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A New Pathway to Synthesize Cyclomercurated Ferrocenylimines Containing Heterocyclic Ring

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Abstract: The cyclomercurated ferrocenylimines containing heterocyclic ring were prepared by the condensation of cyclomercuration of acylferrocene with the appropriate heterocyclic amine. This procedure provides an efficient method for the synthesis of cyclomerucurated ferrocenylimines containing heterocyclic ring which are difficultly synthesized by the conventional method. The reaction mechanism is proposed.

Keywords: Heterocyclic ring containing cyclomercurated ferrocenylimine, synthesis.

The cyclometallation of ferrocenylimines has been systematically studied both in theoretical and applied aspects[1-4]. It was found that some ferrocenylimines containing strong electron-withdrawing group on aryl ring or containing heterocyclic ring have scarcely been successfully synthesized through the conventional condensation of acylferrocene with aromatic or heterocyclic amines[1]. This paper reports a new method for synthesizing some cyclomercurated ferrocenylimines, which could be used as precursor for organic synthesis and transmetallating agent for the synthesis of other cyclometallated ferrocenylimines[5,6]. As far as we know, this synthetic pathway was an efficient method for the synthesis of cyclomercurated ferrocenylimines containing heterocyclic ring.

There are two pathways for synthesis of cyclomercurated ferrocenylimines, **A** and **B**. The former is conventional method and the latter is a new method (**Scheme 1**).

With the method **B**, the cyclomercuration was carried out *prior to* the imination (condensation). The stable intermediate, cyclomercurated acylferrocene **2**, was easily synthesized and separated by preparative TLC[7]. Four cyclomercurated ferrocenylketimines containing pyridyl ring were synthesized *via* pathway **B** and the results obtained are listed in **Table 1**.

As shown in **Table 1**, the reaction was completed within 24 h (entry 3 *vs.* entry 4). **3c** was obtained in highest with yield the same reaction conditions (entry 10). The substitueuted position of aminogroup on pyridine seems to influence the reaction activity. The yield decreased when the reaction was carried out at lower temperature (entries 5 and 6). When chlorobenzene or xylene was used as the solvent at a higher reaction

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Scheme 1

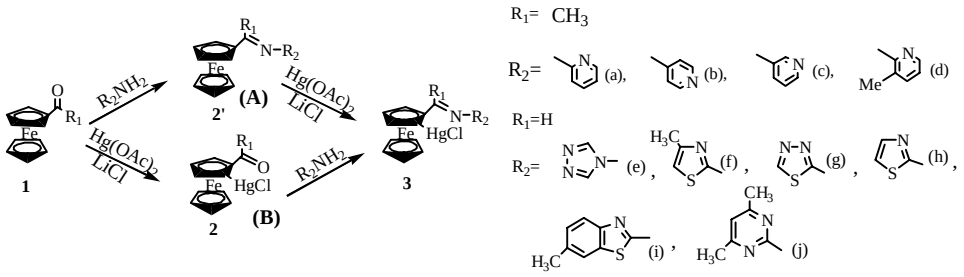


Table 1 The results obtained *via* the new synthetic pathway[1]

Entry	Amine	Product	Solvent	Temp .(^{o}C)	Time (h)	Yield[2] (%)
1	2-aminopyridine	**3a**	Toluene	110	6	45
2	2-aminopyridine	**3a**	Toluene	110	12	56
3	2-aminopyridine	**3a**	Toluene	110	24	72
4	2-aminopyridine	**3a**	Toluene	110	48	72
5	2-aminopyridine	**3a**	THF	66	24	40
6	2-aminopyridine	**3a**	Benzene	80	24	62
7	2-aminopyridine	**3a**	Chlorobenzene	130	24	32
8	2-aminopyridine	**3a**	Xylene	140	24	37
9	4-aminopyridine	**3b**	Toluene	110	24	71
10	3-aminopyridine	**3c**	Toluene	110	24	86
11	6-methyl-2-aminoPy	**3d**	Toluene	110	24	75

1. All reaction were catalized by Al_2O_3. 2. Isolated yield, based on cyclomercurated acetylferrocene.

temperature, the yield was low (entries 7 and 8), which might be due to the cleavage of C-Hg bond. The yields of **3a**, **3b** and **3d** were lower than that of **3c** (entries 3, 9 and 11 *vs*.10), because the amino group of 3-aminopyridine has stronger nucleophilicity than those of other aminopyridines. A somewhat higher yield of **3d** comparing with that of **3a** might result from both the electronic effect and steric hindrance of the methyl group. The former facilitated the nucleophilic attack of amino group on the carbonyl group, but the latter hindered it.

Some other heterocyclic amines **e, f, g, h, i, j** were applied to compare the synthetic methods for cyclomercurated ferrocenylimines **3** from formylferrocene **1** *via* pathway **A** or **B**. According to the conventional method, although **2'e, 2'f, 2'g, 2'h** could be synthesized and were stable in air, in the second step (cyclomercuration), the corresponding mercurated compounds were not obtained probably owing to easy coordination between the mercury atom and various heteroatoms in the heterocyclic ring which resulted in the formation of complicated coordination products.

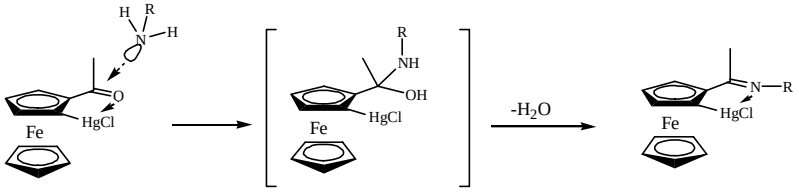
According to the new method, the first step was a well-known reaction. The condensation of **2** with heterocyclic amines gave **3e, 3f, 3g, 3h, 3i**, and **3j** with moderate yields(47-65%), respectively.

In IR, the absorptions at 1000 and 1100 cm^{-1} were indication of an unsubstituted Cp

ring. The C=N absorptions of compounds **3** were appeared in the energy rang from 1580 to 1610 cm^{-1}. The ^{1}H-NMR spectra of compounds **3** were completely consistent with the structure of 1,2-substituted Cp, exhibiting the AMX system for the three different protons on the 1,2-disubstituted Cp ring, and five protons for the unsubstituted Cp ring resonating at higher field. The chemical shifts of the protons 3, 4, and 5 on the substituted Cp ring of compounds **3** were shifted to downfield *ca*. 0.1 ppm in comparison with that of compound **2**. This might be due to that the electronic effect of heterocyclic ring has some influence through the C=N bond on the substituted Cp of the ferrocenyl moiety.

The possible mechanism may be expressed as follows (**Scheme** 2):

Scheme 2 The possible mechanism of the new method



(2) (M) (3)

In the mercurated acylferrocene **2**, Hg atom withdrew the electron from the oxygen atom of the carbonyl group and led to the electron deficiency of the carbonyl group which facilitated the nucleophilic attack of amino group.

Aminopyridines **a, b, c, d** and 2-aminothiazole **h** were purchased from Fluka. 4-Amino-1, 2, 4-triazole **e**, 4-methyl-2-aminothiazole **f**, 2-amino-1, 3, 4-thiadizole **g**, 6-methylbenzo-2-aminothiazole **i** and 4,6-dimethyl-2-aminopyrimidine **j** were synthesized according to literatures[8-12]. Al_2O_3 was activated at 120°C for 2 h before use. All solvents were dried using the appropriate drying agents (toluene, benzene, xylene, THF/Na/benzophenone, MeOH/Mg, CH_2Cl_2/P_2O_5), and freshly distilled *prior to* use. Preparative TLC was performed on dry silica gel plates developed with CH_2Cl_2.

2-(Chloromercuri)-1-acylferrocene **2** were prepared according to literature [7].

General procedure for synthesis of compounds **3:** To a solution of 2-(chloro-mercuri)-1-acylferrocene (0.5 mmol) in toluene (30 mL), heterocyclic amines (1.0 mmol) was added, and the mixture was refluxed with stirring in the presence of activated neutral Al_2O_3 (*ca*. 20 mg) overnight under argon. The resulting mixture was then cooled to room temperature, and the solid was separated by filtration. The filtrate was evaporated *in vacuo* to dryness and the residue was dissolved in a minimum amount of methylene chloride and subjected to a short dry column of silica gel, methylene chloride as eluate. The second band was collected and afforded the product after the evaporation of the solvent and recrystallization from methylene chloride-petroleum ether[13].

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References and Note

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