A convenient Pd-mediated oxidation of 4-methylbenzyl alcohol

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Abstract

A mild and convenient Pd-mediated aerobic oxidation of 4-methylbenzyl alcohol is described. We have applied the catalytic system $Pd(OAc)_2/Et_3N$ to the oxidation of 4-methylbenzyl alcohol to 4-methylbenzyaldehyde. This method has resulted effective at room temperature without oxygen or air stream and without activated molecular sieves.

Keywords

Triethylamine/ 4-Methyl benzylalcohol/ Palladium/ 4-Methylbenzaldehyde

Introduction

The oxidation of alcohols to carbonyl compounds is a fundamental and important transformation for synthetic chemists in both industry and research laboratories [1,2]. Toxic or/and corrosive co-catalysts, large amounts of additives, expensive chemicals and need of molecular sieves are among the most substantial barriers to import synthetic strategies from laboratory to industry.[3] Of the reported oxidations, basic N-donor ligands [4-6] such as Et_3N in combination with $Pd(OAc)_2$ have generally provided active catalyst. Here, we have applied the catalytic system $Pd(OAc)_2/Et_3N$ to the oxidation of 4-methylbenzyl alcohol because generally, benzylic alcohols with electron-donating groups showed good reactivity [3,7,8]. We have investigated the dependence of conversion percentage on temperature and time.

Experimental

All starting materials and reagents were commercially available and were used without further purification^{1}H NMR spectra were recorded on a BRUKER AMX-500 spectrometer in deuterated solvents. *J* values are given in Hertz. Infrared spectra were recorded as KBr pellets either on a Bio-Rad FTS 135 or a Jasco FT/IR-410 spectrophotometer in the range 4000-600 cm^{-1}. Electrospray mass spectra were recorded on a Bruker Microtof spectrometer. Elemental analyses were performed on a Carlo Erba EA 1108 analyzer.

Oxidation of 4-methylbenzyl alcohol to 4-methylbenzaldehyde. Since the oxidation of 4-methylbenzyl alcohol to 4-methylbenzaldehyde was the goal of several experiments, the experimental details of each one of them stated below.

Experiment 1: *Dependence of conversion on temperature*. Five solutions of 4-methylbenzylalcohol (30 mg, 0.25 mmol), $Pd(OAc)_2$ (6.1 mg, 0.03 mmol) and Et_3N (3.5 µl, 0.03 mmol) in tetrahydrofuran (5 mL) were stirred at 10, 20, 40, 60 and 80ºC for 16 h. The resulting orange solutions were centrifuged to separate the very fine black palladium(0) precipitate formed during the heating by palladium acetate decomposition. Then, transparent solutions were concentrated to dryness under vacuum and resulting mixtures were analyzed by NMR. The conversion percentages in obtained crudes were determined by integration of the methyl signal of 4-methylbenzaldehyde against the methyl signals of 4-methylbenzylalcohol and 4-methylbenzaldehyde.

Experiment 2: *Dependence of conversion on time at room temperature.* A solution of 4-methylbenzyl alcohol (30 mg, 0.25 mmol), $Pd(OAc)_2$ (6.1 mg, 0.03 mmol), Et_3N (3.5 µl, 0.03 mmol) in tetrahydrofuran (5 mL) was stirred at 20ºC for 24 h taking samples after 30 min, 7 h, 14 h, 16 h, 17 h and 24 h reaction for NMR monitoring. The samples were concentrated to dryness under vacuum and the obtained crude mixtures were analyzed by NMR. The conversion percentages in the resulting mixtures were determined by integration of the methyl signal of 4-methylbenzaldehyde against the methyl signals of 4-methylbenzylalcohol and 4-methylbenzaldehyde.

Experiment 3: *Dependence of conversion on* NEt_3. A solution of 4-methylbenzylalcohol (30 mg, 0.25 mmol), $Pd(OAc)_2$ (6.1 mg, 0.03 mmol) in tetrahydrofuran (5 mL) was stirred at 20ºC for 16 h. The resulting orange solution was concentrated to dryness under vacuum and the obtained crude mixture was analyzed by NMR. The conversion percentage in the resulting mixture (2%) was determined by integration of the methyl signal of 4-methylbenzaldehyde against the methyl signals of 4-methylbenzylalcohol and 4-methylbenzaldehyde. The addition to the reaction medium of Et_3N (3.5 µl, 0.03 mmol) led to 76% conversion after 16 h reaction.

4-Methylbenzaldehyde. ^1H NMR (400 MHz, DMSO): δ/ppm 9.9 (s, 1H, HCO), 7.8 (d, 2H, *J* = 8.2 Hz, 2xH-2), 7.4 (d, 2H, *J* = 8.2 Hz, 2xH-3), and 2.4 (s, 3H, CH_3). FT-IR (KBr): 1710 ν(CO) cm^{-1}. MS (ESI) 120 *m/z* (100%) $[M+H]^+$. Elemental analysis found: C 79.7; H 6.5%; calcd for C_8H_8O 80.0; H 6.7%.

Results and discussion

Sigman et al. demonstrated aerobic benzyl alcohol oxidation proceeded smoothly even at room temperature by the use of $Pd(OAc)_2$/triethylamine as catalyst system [4,5] using activated molecular sieves under a balloon pressure of oxygen. Inspired by those publications, we will explore the dependence of oxidation of 4-methylbenzyl alcohol on temperature and time without oxygen or air stream and without activated molecular sieves.

In order to establish the influence of temperature on the conversion, we have performed an experiment consisting in five reactions of 4-methylbenzylalcohol in THF charged with $Pd(OAc)_2$/Et_3N at 10, 20, 40, 60 and 80ºC for 16 h (*experiment 1*). Measuring the dependence of conversion percentage on temperature reveals a gradual increasing of the conversion from 80 to 20ºC that falls off considerably at about 10ºC. Fig. 1 shows clearly that room temperature is the most adequate for the oxidation of

4-methylbenzyl alcohol to 4-methylbenzaldehyde, obtaining at 76% conversion after 16 h reaction. ^{1}H NMR spectrum of the mixture obtained at room temperature revealed the formation as minor product of Pd(OAc)$_2$(Et$_3$N) (Fig. 2), which could be the active catalyst; in fact it was proposed as the active catalyst for the oxidation of benzylic alcohol [4,5].

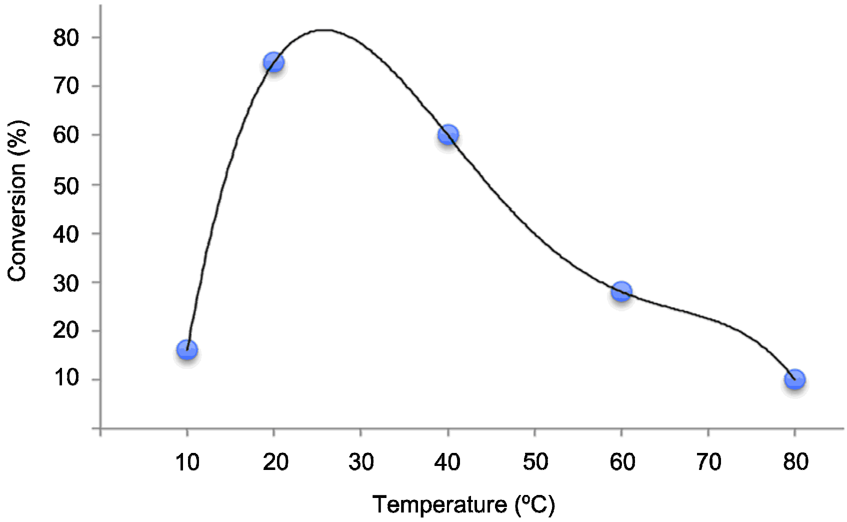

Fig. 1. Dependence of conversion percentage on temperature after 16h reaction using the catalytic system Pd(OAc)$_2$/Et$_3$N.

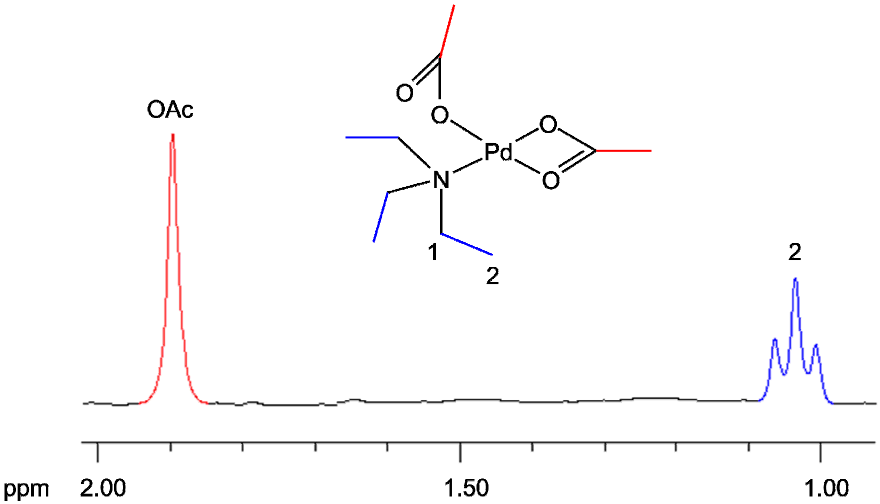

Fig. 2. Partial view of the ^{1}H NMR spectrum of Pd(OAc)$_2$(Et$_3$N). The Et$_3$N-methylene proton signals (1) are obscured by the quintuplet signal of dmso-d_6. The signals corresponding to methyl groups have been highlighted in blue (Et$_3$N-methyl) and red (OAc-methyl) colors, respectively.

We have also studied the influence of time (*experiment 2*) at 20ºC using 10 mol% of the catalytic system Pd(OAc)$_2$/Et$_3$N. Fig. 3 shows that conversion percentages increase gradually from 30 min to 24 h, although the enhancement is quite low after 16 h reaction. Since the spectroscopic detection of Pd(OAc)$_2$(Et$_3$N) in the reaction mixture appears to indicate that this palladium complex is the active catalyst at 20ºC, we have used an equimolar amount of Pd(OAc)$_2$ and Et$_3$N. This led to a 90% conversion after 24 h reaction.

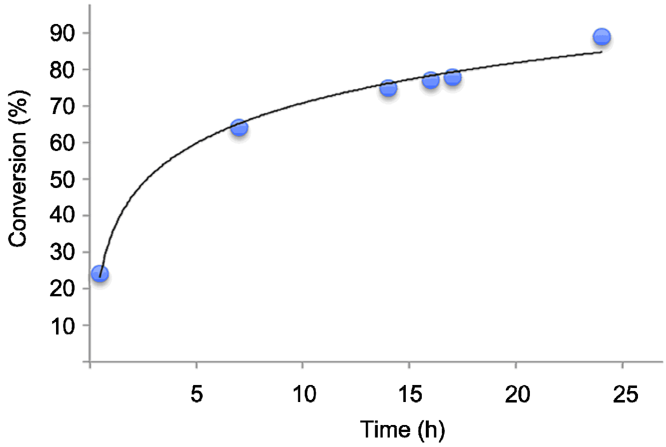

Fig. 3. Dependence of conversion percentage on reaction time using $Pd(OAc)_2/Et_3N$ at room temperature.

Finally, we have verified that Et_3N play a crucial role on the oxidation of 4-methylbenzylalcohol at room temperature (*experiment 3*). After 16 h, 4-methylbenzyl alcohol was oxidized successfully (76% conversion) using $Pd(OAc)_2/Et_3N$ (Fig. 4). In contrast, when we use $Pd(OAc)_2$ conversion percentages were very low (2%).

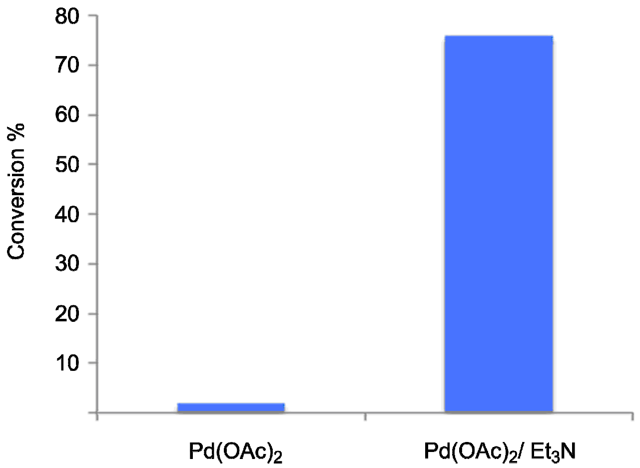

Fig. 4. Bar diagram showing the conversion at 20ºC after 16 h using $Pd(OAc)_2/Et_3N$ and $Pd(OAc)_2$ as catalytic systems.

Conclusions

A convenient aerobic alcohol oxidation, that is effective at room temperature without oxygen or air stream and without activated molecular sieves, has been developed. Using a catalyst loading of 10 mol% $Pd(OAc)_2/Et_3N$, 4-methylbenzyl alcohol can be oxidized to 4-methylbenzaldehyde achieving 90% conversion after 24 h reaction. ^{1}H NMR sepectroscopy provides evidence that the active catalyst may be $Pd(OAc)_2(Et_3N)$.

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