JOC*Note*

1,2-Migration in Rhodium(II) Carbene Transfer Reaction: Remarkable Steric Effect on Migratory Aptitude

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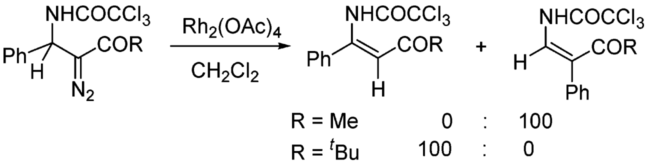
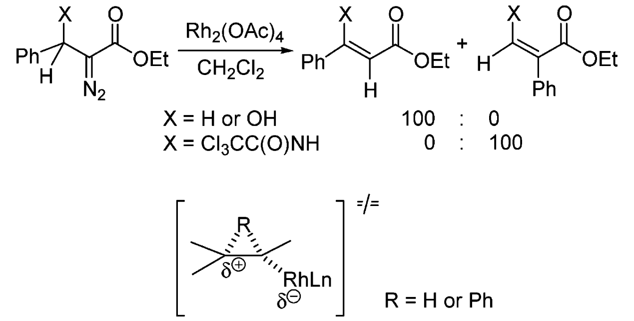


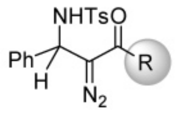
A series of diazo carbonyl compounds bearing different substituents have been prepared in order to investigate the steric effect in 1,2-migration reaction of rhodium(II) carbene. Through the investigation on the diazo decomposition of these compounds with $Rh_2(OAc)_4$, it was found that the steric effect could dramatically influence the migratory aptitude. In many cases, the steric effect could override the inherent electronic effect of the substituent.

1,2-Migration represents a fundamental reaction pathway for both free carbenes and metal-associated carbenes.[1,2] In the cases of singlet carbene, the 1,2-migratory aptitude has been investigated extensively in the past decades. The inherent migratory aptitude is in the order of H > Ar > alkyl. This migratory preference has also been known to be affected by steric and conformational factors.[3] We have recently studied the problem of 1,2-migratory aptitude in the case of rhodium(II)−carbene, which is generated through Rh(II) complex catalyzed reaction of α-diazocarbonyl compounds.[4] Although in 1,2-migration of metal carbenes similar migratory aptitude as in the case of singlet carbene has been known,[2] a dramatic nonmigrating (bystander) effect has been observed. For example, the 1,2-aryl migration becomes completely predominant over 1,2-H migration when there is a nonmigrating substituent $NHCOCl_3$ attached to the migration origin (Scheme 1).[4d] This effect of the bystander has been attributed to their electronic effects. As shown by the transition state in Scheme 1, the migration origin is supposed to have more positive charge development in 1,2-H migration than in 1,2-Ph migration. Thus, a strong π-electron-donating group, such as hydroxy group, will accelerate 1,2-H migration, while relatively less electron-donating group such as $Cl_3CC(O)NH$ has the opposite effect. As a continuation of this investigation, we report in this paper that steric factors also have an important effect on the 1,2-migratory aptitude in the reactions of rhodium(II) carbene.

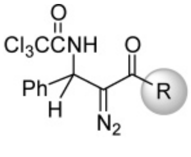
SCHEME 1



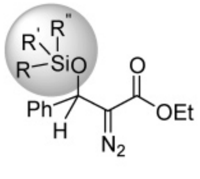
A series of diazo carbonyl compounds **1a**−**f**, **2a**−**e**, and **3a**−**e**, which bear different substituents, have been prepared according to known methods.[4c,5] In the diazo compounds **1a**−**f** and **2a**−**e**, the β substituents are NHTs and $Cl_3CC(O)NH$, respectively. The R is changed from small group to large group (from Me to ^{t}Bu, and from Ph to 2,6-$Cl_2C_6H_3$, respectively). It is easy to expect that with the increase of the bulkiness of R, a large group, in these cases the phenyl group, will become gradually difficult to migrate. In the series of **3a**−**e**, the size of the β substituent is gradually changed from small to large. It is expected that a large β substituent will push a large group (the phenyl) to migrate in order to relieve the steric congestion.



1a, R = Me **1d**, R = Ph
1b, R = ^{i}Pr **1e**, R = 2-ClC_6H_4
1c, R = ^{t}Bu **1f**, R = 2,6-$Cl_2C_6H_3$



2a, R = Me **2d**, R = Ph
2b, R = ^{i}Pr **2e**, R = 2-ClC_6H_4
2c, R = ^{t}Bu



3a, R = R' = R" = Me
3b, R = R" = Me, R' = Ph
3c, R = R" = Me, R' = ^{t}Bu
3d, R = R' = R" = Et
3e, R = R" = Ph, R' = ^{t}Bu

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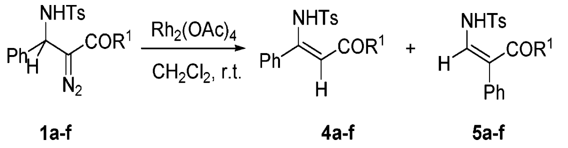
(1) For recent comprehensive reviews, see: (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley-Interscience: New York, 1998. (b) *Carbene Chemistry*; Bertrand, G., Ed.; Fontis Media: Lausanne, Switzerland, 2002.

(2) For 1,2-migration in rhodium(II) carbene, see the following. 1,2-Hydride migration: (a) Pellicciari, R.; Fringuelli, R.; Ceccherelli, P.; Sisani, E. *J. Chem. Soc., Chem. Commun.* **1979**, 959−960. (b) Ikota, N.; Takamura, N.; Young, S. D.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 4163−4166. (c) Hoffmann, K.-L.; Regitz, M. *Tetrahedron Lett.* **1983**, *24*, 5355−5358. (d) Hudlicky, T.; Olivo, H. F.; Natchus, M. G.; Umpierrez, E. F.; Pandolfi, E.; Volonterio, C. *J. Org. Chem.* **1990**, *55*, 4767−4770. (e) Taber, D. F.; Hoerrner, R. S. *J. Org. Chem.* **1992**, *57*, 441−447. (f) Ohno, M.; Itoh, M.; Umeda, M.; Furuta, R.; Kondo, K.; Eguchi, S. *J. Am. Chem. Soc*. **1996**, *118*, 7075−7082. 1,2-Alkyl or 1,2-aryl migration: (g) Nagao, K.; Chiba, M.; Kim, S.-W. *Synthesis*, **1983**, 197−199. (h) Ye, T.; McKervey, M. A. *Tetrahedron* **1992**, *48*, 8007−8022. (i) Kanemasa, S.; Kanai, T.; Araki, T.; Wada, E. *Tetrahedron Lett.* **1999**, *40*, 5055−5058. 1,2-Acetoxy migration: (j) Lopez-Herrera, F. J.; Sarabia-Garcia F. *Tetrahedron Lett.* **1994**, *35*, 6705−6708. (k) Lopez-Herrera, F. J.; Sarabia-Garcia, F. *Tetrahedron* **1997**, *53*, 3325−3346.

10.1021/jo0605391 CCC: $33.50

TABLE 1. $Rh_2(OAc)_4$-Catalyzed Reaction of 1a−f[a]



entry	R	ratio (**4**:**5**)[b]	yield[c] (%)
1	Me	17:83	74
2	^{i}Pr	91:9	90
3	^{t}Bu	100:0	91
4	Ph	15:85	81
5	2-ClC_6H_4	38:62	93[d,e]
6[f]	2,6-$Cl_2C_6H_3$	73:27	56

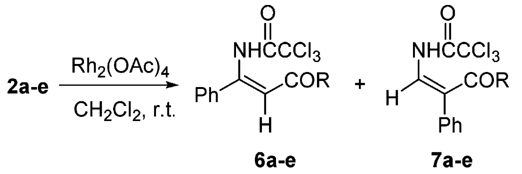
[a] If not specifically noted, the reaction was carried out in CH_2Cl_2 at room temperature with 0.5 mol % $Rh_2(OAc)_4$. [b] Ratio was determined by ^{1}H NMR (400 MHz) of the crude product. [c] If not specifically noted, refer to the isolated yield of the major products, which have *Z* configurations. [d] Both (*Z*)- and (*E*)-isomers of **5e** were isolated. [e] Refer to the combined yield of the two products. [f] The reaction was carried out in refluxing 1,2-dichloroethane.

With these diazo compounds in hand, we then proceeded to examine the diazo decomposition under $Rh_2(OAc)_4$-catalyzed conditions. First, diazo compounds **1a−f** were investigated. The diazo decomposition occurred smoothly with $Rh_2(OAc)_4$ in CH_2Cl_2 at room temperature for **1a−e** to afford the 1,2-migration products in excellent yields (Table 1, entries 1−5). For **1f**, the $Rh_2(OAc)_4$-catalyzed reaction at room temperature was sluggish, presumably due to the steric hindrance around the diazo group which blocks the approach of Rh(II) catalyst. A similar problem has been encountered in our previous studies.[4b] To substantiate this reasoning, **1f** was treated with catalytic TsOH with the expectation that protonic acid-catalyzed diazo decomposition should not be sensitive to steric hindrance. However, the reaction only gave a complex mixture under these conditions. On the other hand, the Rh(II)-catalyzed reaction of **1f** occurred efficiently in refluxing 1,2-dichloroethane (Table 1, entry 6).

The configuration of the products could be easily identified as indicated by ^{1}H NMR the existence of hydrogen bonding between N−H and the carbonyl group. In most cases, only (*Z*)-isomers were obtained for both 1,2-H and 1,2-Ph migrations.

Our previous study has shown that the NHTs group switches the 1,2-migration from 1,2-H to 1,2-Ph. In the case of **1a**, in which the R is a relatively small methyl group, the 1,2-Ph migration predominates (Table 1, entry 1). When R is switched to a bulkier ^{i}Pr group, the ratio is completely reversed (Table 1, entry 2). When the size of R is further increased to ^{t}Bu, only the 1,2-H migration product could be obtained (Table 1, entry 3). For the series of **1d−f**, the trend is similar, although the product ratio change is less sensitive than that for **1a−c**.

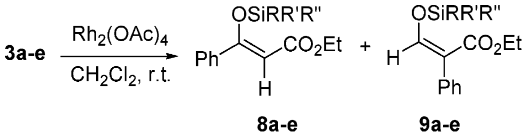
TABLE 2. $Rh_2(OAc)_4$-catalyzed Reaction of 2a−e[a]



entry	R	ratio (**6**:**7**)[b]	yield[c] (%)
1	Me	0:100	87
2	^{i}Pr	65:35	53
3	^{t}Bu	100:0	85
4	Ph	2:98	68
5	2-ClC_6H_4	68:32	97[d]

[a] The reaction was carried out in CH_2Cl_2 at room temperature with 0.5 mol % $Rh_2(OAc)_4$. [b] Ratio was determined by ^{1}H NMR (400 MHz) of the crude product. [c] If not specifically noted, refer to the isolated yield of the major product. [d] Refer to the combined yield of the two products.

TABLE 3. $Rh_2(OAc)_4$-Catalyzed Reaction of 3a−e[a]



entry	**3a−e,** SiRR′R″	ratio (**8**:**9**)[b]	yield[c] (%)
1	**3a**, $SiMe_3$	11:89	57[d]
2	**3b**, $SiMe_2Ph$	10:90	72[d]
3	**3c**, $SiMe_2{}^tBu$	9:91	79
4	**3d**, $SiEt_3$	9:91	82[d]
5	**3e**, Si ^{t}BuPh$_2$	4:96	92

[a] The reaction was carried out in CH_2Cl_2 at room temperature with 0.5 mol % $Rh_2(OAc)_4$. [b] Ratio was determined by ^{1}H NMR (300 MHz) of the crude product. [c] Refer to the isolated yield of the major product. [d] The corresponding enol was obtained after separation with silica gel column.

Next, the $Rh_2(OAc)_4$-catalyzed reaction of **2a−e** was investigated (Table 2). Our previous study has demonstrated that $Cl_3CC(O)NH$ is more efficient than TsNH in promoting 1,2-aryl migration.[4b,d] As shown in Scheme 1, only the 1,2-phenyl migration product is observed in the case of ethyl diazoester. In the $Rh_2(OAc)_4$-catalyzed reaction of **2a−e**, a similar change of migratory aptitude was observed, as shown by the data collected in Table 2. Again, the steric bulkiness effectively overrides the electronic effects.

Finally, the steric effect of β substituent on the 1,2-migration was investigated through $Rh_2(OAc)_4$-catalyzed reaction of **3a−e** (Table 3). The previous study has demonstrated that 1,2-H migration predominates when the bystander is an electron-donating group, such as hydroxyl or alkyl group.[4] In the reaction of **3a**, in which the β substituent is trimethylsiloxy, the ratio of 1,2-phenyl migration vs 1,2-hydride migration is 8:1 (Table 3, entry 1). Since a siloxy substituent is considered an electron-donating group in general, this result is not in accordance with the previous observations. Here, the steric bulkiness of the trimethylsiloxy group might be more determinant in affecting the migratory aptitude. This rationalization is supported by the $Rh_2(OAc)_4$-catalyzed reaction of **3b−e**, in which the size of siloxy substituent is gradually increased. As shown by the data in Table 3, more 1,2-phenyl migration is observed when the β-siloxy substituent becomes bulkier.

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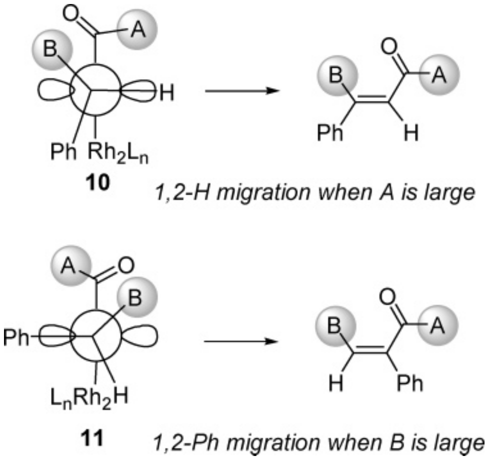
(3) For reviews, see: (a) Nickon, A. *Acc. Chem. Res.* **1993**, *26*, 84−89. (b) Liu, M. T. H. *Acc. Chem. Res.* **1994**, *27*, 287−294. For recent study, see: (c) Farlow, R. A.; Thamattoor, D. M.; Sunoj, R. B.; Hadad, C. M. *J. Org. Chem.* **2002**, *67*, 3257−3265. (d) Keating, A. E.; Garcia-Garibay, M. A.; Houk, K. N. *J. Phys. Chem. A* **1998**, *102*, 8467−8476.

(4) (a) Jiang, N.; Qu, Z.; Wang, J. *Org. Lett.* **2001**, *3*, 2989−2992. (b) Jiang, N.; Ma, Z.; Qu, Z.; Xing, X.; Xie, L.; Wang, J. *J. Org Chem.* **2003**, *68*, 893−900. (c) Shi, W.; Jiang, N.; Zhang, S.; Wu, W.; Du, D.; Wang, J. *Org. Lett.* **2003**, *5*, 2243−2246. (d) Shi, W.; Xiao, F.; Wang, J. *J. Org. Chem.* **2005**, *70*, 4318−4322. (e) Xu, F.; Shi, W.; Wang, J. *J. Org. Chem.* **2005**, *70*, 4191−4194.

(5) For the experimental details of the synthesis of **1a−f**, **2a−e**, and **3a−e** and the characterization data for new compounds, see Supporting Information. (a) Jiang, N.; Wang, J. *Tetrahedron Lett.* **2002**, *43*, 1285−1287. (b) Bardot, V.; Gelas-Mialhe, Y.; Gramain, J.-C.; Remuson, R. *Tetrahedron: Asymmetry* **1997**, *8*, 1111−1114.

SCHEME 2



10 *1,2-H migration when A is large*

11 *1,2-Ph migration when B is large*

The above results clearly demonstrate that steric effects play an important role in affecting the migratory aptitude. In general, the steric effects can override the electronic effects of the bystander group. As previously proposed, the 1,2-migration proceeds through the overlap of the migrating bond with the empty p orbital of the carbene center.[4b,d] The migration is supposed to be a concerted process with a transition state shown in Scheme 1. In the transition state, there is a positive charge development in the migrating origin. This explains the electronic effects of the bystander group. More positive charge is developed in 1,2-H migration than that in 1,2-phenyl migration.[6] Thus, an electron-donating bystander group that is attached to the migrating origin will promote 1,2-H migration, while an electron-withdrawing group, such as Cl_3CCONH, will work in an opposite way.

For the migration to occur, the migrating bond needs to be parallel to the p orbital of the carbene carbon. The conformations **10** and **11** that will lead to 1,2-H or 1,2-Ph migration are depicted in Scheme 2. However, it is difficult to get a clear insight into the substituent effect on migratory aptitude through conformation **10** or **11**. The steric effect observed in this study can be simply rationalized by assuming that the 1,2-migration proceeds through a rather late transition state, as discussed in our previous study.[4d] The transition states resemble the olefin products with the Rh(II) catalyst being departed to a considerable extent. Thus, the migratory aptitude is largely governed by the stability of the products. The steric bulkier group in the migrating origin will obviously favor a large group, such as the phenyl group, to migrate, because the steric hindrance can thus be relieved. On the other hand, when there is a bulkier group attached to the carbene carbon, a small group (H) will migrate in order to relieve steric congestion in the product.

In conclusion, we have demonstrated that, in addition to electronic factors, steric factors play an even more important role in affecting the 1,2-migratory aptitude in rhodium(II)−carbene reactions.[7] These results provide useful information in understanding the mechanism of 1,2-migration reaction of rhodium(II) carbene.

Experimental Section

Caution! Diazo compounds are generally toxic and potentially explosive. They should be handled with care in a well-ventilated fume hood.

General Procedure for $Rh_2(OAc)_4$-Catalyzed Reactions of 1a−f, 2a−e, and 3a−e. To a stirring solution of anhydrous CH_2Cl_2 (10 mL) containing $Rh_2(OAc)_4$ (0.5 mol %) was added the diazo compound **1a**−**f**, **2a**−**e**, or **3a**−**e** (1.0 mmol). The reaction mixture was stirred at room temperature. When the diazo compound disappeared as indicated by thin-layer chromatography, solvent was removed under reduced pressure to give a crude residue, which was purified by silica gel column chromatography.

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Supporting Information Available: Experimental details, including the preparation of the diazo compounds and the characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[6] Keating, A. E.; Garcia-Garibay, M. A.; Houk, K. N. *J. Phys. Chem. A* **1998**, *102*, 8467−8476.

[7] For other examples in which the 1,2-migration is affected by steric/conformational factors, see: (a) Vitale, M.; Lecourt, T.; Sheldon, C. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2006**, *128*, 2524−2525. (b) Aggarwal, V. K.; Sheldon, C. G.; Macdonald, G. J.; Martin, W. P. *J. Am. Chem. Soc.* **2002**, *124*, 10300−10301.