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ABSTRACT OF THE DISCLOSURE

A method is provided for the preparation of ibuprofen by carbonylating 1-(4'-isobutylphenyl)ethanol (IBPE) with carbon monoxide in an acidic aqueous medium, e.g. containing at least 10% of water based on the weight of IBPE initially added, at a temperature of at least about 10°C and a carbon monoxide pressure of at least about 500 psig, and in the presence of (1) a catalyst complex consisting essentially of a palladium compound in which the palladium has a valence of zero to 2 and is complexed with at least one monodentate phosphine ligand miscible with the organic phase of the reaction medium, the phosphorus/palladium mole ratio in said palladium compound and ligand being at least about 2:1 when the palladium/IBPE mole ratio is such that palladium=1 and IBPE=10,000 or more; (2) dissociated hydrogen ions from an acid which is substantially completely ionizable in dilute aqueous solution such that the mole ratio of hydrogen ions to IBPE added to the reaction zone is at least about 0.15; and, (3) dissociated halide ions such that the mole ratio of halide ions to IBPE added to the reaction zone is at least about 0.15. Advantageously, a hydrogen halide is the source of hydrogen ions and halide ions. The carbonylation is preferably integrated with a method of producing IBPE from isobutylbenzene wherein the latter compound is subjected to Friedel-Crafts reaction with an acetylating agent to produce 4-isobutylacetophenone, which is then reduced with hydrogen in the presence of a hydrogenation catalyst, or with a reducing agent containing available hydrogen, to obtain IBPE.

The palladium catalyst complex can be precipitated from an organic phase of the carbonylation reaction which typically includes the ibuprofen product. The precipitated catalyst complex can be recycled without further treatment.

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