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Cobalt and Manganese Salts of *p*-Aminobenzoic Acid Supported on Silica Gel: A Versatile Catalyst for Oxidation by Molecular Oxygen

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Summary. A 1:1 molar ratio of the cobalt and manganese salts of *p*-amino benzoic acid supported on silica gel is an effective catalyst for the oxidation of various organic compounds in reasonable yields using molecular oxygen. The catalyst can be reused several times.

Keywords. Oxidation; Molecular oxygen; Cobalt; Manganese; Silica gel.

Introduction

Solid phase organic synthesis for preparation of various molecules has provided an attractive option for organic synthesis [1–4]. Modification of the activity and product selectivity are the characterizations of this method.

Solid supported reagents for organic reactions were first introduced by *Merrifield* [5] and *Letsinger* [6]. Easy access to the products via a simple filtration for removing unreacted materials has rendered the method very attractive. Organic compounds such as polystyrene and its analogs have long been of interest as solid supports [7, 8]. Inorganic supports such as silica gel, alumina and clays are also of interest [9, 10].

Results and Discussion

During the course of our systematic study on the catalytic oxidation of organic compounds with molecular oxygen, we have recently developed a heterogeneous catalytic method based on Co(II) and Mn(II) salts of *p*-aminobenzoic acid supported on silica gel for the oxidation of different functional organic compounds.

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Table 1. Oxidation of *Hantzsch* 1,4-*DHP* (**1a**) to pyridine (**2a**) using different Co and Mn salts ratio with molecular oxygen (all reactions in heptane at reflux temperature in 3 min; yields refer to pure isolated products)

Entry	Mn/Co Salt Ratio	Yield (%)
1	Mn only	93
2	Co only	96
3	1 : 1	98
4	1 : 2	95
5	2 : 1	92
6	1 : 5	96
7	5 : 1	94

Control experiments of oxidation of 1,4-dihydropyridine (**1a**) to pyridine (**2a**) were done under different conditions to determine the effects of cobalt and manganese salts of *p*-aminobenzoic acid supported on silica gel separately or as a mixture [11]. The best results were obtained when a mixture of 1:1 ratio of the cobalt and manganese salts were used. The results are summarized in Table 1.

In this method silica gel is activated in a pyrolysis apparatus at 260°C in 20 mm Hg to lose its water (5.7%). Then *p*-aminobenzoic acid is reacted with the activated silica gel to bind the acid to the surface of the silica gel which was verified by infrared spectrum [12].

The reaction of the acid bonded to the silica gel with sodium carbonate affords the sodium salt of the acid, which is then converted to the cobalt or manganese salts of *p*-aminobenzoic using cobalt and manganese chloride solutions. The first use of the mixture of Co(II) and Mn(II) salts of *p*-aminobenzoic acid supported on silica gel was the oxidation of alcohols by molecular oxygen to their corresponding aldehydes and ketones [12]. This oxidation method is selective and only allylic and benzylic alcoholes can be oxidized, Table 2.

Table 2. Oxidation of benzylic and allylic alcohols to carbonyl compounds (all reactions at reflux temperature; yields refer to pure isolated products)

Substrate	Product	Time (h)	Yield (%)
$C_6H_5CH_2OH$	C_6H_5CHO	27	80
$4\text{-}(OCH_3)C_6H_4CH_2OH$	$4\text{-}(OCH_3)C_6H_4CHO$	26	85
$4\text{-}(NO_2)C_6H_4CH_2OH$	$4\text{-}(NO_2)C_6H_4CHO$	30	77
$3\text{-}(NO_2)C_6H_4CH_2OH$	$3\text{-}(NO_2)C_6H_4CHO$	30	75
$2\text{-}(NO_2)C_6H_4CH_2OH$	$2\text{-}(NO_2)C_6H_4CHO$	30	60
$4\text{-}(CH_3)C_6H_4CH_2OH$	$4\text{-}(CH_3)C_6H_4CHO$	28	83
$C_6H_5CHOHCH_3$	$C_6H_5COCH_3$	21	88
$(C_6H_5)_2CHOH$	$(C_6H_5)_2CO$	20	95
$C_6H_5CHOHCOC_6H_5$	$C_6H_5COCOC_6H_5$	5	99
$CH_2{=}CHCH_2OH$	$CH_2{=}CHCHO$	35	37
$C_6H_5CH{=}CHCH_2OH$	$C_6H_5CH{=}CHCHO$	23	70
$C_6H_5CH{=}CHCHOHCH$	$C_6H_5CH{=}CHCOCH_3$	33	74

Table 3. Reusability of catalyst for the oxidation of 1-phenylethanol to acetophenone (conditions see Table 1)

Experimental trial	Yield (%)
1st	88
2nd	82
3rd	80
4th	79

Table 3 shows the reusability of catalyst after 4 replicate oxidations of 1-phenylethanol as model substrate to the corresponding ketone. The catalysts were recovered *via* a simple filtration and dried in oven at 135°C for 4 hours.

The oxidation of *Hantzsch* 1,4-dihydropyridines is one of theuniquitous problems in organic chemistry and even in recent years several groups have reported-new methods for aromatization of these compounds. Many methods have been developed for the oxidation of 1,4-*DHP*s [13–27] but some of them suffer from low chemical yields [18, 22], strong oxidative conditions [15, 18, 23], side product formation or dealkylation at 4-position [13, 21]. In this regard, special attention has been focused on the developing of heterogeneous systems in order to support of reagents and to achieve catalytic activities.

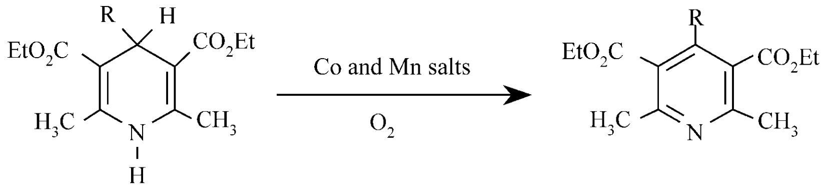
We have reported another application of our heterogeneous catalytic method for the oxidation of *Hantzsch* 1,4-dihydropyridines to corresponding pyridines [28]. The aromatization of 4-alky 1,4-dihydropridines were carried out in *n*-heptane as solvent at 93°C reflux temperature and because of nonsolubility of 4-aryl and 4-heteroaryl 1,4-dihydropridines in *n*-heptane, the oxidation of 4-aryl and 4-heteroaryl 1,4-dihydropridines were carried out in toluene as solvent at 105°C reflux temperature, Table 4. This reactions are selective and only 4-substituted pyridine were obtained.

Following the success of oxidation of *Hantzsch* 1,4-dihydropyridines with Co and Mn salts/O_2 systems we extended this heterogeneous method by raising of temperature. The oxidation reactions in higher temperature led to an oxidative dealkylation of 4-alkyl-1,4-dihydropyridines in *n*-octane at 118°C (reflux temperature), Table 5. However in the case of 4-aryl and 4-heteroaryl 1,4-dihydropyridines no dearylation process occurred by raising of temperature to 150°C. At higher temperatures (up to 150°C) the catalyst was decomposed and the yields dropped drastically.

Table 6 shows the reusability of the catalyst after 4 replicate oxidations of ethyl-1,4-dihydro-2,3-dimethyl-3,5-pyridine dicarboxylate and phenyl-1,4-dihydro-2,3-dimethyl-3,5-pyridine dicarboxylate as model substrates to the corresponding pyridines. The catalyst was recovered quantitatively after each experiment.

The oxidation of phenols to quinones is another application of this catalytic oxidation system. Reagents such as cobalt(II) chelate complex [29], H_2O_2 catalyzed by three methyl oxorenium(VII) [30], *Fermys* salts [31, 32], $C_6H_5SeO_2H$ and $(C_6H_5SeO)_2O$ [33], Pb_2O [34], CrO_3 [35], *DDQ* [36], HgO and $Hg(OCOCF_3)$ [38], *CAN* [39], Ag_2CO_3/Celite [40], and singlet oxygen [41], were reported for the

Table 4. Oxidation of *Hantzsch* 1,4-*DHP*s using molecular oxygen catalyzed by Co and Mn salts (all reactions at reflux temperature; yields refer to pure isolated products)



1a-n **2a-n**

1,4-*DHP*s	4-R	Solvent	Time (min)	Pyridines	Yield (%)
1a	H	*n*-heptane	3	**2a**	98
1b	CH_3	*n*-heptane	15	**2b**	92
1c	CH_2CH_3	*n*-heptane	8	**2c**	98
1d	$CH_2CH_2CH_3$	*n*-heptane	8	**2d**	97
1e	$CH_2CH(CH_3)_2$	*n*-heptane	12	**2e**	97
1f	$CH_2C_6H_5$	*n*-heptane	10	**2f**	95
1g	$CH_2CH_2C_6H_5$	*n*-heptane	10	**2g**	93
1h	C_6H_5	toluene	8	**2h**	95
1i	*p*-$(CN)C_6H_4$	toluene	12	**2I**	91
1j	*m*-$(NO_2)C_6H_4$	toluene	12	**2j**	93
1k	*o*-$(OCH_3)C_6H_4$	toluene	15	**2k**	92
1l	*p*-$(OCH_3)C_6H_4$	toluene	15	**2l**	96
1m	2-furyl	toluene	10	**2m**	92
1n	2-thienyl	toluene	8	**2n**	95

Table 5. Oxidative dealkylation of *Hantzsch* 1,4-*DHP*s at high temperature using molecular oxygen catalyzed by Co and Mn salts (all reactions at reflux temperature; yields refer to pure isolated products)

1,4-*DHP*s	R	Time (min)	Yield (%) of	Pyridines
1b	CH_3	15	**2b** (40)	**2a** (52)
1c	CH_2CH_3	8	**2c** (34)	**2a** (63)
1d	$CH_2CH_2CH_3$	8	**2d** (35)	**2a** (60)
1e	$CH_2CH(CH_3)_2$	12	**2e** (43)	**2a** (51)
1f	$CH_2C_6H_5$	10	**2f** (58)	**2a** (35)
1g	$CH_2CH_2C_6H_5$	10	**2g** (45)	**2a** (50)

oxidation of phenols to quinones. Our Co and Mn salts/O_2 system can also oxidize phenols to quinones [42], Table 7.

Silyl ethers, acetals, and ketals not only are used for the characterization and purification of alcohols and carbonyl compounds, but also play an important role in the protection of organic compounds [43, 44]. A number of methods have been developed for the deprotection of silyl ethers to the alcohols, [45–47] and oxidative cleavage of acetals and ketals to the corresponding carbonyl compounds [48–50]. But some of them have limitations for silyl ethers and some of them, in spite of

Table 6. Reusability of catalyst for the oxidation of *Hantzsch* 1,4-*DHP*s (conditions see Table 3)

Experimental trial	Starting Material	Product	Yield (%)
1st	**1c**	**2c**	98
2nd	**1c**	**2c**	95
3rd	**1c**	**2c**	93
4th	**1c**	**2c**	91
5th	**1c**	**2c**	90
1st	**1h**	**2h**	95
2nd	**1h**	**2h**	90
3rd	**1h**	**2h**	87
4th	**1h**	**2h**	85
5th	**1h**	**2h**	84

Table 7. Oxidation of phenols to quinones using Co and Mn salts/O_2 system (all reactions at reflux temperature; yields refer to pure isolated products)

Substrate	Solvent	Product	Yield (%)
phenol	benzene	1,4-benzoquinone	64
3-methylphenol	toluene	2-methyl-1,4-benzoquinone	53
3,5-dimethylphenol	toluene	2,6-dimethyl-1,4-benzoquinone	57
2-chlorophenol	ethylbenzene	2-chloro-1,4-benzoquinone	39
2-bromophenol	ethylbenzene	2-bromo-1,4-benzoquinone	36
1-naphthol	benzene	1,4-naphthoquinone	65

Table 8. Oxidative deprotection of silyl ethers, acetals and ketals by Co and Mn salts/O_2 system (yields refer to pure isolated products)

Substrate	Product	Time (h)	Yield (%)
$C_6H_5CH_2OSi(CH_3)_3$	$C_6H_5CH_2OH$	12	90
$C_6H_5CH{=}CHCH_2OSi(CH_3)_3$	$C_6H_5CH{=}CHCH_2OH$	15	95
$(C_6H_5)_2CHOSi(CH_3)_3$	$(C_6H_5)_2CHOH$	8.5	96
$CH_2{=}CHCH_2OSi(CH_3)_3$	$CH_2{=}CHCH_2OH$	12	88
$4\text{-}(Cl)C_6H_4CH_2OSi(CH_3)_3$	$4\text{-}(Cl)C_6H_4CH_2OH$	13.5	91
$(C_6H_5)_2C(OCH_2CH_2O)$	$(C_6H_5)_2CO$	8	83
$C_6H_5CH_3C(OCH_2CH_2O)$	$C_6H_5CH_3CO$	10	86
$4\text{-}(OCH_3)C_6H_4CH_3C(OCH_2CH_2O)$	$4\text{-}(OCH_3)C_6H_4CH_3CO$	11	88
$4\text{-}(NO_2)C_6H_4CH(OCH_2CH_2O)$	$4\text{-}(NO_2)C_6H_4CHO$	10	66
$(CH_2)_5CH(OCH_2CH_2O)$	$(CH_2)_5CHO$	10	75

generality, have the drawback of using expensive oxidants and tedious work up, low chemical yields, strong oxidative conditions or side product formation.

Another application of our heterogeneous catalytic system is oxidative deprotection of three methyl silyl ethers to their corresponding original alcohols. Oxidative deprotection of acetals and ketals to aldehydes and ketones can also be done with the Co and Mn salts/O_2 oxidant system under mild and nonaqueous condition [51], Table 8.

Experimental

Chemicals were purchased from Merck, Aldrich, Fluka and Riedel Dehaen AG chemical companies and were used without further purification. IR spectra were recorded on a FT-IR Unicam Mattson 1000 spectrophotometer. ^{1}H-NMR spectra were recorded on a Brucker AC-80 (80 MHz) spectrometer in $CDCl_3$. All products are known compounds and they were identified by their mp's or b p's, IR and ^{1}H-NMR spectroscopic properties. All yields refer to pure isolated products.

Preparation of Activated Silica Gel

In a pyrolysis apparatus silica gel (5 g) was heated at 260°C under reduced pressure (20 mm Hg) using phosphorus pentoxide (5 g) as desiccant. The silica gel was reduced by 0.28 g in weight after 10 h (5.7 wt%).

Reaction of Activated Silica Gel and p-Aminobenzoic Acid

To a mixture of ethyl acetate (70 cm^3) and *p*-aminobenzoic acid (2.13 g, 15 mmol) was added activated silica gel (4.79 g). The reaction mixture was then heated at reflux temperature with magnetic stirring at 80°C for 16 h and then cooled to room temperature and filtered. The solid mass was washed with ethyl acetate for 10 h in a *Soxhlet* apparatus in order to remove unreacted *p*-aminobenzoic acid. The solid was then dried in the oven at 100°C to afford a pale yellow solid (6.05 g); 1.33 g (9.7 mmol) of the acid had reacted.

Preparation of Cobalt and Manganese Salts of p-Aminobenzoic Acid Supported on Silica Gel

The sodium salt of *p*-amino benzoic acid (5 g) supported on silica gel was prepared *via* reaction of the acid and a solution of sodium carbonate to give (5.25 g, 11 mmol, 4.76 wt% increase) of the sodium salt. The presence of sodium salts was verified by X-Ray Fluorescence (XRF) analysis to show a 4.4% wt increase.

Similarly manganese and cobalt salts of the acid were prepared by using manganese chloride and cobalt chloride solutions to give 5.39 g of manganese salt as a white solid (6.1% wt increase) and 5.33 g of cobalt salt as a pink solid (6.0% wt increase). These results were verified by XRF analysis.

Oxidation of p-Methoxybenzyl Alcohol to p-Methoxybenzaldehyde (Typical Procedure)

To a stirred solution of *p*-methoxybenzyl alcohol (1 mmol) in 25 ml chlorobenzene was added the cobalt salt (90 mg 0.1 mmol) and manganese salt (90 mg 0.1 mmol). The reaction mixture was refluxed during bubbling through oxygen at a rate of 15 cm^3 min^{-1} into the solution. The progress of the reaction was monitored by TLC (CCl_4/Et_2O, 1:3). After 26 h, the reaction mixture was cooled to room temperature and filtered to recover the solid material (Co and Mn salts). The filtrate was evaporated and the residue was purified by column chromatography on silica gel (CCl_4/Et_2O, 1:3) to obtain *p*-methoxy benzaldehyde in 85% yield.

Reusability of Catalyst for the Oxidation of 1-Phenylethanol to Acetophenone (Typical Procedure)

Oxidation of 1-phenylethanol as model substrate to corresponding ketone was carried out as described above to give 88% yield of acetophenone. The catalyst was recovered *via* a simple filtration and dried in the oven at 135°C for 4 h. The reaction was repeated using the recovered catalyst to give 82% of product. Reusing of the catalyst for third and fourth times gave 80% and 79% yields, respectively. The catalyst was recovered quantitatively in each experiment.

Oxidation of Phenols to Quinones (General Procedure)

To a stirred solution of phenol (1 mmol) in 25 cm^3 solvent (Table 7) was added the cobalt salt (46 mg, 0.05 mmol) and manganese salt (45 mg, 0.05 mmol). The reaction mixture was heated at reflux temperature for 8 h during which oxygen was bubbled at a rate of 15 $cm^3 min^{-1}$ into the solution and the progress of the reaction was monitored by TLC (hexane/*Et*O*A*c, 4:1). Then the reaction mixture was cooled to room temperature and filtered to recover the solid material (Co and Mn salts). The filtrate was evaporated and the residue was purified by column chromatography on silica gel (hexane/*Et*O*A*c, 4:1) to obtain the desired product.

Oxidative Deprotection of Silyl Ethers, Acetals, and Ketals

To a stirred solution of substrate (1 mmol) in 25 cm^3 of hexane was added the cobalt salt (46 mg, 0.05 mmol) and manganese salt (45 mg, 0.05 mmol). The reaction mixture was heated at reflux temperature during which oxygen was bubbled at a rate of 15 $cm^3 min^{-1}$ into the solution and the progress of the reaction was monitored by TLC (hexane/Et_2O, 4:1). Then the reaction mixture was cooled to room temperature and filtered to recover the solid material (Co and Mn salts). The filtrate was evaporated and the residue was purified by column chromatography on silica gel (hexane/Et_2O, 4:1) to obtain the desired product.

Oxidation of Hantzsch 1,4-Dihydropyridines (General Procedure)

To a stirred solution of 1,4-dihydropyridines (1 mmol) in 25 cm^3 of solvent was added the cobalt salt (90 mg, 0.1 mmol) and manganese salt (90 mg, 0.1 mmol). The reaction mixture was heated at reflux temperature during which oxygen was bubbled at a rate of 15 $cm^3 min^{-1}$ into the solution. Progress of the reaction was monitored by TLC (CH_2Cl_2/*Et*O*A*c 98:2). The reaction mixture was then cooled to room temperature and filtered to recover the solid material (Co and Mn salts). The filtrate was evaporated and the residue was purified by column chromatography on silica gel (CH_2Cl_2/*Et*O*A*c 98:2) to obtain the desired product.

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