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Nickel(II) thiosemicarbazone complex catalyzed Mizoroki-Heck reaction

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ABSTRACT

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Keywords:

Convenient synthesis of a new square planar nickel(II) naphthaldehyde thiosemicarbazone complex has been described. The composition of the complex has been established by elemental analysis, spectral methods and single crystal X–ray crystallography. The new complex acts as an active homogeneous catalyst for the Mizoroki-Heck reaction of electron deficient (activating) and electron rich (deactivating) aryl bromides with various olefins under optimized conditions.

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The chemistry of Schiff base complexes containing transition metal ions is of significant importance due to their potentially beneficial catalytic and biological properties. Thiosemicarbazones form an important class of Schiff base ligand containing nitrogen and sulphur donor atoms. They exhibit thione-thiol tautomerism in solution owing to the presence of the -NH-C=S functional group. Depending on the reaction conditions, basicity of the medium or the metal ions, these ligands coordinate to a metal centre via the azomethine nitrogen either in the neutral thione form or in the anionic thiolate form, as bidentate ligands forming five membered chelate rings.² The ligand can also bind to the metal ion via the hydrazinic nitrogen and the thiolate sulphur as monoanionic bidentate N,S donor forming a four membered chelate ring.³

Transition-metal catalyzed cross-coupling of aryl halides and olefins provides a simple and efficient route for the synthesis of substituted molecules which are of significant importance as intermediates in pharmaceutical industry, as UV absorbers, as antioxidants or as molecular devices.⁴ Since its development in the early 1970s,⁵ palladium catalyzed Mizoroki-Heck reaction has become a powerful tool for the arylation of olefins.⁶ Unlike other C–C coupling reactions, the Mizoroki-Heck reaction has the ability to tolerate a variety of functional groups (such as unprotected amino, hydroxyl, aldehyde, ketone, carboxyl or ester groups) thus avoiding the need for protection and deprotection of functional groups during the organic transformations.⁷ Though palladium complexes show high catalytic activities, one obvious drawback is the prohibitive cost of palladium which has resulted

in the exploration of less costly transition metals as alternatives to palladium systems for cross-coupling reactions while still preserving high levels of efficiency and functional group tolerance.

Nickel appears the most promising for the replacement of palladium as catalyst for carbon-carbon cross-coupling reactions⁸ due to its relative low cost and ability to readily undergo oxidative addition reactions with C-X bonds. However relatively little effort has been dedicated to the development of nickel complexes as catalysts for the Mizoroki-Heck reaction. The earlier attempts to use the Ni(II) complexes, such as [NiCl₂(PPh₃)₂], to catalyze the coupling between activated olefins and aryl halides in the presence of additives like zinc dust gave a mixture of addition and substitution products, resulting in poor selectivity.⁹ However, in subsequent years, nickel complexes containing various ligands such as pincer,¹⁰ phosphine,¹¹ carbene¹² etc., were developed as effective catalysts for Mizoroki-Heck coupling reactions, although so far no nickel catalyst has been able to rival palladium for the Mizoroki-Heck coupling reaction.

Though there are a number of reports on the synthesis, characterization, catalytic and biological applications of nickel(II) thiosemicarbazone complexes,¹³ the use of these complexes as catalyst in the Mizoroki-Heck reaction is not explored in the literature. In this paper we describe the synthesis and structural characterization of air- and moisture-stable square-planar nickel(II) thiosemicarbazone complex, **1**, that can catalyze the Mizoroki-Heck reaction of aryl bromides with various

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olefins. The complex has been characterized by analytical and spectral methods. The structure of the complex **1** has been probed with the help of single crystal X-ray diffraction analysis.

The naphthaldehyde methylthiosemicarbazone ligand (HL) was prepared by the condensation of 1-naphthaldehyde and Nmethyl thiosemicarbazide.¹⁴ Treatment of $(CH_3COO)_2Ni\cdot 4H_2O$ with 2 equivalents of the ligand in ethanol-dichloromethane at room temperature resulted in the formation of the new square planar nickel(II) thiosemicarbazone complex (1) of the formula, $[Ni(L)_2]$ (Scheme 1).



Scheme 1. Synthesis of nickel(II) thiosemicarbazone complex

In the FT-IR spectrum, the $\nu_{C=S}$ and $\nu_{N\!-\!H}$ of the –N–NH–C=S group at 845 cm⁻¹ and 3210 cm⁻¹ respectively in the free ligand disappeared in the complex suggesting enolization and subsequent coordination through the thiolate sulfur to the Ni(II) ion. The complex displays $v_{C=N}$ stretch at 1591 cm⁻¹ which is at a lower frequency than that of the free ligand (1626 cm^{-1}) indicating coordination of azomethine nitrogen to Ni(II) ion.¹⁵ In the ¹H-NMR spectrum of the complex, the signals observed in the region δ 8.3-6.9 ppm have been assigned to the aromatic protons of the coordinated ligand. The singlet due to azomethine proton (\delta 8.7 ppm) in the complex is slightly downfield compared to the free ligand (\delta 8.0 ppm), suggesting deshielding upon coordination to Ni(II) ion. The singlet that appeared for the N–NH–C=S protons of the free ligand in the region δ 11.6 ppm is absent in the complex, supporting enolization and coordination of the thiolate sulphur to the Ni(II) ion.¹

The molecular structure of the complex **1** has been determined by single crystal X-ray diffraction to confirm the coordination mode of the ligand and geometry of the complex. The ORTEP view of complex **1** is shown in Figure 1. The nickel ion is tetra coordinated in a square planar geometry by two ligand molecules acting as monoanionic bidentate NS-donor forming two five-membered rings. The ligand is in trans position with respect to the C-N bond and the complex is centrosymmetric around the nickel centre. The bond lengths and bond angles are in good agreement with reported data on related Ni(II) thiosemicarbazone complexes.¹⁷



Figure 1. ORTEP view of 1 at 30% probability.

The fact, that nickel complexes are becoming increasingly popular as catalyst in bringing about C–C cross coupling reactions of different types,¹⁸ has led us to explore catalytic efficiency of complex **1** in the Mizoroki-Heck reaction. The initial test for the efficacy of the complex in this cross-coupling reaction involved optimization of the base. The cross-coupling reaction between 4-bromoacetophenone (substrate) with *t*-butyl acrylate with **1** as catalyst in DMF solvent at 110 °C was initially examined (Table 1). A controlled experiment indicated that no cross-coupling product was observed in the absence of the catalyst or base. When inorganic bases like K₂CO₃ or Na₂CO₃ were used (entries 1,2), the isolated yields were excellent. The yield of the cross-coupled product was considerably reduced when inorganic acetates or organic bases were used (entries 3-7). Thus, K₂CO₃ has a pronounced effect on the product yield.

Table 1. Optimization of reaction conditions^a

)	+	O'Bu Complex 1 DMF, Base 110 °C, 24 h		O Bu
	Entry	Base	Yield ^b (%)	TON ^c
	1	K ₂ CO ₃	98	98
	2	Na ₂ CO ₃	96	96
	3	CH ₃ COOK	35	35
	4	CH ₃ COONa	31	31
	5	Et ₃ N	<10	<10
	6	Pyridine	<10	<10

 a Reaction conditions: 4-bromoacetophenone (5 mmol), *t*-butyl acrylate (10 mmol), base (6 mmol), complex 1 (1 mol%), DMF (5 mL) at 110 °C for 24 h under N_2 atmosphere.

<10

<10

^b Isolated yield after column chromatography based on 4-bromoacetophenone (average of two runs).

^c TON = Turnover number = ratio of moles of product formed to moles of catalyst used.

Table 2. Effect of catalyst loading^a

Pyrrolidine

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Br + O'Bu O'Bu O'Bu O'Bu		Complex 1 DMF, K ₂ CO ₃ 110 °C, 24 h			O O Bu		
	Entry	Catalyst (mol%	%)	Yield ^b (%)		TON ^c	
	1	1.0		98		98	
	2	0.5		93		186	
	3	0.25		75		300	
	4	0.125		54		432	

 a Reaction conditions: 4-bromoacetophenone (5 mmol), t-butyl acrylate (10 mmol), K_2CO_3 (6 mmol), DMF (5 mL) at 100 $^\circ C$ for 24 h under N_2 atmosphere.

^b Isolated yield after column chromatography based on 4-bromoacetophenone (average of two runs).

^c TON = Turnover number = ratio of moles of product formed to moles of catalyst used.

In order to optimize the effect of catalyst loading, different catalyst:substrate ratios were tested in the cross-coupling reaction of 4-bromoacetophenone with *t*-butyl acrylate to form 4-acetyl-trans-cinnamic acid *tert*-butyl ester (Table 2). The reaction proceeds well when 1.0 or 0.5 mol% of the catalyst is used (entries 1,2). Upon changing the amount of catalyst from 0.25% to 0.125 mol% of the catalyst, the reaction proceeds smoothly accompanied by a drop in the isolated yield (entries 3-5). The isolated yield is good with appreciable TON when 0.5 mol% of the catalyst is used and it was concluded that this catalyst:substrate ratio is the best suitable for the coupling reaction.

Table 3. Mizoroki-Heck reaction of aryl bromides with olefins^a

⇒ .Br	Complex 1 (0.5 mol%)	$a \Rightarrow \mathbf{R}^2$
R^1 R^2	DMF, K ₂ CO ₃ 110 ⁰ C, 24 h	R ¹

Entry	- R ¹	$-\mathbf{R}^2$	Yield ^b (%)	TON ^c
1	-COCH ₃	-COO ^t Bu	93	186
2	-H	-COO ^t Bu	85	170
3	-CH ₃	-COO ^t Bu	76	152
4	-COCH ₃	-COOCH ₃	94	188
5	-H	-COOCH ₃	86	172
6	-CH ₃	-COOCH ₃	77	154
7	-COCH ₃	$-C_6H_5$	80	160
8	-H	$-C_6H_5$	73	146
9	-CH ₃	$-C_6H_5$	67	134
10	-COCH ₃	$-C_{6}H_{4}-4-CH_{3}$	77	154
11	-H	$-C_{6}H_{4}-4-CH_{3}$	69	138
12	-CH ₃	$-C_{6}H_{4}-4-CH_{3}$	60	120
13	-COCH ₃	-C ₆ H ₄ -4-Cl	87	174
14	-H	-C ₆ H ₄ -4-Cl	80	160
15	-CH ₃	-C ₆ H ₄ -4-Cl	72	144

 a Reaction conditions: aryl bromide (5 mmol), olefin (10 mmol), K_2CO_3 (6 mmol), complex 1 (0.5 mol%), DMF (5 mL) at 110 $^\circ C$ for 24 h under N_2 atmosphere.

^b Isolated yield after column chromatography based on aryl bromide (average of two runs).

 $^{\circ}$ TON = Turnover number = ratio of moles of product formed to moles of catalyst used.

Using the above optimized conditions, the Mizoroki-Heck cross-coupling reaction of activated, non- and deactivated aryl bromides with a variety of vinylic substrates (t-butyl acrylate, methyl acrylate, styrene, 4-methyl styrene and 4-chloro styrene) was carried out with complex 1 as catalyst using DMF/K₂CO₃ at 100 °C (Table 3). Only trans products were obtained selectively in all the cases. In general, for a particular aryl bromide, the cross-coupled products were obtained in excellent isolated yield with t-butyl acrylate (entries 1-3) or methyl acrylate (entries 4-6) as the vinylic substrate. The corresponding reactions with styrene as the olefinic partner gave slightly lower yield (entries 7-9). Electron donating substituent (4-methyl) on styrene gave slightly lower yield (entries 10-12) when compared to that of styrene, whereas electron withdrawing substituent (4-chloro) on styrene gave slightly higher yield (entries 13-15) as that compared with styrene. It was also observed that for a particular olefin, activated

electron deficient aryl bromide (4-bromo acetophenone) could effectively couple with the olefins providing the corresponding products in excellent yield after 24 h. The non-activated electron neutral substrate (bromo benzene) and deactivated electron rich substrate (4-bromo toluene) gave moderate amount of products when coupling with the olefins.

The ultimate objective in designing Mizoroki-Heck coupling catalyst is to form active species that can catalyze the coupling of the more difficult aryl chlorides. No catalytic activity was observed in the coupling of 4-chloroacetophenone with t-butyl acrylate using complex **1** in DMF/ K₂CO₃ even after 24 h at elevated temperatures of 150 °C. This trend is consistent with the increasing strength of carbon-halide bonds from aryl bromide to aryl chloride.¹⁹ In terms of TON, the catalytic efficiency of these nickel(II) thiosemicarbazone complexes are superior to the previously reported nickel(II) complexes²⁰ used as catalysts for the Mizoroki-Heck reaction.

In conclusion, nickel(II) complex bearing thiosemicarbazone ligand has been synthesized and characterized. The single crystal X-ray evidenced the N and S coordination mode of the ligand and a distorted square planar geometry around each Ni(II) ion. Furthermore, the nickel(II) thiosemicarbazone complex was found to be highly efficient homogeneous catalyst for the Mizoroki-Heck reaction of aryl bromides with various olefinic substrates.

Supplementary Material

Crystallographic data for the structural analysis have been deposited with Cambridge crystallographic center, CCDC No. 892892. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union roads, Cambridge CB2 1EZ, UK (email: deposit@ccdc.cam.ac.uk). The summary of the data collection and refinement parameters for the complex; Selected bond parameters; Experimental procedures; ¹H-NMR spectrum of the complex **1**; ¹H-NMR data for all the Mizoroki-Heck coupling products. Supplementary data associated with this article can be found, in the online version.

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Graphical Abstract Square planar nickel(II) thiosemicarbazone complex was synthesized and characterized. The new complex acts as an effective homogeneous catalyst for the Mizoroki-Heck reaction of aryl bromides with various olefins. The effects of base and catalyst loading on the catalytic activity of the complex were also investigated.

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Nickel(II) thiosemicarbazone complex catalyzed Mizoroki-Heck reaction				
Pandimuni Kalpaga Suganthy, Rupesh Narayana Prabhu, Venug	opal Shamugham Sreedevi ^{a,} *			
$R^{1} \xrightarrow{\text{Br}} + R^{2} \xrightarrow{\text{R}^{2}} M_{\text{N}}^{\text{S}} \xrightarrow{\text{N}}_{\text{N}}^{\text{S}} \xrightarrow{\text{N}}_{\text{N}}^{\text{N}} \xrightarrow{\text{N}}_{\text{N}} \xrightarrow{\text{N}}_{\text{N}} \xrightarrow{\text{N}}_{\text{N}}^{\text{N}} \xrightarrow{\text{N}}_{\text{N}} \xrightarrow{\text{N}}_{\text{N}} \xrightarrow{\text{N}}_{\text{N}} \xrightarrow{\text{N}} \xrightarrow{\text{N}} \xrightarrow{\text{N}}_{\text{N}} \xrightarrow{\text{N}} \xrightarrow{\text{N}}_{\text{N}} \xrightarrow{\text{N}} \xrightarrow{\text{N}}_{\text{N}} \xrightarrow{\text{N}} N$	R^{2H_3}			