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Asymmetric Catalytic [2,3]-Stevens and Sommelet–Hauser Rearrangements of α-Diazo Pyrazoleamides with Sulfides

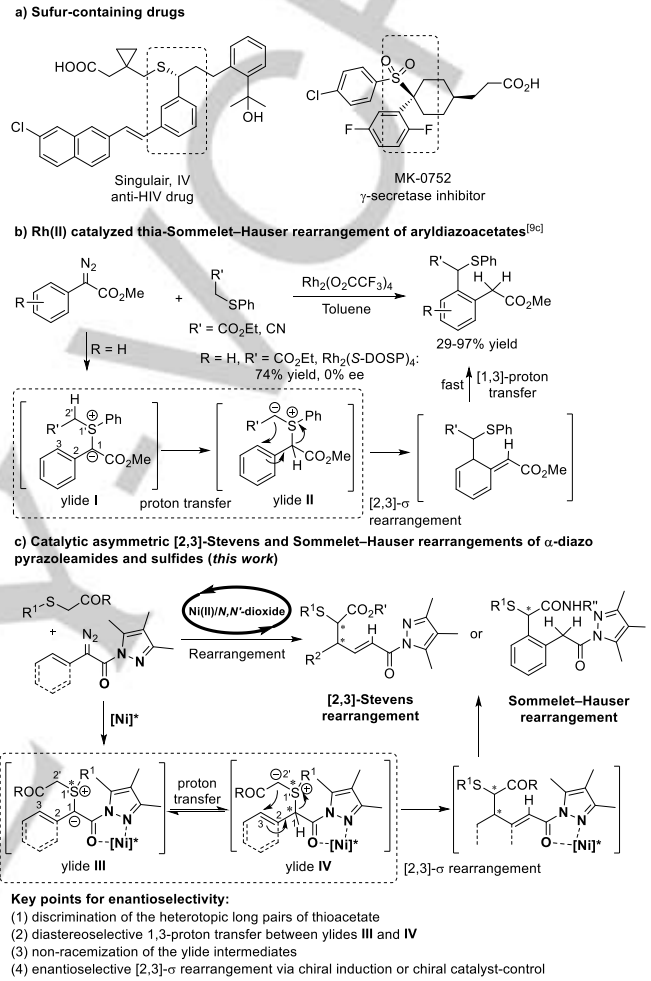
Xiaobin Lin, Wei Yang, Wenkun Yang, Xiaohua Liu,* and Xiaoming Feng*

Abstract: *Catalytic enantioselective [2,3]-Stevens and Sommelet–Hauser rearrangements of α-diazo pyrazoleamides with sulfides were achieved by utilizing chiral N,N'-dioxide/nickel(II) complex catalysts. These rearrangements proceeded well under mild conditions, providing a rapid and facile access to a series of functionalized 1,6-dicarbonyls or sulfane-substituted phenylacetates with high to excellent enantioselectivity. The catalytic system showed excellent stereo-control, discriminating between the heterotopic lone pairs of sulfur and controlling both the 1,3-proton transfer and the [2,3]-σ rearrangement.*

Introduction

Optically active sulfur-containing organic compounds are important in organic chemistry[1] and pharmaceutical applications[2] (Scheme 1a). The development of novel methods for the construction of such compounds has attracted attention in the past decades.[3] Among them, [2,3]-Stevens rearrangement[4] and Sommelet–Hauser reaction[5] of sulfonium ylides provide direct and elegant routes to sulfur-containing variant.[6] Whereas catalytic enantioselective [2,3]-Stevens rearrangement of allylic ammonium salts has been achieved,[7] the related rearrangement of sulfonium ylides remains elusive.[6,8] The asymmetric catalytic Sommelet–Hauser reaction[5] is potentially more challenging because dearomatization and rearomatization steps involved in the process.

One difficulty in [2,3]-Stevens and Sommelet–Hauser rearrangements lies in the generation of ylide intermediates, which usually requires stoichiometric strong bases.[5,7] This issue could be addressed by the use of reaction between transition-metal-carbene and sulfides to generate highly reactive sulfonium ylide intermediates.[9] For example, Wang and co-workers described two examples of Rh(II)-catalyzed thia-Sommelet–Hauser rearrangement of α-diazoesters.[9b-c] However, when the chiral Rh(II) catalyst was used to promote the enantioselective version, only racemic product was yielded (Scheme 1b). In comparison with asymmetric Doyle–Kirmse reaction,[10] enantioselective [2,3]-Stevens and Sommelet–Hauser rearrangements are much more complicated, because there are vicinal *S*- and *C*-stereogenic centers in the reaction intermediate before [2,3]-rearrangement step. In addition, the [2,3]-rearrangement step is a remote functionalization whose



Scheme 1. Sulfur-containing drugs and catalytic asymmetric [2,3]-sigmatropic rearrangements.

stereocontrol is difficult. We propose that the related highly enantioselective versions could be achieved if four points are under control during the whole process. Firstly, chiral sulfonium ylide could be readily generated through the differentiation of the heterotopic lone pairs of the sulfur compound. Secondly, a chiral C1-center in sulfonium ylide tautomer IV generates via diastereoselective proton transfer from C2' of ylide III. Thirdly, racemization or epimerization of the chiral ylide tautomers could be minimized before the following relatively slow [2,3]-sigmatropic rearrangement. Finally, a chiral intermediate-induced or catalyst-controlled [2,3]-sigmatropic rearrangement occurs without steric repulsion in an envelope transition state.

Recently, our group designed α-diazo pyrazoleamides as new carbene precursors for highly enantioselective Doyle–Kirmse reaction in the presence of chiral *N,N'*-dioxide/Ni(II) complex

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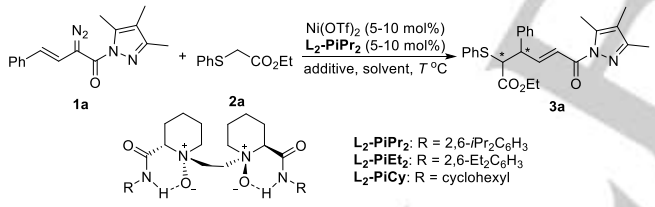
catalysts.[10a,11] We envision that this catalytic system could be adopted for the enantioselective [2,3]-Stevens and Sommelet–Hauser rearrangements of sulfonium ylides by introduction of vinyl or aryl substituent to the α-diazo pyrazoleamides (Scheme 1c). The excellent chiral pocket created by chiral *N,N'*-dioxides might be capable of directing the enantioselective nucleophilic attack to Ni(II)-carbene intermediate, generating a *S*-stereogenic center; and chiral Lewis acid-bounded ylides might govern the issues in 1,3-proton shift and [2,3]-sigmatropic rearrangement. If the hypothesis mentioned above works, it will provide an efficient solution to such challenging reactions. Herein, we report the results in enantioselective [2,3]-Stevens and Sommelet–Hauser rearrangements of vinyl and aryl α-diazo pyrazoleamides with sulfides. Various functionalized 1,6-dicarbonyls and sulfane-substituted phenylacetates are available in high to excellent enantioselectivity.

Results and Discussion

Initially, [2,3]-Stevens rearrangement of vinyl substituted α-diazo pyrazoleamide **1a** with (phenylthio)acetate **2a** was selected as the model reaction (Table 1). $Ni(OTf)_2$ with chiral *N,N'*-dioxide ligands bearing a varied amino acid backbone, amide substituent, and carbon linker was firstly evaluated (See Table S1 for details). It was found that **L_2-PiPr$_2$**/$Ni(OTf)_2$ complex could promote the asymmetric [2,3]-Stevens rearrangement smoothly, providing the desired product **3a** with a promising results (Table 1, entry 1; 48% yield, 75:25 dr, and 81:19 *er*). Next, different types of additives were explored, such as organic and inorganic bases, organic acids, molecular sieves, and others (See Table S4 for details). $AgNTf_2$, in favor of the reactivity and enantioselectivity in Doyle−Kirmse reaction,[10] resulted in quick decomposition of the diazo substrate **1a**, and no desired product was detected (entry 2). Interestingly, the addition of 3-phenylpropanoic acid was advantageous to the overall outcomes, affording the product **3a** in 62% yield with 83:17 dr and 94.5:5.5 *er* (entry 3). Then other parameters including solvent (entry 4), temperature (entry 5), as well as the loadings of additive and catalyst (entries 6 and 7) were carefully investigated (see SI for details), and the optimized conditions for [2,3]-Stevens rearrangement entailed the use of **L_2-PiPr$_2$**/$Ni(OTf)_2$ complex (5 mol%) as the catalyst, and 3-phenylpropanoic acid (20 mol%) as the additive in MeOAc (0.2 M) at 20 °C for 35 minutes. Under such conditions, the product **3a** was isolated in 76% yield with 83:17 dr and 97:3 *er* (entry 7).

Table 1: Condition optimization for asymmetric [2,3]-Stevens rearrangement



Entry[a]	Sol. / Add. / Time	Yield [%][b]	dr[c]	*er*[c]
1	EtOAc / - / 2 h	48	75:25	81:19/73:27
2[d]	EtOAc / $AgNTf_2$ / 10 min	0	--	--
3[e]	EtOAc / acid / 0.5 h	62	83:17	94.5:5.5/87:13
4[e]	MeOAc / acid / 20 min	69	84:16	94.5:5.5/87:13
5[e,f]	MeOAc / acid / 35 min	73	83:17	97:3
6[f, g]	MeOAc /acid / 35 min	76	83:17	97:3
7[h]	MeOAc / acid / 35 min	76	83:17	97:3

[a] Unless otherwise noted, the reactions were carried out with **1a** (0.1 mmol), sulfide **2a** (1.0 equiv), $Ni(OTf)_2$/**L_2-PiPr$_2$** (1:1, 10 mol%) in solvent (0.1 M) at 35 °C. [b] Isolated yields of **3a**. [c] Determined by HPLC on a chiral stationary phase. [d] $AgNTf_2$ (2 mol%) was added. [e] $Ph(CH_2)_2CO_2H$ (10 mol%) was added. [f] At 20 °C. [g] $Ph(CH_2)_2CO_2H$ (20 mol%) was added. [h] **1a** (0.1 mmol), sulfide **2a** (2.5 equiv), $Ni(OTf)_2$/**L_2-PiPr$_2$** (1:1, 5 mol%), $Ph(CH_2)_2CO_2H$ (20 mol%) in MeOAc (0.2 M) at 20 °C.

With the optimized reaction conditions in hand, the substrate generality in the [2,3]-Stevens rearrangement was evaluated (Table 2). This catalytic system was applicable to a range of vinyl substituted α-diazo compounds and aryl thioacetates. In detail, enantioselective [2,3]-Stevens rearrangement of diazo compounds **1b**-**1f** bearing chloride or methyl substituents at different positions of the phenyl groups afforded the targeted products **3b**-**3f** in 55−83% yield with 79:21 to 84:16 dr and 92.5:7.5 to 96.5:3.5 *er* within 70 minutes (entries 2-6). The diazo compounds bearing 2-naphthyl group and heterocyclic rings, also performed well to yield the corresponding products (**3g**-**3j**) in excellent enantio- and diastereoselectivity (entries 7-10). The low yields of the furyl-containing products **3h** and **3i** were attributed to the quick decomposition of the corresponding diazo substrates (39% and 51% yield; entries 8 and 9). Furthermore, if the *Z/E* mixture of **1a** was used for the reaction, it was found that a majority of *Z*-**1a** was recovered, and the *E*-isomer was consumed, yielding the desired product **3a** in 46% yield, 84:16 dr and 97:3 *er*. It indicated that the *Z*-**1a** was unfavorable in this asymmetric [2,3]-Stevens rearrangement.

Subsequently, the scope of the phenylthioacetate derivatives **2** was also examined (Table 2, entries 11-17). The *meta*- or *para*-substituents on the phenyl group of sulfides **2** had little influence on the reactivity, and all the reactions finished in 15−30 min. As shown in Table 2, electron-donating and -withdrawing substituted arylthioacetates **2** could be transformed into the corresponding products (**4a**-**4f**) in 69−84% yield with 78:22 to 83:17 dr and 93:7 to 96:4 *er* (entries 11-16). In comparison, electron-donating substituted sulfides slightly decreased the enantioselectivity (**4a** and **4b** *vs* **4c**; **4d** *vs* **4e**). It was noteworthy that the sulfides with *ortho*-substituent on the phenyl group could not deliver the final product efficiently due to the problem of steric hindrance. In addition, a gram-scale experiment was conducted with phenyl 2-(phenylthio)acetate to yield the product **3z** (entry 17), whose absolute configuration of the major stereoisomer was assigned to be (2*R*,3*S*,*E*) based on the X-ray crystallographic analysis (See SI for details).[12]

Encouraged by the outcomes in the asymmetric [2,3]-Stevens rearrangement, we turned our attention to the enantioselective Sommelet−Hauser rearrangement of aryl

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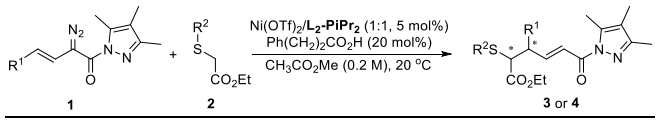
Table 2: Substrate scope for the asymmetric [2,3]-Stevens rearrangement.

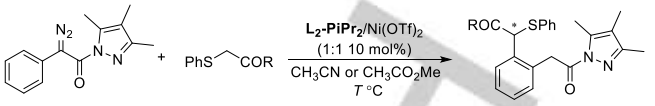


Entry[a]	R^1	R^2	Yield [%][b]	dr[c]	*er*[d]
1	C_6H_5	C_6H_5	76 (**3a**)	83:17	97:3
2	4-MeC_6H_4	C_6H_5	66 (**3b**)	84:16	96:4
3[e]	4-ClC_6H_4	C_6H_5	55 (**3c**)	83:17	94.5:5.5
4	3-MeC_6H_4	C_6H_5	83 (**3d**)	82:18	96.5:3.5
5	3-ClC_6H_4	C_6H_5	62 (**3e**)	79:21	92.5:7.5
6	2-MeC_6H_4	C_6H_5	75 (**3f**)	80:20	96:4
7	2-naphthyl	C_6H_5	61 (**3g**)	84:16	96:4
8	2-furyl	C_6H_5	39 (**3h**)	85:15	96:4
9	3-furyl	C_6H_5	51 (**3i**)	84:16	96.5:3.5
10	3-thienyl	C_6H_5	48 (**3j**)	88:12	96.5:3.5
11	C_6H_5	4-MeC_6H_4	84 (**4a**)	78:22	93:7
12	C_6H_5	4-*i*PrC_6H_4	84 (**4b**)	81:19	93.5:6.5
13	C_6H_5	4-BrC_6H_4	79 (**4c**)	80:20	94.5:5.5
14	C_6H_5	3-MeC_6H_4	83 (**4d**)	81:19	94.5:5.5
15	C_6H_5	3-BrC_6H_4	69 (**4e**)	83:17	96:4
16	C_6H_5	2-naphthyl	79 (**4f**)	81:19	93.5:6.5
17[f]	C_6H_5	C_6H_5	25 (**3z**)	19:1	99:1

[a] The condition is as the same as in footnote [h] in Table 1. [b] Isolated yield. [c] Determined by ^{1}H NMR analysis. [d] Determined by HPLC on a chiral stationary phase. [e] Ni(OTf)$_2$/**L$_2$-PiPr$_2$** (1:1, 10 mol%) in CH_3CO_2Me (0.1 M). [f] **1a** (4.0 mmol), phenyl 2-(phenylthio)acetate (2.5 equiv). The result was obtained after recrystallization.

substituted *α*-diazo pyrazoleamides **5** with sulfides. Initially, the α-diazo(phenyl) pyrazoleamide **5a** and ethyl 2-(phenylthio)acetate **2a** were employed as the model substrates to optimize the reaction conditions (Table 3). Similarly, Ni(OTf)$_2$ was applied to recognize various ligands derived from chiral amino acids, and the same ligand as **L$_2$-PiPr$_2$** was confirmed to be optimal one in CH_2Cl_2 at 35 °C, giving the desired product **6a** in 51% yield with 74:26 er after 3 hours (See Table S8 for details). After careful screening of the solvents, CH_3CN proved to be best choice, and the product **6a** was isolated in 57% yield with 80.5:19.5 er (entry 1). No better results were observed when different ester groups of sulfides **2** were examined (See Table S9 for details). Decreasing the temperature to 0 °C was favorable to the enantioselectivity (entry 2). Next, the survey of the electron-withdrawing group of the sulfides indicated that the phenylcarbamothioates **7** could elevate the er of the Sommelet−Hauser rearrangement, affording the product **8a** in 49% yield with 88.5:11.5 er (entry 3). Further examination of the substituents on the phenyl group of the amides concluded that the

Table 3: Optimization of the reaction conditions of asymmetric Sommelet−Hauser rearrangement



Entry[a]	Sulfide	T (°C)	Time	Yield (%)[b]	er[c]
1	**2a**	35	3 h	57 (**6a**)	80.5:19.5
2	**2a**	0	3 d	62 (**6a**)	85:15
3	**7a**	0	3 d	49 (**8a**)	88.5:11.5
4	**7b**	0	3 d	64 (**8b**)	92.5:7.5
5[d]	**7b**	0	2 d	88 (**8b**)	93:7
6[d,e]	**7b**	0	1.5 d	84 (**8b**)	93:7
7[d,f]	**7b**	0	1.5 d	80 (**8b**)	93:7

[a] Unless otherwise noted, the reactions were carried out with **5a** (0.1 mmol), **2a** or **7** (1.0 equiv), Ni(OTf)$_2$/**L$_2$-PiPr$_2$** (1:1, 10 mol%), and CH_3CN (0.1 M) until the diazo compound **5a** was consumed. [b] Isolated yields. [c] Determined by HPLC on a chiral stationary phase. [d] **7b** (2.5 equiv) under N_2 atmosphere. [e] MeOAc (0.1 M) instead of CH_3CN (0.1 M). [f] $Ph(CH_2)_2CO_2H$ (10 mol%) was added.

sulfide **7b** bearing a trifluoromethoxy group was chosen as the best substrate due to its good solubility in CH_3CN and potential medicinal value of fluorine-containing compounds[13], thus the rearranged product **8b** was generated in 64% yield and 92.5:7.5 er (entry 4). When N_2 atmosphere, and 2.5 equivalents of sulfide **7b** were employed, a yield of 88% with high enantiometric ratio (93:7 er) was obtained (entry 5). The use of CH_3CO_2Me instead of CH_3CN as the reaction solvent enabled the transformation with maintained enantioselectivity and a slightly reduced yield (entry 6). In this case, the additive of 3-phenylpropanoic acid did not play a positive role on enantioselectivity (entry 7). It is noteworthy that the related oxidation byproduct from the diazo compound **5a** was isolated under air atmosphere, but no [1,2]-Stevens rearrangement product was observed.[9a,14]

The substrate scope for Sommelet−Hauser rearrangement was investigated (Scheme 2). CH_3CO_2Me was used instead of CH_3CN in some occasions due to the low solubility of some substrates in CH_3CN at 0 °C. As for α-diazo(aryl) pyrazoleamides **5**, either electron-donating or electron-withdrawing substituent at *para*- or *meta*-position of the phenyl group showed a negative effect on the reactivity and enantioselectivity. The desired products **8c**-**8h** could be isolated in 51-78% yield with 80:20 to 90.5:9.5 *er*. For *meta*-substituted diazo substrates, the reaction occurred at the less sterically hindered *ortho*-position and afforded only one product in moderate to good results (**8e**-**8h**).[15] Additionally, when 2-chlorophenyl substituted α-diazo pyrazoleamide was subjected to the ligand **L$_2$-PiPr$_2$**-based catalyst system, only trace amount of the product **8i** was detected; and a 52% yield with 65:35 *er* was given in the presence of *N,N'*-dioxide **L$_2$-PiCy** instead. α-Diazo(2-naphthyl) pyrazoleamide could undergo the reaction smoothly, to afford the product **8j** in

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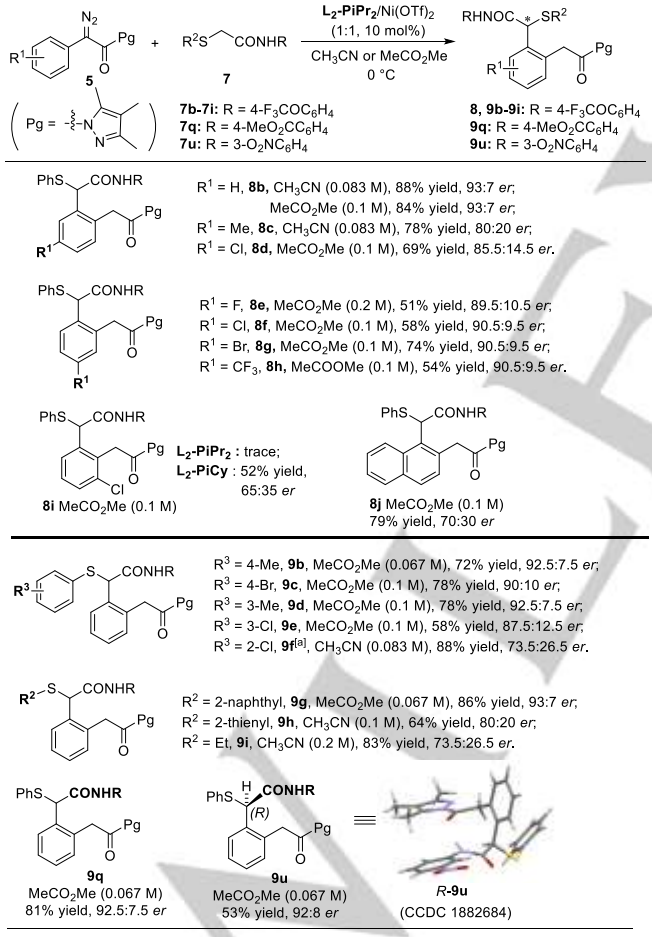
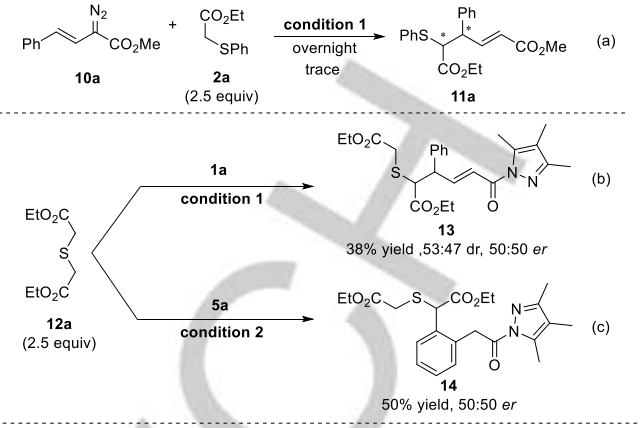
79% yield with 70:30 *er*.[15] Subsequently, various phenylcarbamothioates **7** were investigated by reacting with α-diazo(phenyl) pyrazoleamide **5a**, giving readily the rearrangement products (**9b**-**9e**) in 58-78% yield with 87.5:12.5 to 92.5:7.5 *er*. Phenylthioates containing electron-rich aryl groups gave the desired products in slightly higher enantioselectivities than these with electron-deficient aryl groups. Similarly, when the sulfide **7f** with an *ortho*-chloride substituent was used, the Ni(OTf)$_2$/**L$_2$-PiEt$_2$** complex catalyst proved more efficient. Meanwhile, 2-naphthyl substituted sulfide exhibited high reactivity and enantioselectivity (**9g**; 86% yield, and 93:7 *er*). Moreover, 2- thienyl or ethyl substituted sulfides transformed into the corresponding products **9h** and **9i** in good yields (64% and 83% yields, respectively) with less stereocontrol (80:20 *er* for **9h**; 73.5:26.5 er for **9i**). Additionally, the product **9q** with an ester group and **9u** with a nitro-group at the phenylacetamide unit of sulfides were obtained in 81% and 53% yields with 92.5:7.5 *er* and 92:8 *er*, respectively. The absolute configuration of **9u** was determined to be *R* by using single-crystal *X*-ray diffraction analysis.[16]



[a] **L$_2$-PiEt$_2$** was used instead of **L$_2$-PiPr$_2$**

Scheme 2. Substrate scope for catalytic asymmetric Sommelet−Hauser rearrangement.



Condition 1: **diazo compound** (0.1 or 0.2 mmol), **sulfide** (2.5 equiv), Ni(OTf)$_2$/**L$_2$-PiPr$_2$** (1:1, 10 mol%), Ph(CH$_2$)$_2$CO$_2$H (20 mol%) in MeOAc (0.2 M) at 20 °C.
Condition 2: **5a** (0.1 mmol), **12a** (2.5 equiv), Ni(OTf)$_2$/**L$_2$-PiPr$_2$** (1:1, 10 mol%), in MeOAc (0.2 M) at 0 °C under N$_2$.

Scheme 3. Control experiments with other diazo compound and sulfide.

In order to determine the mechanism of these two types of [2,3]-sigmatropic rearrangement reactions, a series of explored experiments were conducted. Firstly, methyl (*E*)-2-diazo-4-phenylbut-3-enoate **10a** was subjected to the reaction system instead of α-diazo pyrazoleamide **1a** under the standard reaction conditions of the asymmetric [2,3]-Stevens rearrangement (Scheme 3a). But the desired product was formed in only a trace amount as determined by HRMS analysis. The result confirms the necessity of pyrazole group for the reaction reactivity and stereo-control. Moreover, when diethyl 2,2'-thiodiacetate was used for the asymmetric [2,3]-rearrangement reactions, the corresponding products were obtained as racemates (Schemes 3b and 3c). The result was different from the findings in our previous Doyle–Kirmse reaction of diallylsulfane which yield the corresponding product in high enantioselectivity.[10a] This enantioselective Doyle–Kirmse reaction was mainly controlled by the nickel-bounded, less stereo-centered envelope-transition state, and the formation of carbon-carbon bond occurs at the vicinal position of the pyrazoleamide which could by readily controlled by the nearby chiral catalyst. In contrast, when diethyl 2,2'-thiodiacetate was subjected to the asymmetric [2,3]-Stevens and Sommelet–Hauser reactions, the proton in the 1,3-H transfer process could come from two methylene groups of the sulfide **12a**. The formation of ylide IV is less enantioselective. Additionally, carbon-carbon bond occurs at the γ-position of the pyrazoleamides, which is a remote functionalization process and the enantio-control is much more difficult. This might imply that the *S*-stereogenic center generated via discrimination of the heterotopic lone pairs of the sulfur reagent in [2,3]-Stevens and Sommelet–Hauser reactions are important, which will affect the stereochemistry of the sequential proton shift and rearrangement.

Subsequently, deuterium-labelled experiments were carried out to clarify the 1,3-proton transfer process. We synthesized deuterium-labelled sulfide methyl 2-(*p*-tolylthio)acetate-d_2 **15**-d_2 (94% D) for control experiments. All the reactions were purified

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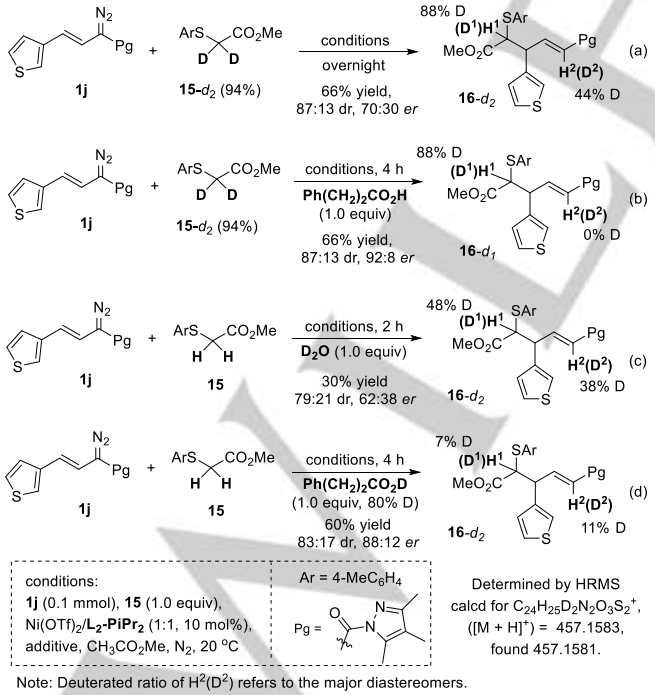
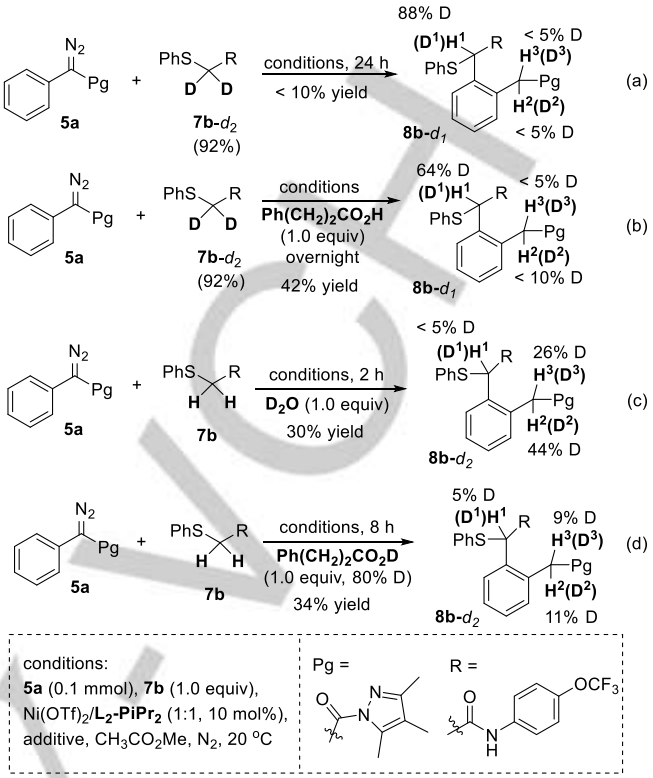
until complete conversion (Scheme 4). As shown in Scheme 4a, when **15**-d_2 was employed for the asymmetric [2,3]-Stevens reaction of diazo compound **1j**, deuterium-labelled product **16**-d_2 was detected after longer reaction time, in which the sulfanylacetate unit (D^1) has around 88% deuterated ratio, and the deuterated ratio of the α-D in the double bond for the major diastereoisomer (D^2) is 44%. It indicates that intermolecular 1,3-proton shift exist in the reaction. The hydrogen atoms (H^2/H^1) in the product might come from the trace amount of water in the catalytic system. The deuterated ratio has discrepancy in multiple experiments due to moisture-sensitivity. Nevertheless, the reaction slows down after strict dehydration. When 3-phenylpropanoic acid was added into the reaction of **15**-d_2, less deuterium (D^2, 0%) is found in the product, and the reactivity and enantioselectivity of the reaction increases obviously (Scheme 4b). It indicates that intermolecular 1,3-proton shift outweighs the direct intramolecular process. Furthermore, if non-deuterium sulfide **15** and deuterated additives (D_2O or $PhCH_2CH_2CO_2D$) were used in the reaction, double-deuterium-labelled product **16**-d_2 were detected (Schemes 4c and 4d). Thus, a reversible transformation might exist between the sulfonium ylide tautomers III and IV, which impacts the stereo-outcome of the reaction (Scheme 1c). The different deuterated ratio and reactivity in these cases shows that water is a faster proton-shuttle than acid, but the isolated yield of the target product is low due to the formation of byproducts. We think that acid could act as a mild proton-shuttle, enabling slower tautomerization process and higher enantioselectivity. Because if reversal tautomerization is dominated, the chiral *S*-center and C1 might undergo a higher racemization risk.[17]



Note: Deuterated ratio of H^2(D^2) refers to the major diastereomers.

Scheme 4. Deuterium-labelled experiments for [2,3]-Stevens rearrangement reaction.



Scheme 5. Deuterium-labelled experiments for Sommelet−Hauser rearrangements.

The deuterium-labelled phenylcarbamothioate **7b**-d_2 (92% D) was examined in the asymmetric Sommelet–Hauser rearrangement reactions (Scheme 5). We carried out the experiments without moisture as much as possible, and found that the reactions slow down dramatically, and low yields were obtained. When **7b**-d_2 was used for the reaction in the absence or presence of the acid additive, the product **8b**-d_1 was found nearly non-deuterium at the methene position (Schemes 5a and 5b). It manifests that the proton (H^2 or H^3) comes from outside rather than sulfide and the tautomerization process became sluggish. When non-deuterium **7b** with deuterated additives (D_2O or $PhCH_2CH_2CO_2D$) were used in the reaction, it is interesting that double-deuterium product **8b**-d_2 was detected (Scheme 5c and 5d). It demonstrates that proton can easily step from outside both in 1,3-H shift step and in the rearomatization step. Water has better proton-transfer ability than acid. Nevertheless, we could not rationalize the reduced deuterium ratio (D^1) shown in Scheme 5b. Neither the sulfide substrates (**7b** and **15**) nor the products (**8b** and **16**) themselves could be deuterium in the catalyst system, but H/D exchange of ylide III or the carbene-insertion intermediate during the reaction process could not be ruled out, because the methylene position is enolisable.

According to our previous work,[10a] the absolute configuration of the major products,[12,17] controlled experiments and deuterium-

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labelled experiments, as well as the general mechanism of [2,3]-sigmatropic rearrangement,[18] the catalytic models for the

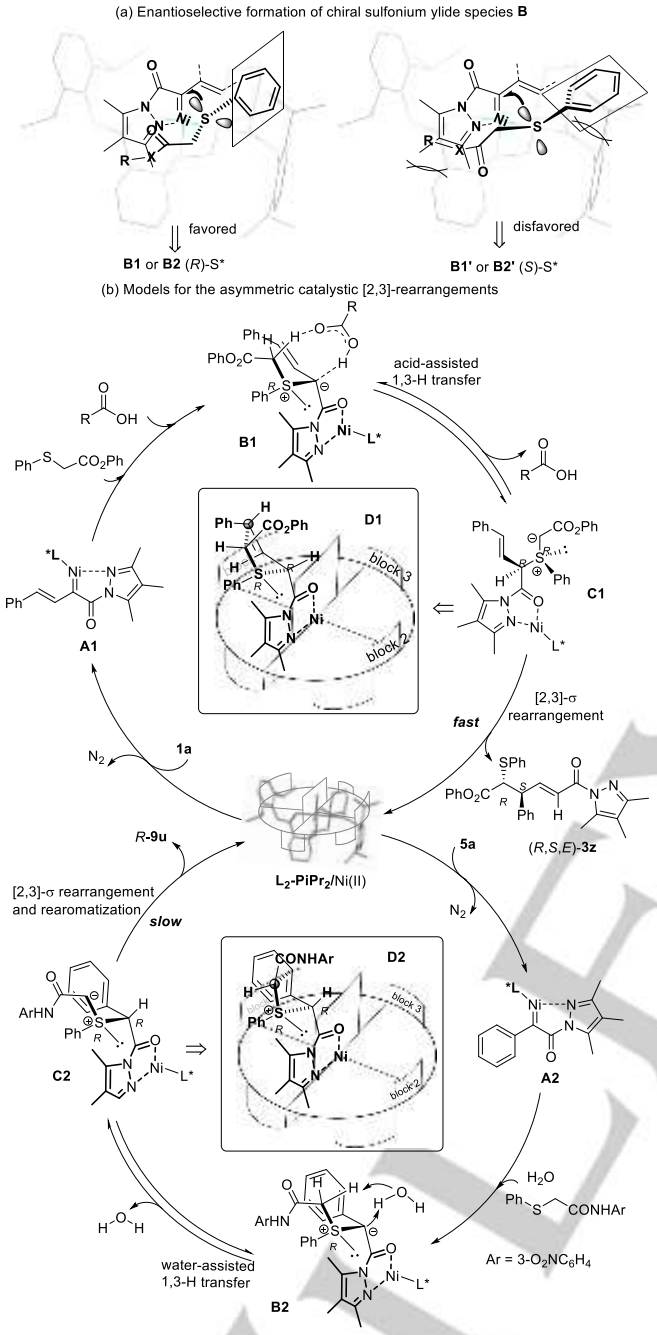

Figure 1. Proposed catalytic models for stereoinduction.

enantiocontrol in [2,3]-Stevens and Sommelet−Hauser rearrangements were proposed (Figure 1). When α-diazo pyrazoleamide **1a** is mixed with the chiral nickel(II) complex catalyst (Figure 1b, top), decomposition via loss of nitrogen proceeds readily to form chiral nickel carbene intermediate **A1**. The (phenylthio)acetate prefers to attack from the *Re*-face of nickel carbene because the opposite *Si*-face is blocked by the left amide unit of the ligand (Figure 1a). As shown in the right model in Figure 1a, due to the steric hindrance of ester group and aryl group of sulfide reagent with the ligand, the discrimination of the heterotopic lone pairs is available. Thus, (*R*)-configured sulfonium ylide species **B1** and **B2** are favorable (Figure 1a, left). Next, carbonic acid additive might act as a proton shuttle to assist the carbanion translocation to yield a tautomeric ylide (Scheme 4).[19] As shown in transition state **B1**, due to the chiral induction raised from sulfur center and chiral catalyst, diastereoselective intermolecular proton transfer occurs to generate (*R*,*R*)-intermediate **C1**. Fortunately, the strong Lewis acid-bounded ylide intermediate by introducing a pyrazoleamide group and the perfect chiral environment in concert benefit the enantioselective 1,3-proton transfer. Next, as shown in **D1**, [2,3]-σ rearrangement process occurs for the β-*Si* face of (*E*)-type C=C double bond via an envelope transition state, in which all the larger substituents (Ph, CO_2Ph, and pyrazoleamide) locate at the opposite sites to exclude the steric hindrance. The chiral catalyst benefits the match of multiple stereogenic centers, and the desired (*2R*,*3S*,*E*)-configured product **3z** was generated as the major isomer.

Similarly, the formation of sulfonium ylide intermediate **B2** for Sommelet–Hauser rearrangement occurs readily (Figure 1b, bottom), but it undergoes an enantioselective intermolecular 1,3-proton shift from trace amount of water in the system. The tautomeric ylide **C2** with uniform stereo-selection performs the [2,3]-σ rearrangement process at the *ortho*-position of the aryl group, which is proposed to be slower than 1,3-proton transfer step due to the high activation energy of the dearomatization step. As shown in **D2**, the amide substituent is opposite to the phenyl group at sulfur atom in the envelope transition state to release the steric hindrance. The attack of prochiral C'-2-atom with its *Re*-face to the aryl substituent, following another 1,3-proton shift to generate rearomatization product (*R*)-**9u** as the major product.

Conclusion

In summary, we have developed the unique examples of asymmetric catalytic [2,3]-Stevens and Sommelet–Hauser rearrangements of sulfonium ylides generated in situ from α-diazo carbonyl compounds and sulfides. The introducing vinyl or aryl substituted α-diazo pyrazoleamides, and the use of chiral *N,N'*-dioxide-Ni(II) complex, as well as additives are critical to the outcome of the two kinds of rearrangements. A series of α-diazo pyrazoleamides and sulfides could undergo the reaction smoothly, affording functionalized 1,6-dicarbonyls and sulfane-substituted phenylacetates with good outcomes. Beside of high reactivity, the catalytic system showed an excellent stereo-control performance for fine discrimination of the heterotopic long pairs of sulfur, enantioselective 1,3-proton transfer, and [2,3]-σ rearrangement as well. Intermolecular 1,3-proton transfer was confirmed by deuterium-labelled experiments. Further application of the functional group-direct-strategy with chiral *N,N'*-dioxide-metal complex catalysts to other enantioselective synthesis are ongoing in our laboratory.

Experimental Section

General procedure for enantioselective [2,3]-Stevens rearrangement of vinyl substituted α-diazo pyrazoleamides 1: A dry reaction tube was charged with **L_2-PiPr$_2$** (0.005 mmol), $Ni(OTf)_2$ (0.005 mmol) and $Ph(CH_2)_2CO_2H$ (0.02 mmol) under an N_2 atmosphere. Then CH_3CO_2Me (0.5 mL) was added and the mixture was stirred at 35 °C for 40 minutes. Subsequently, sulfide **2** (0.25 mmol) and diazo compound **1** (0.1 mmol) were added successively at 20 °C. The reaction was detected by TLC. After the diazo compound **1** was consumed (detected by TLC), the residue was purified by column chromatography on silica gel to afford the product (Pet/EtOAc = 25/1 as eluent).

General procedure for enantioselective Sommelet–Hauser rearrangement of α-diazo(aryl) pyrazoleamides 5: A dry reaction tube was charged with **L_2-PiPr$_2$** (0.01 mmol) and $Ni(OTf)_2$ (0.01 mmol) under an N_2 atmosphere. Then CH_2Cl_2 (1.0 mL) was added and the mixture was stirred at 35 °C for 40 minutes. Then the solvent CH_2Cl_2 was removed in vacuum. Subsequently, sulfide **7** (0.25 mmol) and diazo compound **5** (0.1 mmol) were added successively. The reaction tube was charged with N_2 in 5 cycles again. The solvent was added at 0 °C. After the diazo compound **5** was consumed (detected by TLC), the residue was purified by column chromatography on silica gel to afford the product (Pet/EtOAc = 15/1 to 10/1 as eluent).

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Keywords: [2,3]-σ rearrangement • sulfonium ylides • α-diazo compound • sulfide • chiral nickel(II) complex

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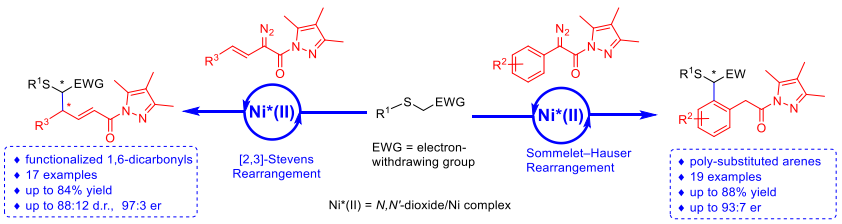

Chiral *N,N'*-dioxide-Ni(II) complex catalysts were found to work efficiently in the asymmetric catalytic [2,3]-Stevens and Sommelet–Hauser rearrangements of α-diazo pyrazoleamides with sulfides. The catalytic system showed excellent stereo-control, discriminating between the heterotopic lone pairs of sulfur and controlling both the 1,3-proton transfer and the [2,3]-σ rearrangement.

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Asymmetric Catalytic [2,3]-Stevens and Sommelet–Hauser Rearrangements of α-Diazo Pyrazoleamides with Sulfides