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Iron-catalysed 1,2-aryl migration of tertiary azides

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Received 00th January 20xx, Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

1,2-Aryl migration of α, α -diaryl tertiary azides was achieved by using the catalytic system of FeCl₂/*N*-heterocyclic carbene (NHC) SIPr·HCl. The reaction generated aniline products in good yields after one-pot reduction of the migration-resultant imines.

Transition metal-catalysed amination reactions involving azides as precursors have aroused great interest because of their potential usefulness in the synthesis of amines and amides.¹ In this context, much attention has been paid recently to the iron-catalysed aminaton reactions of azides² because of the benefits of using iron as catalyst.³ Iron salts and complexes can react with the azido group to form iron-imido species, which are highly reactive as nitrene transfer agents for amination reactions such as C–H insertion, cycloaddition and amination of heteroatoms.^{2a-d} Considering the versatile properties of nitrene species, it is expected that more reaction patterns will be found for the iron-catalysed reactions of azides.

1,2-Group migration from a carbon atom to a neighbouring nitrogen atom constitutes an important type of rearrangement that has long attracted interest of organic chemists.^{4,5}. It has been known that aryl substituted tertiary alkyl azides can undergo 1,2-aryl carbon to nitrogen migration via a nitrene intermediate or in a concerted way to afford imines at high temperature or when irradiated by UV light.⁶ A 1,2-aryl radical rearrangement of alkyl azides has also been realized under the condition of Bu₃SnH/AIBN.⁷ Despite these previous studies, however, similar 1,2-aryl rearrangement by transition metal catalysis has not been reported so far to our knowledge. Recently, we found that iron(II) salts and complexes are capable of promoting the 1,2-acyl migration of tertiary α -azido ketones to afford enamides and hereocycles such as

+ Footnotes relating to the title and/or authors should appear here. Electronic Supplementary Information (ESI) available: See DOI: 10.1039/x0xx00000x isoquinolone and 2-benzazepin-1-one.⁸ Encouraged by this result, we envisioned that iron catalysis might enable as well the 1,2-aryl migration from carbon to nitrogen when applied to α -aryl azides. Indeed, by using a catalytic system of FeCl₂ and *N*-heterocyclic carbene (NHC) SIPr·HCl, the expected 1,2-aryl migration was realized; *in situ* reduction of the thus formed imines by NaBH₄ delivered aniline products. Herein we report our result.

Previous work (ref. 8):



Scheme 1 Iron-catalysed 1,2-group rearrangement.

At the initial stage of this study, azide 1a was chosen as the model compound for searching for screening of the reaction conditions. Our previous work shows that the catalytic system of FeCl₂ and β -diketiminate ligand L₁ can promote intramolecular C–H amination of α -azido amides.⁹ Thus, this catalytic system was firstly employed to effect the reaction of 1a. It was found that the anticipated 1,2-phenyl migration did occur in a solvent such as chlorobenzene or 1,2-dichloroethane (DCE) under the condition of FeCl₂ and L_1 at 80 °C, giving rise to the anticipated imine product 1,3-triphenylpropan-1-imine. As imines are liable to hydrolysis, the product 1,3triphenylpropan-1-imine was then reduced by NaBH₄ in a onepot fashion to afford N-(1,3-diphenylpropyl)aniline 2a, which is easier to purify. This one-pot procedure was employed for the subsequent examination of reaction conditions. The result is summarized in Table 1.

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Table 1. Screening of reaction conditions

$Ph \xrightarrow{N_3} Ph \xrightarrow{Ph} (2) NaBH_4, MeOH Ph \xrightarrow{Ph} Ph$				
Entry	Ligand	Time (h)	Yield (%) ^b	
1	none	8	N.R. ^c	
2	L1	8	73	
3	L ₂	8	77	
4	L3	8	trace ^d	
5	L ₄	8	trace ^d	
6	Ls	8	27	
7	L ₆	8	87	
8	L ₇	8	trace ^d	
9	L ₈	8	trace ^d	
10	L9	8	86	
11	L ₁₀	8	35	
12	L ₆	2	85	
13	L ₆	8	69 ^e	
14	L ₆	8	<i>89</i> ^f	
15	L ₆	8	N.R. ^g	
16	L ₆	8	N.R. ^h	

^{*a*} The reaction was conducted on 0.3 mmol scale in 2.5 mL solvent. After the migration reaction finished, the reaction mixture was subjected to 0.6 mmol of NaBH₄ in 3.0 mL of methanol to convert the thus formed 1,3-triphenylpropan-1-imine to **2a**.^{*b*} Isolated yield. ^{*c*} No reaction took place. ^{*d*} Most of **1a** was recovered. ^{*e*} 5 mol % of FeCl₂ and **L**₆ were used. ^{*f*} 20 mol % of FeCl₂ and **L**₆ were used. ^{*f*} In the absence of FeCl₂.



Figure 1 The structures of tested ligands.

As shown in Table 1, compound **1a** reacted well in chlorobenzene at 80 °C under the condition of 10 mol % of FeCl₂ and L₁, affording **2a** in 73% yield after reduction (entry 2). Besides L₁, β -diketiminate ligands L₂-L₅ were also tested, among which, L₂ exhibited better efficacy (entry 3), while the other three were found to be much less effective (entries 4-6). Control experiment shows that the reaction did not occur in the absence of the ligand (entry 1).

Encouraged by this initial success, we went on to test other types of ligands. *N*-Heterocyclic carbenes (NHCs) belongs to a unique class of stable carbene compounds that can form ligands with a variety of transition metals.¹⁰ As such, many iron-NHC complexes of different structure features have been prepared and investigated concerning their catalytic capacities.¹¹ Recent studies demonstrate that iron-NHC complexes can be used to catalyse various transformations including cross coupling,¹² C–X bond formation¹³ and polymerization.¹⁴ Their catalytic capacity for azide-based amination reactions has also been investigated.^{10,15,16} It is to

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our interest to see that if NHCs ligands are capable to promote the phenyl migration reaction of 1a. Webchoselfise corrorationly used NHCs compounds (L₆-L₁₀), and used them together with FeCl₂ on **1a** in PhCl at 80 °C (entries 7-11). It was found that among these NHCs ligands, L₆ and L₉ exhibited good catalytic performance, while L_7 and L_8 were ineffective. The reactions also took place when L_{10} was used, but the yield was low. Apparently, the counter anion of NHCs exerted a critical influence under the current circumstance. Notably, using L_{6} and L_a delivered higher yield of **2a** (87% and 86%, respectively) than using β -diketiminate ligand L_1 under the otherwise same conditions. 80 °C proved to be the optimal reaction temperature. Under the condition of 10 mol % of FeCl₂ and L₆ in PhCl at 80 °C, **1a** was nearly completely consumed in 2 h (entry 12) (see Table S2 in Supplementary Information (SI)). Oxygen is detrimental to the reaction (entry 15). Apart from FeCl₂, several other ferrous salts were also tested, but they were all found to be inferior to FeCl₂ for this reaction (See Table S1 in SI).

The optimal conditions were then applied to a variety of α , α -diphenyl tertiary azides bearing different alkyl chains, and the result is illustrated in Scheme 2. The desired 1,2-phenyl migration reaction took place for all these substrates, and the yields were good in general except for **1i** and **1j**. In the cases of **1i** and **1j**, no other products apart from **2i** and **2j** were obtained, and both **1i** and **1j** were consumed completely. Notably, the reaction can be implemented on gram scale with little loss in yield (footnote *a* in Scheme 2). Triphenylmethyl azide also reacted well under the standard conditions (**2v**). However, when one phenyl group was replaced with a thienyl or a pyridyl group, as in the case of **1w** and **1x**, no migration product was generated.

Subsequent examination showed that compound **1y** or **1z** was unreactive under the standard conditions, indicating that the presence of two phenyl groups at the α -position is necessary for the reaction to take place (Scheme 3, (1)).



When compound **1aa**, was subjected to the standard conditions, **2aa** was generated in a yield of 96%. The *para*methyl group apparently has a beneficial effect on the reaction. To gain more insight into the impact of the substituent effect, the reactions of compounds **3a-d** were investigated. The result is presented in Scheme 4. It can be seen clearly that the migrating capacity of the phenyl ring is largely dependent on its electronic nature. The more electron-rich the phenyl ring, the stronger the aptitude for it to migrate. In the case of compound **3d**, the reaction only afforded **4d**, with its Phmigrating isomer not obtained at all.

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The reactions were carried out on 0.3 mmol scale. Isolated yields. ^a The reaction was carried out on 5.0 mmol scale. ^b 1w was decomposed. ^c No reaction took place.



Scheme 4 Electronic effect on the reaction.

As aforementioned, iron complexes can effectively promote the intramolecular $C(sp^3)$ -H insertion of alkyl azides.¹⁷⁻²¹ However, under the current circumstances, no $C(sp^3)$ -H insertion was observed for the substrates that can potentially undergo this reaction. As Boc₂O was generally used in the previously reported methods,¹⁷⁻²¹ subsequent experiment was conducted with **1z** in the presence of Boc₂O to see if the $C(sp^3)$ -H insertion could be effected (Scheme 5). The result showed that even without the competition of phenyl migration, **1z** still failed to undergo the anticipated intramolecular $C(sp^3)$ -H insertion.

∕ Ph	FeCl ₂ (10 mol %) L ₆ (10 mol %) Boc ₂ O (2.0 equiv.)	
N ₃	PhCl, 120 °C, Ar, 8 h	N.R.
1z		
Scheme 5 Reaction	of 1z in the presence of Bo	c ₂ O.

Recent mechanistic studies reveal that Iron(II) salts and complexes can react with azides to form high valent iron(IV)imido species or radical-type iron(III)-iminyl complexes, which would react in a way analogous to nitrenes.^{2a-d} According to these studies as well as the previous reports on the 1,2-aryl migration of azides, a plausible mechanism is proposed to account for the aryl migration of compounds **1** (and **3**). As shown in Scheme 6, **1** might first react with the *in situ* formed iron-NHC complex to form an iron-imido species **A** or an iron(III)-iminyl species **B**, which would then undergo 1,2phenyl migration to generate the imine product (path (a)), with the iron catalyst being released at the same time. That compounds **1y** and **1z** failed to react suggests the α -carbon atom bear a lot of positive charge at the transition state, so a stabilizing phenyl group is required for the migration to take place. It is even possible that a carbocation intermediate (**C**) is involved during the migration (path (b)). Apart from these mechanisms, a radical mechanism similar to that under the condition of n-Bu₃SnH and AIBN⁷ might also operate for the present reactions (path (c)). Iron(III)-iminyl complexes have a radical character at the nitrogen atom, and thus **B** might behave like typical nitrogen radicals to attack the phenyl ring to give a spiro cyclohexadienyl radical **D**. This nitrogen radical-mediated aryl migration is also expected to be sensitive to substituent effect.⁷





Scheme 7 Preparation of phenanthridines.

This method can be applied to the preparation of phenanthridines. As such, when 9-azidofluorenes **6a** and **6b**

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were used as the substrates, phenanthridines **7a** and **7b** were generated in yield of 55% and 59%, respectively (Scheme 7). The yields are much higher than those obtained under the condition of n-Bu₃SnH and AIBN.⁷

In conclusion, we have demonstrated that the catalytic system of FeCl₂/NHC SIPr·HCl (L_6) can enable diphenyl tertiary azides to be converted to imines via 1,2-phenyl migration. One-pot reduction of the thus formed imines by NaBH₄ provides aniline products in high yield. Further study is undergoing in our lab to elucidate the mechanistic issues as well as to exploit the catalytic capacity of FeCl₂/NHC system for other types of azide-involved amination reactions.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The authors thank the National Natural Science Foundation of China (No. 21772077) and State Key Laboratory of Applied Organic Chemistry for financial support.

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Table of contents

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1,2-Carbon to nitrogen aryl migration of α , α -diaryl tertiary azides was realized by using FeCl₂ and *N*-heterocyclic carbene SIPr·HCl as catalyst.