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Catalytic Transfer Reduction of Electron Deficient Alkenes and an Imine Using Potassium Formate and Catalytic Palladium Acetate

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Abstract. Chemoselective reduction of α, β-unsaturated cyanostannyl esters, ketones and an imine with potassium formate as hydrogen donor and palladium acetate as homogeneous catalyst in DMF was observed to proceed readily with saturation of C-C and C-N double bonds, without any concomitant reduction of cyano, carboxylate, halogen or carbonyl groups and demetallation.

Keywords: catalytic transfer hydrogenation, potassium formate, palladium acetate, electron deficient alkenes, catalytic transfer, catalytic reduction, chemoselective hydrogenation, transition metal-hydrides

Introduction

Homogeneous hydrogenation of unsaturated compounds with transition-metal complexes proceeds in a stepwise manner *via* metal hydride species. Molecular hydrogen readily reacts with various transition-metal complexes resulting in metal monohydrides or dihydrides. Chemoselective hydrogenation of carbon-carbon multiple bonds in conjugated carbonyl functions has been a long desired synthetic transformation. In terms of chemoselectivity and regio- and stereocontrol, transition-metal hydrides offer a number of advantages over the more traditional methods of catalytic hydrogenation (Augustin, 1965) and dissolving metal reduction methods (House, 1972). Despite the bewildering variety of reducing agents available for synthetic chemistry, new and ever more selective reductants are in constant demand. In many cases, the carbon-carbon multiple bonds can be carried out by means of a hydrogen donor. This process is termed as catalytic transfer hydrogenation (Zassinovich *et al.*, 1992). The transition-metal catalyzed hydrogen transfer reaction, with the aid of hydrogen donors such as trialkylammonium formate (Cortese and Heck, 1978), n-Bu_3SnH (Keinan and Gleiz, 1982), $Ph_2SiH_2/ZnCl_2.H_2O$ (Keinan and Greenspoon, 1986), triethoxysilane and H_2O (Tour *et al.*, 1990), and NaH_2PO_2/H_2O (Sala *et al.*, 1984) are some of the examples employed for selective conjugate reduction. Sodium salts of formic acid, phosphinic acid and phosphorous acid have also been reported as hydrogen donors in catalytic transfer hydrogenation (Johnstone *et al.*, 1985). Conjugate reduction of α, β-unsaturated cyano esters to the corresponding saturated cyano esters in the presence of $HCOOK/Pd(OAc)_2$ has been recently reported by research group of the present author (Basu *et al.*, 2003a). That line of research was further investigated by using a new series of electron deficient alkenes, which possessed other sensitive functional groups and an imine, the results of which study are reported here.

Materials and Methods

The ^1H- and ^{13}C-NMR were measured on Bruker AC 200 spectrometer using $CDCl_3$ as the solvent, and chemical shifts were expressed as 'δ' values in ppm against TMS as an internal standard. Silica gel thin layer chromatography was routinely used to check the purity of the compounds. The TLC spots were exposed in iodine vapours for visualization.

General method for the preparation of compound 2 (unsaturated stannyl esters). Unsaturated cyanoesters (compound **1**, 5 mmol) and *bis*-tri-*n*-butyltin oxide (5 mmol) in toluene (40 ml) was refluxed for 12-14 h. The solvent was then evaporated *in vacuo* and the crude product was purified by column chromatography.

Tri-*n*-butylstannyl 2-cyano-3-(4-methoxyphenyl)acrylate, compound 2a. Viscous liquid; yield: 84%. ^1H NMR ($CDCl_3$): δ 7.88 (s, 1H), 7.71 (d, 2H, J = 6.6 Hz), 6.8 (d, 2H, J = 6.6 Hz), 3.62 (s, 3H), 1.69 (m, 6H), 1.35 (m, 12H), 0.95 (t, 9H, J = 6.6 Hz).

Tri-*n*-butylstannyl 2-cyano-3-(4-hydroxyphenyl)acrylate, compound 2b. Viscous liquid; yield: 80%. ^1H NMR ($CDCl_3$): δ 8.12 (s, 1H), 7.90 (d, 2H, J = 8.73 Hz), 6.99 (d, 2H, J = 8.73 Hz), 1.70 (m, 6H), 1.37 (m, 12H), 0.92 (t, 9H, J = 6.6 Hz).

Tri-*n*-butylstannyl 2-cyano-3-(4-chlorophenyl)acrylate, compound 2c. Viscous liquid; yield: 75%. ^1H NMR ($CDCl_3$): δ 8.21 (s, 1H), 7.74 (d, 2H, J = 8.6 Hz), 7.49 (d, 2H, J = 8.6 Hz), 1.71 (m, 6H), 1.39 (m, 12H), 1.00 (t, 9H, J = 6.6 Hz).

Tri-*n*-butylstannyl 2-cyano-3-(furan-2-yl)acrylate, compound 2d. Viscous liquid; yield: 76%. ^1H NMR ($CDCl_3$): δ

8.03 (s, 1H), 7.76 (d, 1H, *J* = 1.6 Hz), 7.40 (d, 1H, *J* = 4.0 Hz), 6.88 (dd, 1H, *J* = 4.0; 1.6 Hz), 1.69 (m, 6H), 1.37 (m, 12H), 0.98 (t, 9H, *J* = 6.6 Hz).

Tri-*n*-butylstannyl 2-cyano-3-phenyl-2-butenoate, compound 2e. Viscous liquid; yield: 75%. ^{1}H NMR ($CDCl_3$): δ 7.60 (m, 5H), 2.60 (s, 3H), 1.70 (m, 6H), 1.32 (m, 12H), 0.96 (t, 9H, *J* = 6.6 Hz).

General method for the preparation of compound 4 (chaleones). To a solution of NaOH (0.8 g) in water (8 ml) and rectified spirit (5 ml), immersed in a bath of crushed ice, acetophenone (15 mmol) was added. Then, aromatic aldehyde (15 mmol) was added dropwise. The temperature of the mixture was maintained at 25 °C and stirred vigorously for 3 h. The reaction mixture was kept in a refrigerator, overnight. The product was filtered with suction on Buckner funnel, washed with cold water until the washings were neutral to litmus. The solid was recrystallized from rectified spirit.

1-(4-Chlorophenyl)-3-(furan-2-yl)-2-propen-1-one, compound 4a. Yellow crystals; yield: 80%; m. p. 83-84 °C. IR 3129, 3083, 1747, 1655, 1598, 1475, 1409, 1301, 1224 cm^{-1}.

1-(4-Bromoorophenyl)-3-(4-methoxyphenyl)-2-propen-1-one, compound 4b. Yellow crystals; yield: 72%; m. p. 143-144 °C. IR 3012, 2935, 1670, 1588, 1465, 1337, 1301 cm^{-1}.

General method for the preparation of compounds 3, 5 and 7 (saturated derivatives of electron deficient alkenes). To a solution of compounds **2** or **4** or **6** (electron deficient alkenes, compounds **2** or **4**; imine, compound **6**; 2 mmol) in DMF (5 ml), $Pd(OAc)_2$ (2 mol%) and HCOOK (4 mmol) were added and stirred in a sealed tube (screw-cap) under nitrogen at 45 °C for 3-4 h. After cooling, the mixture was diluted with water and then extracted with ether (3 x 20 ml). The solvent was evaporated and the residue was purified by column chromatography on silica gel eluting with petroleum ether/ethyl acetate (80 : 20).

Tri-*n*-butylstannyl 2-cyano-3-(4-methoxyphenyl) propionate, compound 3a. Viscous liquid; yield: 85%. IR 2225, 1750 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.96 (d, 2H, *J* = 8.73 Hz), 6.97 (d, 2H, *J* = 8.73 Hz), 3.83 (s, 3H), 3.76 (dd, 1H, *J* = 8.3; 6.06 Hz), 3.22 (m, 2H), 1.66 (m, 6H), 1.37 (m, 12H), 0.93 (t, 9H, *J* = 7.23 Hz). ^{13}C NMR ($CDCl_3$): δ 163.5, 153.2, 133.2, 129.9, 125.2, 114.7, 55.6, 47.8, 28.3, 27.9, 27.1, 17.0, 13.8.

Tri-*n*-butylstannyl 2-cyano-3-(4-hydroxyphenyl) propionate, compound 3b. Viscous liquid; yield: 82%. IR 2242, 1742 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 6.94 (d, 2H, *J* = 8.40 Hz), 6.83 (d, 2H, *J* = 8.40 Hz), 3.73 (dd, 1H, *J* = 8.1; 5.8 Hz), 3.16 (m, 2H), 1.68 (m, 6H), 1.39 (m, 12H), 0.92 (t, 9H, *J* = 7.23 Hz). ^{13}C NMR ($CDCl_3$): δ 166.1, 154.4, 133.6, 130.4, 129.8, 116.5, 63.2, 40.2, 35.2, 27.5, 17.1, 13.7.

Tri-*n*-butylstannyl 2-cyano-3-(4-chloroyphenyl) propionate, compound 3c. Viscous liquid; yield: 86%. IR 2372, 1745, 1674, 1495 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.90 (d, 2H, *J* = 8.60 Hz), 7.40 (d, 2H, *J* = 8.60 Hz), 3.69 (dd, 1H, *J* = 8.0; 5.9 Hz), 3.20 (m, 2H), 1.70 (m, 6H), 1.40 (m, 12H), 0.93 (t, 9H, *J* = 7.22 Hz). ^{13}C NMR ($CDCl_3$): δ 166.1, 138.7, 132.0, 130.5, 129.5, 116.4, 62.8, 37.3, 37.1, 27.8, 17.2, 13.7.

Tri-*n*-butylstannyl 2-cyano-3-(furan-2-yl)propionate, compound 3d. Viscous liquid; yield: 84%. IR 2244, 1747 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.91 (s, 1H), 7.67 (s, 1H), 6.60 (s, 1H), 3.79 (m, 1H), 3.28 (m, 2H), 1.67 (m, 6H), 1.38 (m, 12H), 0.91 (t, 9H, *J* = 7.22 Hz). ^{13}C NMR ($CDCl_3$): δ 166.8, 149.4, 147.7, 120.4, 116.8,113.9, 63.3, 37.3, 28.1, 27.4, 17.4, 14.0.

Tri-*n*-butylstannyl 2-cyano-3-phenylbutanoate, compound 3e. Viscous liquid; yield: 75%. IR 2242, 1746, 1594, 1446,1250 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.42 (m, 5H), 3.65 (m, 1H), 3.52 (m, 1H), 1.72 (m, 6H), 1.50 (d, 3H, *J* = 7.0 Hz), 1.38 (m, 12H), 0.92 (t, 9H, *J* = 7.22 Hz).

1-(4-Chlorophenyl)-3-(furan-2-yl)propanone, compound 5a. Viscous liquid; yield: 80%. IR 1726, 1685, 1598, 1450, 1363, 1214 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.97 (d, 2H, *J* = 7.8 Hz), 7.47 (d, 2H, *J* = 7.8 Hz), 7.57 (m, 1H), 7.44 (m, 1H), 7.31 (m, 1H), 3.34 (t, 2H, *J* = 7.8 Hz), 3.09 (t, 2H, *J* = 7.8 Hz). ^{13}C NMR ($CDCl_3$): δ 198.6, 154.7, 141.1, 136.6, 133.1, 128.6, 128.0, 110.2, 105.3, 36.9, 22.4.

1-(4-Bromoorophenyl)-3-(4-methoxyphenyl)propanone, compound 5b. Yellow crystals; yield: 82%; m. p. 67-68 °C. IR 2991, 2940, 1680, 1603, 1505, 1450, 1378, 1301, 1240 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.94 (d, 2H, *J* = 7.2 Hz), 7.43 (d, 2H, *J* = 7.2 Hz), 7.14 (d, 2H, *J* = 8.5 Hz), 6.83 (d, 2H, *J* = 8.5 Hz), 3.76 (s, 3H), 3.24 (t, 2H, *J* = 7.2 Hz), 3.00 (t, 2H, *J* = 7.2 Hz). ^{13}C NMR ($CDCl_3$): δ 201.1, 159.7, 138.6, 135.0, 134.7, 131.1, 130.3, 129.8, 115.7, 57.0, 42.4, 31.0.

Tri-n-butylstannyl butanoate, compound 5c. Viscous liquid; yield: 65%. ^{1}H NMR ($CDCl_3$): δ 1.67 (m, 10H), 1.59 (t, 3H, *J* = 7.32 Hz), 1.37 (m, 12H), 0.93 (t, 9H, *J* = 7.32 Hz). ^{13}C NMR ($CDCl_3$): δ 166.6, 27.8, 26.8, 17.5,13.6.

Benzylaniline, compound 7. Colourless oil; yield: 70%. ^{1}H NMR ($CDCl_3$): δ 7.50 (m, 5H), 7.31 (m, 5H), 4.22 (br, 1H), 3.80 (s, 2H).

Results and Discussion

A series of α, β-unsaturated cyano esters, compounds **1**, have been prepared from their carbonyl substrates condensed with ethyl cyanoacetate under Knoevenagel condition (Furniss *et al.,* 1989). The unsaturated stannyl esters (compounds, **2a-e**) were prepared by transesterification method (Deb and Basu, 1993a) from their corresponding esters, compounds **1**, by treating with *bis*-tri-*n*-butyltin oxide in refluxing toluene. All the stannyl esters were obtained in pure form after chromatography in good to excellent yields and were characterized by spectral analyses.

Chalcones (compounds, **4a-b**) were prepared by base catalyzed condensation reaction of aldehyde with the appropriate acetophenone derivative, in accordance with the reported procedure (Furniss *et al.,* 1989).

Catalytic transfer reduction of electron deficient alkenes (compounds, **2a-e; 4a-c**) and imine (compound **6**) using potassium formate and catalytic palladium acetate in DMF under nitrogen afforded the corresponding saturated derivatives, (compounds **3**, **5** and **7**) in good to excellent yields, respectively as schematically shown in Fig. 1. The structures were characterized from their ^{1}H- and ^{13}C-NMR spectral data. Compounds **5a-b** were comparable with the data reported in literature (Basu *et al.,* 2003b).

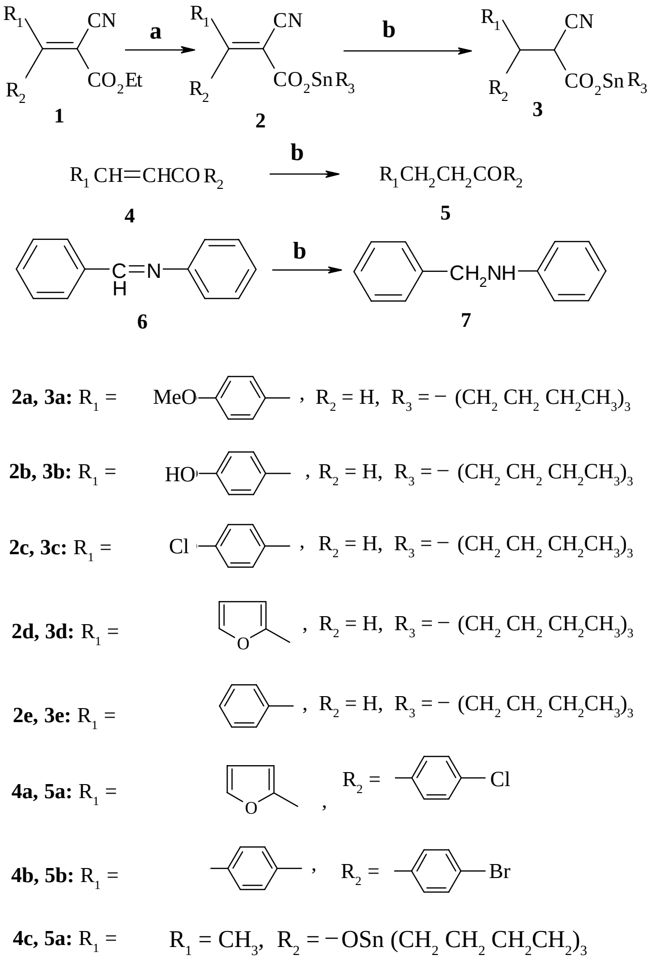

Fig. 1. Schematic presentation of reduction of electron deficient alkenes and an imine using less expensive reagents: **(a)** (n-$Bu_3Sn)_2O$, toluene, reflux; **(b)** HCOOK, $Pd(OAc_2)$, DMF, 45-55 °C, 3 - 4 h.

Although dehalogenation of haloaromatics is known under transfer reduction using heterogeneous catalyst (Entwistle *et al.,* 1977), the present method did not proceed with cleavage of carbon-halogen bond. Furthermore, conjugated cyano esters have been repotred to often reduce to the saturated cyano alcohols (Marshal and Carroll, 1965), however, the stannyl esters survived demetallation under the reaction conditions (Deb and Basu, 1993b). Moreover, reduction of conjugated nitriles and cyanoesters using molecular hydrogen or Pd-catalyzed hydride transfer afforded with reduction of cyano group as well (Brieger and Nestric, 1974). Thus, the reduction of electron deficient alkenes can be accomplished with less expensive HCOOK and $Pd(OAc)_2$ without affecting the reduction of any reducible substituents. The yields are virtually quantitative and analytically pure. The obvious advantages of the presently reported method over those reported previously are: (i) selective reduction of C-C and C-N double bonds, in the presence of other reducible groups, (ii) easy to operate, (iii) rapid reduction, (iv) no requirement of pressure apparatus, and (v) less expensive.

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