ORGANIC LETTERS

2003
Vol. 5, No. 15
2619−2621

Doyle−Kirmse Reaction of Allylic Sulfides with Diazoalkane-Free (2-Furyl)carbenoid Transfer

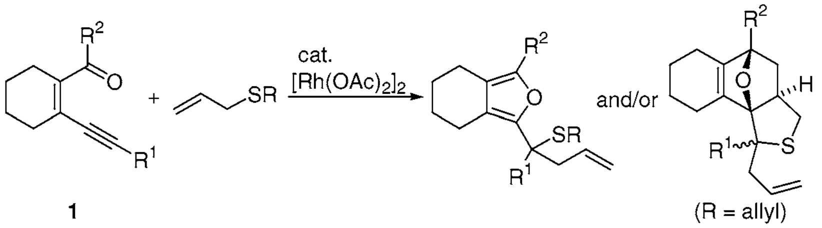
Yumiko Kato, Koji Miki, Fumiaki Nishino, Kouichi Ohe,* and Sakae Uemura*

Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan

ohe@scl.kyoto-u.ac.jp; uemura@scl.kyoto-u.ac.jp

Received May 1, 2003

ABSTRACT

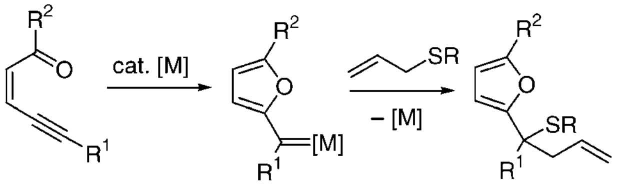


1

In the presence of rhodium catalyst, (2-furyl)carbenoids generated from conjugated ene-yne-carbonyl compounds 1 efficiently undergo carbene transfer reactions with allylic sulfides followed by [2,3]sigmatropic rearrangement of sulfur ylides to give furan-containing sulfides in good yields. When diallyl sulfide is employed, heteroatom-containing polycyclic compounds are obtained by sequential intramolecular Diels–Alder cyclization reaction with a constructed furan ring as an enophile.

The Doyle−Kirmse reaction of allylic sulfides and diazo compounds ([2,3]sigmatropic rearrangement of sulfur ylides) is a powerful synthetic method for creating new C−C bonds.[1,2] The reaction presumably involves carbenoid complexes as intermediates. We report herein the rhodium(II)-catalyzed Doyle−Kirmse-type reaction using (2-furyl)carbenoid precursors **1** without involving the corresponding diazoalkanes, as shown in Scheme 1. We have already reported the cyclopropanation of alkenes via (2-furyl)carbenoid complexes **2a** generated from **1a**, which can be catalyzed by a wide range of transition metal complexes (Scheme 2).[3,4] The following investigation demonstrates the efficacy of electron-withdrawing groups introduced at the R^1 position of **1**, as well as catalysis by a rhodium(II)

Scheme 1



1 **2**

---

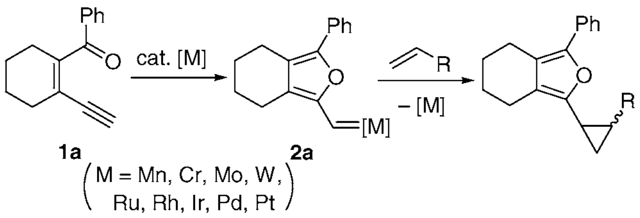
(1) For reviews, see: (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; John Wiley&Sons: New York, 1998. (b) Li, A.-H.; Dai, L.-X.; Aggarwal, V. K. *Chem. Rev.* **1997**, *97*, 2341. (c) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon: Oxford, 1995; Vol. 12, pp 421−468.

(2) For leading references, see: (a) Zhang, X.; Qu, Z.; Ma, Z.; Shi, W.; Jin, X.; Wang, J. *J. Org. Chem.* **2002**, *67*, 5621. (b) Simonneaux, G.; Galardon, E.; Paul-Roth, C.; Gulea, M.; Masson, S. *J. Organomet. Chem.* **2001**, *617−618*, 360. (c) Carter, D. S.; Van Vranken, D. L. *Org. Lett.* **2000**, *2*, 1303. (d) Carter, D. S.; Van Vranken, D. L. *Tetrahedron Lett.* **1999**, *40*, 1617. (e) Aggarwal, V. K.; Ferrara, M.; Hainz, R.; Spey, S. E. *Tetrahedron Lett.* **1999**, *40*, 8923. (f) Gulea, M.; Marchand, P.; Masson, S.; Saquet, M.; Collignon, N. *Synthesis* **1998**, 1635. (g) Meyer, O.; Cagle, P. C.; Weickhardt, K.; Vichard, D.; Gladysz, J. A. *Pure Appl. Chem.* **1996**, *68*, 79. (h) Cagle, P. C.; Arif, A. M.; Gladysz, J. A. *J. Am. Chem. Soc.* **1994**, *117*, 3655. (i) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094. (j) Kirmse, W.; Kapps, M. *Chem. Ber.* **1968**, *101*, 994.

(3) Miki, K.; Nishino, F.; Ohe, K.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 5260. For isolation of chromium (2-furyl)carbenoid, see: Miki, K.; Yokoi, T.; Nishino, F.; Ohe, K.; Uemura, S. *J. Organomet. Chem.* **2002**, *645*, 228. For vinylcarbenoids as related carbenoid species, see: Miki, K.; Ohe, K.; Uemura, S. *Tetrahedron Lett.* **2003**, *44*, 2019.

10.1021/ol034731q CCC: $25.00

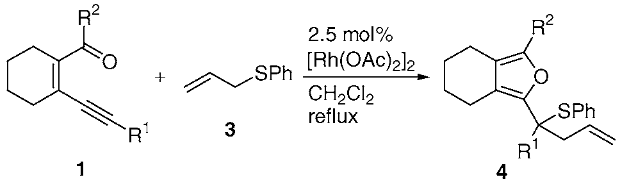
Scheme 2



complex for the Doyle–Kirmse reaction of allylic sulfides. When the Doyle–Kirmse reaction was carried out with newly prepared **1b**–**d** as carbenoid precursors in the presence of $[Rh(OAc)_2]_2$ as a catalyst, the reaction was found to proceed more efficiently than with **1a**.

First, the reactions of **1** with allyl phenyl sulfide **3** as a carbenoid acceptor were examined. Results are shown in Table 1. The reaction of **1a** with **3** in the presence of 2.5 mol % of $[Rh(OAc)_2]_2$ at room temperature or under refluxing conditions gave a complex mixture, but none of the desired product was obtained (entry 1). Thus, we next examined the reaction of **3** using ene-yne-carbonyl compounds **1b**–**d** having electron-withdrawing groups at the R^1 position, which could be expected to enhance the electrophilicity of the intermediary carbenoid species to the sulfur atom. The reaction of benzoyl group containing ene-yne-carbonyl compound **1b** with **3** gave **4b** quantitatively (entry 2). Ene-yne-carbonyl compounds **1c** and **1d**, having acetyl or methoxycarbonyl moiety, also reacted with **3** to give **4c** and **4d**[5] in good yields (entries 3 and 4). Since slow addition of diazoalkane is necessary in most cases of Doyle–Kirmse reaction using diazoalkanes,[2] it is noted that slow addition of **1** is not required in the present diazoalkane-free reaction.

Table 1. Rh-Catalyzed Carbene Transfer Reaction with Sulfide **3**[a]

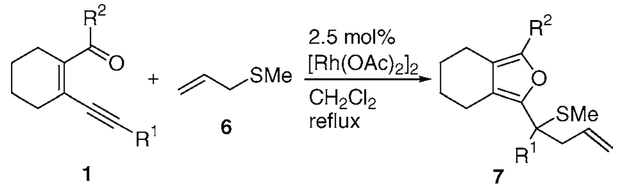


entry	1	R^1	R^2	time (h)	isolated yield
1	**1a**	H	Ph	4	complex mixture
2	**1b**	Bz	H	10	98%
3	**1c**	Ac	H	7	94%
4	**1d**	CO_2Me	H	12	83%

[a] Reaction conditions: **1** (0.25 mmol), sulfide **3** (2.5 mmol), $[Rh(OAc)_2]_2$ (0.006 mmol) in CH_2Cl_2 (1 mL) at reflux temperature.

Diazoalkane-free carbenoid transfer reaction using **1** was also effective for more nucleophilic allyl methyl sulfide **6**.[2b,f] These results are summarized in Table 2. The reaction of **6** using **1a**, which gave an unsatisfactory result with **3**, afforded the corresponding expected product **7a** in 60% yield (entry1). Reactions of **1b**–**d** with sulfide **6** also gave products **7b**–**d** in fair to good yields, respectively, although prolonged reaction periods (48–120 h) were required for each reaction (entries 2–4).

Table 2. Rh-Catalyzed Carbene Transfer Reaction with Sulfide **6**[a]



entry	1	R^1	R^2	time (h)	isolated yield
1	**1a**	H	Ph	7	60%
2	**1b**	Bz	H	120	77%[b]
3	**1c**	Ac	H	48	72%
4	**1d**	CO_2Me	H	48	91%

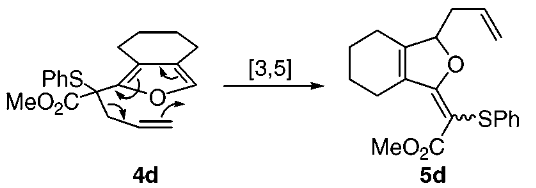
[a] Reaction conditions: **1** (0.25 mmol), sulfide **6** (2.5 mmol), $[Rh(OAc)_2]_2$ (0.006 mmol) in CH_2Cl_2 (1 mL) at reflux temperature. [b] **1b** (11%) was recovered.

Next, we carried out the rhodium-catalyzed reaction of **1** with diallyl sulfide **8**. Results are shown in Table 3. The reaction of **1a** with **8** in refluxing CH_2Cl_2 gave the product **9a**, in which the reaction occurred at one end of two allylic moieties (entry 1). On the other hand, the reaction using **1b** under the same conditions produced **9b** in 32% yield together with tetracyclic product **10b** in 43% yield as a mixture of two isomers (ratio = 79/21)[6] (entry 2). The latter product **10b** was considered as the subsequent intramolecular Diels–Alder product from an initially produced **9b**. Prolonging the reaction time did not affect the product ratio of **9b** and **10b**, but carrying out the reaction at 80 °C in 1,2-dichloroethane

---

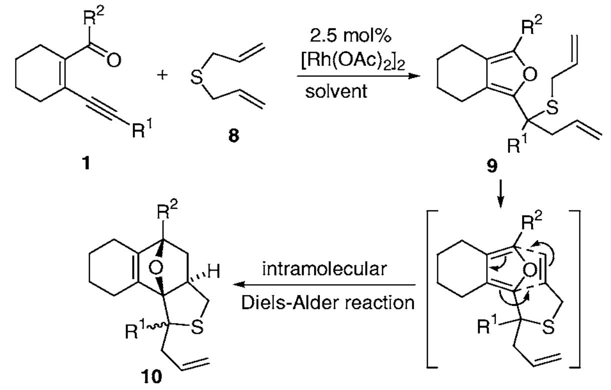
[4] For rhodium-catalyzed (2-pyrrolyl)carbenoid transferred cyclopropanation using ene-yne-imino ethers, see the immediately following Letter: Nishino, F.; Miki, K.; Kato, Y.; Ohe, K.; Uemura, S. *Org. Lett.* **2003**, *5*, 2615.

[5] The isolated product **4d** was thermally labile, which gradually isomerized to another structural form **5d** at ambient temperature. Although the precise isomerism of **4d** is not clear at present, [3,5]sigmatropic rearrangement of an allylic moiety is a likely process for the isomerization. For precedents of [3,5]sigmatropic rearrangement, see: Battye, P. J.; Jones, D. W. *J. Chem. Soc., Chem. Commun*. **1986**, 1807 and references therein.



[6] Two isomers stemmed from epimers at quaternary carbon having R^1 and allyl groups of tetrahydrothiophene, although the configuration is not yet clear. The intramolecular Diels–Alder reaction involving furan moieties as enophiles might take place via *exo*-cyclization. Similar stereochemical outcomes in the intramolecular Diels–Alder reactions have already been reported: Klein, L. L. *J. Am. Chem. Soc.* **1985**, *107*, 2573. Klein, L. L.; Shanklin, M. S. *J. Org. Chem.* **1988**, *53*, 5202. Sternbach, D. D.; Rossana, D. M. *J. Am. Chem. Soc.* **1982**, 104, 5853.

Table 3. Rh-Catalyzed Carbene Transfer Reaction and Sequential Diels−Alder Reaction with **8**[a]



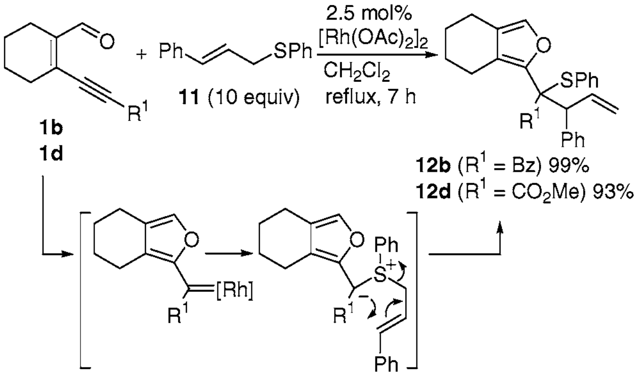
entry	**1**	R^1	R^2	solvent	temp	time (h)	isolated yield	
							9	**10**[b]
1	**1a**	H	Ph	CH_2Cl_2	reflux	7	43%	–
2[c]	**1b**	Bz	H	CH_2Cl_2	reflux	120	32%	43% (79/21)
3	**1b**	Bz	H	DCE[d]	80 °C	72	–	92% (79/21)
4	**1c**	Ac	H	DCE[d]	80 °C	54	–	80% (67/33)
5	**1d**	CO_2Me	H	CH_2Cl_2	reflux	120	trace	90% (73/27)

[a] Reaction conditions: **1** (0.25 mmol), sulfide **8** (2.5 mmol), $[Rh(OAc)_2]_2$ (0.006 mmol) in CH_2Cl_2 (1 mL). [b] The values in the parentheses indicate diastereomeric ratio determined by ^1H NMR. [c] **1b** (9%) was recovered. [d] DCE = $ClCH_2CH_2Cl$.

(DCE) considerably improved the yield of the Diels−Alder adduct **10b** (entry 3). The absence of Diels−Alder adduct **10a** in the reaction using **1a** might be attributed to the lack of the sterically demanding R^1 group. In reactions of **1c** and **1d** with **8**, Diels−Alder adducts **10c** and **10d** were obtained with complete selectivity, respectively (entries 4 and 5). Notably, in the reaction using **1d**, reflux temperature in CH_2Cl_2 was sufficient for the Doyle−Kirmse-type reaction and subsequent intramolecular Diels−Alder reaction. This clearly shows that introduction of an electron-withdrawing methoxycarbonyl moiety into **1** prominently facilitates intramolecular Diels−Alder reaction as well as ylide formation by carbenoid transfer.

Finally, the reaction with cinnamyl phenyl sulfide **11** using **1** as a carbenoid source was examined in order to elucidate the reaction pathway. In the presence of 2.5 mol % $[Rh(OAc)_2]_2$, the reactions of **1b** and **1d** with **11** gave **12b** and **12d** as a single diastereomer, in 99% and 93% yields, respectively (Scheme 3). These results clearly indicate that the rearrangement of sulfur ylides generated by (2-furyl)-carbenoid transfer proceeds via [2,3]sigmatropy accepted for Doyle−Kirmse reaction.

Scheme 3



In summary, we have demonstrated catalytic carbene transfer reactions with allylic sulfides leading to ylide formation on the basis of the in situ generation of (2-furyl)-carbenoids from conjugated ene-yne-carbonyl compound. The resulting sulfur ylides efficiently undergo [2,3]sigmatropic rearrangement to give furan-containing sulfides. A reaction cascade of [2,3]sigmatropy followed by intramolecular Diels−Alder reaction employing diallyl sulfide allows the one-pot synthesis of polycyclic heterocycles.

Acknowledgment. This work was supported by a Grant-in-Aid for 21st Century COE program of a United Approach to New Materials Science from the Ministry of Education, Culture, Sports, Science, and Technology. Financial support by Scientific Research (B) (no. 14350468) and Priority Areas (A) “Exploitation of Multi-Element Cyclic Molecules” from the Japan Society for the Promotion of Science is gratefully acknowledged.

Supporting Information Available: Full experimantal details and spectral data for all transformations and compounds are described. This material is available free of charge via the Internet at http://pubs.acs.org.

OL034731Q