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Efficient Metallo-Ene Reactions in Organoaqueous Phase

Supporting Information :
General experimental procedures for metallo-ene reactions.
All manipulations were carried out under nitrogen using a dry box ($Ni(COD)_2$) and Schlenk techniques. $PdCl_2$, $NiCl_2.6H_2O$ and $Ni(OAc)_2$ were purchased from Aldrich. $[Rh(COD)Cl]_2$ and $Ni(COD)_2$ were purchased from Strem. TPPTS was generously given by Rhodia, France as a water-solution (30% in weight). Water, tetrahydrofuran, ethanol and dioxane were degassed by sparging with nitrogen and/or exposure to vacuum. Column chromatography was performed with E. Merck 0.040-0.063 mm Art. 11567 silica gel.

Pd-catalyzed ene-reaction : $Pd(TPPTS)_2$ was preformed in water (2.5ml/mmol Pd) by mixing 10 mol% $PdCl_2$ and 30 mol% TPPTS at 60°C during 30 minutes. To the red colored catalyst was added a dioxane (1.5 ml / mmol) solution of the substrate. The homogeneous mixture was heated at 60°C until completion of the reaction (TLC) and then at room diluted in water. The aqueous phase was extracted three times with ether. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. Products were purified by chromatography on silica gel with the appropriate eluent.

Rh-catalyzed ene-reaction : $RhCl(TPPTS)_3$ was prepared by adding a solution of $[Rh(COD)Cl]_2$ in degassed THF to a mixture of TPPTS (20 mol%) and NaCl (47 mg / mmol) in water (0.5 ml/mmol). The resulting solution was stirred 15 minutes at room temperature and THF was then evaporated under high vacuum. Another 40 mol% of TPPTS was then added and the red catalyst was formed overnight at room temperature. A dioxane solution of the substrate (4 ml/mmol) was added and the mixture was heated at 60°C until completion (TLC) and then at room diluted in water. The aqueous phase was extracted three times with ether. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. Products were purified by chromatography on silica gel.

Ni-catalyzed ene-reaction : $Ni(TPPTS)_3$ was prepared according to two different procedures.
From Ni(II) : to a solution of $NiCl_2.6H_2O$ or $Ni(OAc)_2$ (10 mol%) and TPPTS (50 mol%) in a 5/3 ethanol/water mixture (27 ml/mmol Ni) at –10°C was slowly added a solution of $NaBH_4$ (3 equiv. / Ni) in a 1/1 mixture ethanol/water (3.4 ml/mmol). The reddish resulting mixture was allowed to come back to room temperature and stirred three hours. Ethanol was evaporated under high vacuum.
From Ni(0) : a mixture of $Ni(COD)_2$ (10 mol%) and TPPTS (50 mol%) was heated at 80°C in water (17 ml/mmol) during 30 minutes.
Ene-reaction : a solution of the substrate in dioxane (1.7 ml/mmol) was added *via* cannula to the red catalyst. The homogeneous solution was stirred overnight at room temperature and then filtered through a bed of Florisil® (100-200 mesh) using ethyl acetate as eluent. After evaporation under vacuum, the crude product was purified by chromatography on silica gel.

Examples of $Ni(COD)_2$/TPPTS catalysis :
Cyclization of dimethyl 2-(4-acetoxybut-2-enyl)-2-prop-2-enyl)propanedioate **2a**
To a solution of $Ni(COD)_2$ (20 mg) and TPPTS (688 mg of water-solution corresponding to 206 mg of TPPTS and 0.48 ml H_2O) in water (0.72 ml) preheated at 80°C during 30 minutes, was added at room temperature a solution of **2a** in dioxane (1.2 ml). The easy work-up gave 152 mg (92%) of the desired compound.
Cyclization under anhydrous conditions was only performed with palladium catalyst, AcOH at 80°C, giving **5a** with 77% yield : Oppolzer, W. *Pure and Appl. Chem.* **1988**, *60*, 39.

Cyclization of 5,5'-bis(phenylsulfonyl)octa-2,7-dienyl acetate **2b**
To a solution of $Ni(COD)_2$ (6.6 mg) and TPPTS (46 mg of water-solution corresponding to 14 mg of TPPTS and 0.03 ml H_2O) in water (0.37 ml) preheated at 80°C during 30 minutes, was added at room temperature a solution of **2b** in dioxane (0.4 ml). The easy work-up gave 62 mg (65%) of the desired compound.

Cyclization under anhydrous conditions was performed with nickel catalyst, at room temperature, giving **5b** with 83% yield : Oppolzer, W.; Bedoya-Zurita, M.; Switzer, C.Y. *Tetrahedron Lett.* **1988**, *29*, 6433.