Ruthenium Complex-Catalyzed Reaction of Isocyanoacetate and *N*-Sulfonylimines: Stereoselective Synthesis of *N*-Sulfonyl-2-Imidazolines

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Ruthenium(II)-catalyzed reaction of *N*-sulfonylimines with methyl isocyanoacetate proceeds efficiently under neutral, mild conditions to give *trans*-2-imidazolines stereoselectively in high yields. 2,3-Diamino acids can be easily acquired via the hydrolysis of the imidazolines in excellent yields. A possible mechanism for the ruthenium-catalyzed aldol reaction of the imines under neutral conditions is discussed.

The construction of five-membered nitrogen-containing heterocycles, such as oxazoline and imidazoline, has received considerable attention because of the wide application of these compounds to the synthesis of biologically active compounds.[1] The aldol reaction has been used in the synthesis of oxazoline which bears a 1,3-*O*,*N*-ring system in the heterocycle.[2] During the past decade, considerable effort has been devoted to developing effective catalytic, stereoselective aldol reactions.[3,4,5] Recently, transition metal-catalyzed aldol reactions of isocyanoacetate and aldehydes have been reported to give 4,5-disubstituted-2-oxazolines.[6] A successful method has been reported by Ito et al. who used a gold-complex and a chiral ligand in the asymmetric version of this reaction, giving high yields and enantiomeric excesses.[7] For the synthesis of 2-imidazoline, existing methods include base-promoted aldol reaction,[8] 1,3-dipolar addition,[9] and others.[10] There have been few reports on the catalytic reaction of imines with isocyanoacetate because of the low reactivity of imines.[11] Herein, we report an efficient method for the synthesis of 2-imidazolines from isocyanoacetate and *N*-sulfonylimines catalyzed by transition metal complexes.

Results and Discussion

We have studied iridium complex-catalyzed aldol reactions of isocyanoacetates with various aldehydes in order to obtain *trans*-(4,5)-disubstituted-2-oxazolines in high yields under neutral conditions.[12] When *N*-aryl- or *N*-alkyl-substituted imines were used instead of aldehydes in this reaction, no products were isolated. Given the low reactivity of imines in nucleophilic addition, a strong electron-withdrawing group, i.e. sulfonyl, was introduced on the nitrogen atom of the imines in order to activate the C=N bond. We found that the iridium polyhydride complex-catalyzed aldol reaction of the activated imine and isocyanoacetate did occur and afforded imidazolines. In addition to the iridium complex, ruthenium dihydride complex, Pd-complexes, and Fe-complex are effective catalysts for this reaction. $RuH_2(PPh_3)_4$ is the best among the catalysts examined when the reaction of *N*-sulfonylimines with isocyanoacetate is carried out in the presence of a catalytic amount of phosphine ligand dppe in CH_2Cl_2 at 25 °C. The catalytic activity of the various metal complexes is shown in Table 1.

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Table 1. Catalytic Activity of Metal Complexes for the Aldol Reaction of Imine in CH_2Cl_2[a]

entry	catalyst (% mol)	ligand, dppe (% mol)	solvent	reaction time (h)	ratio of *trans*:*cis*[b]	yield, (%)[c]
1	$RuH_2(PPh_3)_4$ (1)	10	CH_2Cl_2	7	86:14	92
2	$RuH_2(PPh_3)_4$ (1)	5	CH_2Cl_2	7	80:20	88
3	$RuH_2(PPh_3)_4$ (1)	0	CH_2Cl_2	7	77:23	90
4	$RuH_2(PPh_3)_4$ (1)	0	CH_2Cl_2/CH_3OH	7	95:5	95
5	$IrH_5(i\text{-}Pr_3P)_2$ (1)	0	CH_2Cl_2	7	63:37	88
6	$IrH_5(i\text{-}Pr_3P)_2$ (1)	10	CH_2Cl_2	7	70:30	85
7	$IrH_5(i\text{-}Pr_3P)_2$ (1)	0	CH_2Cl_2/CH_3OH	7	93:7	95
8	$FeH_2(dppe)_2$ (1)	0	CH_2Cl_2	10	80:20	86
9	$FeH_2(dppe)_2$ (1)	0	CH_2Cl_2/CH_3OH	10	86:14	88
10	$Pd(PPh_3)_4$ (5)	10	CH_2Cl_2	2	83:17	90
11	$Pd(PPh_3)_4$ (5)	0	CH_2Cl_2/CH_3OH	2	84:16	90
12	$Pd_2(dba)_2$ (5)	10	CH_2Cl_2	5	81:19	90
13	$Pd_2(dba)_2$ (5)	0	CH_2Cl_2/CH_3OH	3	80:20	86
14	$PdCl_2(CH_3CN)_2$ (5)	10	CH_2Cl_2	24	48:52	85
15	$PdCl_2(CH_3CN)_2$ (5)	0	CH_2Cl_2/CH_3OH	24	60:40	81
16	$PdCl_2$(dppf) (5)	0	CH_2Cl_2	36	70:30	66

[a] The reaction was carried out with various catalysts in the presence or absence of dppe at 25 °C. **1a**/**2** = 1/1.1. [b] Determined by ^{1}H NMR analysis. [c] Isolated yields of a mixture of *trans*/*cis* isomers based on *N*-sulfonylimines **1a**.

Scheme 1

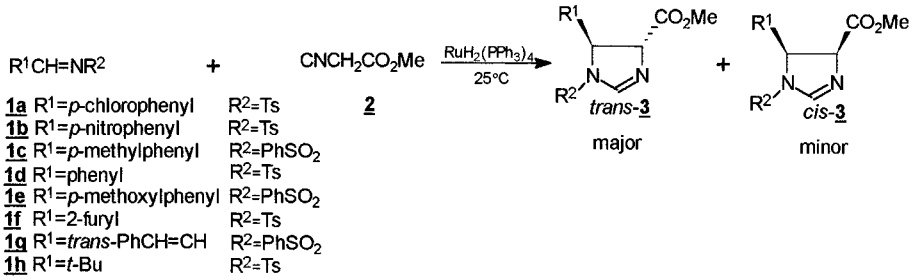


Table 2. Reaction of 1a with Methyl Isocyanoacetate 2 Catalyzed by $RuH_2(PPh_3)_4$ in Various Solvents[a]

entry	solvent	ligand, dppe (%)	time (h)	*trans*:*cis*[b]	yield, %[c]
1	THF	0	7	68:32	88
2	THF	10	7	73:27	88
3	CH_2Cl_2	0	7	77:23	90
4	CH_2Cl_2	10	7	86:14	92
5	CH_3CN	0	7	70:30	72
6	CH_3CN	10	7	68:32	78
7	CH_3OH	0	7	84:16	80
8	CH_3OH	10	7	86:14	83
9	toluene	0	7	60:40	65
10	toluene	10	7	60:40	69
11	1,4-dioxane	10	7	70:30	86

[a] The reaction was carried out at 25 °C. **1a**/**2**/catalyst = 1/1.1/0.01. [b] Determined by ^{1}H NMR analysis. [c] Isolated yields of a mixture of *trans*/*cis* isomers based on *N*-sulfonylimine **1a**.

Table 3. The Effect of ligand on the Reactivity of 1a with Methyl Isocyanoacetate 2 Catalyzed by $RuH_2(PPh_3)_4$[a]

entry	ligand	time (h)	ratio of *trans*:*cis*[b]	yield, %[c]
1	*n*-Bu_3P	7	85:15	85
2	(c-hexyl)$_3$P	7	83:17	42
3	$(CH_3O)_3P$	7	60:40	83
4	dppe	7	86:14	92
5	dppf	7	80:20	68
6		7	77:23	90

[a] The reaction was carried out in CH_2Cl_2 at 25 °C. **1a**/**2**/catalyst/ligand = 1/1.1/0.01/0.1. [b] Determined by ^{1}H NMR analysis. [c] Isolated yields of a mixture of *trans*/*cis* isomers based on *N*-sulfonylimine **1a**.

The reaction of methyl isocyanoacetate and *N*-sulfonylimines catalyzed by $RuH_2(PPh_3)_4$ complex is illustrated in Scheme 1. The effects of solvents and phosphine ligands on the catalytic aldol reaction of the imine were examined, and the results are listed in Tables 2 and 3, respectively. Table 2 shows that CH_2Cl_2 is a suitable solvent in the sense of yield and selectivity and that MeOH is effective in terms of selectivity. Addition of an electron-donating phosphine ligand to the catalytic system in CH_2Cl_2 gave higher trans/cis stereoselectivity. 1,2-Bis(diphenylphosphino)ethane (dppe) was the most effective ligand among those examined (Table 3). However, addition of the phosphine ligand dppe did not improve the stereoselectivity and reactivity of the reaction in toluene (Table 2). The bulky phosphine, dppf (entry 5, Table 3) and tricyclohexylphosphine (entry 2, Table 3) reduced the yield significantly.

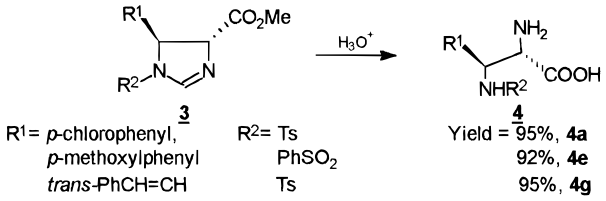
Thus, when the reaction of *N*-tosyl-*p*-chlorobenzaldimine and methyl isocyanoacetate was catalyzed by the $RuH_2(PPh_3)_4$ complex in CH_2Cl_2 at 25 °C, the 2-imidazoline was obtained in 90% yield with a *trans*:*cis* ratio of 77:23. Upon addition of dppe ligand, the stereoselectivity improved to 86:14 with 92% yield of 2-imidazoline. The selectivity as well as the yield further improved to 95:5 and 95% when a mixed solvent of methanol and dichloromethane was used, even in the absence of dppe (entry 4, Table 1). The use of a mixed solvent has almost no effect in the Pd and Fe systems (entries 9, 11, 13, Table 1). The above reaction conditions were then employed in the remainder of this study. The reaction occurs with *N*-sulfonylimines prepared from aromatic, heterocyclic, α,β-unsaturated, and *t*-Bu-aldehydes (Table 4). In all cases, the *trans*-2-imidazolines were obtained with high selectivity and in high yield. The results indicate that Ru(II)-complex-catalyzed aldol reactions of *N*-sulfonylimines are highly efficient in yield and stereoselectivity under neutral conditions.

Table 4. Reaction of *N*-sulfonylimines 1 with Isocyanoacetate 2 Catalyzed by $RuH_2(PPh_3)_4$ Complex[a]

entry	*N*-sulfonylimines	R^1	R^2	time (h)	ratio of *trans*:*cis*[b]	yield % (*trans*-**3**)[c]
1	**1a**	*p*-chlorophenyl	Ts	7	95:5	90
2	**1b**	*p*-nitrophenyl	Ts	5	91:9	86
3	**1c**	*p*-methylphenyl	$PhSO_2$	9	93:7	88
4	**1d**	phenyl	Ts	9	87:13	80
5	**1e**	*p*-methoxylphenyl	$PhSO_2$	12	92:8	89
6	**1f**	2-furyl	Ts	7	95:5	90
7	**1g**	*trans*-PhCH=CH	$PhSO_2$	12	84:16	75[d]
8	**1h**[e]	*t*-Bu	Ts	16	95:5	90[d]

[a] The reaction was carried out in a mixed solvent of methanol and CH_2Cl_2 (3:1) at 25 °C. **1**/**2**/catalyst = 1/1.1/0.01. [b] Determined by ^1H NMR analysis before isolations. [c] Isolated yields of *trans*-isomer based on *N*-sulfonylimines **1**. [d] Use 3% mol catalyst. [e] The reaction was carried out in CH_2Cl_2.

Scheme 2



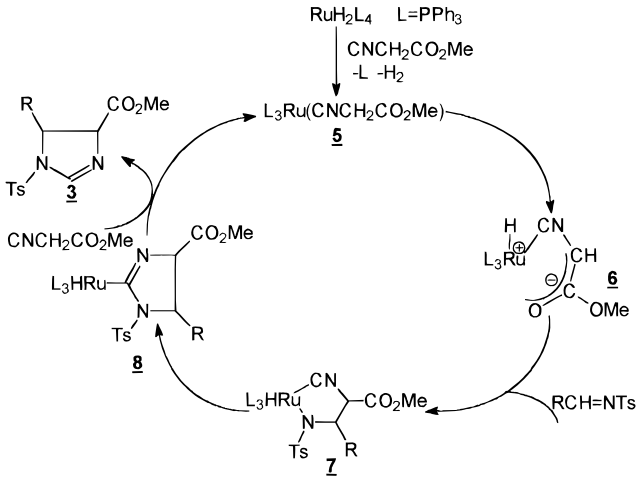
The configuration of the *trans* isomer was assigned on the basis of ^1H NMR coupling constants between 4-H and 5-H (J = 7.12 Hz, for **3a**).[13] It was further confirmed by an X-ray crystallographic analysis of **3d**.[32]

The imidazolines obtained by this reaction can be used in the synthesis of various substituted 2,3-diamino acids or diamino alcohols,[14] which are constituents of some peptidic antibiotics[15] as well as other biologically active molecules.[16] In general, the efficient synthesis of 2,3-diaminio acids begins with individual amino acids.[17] Now, the diamino acids can be easily obtained by hydrolysis of imidazolines in high yields (Scheme 2). The diamino acids obtained by this method may have various R^1 groups at the 3-position.

The importance of the *N*-sulfonyl-2-imidazolines as synthetic intermediates lies not only in their usefulness in preparing *N*-protected 2,3-diamino acids which can be readily converted to 2,3-diamino acids and other amino acids or peptides, but also in the further preparation of *N*-sulfonyl-*β*-lactams from the *N*-sulfonyl diamino acids using DCC/4-PPY.[18]

Recently, transition metal complexes have been reported to be effective catalysts for aldol and Michael reactions under neutral and mild conditions.[3−5] The mechanism of the aldol reaction of nitriles with carbonyl

Scheme 3



compounds catalyzed by divalent ruthenium complex has been studied by Murahashi very recently.[19] The catalytically active species of these reactions seems to be a zerovalent ruthenium complex. In the present reaction, the formation of active species **5** seemed reasonable by the coordination of the isocyano group to "L_3RuH_2" and subsequent reductive elimination of molecular hydrogen. A postulated catalytic cycle is shown in Scheme 3.

A possible pathway for the ruthenium-catalyzed aldol reaction of imines under neutral conditions may include a ruthenium enolate intermediate which is probably formed by the oxidative addition of the active methylene C−H bond to the metal after the coordination of the isocyano group. In our proposed catalytic scheme, oxidative addition of the active methylene C−H bond of isocyanoacetate to the metal may afford a hydrido-α-isocyanoalkylruthenium intermediate which is converted to hydrido(enolato)−ruthenium(II) complex **6**. Although we have as yet no experimental evidence, this process is similar to that suggested by Murahashi for the aldol reaction of nitriles.[19a] Furthermore, the oxidative addition product of the reaction of alkyl cyanoacetate with $RuH_2(PPh_3)_4$ has been isolated by Komiya et al.[19b] The formation of **6** is thus a reasonable intermediate in our reaction. Direct interaction of **6** with an imine takes place to give **7**, probably by intramolecular nucleophilic addition. However, nucleophilic addition of the imine in an intermolecular manner cannot be ruled out if the solvent, ligand, or the second molecular isocyanoacetate can coordinate with intermediate **6**. The η^1-*O*-enolato or

(13) A small amount of *cis* isomer **3a** displayed a vicinal (H_4-H_5) coupling constant of 11.3 Hz. *trans*-4,5-disubstituted-2-imidazolines always display smaller vicinal coupling constants than do *cis* isomers. This is in accord with the *trans*/*cis* coupling constants for five-membered ring compounds.

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η^3-oxaallylic moiety is responsible for the nucleophlic addition to a sulfonyl activated C=N bond of imine. The addition product **7** underwent cyclization to **8** and then regeneration of **5** after reductive elimination. The stereochemistry of the disposition of R and COOR in a trans-fashion is probably controlled by a stereofavorable factor. The path for the formation of metal enolate in this case is different from that of the Au-complex-catalyzed aldol reaction of aldehyde with isocyanoacetate reported in the presence of an amino group by Ito. In our case, the reaction conditions are neutral, without the necessary presence of amine, and the transition metal plays a key role in forming the Ru-enolate. Further studies on this new catalyzed reaction are now in progress.

In summary, we have demonstrated a new catalytic approach for the convenient synthesis of 2-imidazolines from isocyanoacetates and *N*-sulfonylimines under neutral conditions. The mildness of the reaction conditions, the simplicity of the procedure, and the high yields and stereoselectivity of the nucleophilic addition should offer great promise for the synthesis of nitrogen-heterocyclic compounds as well as useful diamino acids, β-lactams and many others. Investigations of further extensions and enantioselective synthetic applications of our method are in progress.

Experimental Section

Materials and General Procedure. All *N*-sulfonylimines **1** and methyl isocyanoacetate were prepared according to literature methods.[20,21] THF was distilled immediately prior to use from sodium/benzophenone under nitrogen. The other solvents were treated according to standard methods.

Catalytic Activity of Metal Complexes for the Aldol Reactions of Imines. A mixture of *N*-sulfonylimine (**1a**, 0.46 mmol), methyl isocyanoacetate (**2**, 0.50 mmol), and catalyst (1% mol) was stirred in CH_2Cl_2 at 25 °C for 2−36 h under nitrogen. After removal of the solvent, the residue was isolated by preperative TLC eluting with a mixture of petroleum ether (60−90 °C) and ethyl acetate (2:1) to give 4,5-disubstituted-2-imidazoline. The yields are shown in Table 1. The *trans*/*cis* ratio was determined by ^{1}H NMR spectra. The catalysts $IrH_5(i\text{-}Pr_3P)_2$,[22] $RuH_2(CO)(PPh_3)_3$,[23] $Pd(PPh_3)_4$,[24] $PdCl_2(CH_3CN)_2$,[25] $PdCl_2(dppf)$,[26] $RuH_2(PPh_3)_4$,[27] $FeH_2(dppe)_2$,[28] and $Pd_2(bda)_3$[29] were prepared according to literature methods.

The Effect of Phosphine Ligands on the Reaction of 1a with 2 Catalyzed by $RuH_2(PPh_3)_4$. *N*-Sulfonylimine (0.46 mmol), methyl isocyanoacetate (0.50 mmol), and $RuH_2(PPh_3)_4$ (0.005 mmol) were dissolved in 4.0 mL of solvent. To this solution was added phosphine ligand (0.05 mmol). This mixture was stirred at 25 °C for 7 h. After removal of the solvent, the residue was isolated by preparative TLC (petroleum ether (60−90 °C):ethyl acetate, 2:1) to give 4,5-disubstituted-2-imidazoline (**3a**). The yields are shown in Table 2. The *trans*/*cis* ratio was determined by ^{1}H NMR spectra. The phosphine ligands dppe[30] and dppf [31] were prepared by literature procedures. n-Bu_3P, $(CH_3O)_3P$, $(c\text{-}C_6H_{11})_3P$ were bought from commerial suppliers and used without further purification.

General Procedure for the Ruthenium-Catalyzed Reaction of *N*-Sulfonylimines (1a) with Methyl Isocyanoacetate (2). A mixture of *N*-sulfonylimine (**1a**, 0.46 mmol), methyl isocyanoacetate (**2**, 0.5 mmol), and $RuH_2(PPh_3)_4$ complex (5.3 mg, 1% mol) was stirred in 4.0 mL of a mixed solvent of methanol and CH_2Cl_2 (CH_3OH/CH_2Cl_2 = 3/1) at rt for 7 h under nitrogen. After removal of the solvent, the residue was isolated by preparative TLC (petroleum ether (60−90 °C):ethyl acetate, 2:1) to give *trans*-(4,5)-2-imidazoline (**3a**). The *cis* isomer was not isolated. The *trans*/*cis* ratio was determined by ^{1}H NMR spectra before isolation.[13]

***trans*-4-(Methoxycarbonyl)-5-(4-chlorophenyl)-1-*N*-tosyl-2-imidazoline (3a).** ^{1}H NMR ($CDCl_3$/TMS): δ 2.42 (s, 3 H), 3.71 (s, 3 H), 4.62 (d, J = 7.12 Hz, 1 H), 5.06 (d, J = 7.12 Hz, 1 H), 7.10 (d, J = 8.11 Hz, 2 H), 7.20−7.21 (m, 4 H), 7.47 (d, J = 8.11 Hz, 2 H), 7.68 (s, 1 H). IR: 1740, 1620 cm^{-1}. MS m/z 393 (M^+ + 1, 1), 333 (13), 237 (100), 155 (43), 91 (66), 59 (2). Anal. Calcd for $C_{18}H_{17}ClN_2O_4S$: C, 55.03; H, 4.36; N,7.13. Found: C, 55.12; H, 4.48; N, 7.01.

***trans*-4-(Methoxycarbonyl)-5-(4-nitrophenyl)-1-*N*-tosyl-2-imidazoline (3b).** ^{1}H NMR ($CDCl_3$/TMS): δ 2.47 (s, 3 H), 3.74 (s, 3 H), 4.62 (dd, J = 7.58, 2.12 Hz, 1 H), 5.13 (d, J = 7.58 Hz, 1 H), 7.26 (d, J = 8.31 Hz, 2 H), 7.39 (d, J = 8.72 Hz, 2 H), 7.54 (d, J = 8.31 Hz, 2 H), 7.68 (d, J = 2.12 Hz, 1 H), 8.15 (d, J = 8.72 Hz, 2 H). IR: 1740, 1650 cm^{-1}. MS m/z 404 (M^+ + 1), 344 (19), 248 (63), 155 (54), 91 (100). Anal. Calcd for $C_{18}H_{17}N_3O_6S$: C, 53.59; H, 4.24; N, 10.41. Found: C, 53.66; H, 4.33; N, 10.28.

***trans*-4-(Methoxycarbonyl)-5-(4-methylphenyl)-1-*N*-benzenesulfonyl-2-imidazoline (3c).** ^{1}H NMR ($CDCl_3$/TMS): δ 2.23 (s, 3 H), 3.62 (s, 3 H), 4.59 (dd, J = 7.44, 2.16 Hz, 1 H), 4.98 (d, J = 7.44 Hz, 1 H), 6.96 (s, 4 H), 7.19−7.53 (m, 5 H), 7.58 (d, J = 2.16 Hz, 1 H). IR: 1740, 1610 cm^{-1}. MS m/z 359 (M^+ + 1, 5), 299 (15), 217 (100), 141 (11), 77 (37). Anal. Calcd for $C_{18}H_{18}N_2O_4S$: C, 60.32; H, 5.06; N, 7.81. Found: C, 60.03; H, 5.10; N, 7.98.

***trans*-4-(Methoxycarbonyl)-5-phenyl-1-*N*-tosyl-2-imidazoline (3d).** ^{1}H NMR ($CDCl_3$/TMS): δ 2.40 (s, 3 H), 3.70 (s, 3 H), 4.70 (dd, J = 7.42, 2.07 Hz, 1 H), 5.10 (d, J = 7.42 Hz, 1 H), 7.14−7.26 (m, 7 H), 7.47 (d, J = 8.32 Hz, 2 H), 7.65 (d, J = 2.07 Hz, 1 H). IR: 1740, 1610 cm^{-1}. MS m/z 359 (M^+ + 1, 1), 299 (20), 203 (100), 155 (34), 91 (59), 59 (1). Anal. Calcd for $C_{18}H_{18}N_2O_4S$: C, 60.32; H, 5.06; N, 7.81. Found: C, 60.12; H, 5.09; N, 7.95.

***trans*-4-(Methoxycarbonyl)-5-(4-methoxyphenyl)-1-*N*-benzenesulfonyl-2-imidazoline (3e).** ^{1}H NMR ($CDCl_3$/TMS): δ 3.70 (s, 3 H), 3.80 (s, 3 H), 4.65 (d, J = 7.20 Hz, 1 H), 5.10 (d, J = 7.20 Hz, 1 H), 6.73 (d, J = 8.42 Hz, 2 H), 7.04 (d, J = 8.42 Hz, 2 H), 7.40 (m, 2 H), 7.56 (m, 3 H), 7.70 (s, 1 H). IR: 1740, 1620 cm^{-1}. MS m/z 374 (M^+, 1), 315 (6), 233 (77), 141 (4), 77 (24). Anal. Calcd for $C_{18}H_{18}N_2O_5S$: C, 57.74; H, 4.84; N, 7.48. Found: C, 57.52; H, 4.96; N, 7.48.

***trans*-4-(Methoxycarbonyl)-5-furyl-1-*N*-tosyl-2-imidazoline (3f).** ^{1}H NMR ($CDCl_3$/TMS): δ 2.40 (s, 3 H), 3.73 (s, 3 H), 4.91 (d, J = 7.48 Hz, 1 H), 5.31 (d, J = 7.48 Hz, 1 H), 6.25 (d, J = 1.78 Hz, 1 H), 6.40 (d, J = 3.15 Hz, 1 H), 7.15 (s, 1 H), 7.26 (d, J = 8.00 Hz, 2 H), 7.50 (d, J = 8.00 Hz, 2 H), 7.62 (s, 1 H). IR: 1740, 1620 cm^{-1}. MS m/z 349 (M^+ + 1, 5), 289 (5), 193 (100), 155 (11), 91 (38), 59 (2). Anal. Calcd for $C_{16}H_{16}N_2O_5S$: C, 55.16; H, 4.62; N, 8.04. Found: C, 54.89; H,4.67; N, 7.91.

***trans*-4-(Methoxycarbonyl)-5-(*trans*-phenylvinyl)-1-*N*-benzenesulfonyl-2-imidazoline (3g).** ^{1}H NMR ($CDCl_3$/TMS): δ 3.72 (s, 3 H), 4.60 (dd, J = 7.72, 1.85 Hz, 1 H), 4.80 (dd, J = 8.32, 7.72 Hz, 1 H), 5.85 (dd, J = 15.78, 8.32 Hz, 1

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H), 6.63 (d, J = 15.78 Hz, 1 H), 7.3−7.8 (m, 11 H). IR: 1740, 1620 cm^{-1}. MS m/z 370 (M^+, 3), 311 (5), 229 (100), 141 (5), 59 (1). Anal. Calcd for $C_{19}H_{18}N_2O_4S$: C, 61.60; H, 4.89; N, 7.56. Found: C, 61.51; H, 5.02; N, 7.34.

***trans*-4-(Methoxycarbonyl)-5-*tert*-butyl-1-*N*-tosyl-2-imidazoline (3h).** ^{1}H NMR ($CDCl_3$/TMS): δ 0.95 (s, 9 H), 2.43 (s, 3 H), 3.48 (s, 3 H), 3.71 (d, J = 3.25 Hz, 1 H), 4.45 (s, 1 H), 7.32 (d, J = 8.01 Hz, 2 H), 7.53 (s, 1 H), 7.65 (d, J = 8.01 Hz, 2 H). IR: 1620 cm^{-1}. MS m/z 339 ($M^+ + 1$, 5), 281 (77), 183 (3), 155 (81), 91 (83), 59 (1). Anal. Calcd for $C_{16}H_{22}N_2O_4S$: C, 56.78; H, 6.55; N, 8.27. Found: C, 56.41; H, 6.64; N, 8.07.

General Procedures for the Preperation of Diamino Acids from the Hydrolysis of 2-Imidazoline. Procedure A (for **4a**, **4e**): A mixture of *trans*-2-imidazoline (0.3 mmol) and 2 mL of 40% HBr was refluxed for 3 h. After concentration under vacuum, 5 mL of 2 N NaOH was added. The reaction mixture was filtered to remove inorganic salts. To the filtrate was dropwise added 6 N HCl at 80 °C until the solid was precipitated (pH = 7). The precipatates were washed with water and then ethyl ether to give a white solid, diamino acid. **Procedure B** (for **4g**): The procedure is the same with procedure A except 40% HBr was replaced by 30% HCl.

2-Amino-3-(*N*-tosylamino)-3-(4-chlorophenyl)propanoic Acid (4a). ^{1}H NMR (CF_3COOD): δ 2.50 (s, 3 H), 4.86 (d, J = 8.88 Hz, 1 H), 5.06 (d, J = 8.88 Hz, 1 H), 7.06 (d, J = 8.27 Hz, 2 H), 7.30 (m, 4 H), 7.63 (d, J = 8.27 Hz, 2 H). Anal. Calcd for $C_{16}H_{17}ClN_2SO_4$: C, 52.10; H, 4.64; N, 7.59. Found: C, 51.49; H, 4.60; N, 7.48.

2-Amino-3-(*N*-benzenesulfonylamino)-3-(4-methoxyphenyl)propanoic Acid (4e). ^{1}H NMR (CF_3COOD): δ 3.81 (s, 3 H), 4.71 (d, J = 8.32 Hz, 1 H), 4.93 (d, J = 8.32 Hz, 1 H), 6.75 (d, J = 8.55 Hz, 2 H), 6.94 (d, J = 8.55 Hz, 2 H), 7.33 (d, J = 7.77 Hz, 2 H), 7.51 (m, 1 H), 7.61 (d, J = 7.77 Hz, 2 H). Anal. Calcd for $C_{16}H_{18}N_2SO_5$: C, 54.84; H, 5.17; N, 7.99. Found: C, 54.56; H, 4.99; N, 7.78.

2-Amino-3-(*N*-tosylamino)-3-(*trans*-phenylvinyl)propanoic Acid (4g). ^{1}H NMR (CF_3COOD): δ 2.28 (s, 3 H), 4.64 (m, 2 H), 5.88 (m, 1 H), 6.20 (d, J = 15.66 Hz, 1 H), 7.08 (d, J = 7.91 Hz 2 H), 7.33 (m, 5 H), 7.79 (d, J = 7.91 Hz, 2 H). Anal. Calcd for $C_{18}H_{20}N_2SO_4$: C, 59.98; H, 5.59; N, 7.77. Found: C, 59.88; H, 5.56; N, 7.60.

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