Rhodium-Catalyzed Carbene-Transfer Reactions via Thienylcarbene Complexes Generated from Thiocarbamoyl-ene-yne Compounds

Tsuneishi, Asuka; Okamoto, Kazuhiro; Ikeda, Yuji; Murai, Masahito; Miki, Koji; Ohe, Kouichi


ISSUE DATE:
2011-03

URL:
http://hdl.handle.net/2433/156437

RIGHT:
© Georg Thieme Verlag Stuttgart • New York; This is not the published version. Please cite only the published version.; この論文は出版社版ではありません。引用の際には出版社版をご確認ご利用ください。
Rhodium-catalyzed carbone transfer reactions via thienylcarbene complexes generated from thiocarbamoyl-ene-yne compounds

Asuka Tsumeshi, Kazuhiro Okamoto, Yuji Ikeda, Masahito Murai, Koji Miki, and Kouichi Ohe*
Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Katsura, Nishikyo-ku, Kyoto 615-8510, Japan
Fax +81(75)3832499; E-mail: ohe@sci.kyoto-u.ac.jp
Received XXXX 2010

Abstract: Catalytic thienylcarbene transfer reactions have been developed. The rhodium-catalyzed reaction of alkenes, furans, and thiophenes with a thiocarbamoyl-ene-yne compound as a carbone source gave the cyclopropanation products or ring-opened products of heterocycles. These processes provide efficient synthetic methods for thiophene-containing complex molecules.

Key words: thiocarbamoyl-ene-yne, rhodium, carbene complex, cyclopropanation, ring-opening reaction

Transition metal-catalyzed transformations involving carbone complexes are powerful methods especially for carbon–carbon bond formation. Although diazoalkanes have been widely used as some of the most common precursors for carbenoid generation, such compounds must be handled carefully because of their explosive nature. The activation of alkynes by transition metal catalysts giving carbene complexes with cyclization or rearrangement has emerged as an alternative method. Among them, reactions involving carbone complexes generated with the formation of furan or pyrrole rings as a driving force are efficient processes in terms of atom-efficiency (Scheme 1, Y = O, NR). However, no such reaction with the formation of thiophene rings has been reported (Scheme 1, Y = S). Here we report the catalytic carbone transfer reactions via thienylcarbene complexes generated from thiocarbonyl-ene-yne compounds.

Since thioaldehydes and thioketones are generally unstable, we employed an ene-yne compound with a thiocarbamoylo moiety (1)3–8 as a substrate for the rhodium-catalyzed cyclopropanation of alkenes, which was reported by us using carbonyl-ene-ynes or imino-ene-ynes as carbone sources. The reaction of thiocarbamoyl-ene-yne 1 with tert-buty1 vinyl ether in the presence of 2.5 mol% of [Rh(OAc)2]2 at room temperature gave the expected thienylcyclopropane 2a in 84% yield (Table 1, entry 1).8,10 It turned out that the major diastereomer of product 2a was cis isomer (cis/trans = 81/19). The reaction of 1 with styrene gave 91% yield of 2b, which was in turn trans-rich mixture (cis/trans = 30/70; Table 1, entry 2). The reaction with 1,1-diphenylethylene also gave the corresponding cyclopropane 2c in 80% yield (Table 1, entry 3).

Table 1 Rhodium-catalyzed cyclopropanation of alkenes via a thienylcarbene complex

<table>
<thead>
<tr>
<th>Entry</th>
<th>R1</th>
<th>R2</th>
<th>Yield (cis/trans)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Br</td>
<td>H</td>
<td>84% (81/19)</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>H</td>
<td>91% (30/70)</td>
</tr>
<tr>
<td>3</td>
<td>Ph</td>
<td>Ph</td>
<td>80%</td>
</tr>
</tbody>
</table>

*The reaction was carried out with 1 (0.30 mmol), alkene (1.5 mmol), and [Rh(OAc)2]2 (2.5 mol%) in THF (3.0 mL) at rt for 2 h. Isolated yield. Determined by 1H NMR.

Table 2 Rhodium-catalyzed ring-opening reaction of furans

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OMe</td>
<td>3a</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>3b</td>
<td>48*</td>
</tr>
<tr>
<td>3</td>
<td>Et</td>
<td>3c</td>
<td>64*</td>
</tr>
<tr>
<td>4</td>
<td>4-MeC6H4</td>
<td>3d</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td>4-MeOC6H4</td>
<td>3e</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>3-MeOC6H4</td>
<td>3f</td>
<td>94</td>
</tr>
<tr>
<td>7</td>
<td>2-MeOC6H4</td>
<td>3g</td>
<td>96</td>
</tr>
<tr>
<td>8</td>
<td>4-CNC6H4</td>
<td>3h</td>
<td>94</td>
</tr>
<tr>
<td>9</td>
<td>4-CF3C6H4</td>
<td>3i</td>
<td>89</td>
</tr>
</tbody>
</table>

* The reaction was carried out with 1 (0.30 mmol), furan (1.5 mmol), and [Rh(OAc)2]2 (2.5 mol%) in 1,2-dichloroethane (3.0 mL) at rt for 2 h. Isolated yield. In THF.

In the reaction of furans with carbene complexes, we have to consider several pathways including...
cyclopropanation, C–O insertion, and ring-opening of furans. In some cases, the selective ring-opening reaction proceeds. A thienylcarbene complex generated from thiocarbamoyl-ene-yn is also expected to react with furans. Indeed, 2-methoxyfuran reacted with thiocarbamoyl-ene-yn 1 to give thienylidencya 3a in 90% yield (Table 2, entry 1). This reaction is applicable to various 2-substituted furans to give the corresponding ring-opening products in the optimized solvents (THF or 1,2-dichloroethane). In the case of 2-alkylfurans, the products were obtained only in moderate yields (Table 2, entries 2, 3). The reaction with aromatic-substituted furans at 2-position gave the dienone 3b–3g in high yields (Table 2, entries 4–9).

We next examined the ring-opening reactions of thiophenes, which are anticipated to be less reactive than furans because of their resonance stability. Under the above reaction conditions, the reaction of thiocarbamoyl-ene-yn 1 with 2-methoxythiophene gave the ring-opening product 4a in 62% yield (Table 3, entry 1). The instability of the methoxythiocarbonyl group of the product 4a resulted in a low yield. Therefore, we employed 2-aminothiophenes, which were expected to provide more stable products having thioamide moieties. As expected, the use of pyrrolidino-, piperidino-, diethylamino-, and morpholinothiophene resulted in high yields of the ring-opening products (Table 3, entries 2–5).

Interestingly, ethyl diazoacetate, which is widely used as a common carbene source, showed a different reactivity from thiocarbamoyl-ene-yn 1 in the rhodium-catalyzed reaction with 2-aminothiophenes. As shown in Scheme 2, we examined the reaction of 2-pyrrolidinothiophene with ethyl diazoacetate under the above conditions, and found that C–H insertion products were obtained as major products in 64% yield (3-substituted/5-substituted = 67/33). Other carbene sources were also examined. Carbonyl-ene-yn compound 7, a previously reported carbene source, was also reacted with 2-pyrrolidinothiophene. However, the yield of ring-opening product 8 was only 67% (Scheme 3).

In summary, we have developed catalytic carbene transfer reactions via a thienylcarbene complex from thiocarbamoyl-ene-yn 1. This type of carbene source was applicable to not only cyclopropanation reaction, which has been achieved by the use of furyl- or pyrrolylcarbene complexes, but also ring-opening reactions of furans and thiophenes. Especially, the ring-opening of 2-aminothiophenes succeeded specifically in the reaction of thiocarbamoyl-ene-yn 1, while other carbene sources resulted in lower yields of ring-opening products or in the formation of C–H insertion products. Synthetic applications of thienylcarbene complexes to preparation of conjugated heterocycles are underway in our laboratory.

### References and Notes


(5) Thio carbamoyl moiety was also used for the generation of vinylcarbene complexes. See: Bedia, Y.; Murai, M.; Abo, T.; Miki, K.; Ohe, K. Tetrahedron Lett. 2007, 48, 6651.

(6) Thio carbamoyl-ene 1 was synthesized in two steps from 1,2-dibromocyclohexene, which was prepared according to the known procedure. See: Voigt, K.; von Zeeschwitz, P.; Rosauer, K.; Lansky, A.; Adams, A.; Reiser, O.; de Mejia, A. Eur. J. Org. Chem. 1998, 1521.

(7) Synthesis of 1-bromo-2-trimethylsilylthelylenecyclohex-1-ene.

To a solution of trimethylsilylacetylene (1.96 g, 20 mmol) in toluene (40 mL) were added tert-butylamine (5 mL) and 1,2-dibromocyclohexene (9.6 g, 40 mmol) at room temperature under N2. Cul (0.68 g, 3.6 mmol) and Pd(PPh3)4 (1.35 g, 1.2 mmol) were added to the solution and the mixture was stirred at 60 °C for 2 h. The reaction mixture was filtered through a pad of silica gel with Et2O. The filtrate was removed under reduced pressure and the residue was purified by column chromatography on silica gel with hexane as the eluent.


Typical procedure for rhodium-catalyzed ring-opening reaction of thio carbamoyl-ene 1 with 2-methoxyfuran.

To a solution of [Rh(OAc)2](3.3 mg, 0.0075 mmol) in anhydrous 1,2-dichloroethane (3.0 mL) were added thio carbamoyl-ene 1 (59 mg, 0.30 mmol) and 2-methoxyfuran (150 mg, 1.50 mmol) under N2. The mixture was stirred at room temperature for appropriate time. The mixture was diluted with EtOAc (10 mL), and the solution was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with hexane/AcOEt (ν/v = 10/1).

Compound 3a (90% yield, 1,4,4'-DIEZ-E = 99%); an orange solid; mp 108.5-109.5 °C; IR (KBr) 877, 1008, 1237, 1332, 1394, 1590, 1701, 2831, 2938 cm−1; (1H-E)-3a: 3H NMR (300 MHz, CDCl3) δ 1.63 – 1.78 (m, 4H), 2.41 – 2.56 (m, 2H), 2.62 – 2.71 (m, 2H), 2.79 (s, 6H), 3.73 (s, 3H), 5.80 (d, J = 15.0 Hz, 1H), 6.38 (dd, J = 15.0, 11.3 Hz, 1H), 6.96 (d, J = 15.0 Hz, 1H), 7.39 (dd, J = 15.0, 11.3 Hz, 1H); 13C NMR (75.5 MHz, CDCl3) δ 22.9, 23.2, 25.2, 25.4, 44.7, 51.2, 116.7, 120.5, 123.5, 124.5, 132.1, 140.9, 145.7, 154.9, 167.9. (1I-E)-3a: 3H NMR (300 MHz, CDCl3) δ 1.63 – 1.78 (m, 4H), 2.41 – 2.56 (m, 2H), 2.62 – 2.71 (m, 2H), 2.82 (s, 6H), 3.76 (s, 3H), 5.51 (d, J = 11.5 Hz, 1H), 6.66 (dd, J = 11.5, 11.5 Hz, 1H), 6.89 (d, J = 15.0 Hz, 1H), 7.69 (dd, J = 15.0, 11.5 Hz, 1H); 13C NMR (75.5 MHz, CDCl3) δ 23.1, 25.2, 25.4, 44.8, 50.1, 112.7, 119.8, 123.9, 124.3, 143.0, 140.9, 145.0, 155.7, 167.4. Anal. Calcd for C11H14NO·S: C, 65.95; H, 7.26. Found: C, 66.06; H, 7.22.

Compound 4e (76% yield); a red solid; mp 79.0-80.0 °C; IR (KBr) 1119, 1269, 1396, 1558 cm−1; 1H NMR (400 MHz, CDCl3) δ 1.60 – 1.75 (m, 4H), 2.50 – 2.55 (m, 2H), 2.68 – 2.77 (m, 2H), 2.80 (s, 6H), 3.78 (br s, 4H), 4.20 – 4.40 (m, 2H), 6.45 (t, J = 13.2 Hz, 1H), 6.52 (d, J = 14.2 Hz, 1H), 7.03 (d, J = 15.1 Hz, 1H), 7.73 (t, J = 12.7 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 15.2, 22.9, 23.2, 25.2, 25.5, 44.7, 50.3, 65.8, 66.6, 121.5, 123.3, 124.0, 124.7, 131.9, 141.1, 147.9, 154.8, 194.9. HRMS (FAB): calcd for C9H8N2O·S·H2O (M+), 362.1487; found, 362.1473.


Rhodium-catalyzed ring-opening reaction of 2-methoxythiophene with ethyl diazoacetate has been reported. See: Tranmer, G. K.; Capreta, A. Tetrahedron 1998, 54, 15499.

(14) Catalytic ring-opening reaction of 2-methoxythiophene with propargyl acetate as carbene sources has been reported. See: Tranmer, G. K.; Capreta, A. Tetrahedron 1998, 54, 15499.

(15) Aminothiophenes were synthesized according reported procedures. See: Lu, Z.; Twieg, R. J. Tetrahedron 2005, 61, 903.


(16) The reaction of 1,1-dimethyl-2-propinyl acetate and 2-pyridinolinethione in the presence of [RuCl2(CO)3]2 or PdCl2 as a catalyst gave no ring-opening product.
Compared with ref. 13, the reactivity of 2-aminothiophenes towards ring-opening seems to be lower than that of furans or 2-methoxythiophene.