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CATALYST TYPE AND CONCENTRATION DEPENDENCE IN CATALYTIC TRANSFER HYDROGENOLYSIS OF α,β -UNSATURATED CARBONYLS AND NITRILES VIA AMMONIUM FORMATE

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<u>Abstract</u>: The catalytic reduction of a variety of α , β -unsaturated compounds into saturated analogs in the presence of other reducible moieties is described using ammonium formate as a hydrogen source. The rate dependence on the concentration of Pd-C catalyst as well as on 5% Pd-BaSO₄ and Ra-Ni are also characterized.

Fast and efficient methods for chemoselective reductions are a continuing quest in synthetic chemistry.¹ Here we demonstrate the usefulness of Pd-C with ammonium formate as a catalytic hydrogen transfer agent for the reduction of α,β -unsaturated ketones, esters, and nitriles. In an accompanying communication we describe the use of temperature and solvent control for reduction of aromatic aldehydes and ketones to either alcohols or methylene derivatives.² The use of

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Substrate	Reaction time in min	Product ^a	Yield ^b X	Retention time of product ^C GC
C ₆ H ₅ CH-CHCO ₂ C ₂ H ₅ (Trans)	8	с ₆ н ₅ сн ₂ сн ₂ со ₂ с ₂ н ₅	92	6.94
CH ₃ CH=CHCO ₂ C ₂ H ₅ (Trans)	8	сн ₃ сн ₂ сн ₂ со ₂ с ₂ н ₅	91	1.26
C ₆ H ₅ CH-CHCONH ₂ (Trans)	10	с6н5сн5сн5сн5соин5	65	1.60 ^d
C2H502CCH-CHC02C2H5 (C1s)	8	с ₂ н ₅ 0 ₂ ссн ₂ сн ₂ со ₂ с ₂ н ₅	93	5.92
сн ₂ -снсо ₂ с ₂ н ₅	20	сн ₃ сн ₂ со ₂ с ₂ н ₅	88	0.95
(C6H5CH=CH)2CO	10	(C6H5CH2CH2)2CO	88	1.90 ^e
C ₆ H ₅ CH=CH-CN (Trans)	10	с ₆ н ₅ сн ₂ сн ₂ сн	92	6.23
CH ₃ CH-CHCN (Trans)	20	сн ₃ сн ₂ сн ₂ си	64	0.92
C ₂ H ₅ O ₂ CCH=CHCO ₂ C ₂ H ₅ (Trans)	5	с ₂ н ₅ 0 ₂ ссн ₂ сн ₂ со ₂ с ₂ н ₅	90	6.05
C ₆ H ₅ CH=CHCOCH ₃ (Trans)	5	с ₆ н ₅ сн ₂ сн ₂ сосн ₃	92	6.34 ^c

Table. Reduction of $\alpha\,,\beta$ -unsaturated compounds to saturated analogs using ammonium formate and Pd-C at $110^{6}C$.

^aAll products were characterized by ¹H NMR, TLC and m.p. ^bIsolated yields. ^c5% methyl silicone oil, 0V-101, column size 50 cm x 1/8", temperature programmed 50°C (3 min hold) to 275°C (5 min hold) with rate of 25°C/min, helium flow rate 30 ml min. ^dInitial column temperature 150°C. ^eInitial column temperature hold time 1 min.

ammonium formate as a catalytic hydrogen transfer agent has been reviewed³ and recently a variety of applications have been reported.⁴⁻¹⁴ For α,β -unsaturated nitroalkenes good yields of the corresponding oximes are reported in 20 min to 18 h at room temperature using ammonium formate with 5% Pd-C as the reducing system.⁴ The α,β -unsaturated carbonyls and nitriles studied here are rapidly reduced to the corresponding saturated analogs



Where R = H, alkyl, aryl, $-CO_2C_2H_5$ $R_1 = -OC_2H_5$, $-NH_2$, $-CH_3$, $-CH=CHC_6H_5$



with 10% Pd-C/HCO₂NH₄ in generally high yields within 5-20 min at 110° C as shown in the Table.

We propose the mechanism in Scheme I for this reaction although the palladium formate intermediate indicated may very well be demetallated via a concerted process involving a cyclic transition state.

In an effort to characterize and optimize this group of catalytic hydrogenolysis reactions, we have focused on the catalyst, its support and the acidity of the reaction medium. Using reduction of ethyl cinnamate as a model reaction, we have studied a variety of concentrations of Pd-C catalyst as well as



Figure 1. Conversion of ethyl cinnamate into ethyl 3-phenylpropionate using ammonium formate as the hydrogen source. All cases are in an acid medium except b. which is neutral.

Pd-BaSO₄ and Raney Nickel (Ra-Ni) for comparison. We have found reduction with 3%, 5%, or 10% Pd-C in acetic acid at 100° C is rapid and efficient, being over within 5 min. However, the rate of reaction with 1% Pd-C is considerably slower yielding only 64% product in 15 min for example. Under similar reaction conditions, conversion of ethyl cinnamate to ethyl 3-phenylpropionate with 5% Pd-BaSO₄ at 5, 10, 15, and 25 min was 49%, 69%, 89% and 100%, respectively. These results are graphically illustrated in Figure 1. In the case of Raney Nickel under similar reaction conditions, only 25% product formation was observed at 90 min. These results clearly demonstrate that Pd-C loaded at >3% is the most efficient catalyst of this series.

We have also investigated the role of acetic acid and neutral solvents for this reaction. The reduction of ethyl cinnamate in CH₃OH, for example, with 5% Pd-C and ammonium formate under reflux conditions produced the following yields of ethyl 3-phenylpropionate after 5, 8, 10, 20, and 35 min respectively: 27%, 40%, 54%, 95% and 100%. In acetic acid, however, reaction was over within 5 min. Based on the above results, we suggest Pd-C and glacial acetic acid as the choice of catalyst and solvent, respectively, for this reduction method.

These and the other results cited demonstrate that catalytic transfer hydrogenolysis by ammonium formate is rapid, chemoselective, and applicable to a variety of substrates under moderate reaction conditions. Ammonium formate also has the advantage of being readily available, inexpensive, stable, and nontoxic and can be used in conjunction with either Pd-C, Pd-BaSO₄, or Raney Nickel catalysts; although the latter two are less effective.

Experimental Section:

All chemicals and solvents were obtained from Aldrich Chemical Company and were used without further purification. ¹H NMR spectra were obtained on General Electric GN-300 MHz and GN-500 MHz spectrometers. GC analysis was carried out using a 5% methyl silicone oil, OV-101 column. Most of the reactants and products in these reactions were identified by comparison of retention time with those from commercially available authentic samples. Otherwise, identification was based on ¹H NMR, IR, and mass spectral data.

Preparation of Ethyl 3-phenylpropionate:

Since the reactions reported are similar in many aspects, a typical reaction is described as a specific example. To a stirred solution of ethyl cinnamate (0.90 g, 0.0051 mol) in glacial acetic acid (10 ml), 5% Pd-C (0.3 g) was added under an argon atmosphere, followed by the addition of ammonium formate (0.902 g, 0.0143 mol) in a single portion. The resulting mixture was stirred at 110°C and the progress of the reaction was monitored by GC analysis¹⁵ at 3-5 min intervals. At completion, the reaction mixture was cooled to room temperature and diluted with dichloromethane (80 ml), or diethyl ether. The catalyst was removed via filtration through a celite pad and the filtrate was washed with water (30 ml), and then with 7% aqueous solution of NaOH (25 ml). The organic layer was dried over Na2SO4 and filtered off. The filtrate, on evaporation under reduced pressure, gave 0.84 g of ethyl 3-phenylpropionate (92.3%) as a colorless oil. ¹H NMR spectral data and GC retention time of this laboratory synthesized material were identical with those from authentic material.

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