(hydrocarbon internal standards) which showed that ca. 10% of the former nitrile and ca. 15-20% of the latter nitrile were lost. The weight losses which occurred as a result of these reactions suggested that the products of these reactions were water soluble. Similar treatment of isobutyronitrile and pivalonitrile gave principally water soluble products, and IR and GLC analyses of the small amounts of organic products from these nitriles showed the absence of starting materials.

Conversion of Phenylacetonitrile to Benzonitrile. To a solution of 1.76 g (15 mmol) of phenylacetonitrile in 30 mL of CCl$_4$ was added 2.7 g of *N*-bromosuccinimide (NBS) and 25 mg of benzoyl peroxide. This solution was heated at reflux in the presence of a sunlamp for 30 min, the succinimide was removed, and the solution was concentrated to a yellow oil. This oil was added dropwise over a period of ca. 5 min to a solution of 3 g of sodium azide in 50 mL of Me$_2$SO at room temperature. The solution was stirred for 15 min, poured into 1% NaOH solution, and extracted with pentane. The organic layer was dried, concentrated, and distilled to give 1.28 g (80%) of benzonitrile which was identified by comparison with an authentic sample.

Acknowledgment. P. E. Nicholas thanks the Gillette Corp. for a fellowship.

New Hydrogenation Catalyst: Palladium-Poly(ethylenimine) "Ghosts". Applications in Peptide Synthesis

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Received February 5, 1980

Polymer "ghosts" are made in a three-step process: (1) The polymer is adsorbed to a porous inorganic bead. (2) The polymer layer is then cross-linked. (3) The inorganic core is leached out to yield a macroporous spheroid with very high surface area and functional group density.[1] Poly(ethylenimine) (PEI) "ghosts" have good mechanical and chemical stability which led us to investigate their use as a support for metal catalysts. Pd-PEI "ghosts" were made with Pd(Ac)$_2$, NaBH$_4$, and PEI "ghosts". They exhibit high catalytic activity and stability in the hydrogenolysis of the carbobenzoxy (Cbz) group. Formic acid was used as the hydrogen donor.[2] The Merrifield peptide (H-Leu-Ala-Gly-Val-OH) was synthesized in high purity by using the active ester method.

Results and Discussion

The catalytic efficiency of Pd-PEI "ghosts" is quite good when compared to that of Pd-carbon and Pd-black which are commonly used in catalytic hydrogenation in peptide synthesis and reduction of functional groups. Cbz-alanine was deblocked with formic acid as shown in Figure 1.

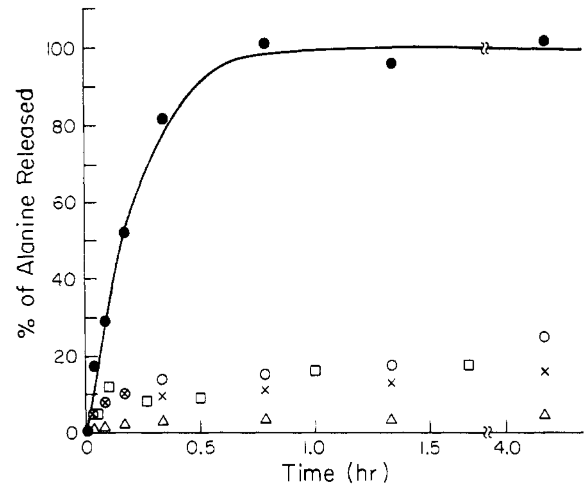

Figure 1. Rate of Pd-catalyzed hydrogenolysis of Cbz-alanine using formic acid as the hydrogen donor. Pd-PEI "ghosts", 100 mg (●); Aldrich 10% Pd on charcoal, lot no. 031597, 10 mg (□); Research Inorganic/Organic Chemical 10% Pd on charcoal, two different samples, 10 mg (X and O); Pd-black, 1 mg (Δ).

To demonstrate the utility of our catalytic system in sequential synthesis of peptides, we prepared H-Leu-Ala-Gly-Val-OH. As judged by TLC, the deblocking reactions at room temperature were complete in 20 min or less. Cbz-Leu-Ala-Gly-Val-OMe was treated with immobilized carboxypeptidase Y to hydrolyze the ester.[3] The final deblocking of the amino terminus was done by the usual procedure. The respective yields following removal of the Cbz groups were 99, 100, and 97%. Coupling yields using the formate salt of the amine component and the *N*-hydroxysuccinimide ester of the Cbz amino acids were 78, 71, and 58%. The product was judged pure by TLC: R_f 0.46 (1-BuOH-AcOH-H$_2$O 4:1:5), R_f 0.05 (CHCl$_3$-MeOH-AcOH 16:3:1), R_f 0.62 (2-BuOH-88% HCOOH-H$_2$O 15:3:2), and R_f 0.34 (2-BuOH-3% NH$_3$ 71:29). Amino acid analysis of the acid hydrolysate resulted in the following: Leu 1.02, Ala 0.99, Gly 0.96, Val 1.00. Digestion by leucine aminopeptidase[4] demonstrated the optical purity of leucine and alanine: Leu 1.00, Ala 1.03, Gly 0.99, Val 0.98. Also, C-terminal valine was released by immobilized carboxypeptidase Y (pH 6) to the extent of 95%. The optical rotation of our product was similar to that reported previously: $[\alpha]^{25}_D$ +17.8 (product, 2% in EtOH) and $[\alpha]^{25}_D$ +17.5 (lit.,[5] 2% in EtOH).

Catalytic hydrogenolysis of the Cbz group with the use of Pd-PEI "ghosts" and formic acid is convenient, rapid, and mild. The catalyst beads are mechanically stable and rapidly settle out when agitation is stopped. The storage and operational stability of the catalyst are excellent. One batch of catalyst has been used 10 times with no apparent loss of activity. Pd-PEI "ghosts" do not appear to be pyrophoric. The high activity of our catalyst compared to Pd-carbon and Pd-black may be explained by the attraction of the formic acid to the PEI matrix and/or by the distribution of palladium over a large surface area. Since the PEI matrix is easily modified, we hope to build in chiral and structural substrate specificity for other hydrogenation reactions.

Experimental Section

PEI "ghosts" were made as previously described[1] by using porous silica beads (Corning 5011-S, average pore diameter 350 Å, 40 mesh) rather than alumina. The silica core was leached by treatment with 5 N NaOH. PdCl$_2$ (1.7 g) was dissolved in 20 mL of 1 N HCl by heating to boiling. This solution was mixed with 100 mL of a sodium acetate solution (15 g NaAc·3H$_2$O/100 mL). Dry PEI "ghosts" (100 g) were added with gentle agitation and a vacuum was applied to remove trapped air from the particles. The damp "ghosts" were then added to a 1% solution of sodium borohydride in ethanol. The blackened beads were washed with 18% formic acid solution, methanol, and ether and then dried in vacuo.

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Cbz-alanine deblocking was carried out at 25 °C with either 100 mg of Pd–PEI "ghosts" (1 mg of Pd), 10 mg of the Pd–carbon samples (1 mg of Pd), or 1 mg of Pd-black in 3 mL of $HCOOH/MeOH/H_2O$ (14:28:58) containing 0.1 g of Cbz-alanine at the start of the reaction. The reaction mixture was agitated with a wrist-action shaker. The amount of free alanine was determined by amino acid analysis. Elution time was 13.8 min, using buffer B only on a Beckman 119CL amino acid analyzer.

L-Leucyl-L-alanylglycyl-L-valine. The synthesis was begun with Val-OMe. The other residues were successively added as the *N*-hydroxysuccinimide esters of the Cbz-amino acids.[6] Hydrogenolysis of the Cbz group was accomplished by using the following conditions: 1–5 mmol of peptide, 30 mL of THF, 30 mL of water, 6 mL of formic acid (97%), and about 5 g of Pd–PEI "ghosts". The reaction mixture was shaken in a round-bottom flask with a wrist-action shaker. A rotary evaporator may also be used for agitation.

Thin-layer chromatography was performed on silica gel G plates (Analtech) with $MeOH-CHCl_3$ (1:50). After development, the plates were exposed to HBr–AcOH fumes for 15 min, heated at 100 °C for 10 min, sprayed with ninhydrin, and heated for 10 min at 100 °C.

Acknowledgment. G.P.R. is a recipient of a Public Health Service Research Career Development Award. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. The financial assistance of Pierce Chemical Co. is also acknowledged.

Registry No. PEI, 9002-98-6; Cbz-alanine, 1142-20-7; L-leucyl-L-alanylglycyl-L-valine, 17195-26-5.

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Rhodium(I)-Catalyzed Biphasic Isomerization of Allylic Alcohols

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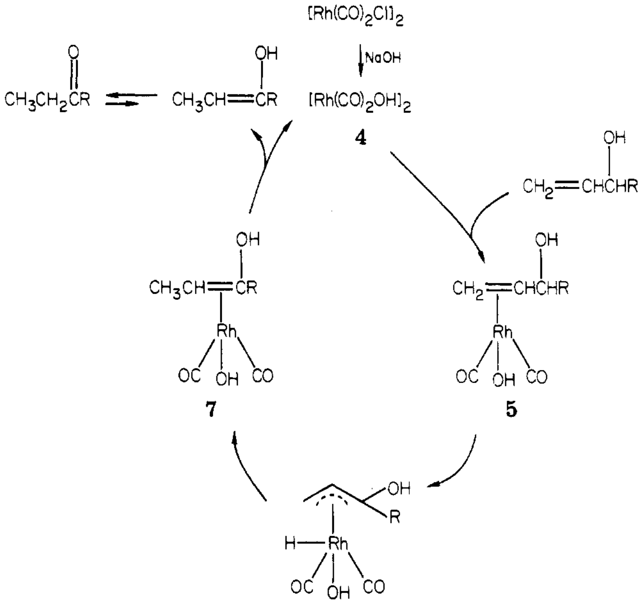
Received August 31, 1979

The isomerization of allylic alcohols to carbonyl compounds is an important reaction in organic chemistry. This transformation can be effected by thermolysis of the allyl alcohol at 302–368 °C.[1] Somewhat less drastic conditions could be used when the reaction was induced by metal species such as iron pentacarbonyl (130 °C, 16 h),[2] hydridochlorotris(triphenylphosphine)ruthenium(II) (110 °C, 1 h),[3] and hydridocarbonyltris(triphenylphosphine)rhodium(I) (70 °C, 3 h).[4] The use of 2 equiv of *n*-butyllithium also results in isomerization.[5]

Scheme I



We have been investigating the application of phase transfer catalysis to metal-catalyzed processes.[6-8] This note describes the rearrangement of allylic alcohols to carbonyl compounds under remarkably mild conditions by use of a two-phase system. This method does not generally require a phase-transfer catalyst, although the use of one results in cleaner reactions (no by-products).

Treatment of a methylene chloride solution of 1-hexen-3-ol (1) with a catalytic amount of chlorodicarbonylrhodium(I) dimer (2) (50:1 ratio of 1:2), sodium hydroxide (8 M), and benzyltriethylammonium chloride as the phase-transfer catalyst, at room temperature for 6–10 h, affords 3-hexanone (3) in quantitative yield. Repetition of the experiment in the absence of the phase-transfer catalyst resulted in a 90–93% yield of 3-hexanone. The conversion of 3-penten-2-ol to 2-pentanone also proved to

$$\underset{\mathbf{1}}{CH_2{=}CHCH(OH)CH_2CH_2CH_3} + \underset{\mathbf{2}}{[Rh(CO)_2Cl]_2} \xrightarrow[\substack{CH_2Cl_2 \\ PhCH_2N(C_2H_5)_3{}^+Cl^-}]{8\ M\ NaOH} \underset{\mathbf{3}}{C_2H_5C(O)CH_2CH_2CH_3}$$

Table I. Products Obtained from the Biphasic Rh(I)-Catalyzed Isomerization of Allylic Alcohols

allyl alcohol	$PhCH_2N(C_2H_5)_3{}^+Cl^-$	product[a]	yield, %
$CH_2{=}CHCH(OH)C_3H_7$ (**1**)	yes	$C_2H_5COC_3H_7$ (**3**)	100
	no	$C_2H_5COC_3H_7$	90–93
$CH_3CH{=}CHCH(OH)CH_3$	yes	$CH_3CH_2CH_2COCH_3$	98
	no	$CH_3CH_2CH_2COCH_3$[b]	80
$PhCH(OH)CH{=}CH_2$	no	$PhCOCH_2CH_3$	71
$PhCH{=}CHCH(OH)CH_3$	yes	$PhCH_2CH_2COCH_3$	94
$CH_3CH(OH)CH{=}CHCH(OH)CH_3$	no	$CH_3C(O)CH_2CH_2CH(OH)CH_3$[b]	58

[a] Products were identified by comparison with authentic samples. [b] An unidentified by-product was also formed.

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