was distilled to give 4.2 g of 4-isobutylstyrene having the following physical properties.

Yield: 78 mole %.

boiling point: 82—84°C/2.4 mmHg

colorless liquid, $n_D^{20} = 1.5218$

Infrared absorption spectrum: 1625, 1381, 990, 904, 910 cm^{-1}

Nuclear magnetic resonance spectrum (in $CDCl_3$) δ ppm

0.89 (6H, c)

1.5 —2.2 (1H, m)

2.42 (2H, d)

5.11 (1H, dd)

5.60 (1H, dd)

6.65 (1H, dd)

6.9 —7.4 (4H, m)

Elemental analysis: theoretical
C: 89.94, H: 10.06 found
C: 89.96, H: 9.92

The 4-isobutylstyrene thus obtained was of a high purity, and after a single distillation was used for the following reaction.

2) Into an autoclave 100 ml. in capacity were charged 4.2 g of 4-isobutylstyrene, 40 ml. of ethyl alcohol, 0.2 g of bis(triphenylphosphine)dichloropalladium and 0.2 g of boron trifluoride etherate. The autoclave was further charged with carbon monoxide until the pressure therein reached 80 kg/cm². Reaction was carried out at 70°C until absorption of carbon monoxide ceased. After cooling, the resultant reaction liquor was washed with an aqueous solution of calcium chloride. The ester layer thus obtained was dried over magnesium sulfate, followed by distillation to give 4.8 g of ethyl α-(4-isobutylphenyl)-propionate. b.p.: 102—104°C/0.8 mmHg.

3) Into 20 ml. of a 30% aqueous solution of NaOH was added 4.8 g of ethyl α-(4-isobutylphenyl) propionate, and the mixture was refluxed for 2 hours. After cooling of the mixture, insoluble matter was removed by extraction with ether, and the resultant aqueous layer was acidified with hydrochloric acid, followed by extraction with ether. After the ether layer thus obtained was washed with water and dried over magnesium sulfate, the ether was distilled off. The resultant crude crystals were recrystallized from *n*-hexane to give 3.5 g of α-(4-isobutylphenyl)propionic acid.

Yield: 81 mole %
m.l.: 75—76°C

Example 18.

1) To 20 g of α-(4-isobutylphenyl)ethyl chloride was added 80 ml. of pyridine, and the mixture was heated at 115°C for 6 hours. The resultant product was poured into a mixture of 130 ml. of concentrated hydrochloric acid — 370 g of ice, followed by extraction with chloroform.

After the chloroform solution thus obtained was dried with magnesium sulfate, the chloroform in the solution was distilled off. The resultant residue was further subjected to distillation to give 11.7 g of 4-isobutylstyrene. Yield: 65 mole %.

2) Into an autoclave 100 ml. in capacity were charged 10 g of 4-isobutylstyrene, 12 ml. of a 10% methyl alcohol solution of hydrogen chloride and 0.2 g of bistriphenylphosphinedichloropalladium. Carbon monoxide was introduced into the autoclave at room temperature until the pressure therein reached 300 kg/cm², and, after the reaction mixture was heated to 90°C, a further quantity of carbon monoxide was introduced until the pressure therein reached 700 kg/cm². Reaction was carried out until no absorption of carbon monoxide was observed. After cooling, the resultant reaction liquor was washed with an aqueous solution of calcium chloride, and then subjected to extraction with ether. The ether layer thus obtained was dried over magnesium sulfate, and then distilled to give 9.7 g of methyl α-(4-isobutylphenyl)propionate having a boiling point of 99 to 101°C/1 mmHg.

3) To 40 ml. of 30% aqueous solution of NaOH was added 9.7 g of methyl α-(4-isobutylphenyl)propionate, and the mixture was refluxed for 2 hours.

After cooling, insoluble matter was removed by extraction with ether. The resultant aqueous layer was acidified with hydrochloric acid, followed by extraction with ether. After the ether layer thus obtained was washed with water and dried with magnesium sulfate, the ether was distilled off under reduced

pressure. The crude crystals thus produced were recrystallized from petroleum ether to give 7.7 g of α-(4-isobutylphenyl)propionic acid.
m.p.: 75—77°C

Example 19.

Into an autoclave 100 ml. in capacity were charged 6 g of 4-isobutylstyrene, 20 g of 10% aqueous solution of hydrochloric acid, 0.2 g of bistriphenylphosphine dichloropalladium, 10 g of benzene and 0.6 g of m-dinitrobenzene. Carbon monoxide was introduced into the autoclave at room temperature until the pressure therein reached 300 kg/cm².

Reaction was carried out by heating the mixture at 100°C until absorption of the carbon monoxide ceased. After cooling, the benzene layer was separated, and subjected to extraction with a saturated aqueous solution of sodium hydrogencarbonate. Then the resultant extract was acidified with hydrochloric acid and further extracted with ether. The extract thus obtained was washed with water, and dried over magnesium sulfate, followed by distillation of the ether under reduced pressure. The resultant residue was recrystallized from hexane to give 6.4 g of α-(4-isobutylphenyl)propionic acid.
Yield: 81 mole %
m.p.: 75—77°C

Example 20.

1) Through a glass tube which was packed with alumina and heated at 270°C were passed downward 1590 g of α-(4-isobutylphenyl)ethyl alcohol and nitrogen gas at a liquid hourly space velocity of 1.0 hr^{-1} and space velocity of 2100 hr^{-1}. Effluent gas was collected by a receiver cooled with dry ice-methanol to give 1360 g of 4-isobutylstrene.
Yield: 95 mole%

2) Into an autoclave 5 liter in capacity were charged 643 g of 4-isobutylstyrene, 1400 ml. of ethyl alcohol, 4.0 g of bistriphenylphosphinc dichloropalladium, 4.0 g of boron trifluoride etherate and 10 g of m-dinitrobenzene as a polymerization inhibitor. Carbon monoxide was introduced into the autoclave at room temperature until the pressure therein reached 76 kg/cm². Reaction was carried out at 88°C until absorption of carbon monoxide ceased. After cooling, the resultant reaction liquor was washed with water, and dried over magnesium sulfate. Then the solvent was distilled off under reduced pressure, and the resultant residue was distilled to give 733 g of ethyl α-(4-isobutylphenyl)propionate.
Yield: 78 mole %, b.p.: 102—104°C/0.8 mmHg

3) To 500 ml. of a 30% aqueous solution of NaOH was added 733 g of ethyl α-(4-isobutylphenyl)propionate, and the mixture was refluxed for 2 hours. After cooling, the aqueous layer was separated and acidified with hydrochloric acid. The resultant precipitate was separated by filtration, dried, and then recrystallized from petroleum ether to give 536 g of α-(4-isobutylphenyl)-propionic acid.
Yield: 83 mole %, m.p.: 75—76°C.

Example 21.

To 40 ml. of anhydrous tetrahydrofuran solution containing phenylmagnesium bromide prepared from 0.53 g of magnesium and 3.4 g of bromobenzene was added dropwise at room temperature 20 ml. of an anhydrous tetrahydrofuran solution containing 2.3 g of 3-cyanostyrene. After agitation for 2 hours at room temperature, 30 ml. of 1 N aqueous hydrochloric acid was added dropwise to the tetrahydrofuran solution, and the resultant mixture was agitated for further 30 minutes.

The tetrahydrofuran layer was separated, washed with water, aqueous sodium hydrogen carbonate, and then water again, followed by drying over magnesium sulfate. Tetrahydrofuran was distilled off, and the residue was subjected to column chromatography, whereupon 1.9 g of 3-vinylbenzophenone were obtained.
Yield: 51 mole %, n_D^{24}: 1.6174
Nuclear magnetic resonance spectrum ($CDCl_3$) δ ppm

5.31 (1H, dd)

5.78 (1H, dd)

6.79 (1H, dd)

7.36—8.01 (9H, m)

The product of this example was used as the starting material of Example 9.

Example 22.

1) In 20 ml. of absolute ethyl alcohol was dissolved 0.38 g of sodium borohydride to which 2.32 g of 4-acetyl-2,2′-difluorobiphenyl in ethyl alcohol was added dropwise at room temperature. The resultant solution was agitated overnight and then maintained at 50°C for 1 hour, whereupon the reaction was completed.

The reaction solution was poured into 100 ml. of water and, after neutralization with acetic acid, subjected to extraction with ethyl ether. The ethyl ether layer thus obtained was washed with water and dried with calcium sulfate. Then the ether was distilled off under reduced pressure, and 2.11 g of crude α-(2,2′-difluoro-4-biphenylyl)ethyl alcohol was obtained as an oily substance.

Yield: 90 mole %

Nuclear magnetic resonance spectrum ($CDCl_3$) δ (ppm)

1.47 (3H, d)

2.80 (1H, s)

4.90 (1H, q)

6.90—7.60 (7H, m)

Infrared absorption spectrum:

3390, 2995, 1490, 1420, 1220, 765 (cm^{-1})

2) In 20 ml. of dimethyl sulfoxide was dissolved 2.0 g of crude α-(2,2′-difluoro-4-biphenyl)ethyl alcohol. The resultant solution was subjected to reaction at 170°C for 28 hours. After cooling, the reaction solution was poured into 100 ml. of water, extracted with ethyl ether, washed with water, and then dried with calcium sulfate. The ethyl ether was distilled off under reduced pressure, and the residue was subjected to silica gel column chromatography, whereupon 1.12 g of 2,2′-difluoro-4-vinylbiphenyl were obtained.

Yield: 61 mole %

m.p.: 40.5—41.5°C

Infrared spectrum:

1487, 1419, 1223, 762 (cm^{-1})

Nuclear magnetic resonance spectrum ($CDCl_3$) δ (ppm)

5.32 (1H, dd)

5.81 (1H, dd)

6.72 (1H, dd)

6.95—7.63 (7H, m)

WHAT WE CLAIM IS:—

1. A process for the preparation of an α-aryl propionic acid and/or an ester thereof represented by the general formula (A):

$$R^1—\underset{\displaystyle COOR^2}{\underset{|}{CH}}—CH_3 \qquad (A)$$

wherein R^1 stands for an isobutylphenyl, a phenoxyphenyl, a benzoylphenyl, a mono- or dihalo biphenylyl, a xanthenyl, a fluorenyl or a biphenylenyl radical, and R^2 stands for hydrogen or a C_1—C_4 alkyl radical,

which comprises reacting an aryl ethylene represented by the general formula (C):

$$R^1—CH=CH_2 \qquad (C)$$

wherein R^1 is as defined above,

with carbon monoxide under pressure in the presence of a carbonylation catalyst and in the presence of water and/or a lower alcohol of the formula: R^2OH, where R^2 is a C_1—C_4 alkyl radical, thereby to carbonylate the aryl ethylene into the α-aryl propionic acid and/or ester thereof.

2. A process as claimed in Claim 1, in which the aryl ethylene starting material has been produced by dehydration of the corresponding α- or β- aryl ethyl alcohol.

3. A process as claimed in Claim 1, in which the aryl ethylene starting material has been produced by dehydrohalogenation of the corresponding α- or β- aryl ethyl halide.

4. A process as claimed in any one of Claims 1 to 3, in which the aryl ethylene is carbonylated over a carbonylation catalyst which comprises a complex of from zero- to bivalent palladium.

5. A process as claimed in Claim 4, in which the complex of bivalent palladium has the general formula: PdZ_2L_2 wherein Z is a halogen atom and L is a ligand consisting of a trivalent phosphorus compound, a π-allyl group, an amine, a nitrile, an oxime, an olefin or carbon monoxide.

6. A process as claimed in Claim 5, in which the complex of bivalent palladium has the general formula PdZ_2L_2 wherein Z is chlorine, bromine or iodine, and L is a phosphorus compound having a hydrocarbon radical consisting of an aromatic hydrocarbon radical having from 6 to 12 carbon atoms or an aliphatic hydrocarbon radical having from 3 to 10 carbon atoms.

7. A process as claimed in Claim 6, in which the phosphorus compound is a phosphine.

8. A process as claimed in any of Claims 1 to 7, in which the aryl ethylene is carbonylated in the presence of an alcohol to produce an ester of the α- aryl propionic acid.

9. A process as claimed in Claim 8, in which the ester is further subjected to hydrolysis to produce an α- aryl propionic acid.

10. A process as claimed in Claim 8, in which the aryl ethylene is carbonylated in the presence of a carbonylation catalyst which comprises a complex of from zero- to bivalent palladium at a temperature of from 100°C to 250°C and under a carbon monoxide pressure of from 90 to 800 atmospheres.

11. A process as claimed in Claim 8, in which the aryl ethylene is carbonylated in the presence of a carbonylation catalyst which comprises a complex of from zero- to bivalent palladium in the presence of hydrogen chloride, boron trifluoride or boron trifluoride etherate.

12. A process as claimed in Claim 8, in which the aryl ethylene is carbonylated in the presence of a carbonylation catalyst which comprises a complex of from zero- to bivalent palladium in the presence of hydrogen chloride in a quantity of 1 to 20 percent by weight of the alcohol at a temperature of 40 to 150°C and under a carbon monoxide pressure of 100 to 800 atmospheres.

13. A process as claimed in Claim 8, in which the aryl ethylene is carbonylated in the presence of a carbonylation catalyst which comprises a complex of from zero- to bivalent palladium in the presence of boron trifluoride or an etherate thereof in a quantity of 0.8 to 15 moles per mole of the complex of palladium at a temperature of 40 to 120°C and under a carbon monoxide pressure of 10 to 150 atmospheres.

14. A process as claimed in any of Claims 1 to 7 in which the aryl ethylene is carbonylated in the presence of water to produce the α- aryl propionic acid.

15. A process as claimed in Claim 14, in which the aryl ethylene is carbonylated in the presence of a carbonylation catalyst which comprises a complex of from zero- to bivalent palladium in the presence of hydrogen chloride in a quantity of 1 to 20 percent by weight of the water at a temperature of 40 to 150°C and under a carbon monoxide pressure of 100 to 800 atmospheres.

16. A process as claimed in Claim 14, in which the α- aryl propionic acid consists of α-(4'-fluoro-4-biphenylyl) propionic acid, α-(3'-fluoro-4-biphenylyl) propionic acid, α-(2'-fluoro-4-biphenylyl)propionic acid, α-(2-fluoro-4-biphenylyl)-propionic acid α-(2,2'-difluoro-4-biphenylyl)propionic acid, α-(4-phenoxyphenyl)-propionic acid, α-(3-phenoxyphenyl)propionic acid, α-(4-benzoylphenyl)propionic acid, α-(3-benzoylphenyl)propionic acid, α-(2-xanthenyl)propionic acid, α-(2-fluorenyl)propionic acid, α-(2-biphenylenyl)propionic acid or α-(4-isobutylphenyl)-propionic acid.

17. A process as claimed in any of Claims 1 to 7, in which the aryl ethylene consists of 4'-fluoro-4-vinylbiphenyl, 3'-fluoro-4-vinylbiphenyl, 2'-fluoro-4-vinyl-biphenyl, 2-fluoro-4-vinylbiphenyl, 2,2'-difluoro-4-vinylbiphenyl, 4-phenoxy-

styrene, 3-phenoxystyrene, 4-vinylbenzophenone, 3-vinylbenzophenone, 2-vinylxanthene, 2-vinylfluorene, 2-vinylbiphenylene, or 4-isobutylstyrene.

18. A process as claimed in any of Claims 1 to 17, in which the aryl ethylene is produced by dehydration or dehydrohalogenation of an α- or β- aryl ethyl alcohol or an α- or β- aryl ethyl halide represented by the general formula (B):

$$R^1—CH(X)—CH_2(Y)$$

wherein R^1 stands for an isobutylphenyl, a phenoxyphenyl, a benzoylphenyl, a mono- or dihalo biphenylyl, a xanthenyl, a fluorenyl or a biphenylenyl radical, and one of X and Y stands for hydrogen and the other for hydroxyl or a halogen atom consisting of chlorine, bromine or iodine.

19. A process as claimed in Claim 18, in which the α- or β-aryl ethyl alcohol is heated in the liquid phase to dehydrate the alcohol.

20. A process as claimed in Claim 18, in which the α- or β- aryl ethyl alcohol is contacted in the vapour phase with a dehydration catalyst consisting of activated alumina or a caustic alkali to dehydrate the alcohol.

21. A process as claimed in Claim 18, in which the α- or β- aryl ethyl alcohol consists of α- or β-(2,2'-difluoro-4-biphenylyl)ethyl alcohol, α- or β-(3'-fluoro-4-biphenylyl)ethyl alcohol, α- or β-(4'-fluoro-4-biphenylyl)ethyl alcohol, α- or β-(4-phenoxyphenyl)ethyl alcohol, α- or β-(3-fluoro-4-biphenylyl)-ethyl alcohol, α- or β-(2'-fluoro-4-biphenylyl)-ethyl alcohol, α- or β-(3-phenoxyphenyl)ethyl alcohol, α- or β-(4-isobutylphenyl)ethyl alcohol, α- or β-(2-fluoro-4-biphenylyl)-ethyl alcohol, α- or β-(4-benzoylphenyl)ethyl alcohol, α- or β-(3-benzoylphenyl)ethyl alcohol, α- or β-(2-xanthenyl)ethyl alcohol, α- or β-(2-fluorenyl)ethyl alcohol or α- or β-(2-biphenylenyl)ethyl alcohol.

22. A process as claimed in Claim 18, in which the α- or β- aryl ethyl halide is heated in the liquid phase in the presence of a base to dehydrohalogenate the halide.

23. A process as claimed in Claim 22, in which the base consists of pyridine, quinoline, piperidine, piperazine, aniline, N,N-dimethyl-aniline, sodium hydroxide or potassium hydroxide.

24. A process as claimed in Claim 18, in which the α- or β- aryl ethyl halide is passed through a bed of a molten secondary or tertiary amine hydrochloride to dehydrohalogenate the halide.

25. A process as claimed in Claim 24, in which the secondary or tertiary amine consists of diamylamine, triamylamine, dihexylamine or trihexylamine.

26. A process as claimed in Claim 18, in which the α- or β- aryl ethyl halide consists of α- or β-(4-benzoylphenyl)ethyl chloride, α- or β-(2-fluoro-4-biphenylyl)-ethyl bromide, α- or β-(2-chloro-4-biphenylyl)ethyl chloride, α- or β-(2-xanthenyl)-ethyl bromide, α- or β-(3-benzoylphenyl)ethyl chloride, α- or β-(2-fluorenyl)ethyl bromide, α- or β-(4-isobutylphenyl)ethyl chloride, α- or β-(4'-fluoro-4-biphenylyl)-ethyl chloride, α- or β-(3'-fluoro-4-biphenylyl)ethyl chloride, α- or β-(2'-fluoro-4-biphenylyl)ethyl chloride, α- or β-(2,2'-difluoro-4-biphenylyl)ethyl chloride, α- or β-(4-phenoxyphenyl)ethyl chloride, α- or β-(3-phenoxyphenyl)-ethyl chloride, or α- or β-(2-biphenylenyl)ethyl chloride.

27. A process for producing α- aryl propionic acids and/or esters thereof substantially as herein described with reference to any of the specific Examples 1 to 12 and 17 to 20.

28. α- Aryl propionic acids and/or esters thereof when produced by a process as claimed in any of Claims 1 to 27.

ELKINGTON AND FIFE,
Chartered Patent Agents,
High Holborn House,
52—54 High Holborn,
London WC1V 6SH.
Agents for the Applicants.

Printed for Her Majesty's Stationery Office by the Courier Press, Leamington Spa, 1980.
Published by the Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.