LETTER

# Carbon–Carbon Double-Bond Isomerization and Diels–Alder Reaction of Dimethyl 5-Methylene-4-isopropylidene-2-cycloheptene-1,1-dicarboxylate with Dienophiles

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**Abstract:** Tricyclic compounds were obtained as a single diastereomer via carbon–carbon double-bond isomerization–Diels–Alder reaction of dimethyl 5-methylene-4-isopropylidene-2-cycloheptene-1,1-dicarboxylate with dienophiles under the catalysis of [RhCl(cod)<sub>2</sub>]<sub>2</sub>/dppe/AgOTf. Further experiments provided the proof of isomerization of carbon–carbon double bond. Meanwhile a sequential double Diels–Alder reaction took place without carbon– carbon double-bond isomerization when 4-phenyl-4*H*-1,2,4-triazole-3,5-dione used as a dienophile.

**Key words:** Diels–Alder reactions, isomerizations, rhodium, stereoselectivity, carbocycles

The Diels–Alder reaction is a powerful tool for construction of complicated six-membered derivatives with good to excellent selectivity.<sup>1</sup> After the first report of rhodiumcatalyzed Diels–Alder reaction by Livinghouse and coworkers,<sup>2</sup> the chemistry of this catalytic reaction has been greatly explored.<sup>3</sup> Recently, the catalytic enatioselective reactions have also been independently achieved by Mikami's group<sup>4</sup> and Hayashi's group<sup>5</sup> using chiral rhodium catalysts.

Recently, we have observed that the cyclometallation of 9,9-disubstituted 1,2,7,8-tetraenes under the catalysis of [RhCl(CO)<sub>2</sub>]<sub>2</sub> (2 mol%) or [RhCl(cod)]<sub>2</sub> (2.5 mol%)/dppp (5 mol%) afforded the seven-membered cross-conjugated trienes 2 (Equation 1).<sup>6</sup> We reasoned that the Diels–Alder reaction of the diene unit of the cross-conjugated triene 2 with dienophile would afford complex polycyclic compounds efficiently, if the issue of selectivity can be addressed. Interestingly, when 2a was treated with N-ethyl maleimide under the catalysis of [RhCl(cod)]<sub>2</sub>/dppe/AgO-Tf, instead of the normal [4+2] product **3a**,<sup>7</sup> tricyclic product 4a was isolated as a single diastereomer in 97% yield, probably via in situ generated triene **5a** (Scheme 1).<sup>8</sup> The structure of this product was unambiguously established by X-ray diffraction studies (Figure 1).<sup>9</sup> The reaction was much slower at 80 °C; however, a 89% yield could also be achieved for 4a after 42 hours.

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**Equation 1** 



Scheme 1



Figure 1 ORTEP representation of 4a

When *N*-phenyl maleimide or *p*-iodophenyl maleimide was treated with **2a** under the same conditions, the corresponding tricyclic products **4b** or **4c** could be isolated as a single diastereomer in 86% yield (Scheme 2). The tricyclic product **4d** was also formed in 66% yield as the only diastereomer when maleic anhydride was used as the dienophile.



### Scheme 2

When a less active dienophile, for example, 1,4-diacetoxy-2-butyne, was used instead of the expected tricyclic compound, we isolated the carbon–carbon double-bond migration product 5a in 53% yield, together with another carbon–carbon double-bond isomer 5a' in ca. 40% yield, which was contaminated with unidentified byproducts (Equation 2). This reaction clearly indicated that the cycloaddition reaction shown in Schemes 1 and 2 took place after the formation of the carbon–carbon double-bond migration product 5a.



#### **Equation 2**

Further study led to the observation that in the absence of the dienophile the reaction of 2a – under the same conditions – afforded the carbon–carbon double-bond isomerization product 5a in the yield of 62% highly selectively, together with another carbon–carbon double-bond isomer 5a' in only 4% yield. The product 5a' was also formed exclusively in the presence of Lewis acid AlCl<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> (Scheme 3).

Treatment of triene **5a** with 4-phenyl-4H-1,2,4-triazole-3,5-dione (**6**) could also smoothly afford the tricyclic compound **4e** in 95% yield (Scheme 4). The structure of









Figure 2 ORTEP representation of 4e

**4e** was also unambiguously confirmed by the X-ray diffraction studies (Figure 2).<sup>10</sup>

When this active dienophile **6** was treated with **2a** under the catalysis of  $[RhCl(cod)]_2/dppe/AgOTf$  at room temperature, surprisingly the polycyclic product **7** was isolated as a single diastereomer in 23% yield (Scheme 5). The structure of **7** was unambiguously confirmed by the X-ray diffraction studies (Figure 3).<sup>11</sup> Obviously, the normal Diels–Alder tricyclic product **8** was formed firstly, followed by the further reaction with 4-phenyl-4*H*-1,2,4-triazole-3,5-dione. Furthermore, in the absence of this



Scheme 5



Figure 3 ORTEP representation of  $7.2CH_2Cl_2$ 

catalyst, the reaction also took place to afford **7** in 94% yield with 4 equivalents of dienophile **6**.

In conclusion, we observed here some interesting cycloaddition reactions of dimethyl 5-methylene-4-isopropylidene-2-cycloheptene-1,1-dicarboxylate with different dienophiles: with maleimide or maleic anhydride, the carbon-carbon double-bond isomerization took place under the catalysis of cationic rhodium catalyst first, followed by Diels-Alder reaction, providing an efficient strategy to the construction of tricyclic compounds with high stereoselectivity. On the other hand, the polycyclic product 7 could also be obtained via a sequential double Diels-Alder reaction when 4-phenyl-4H-1,2,4-triazole-3,5-dione (**6**) was used. In this reaction, the carbon-carbon double-bond isomerization was not observed. Further studies in this area are being pursued in this laboratory.

**Supporting Information** for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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- (9) **Crystal Data for Compound 4a**   $C_{21}H_{27}NO_6$ , *MW* = 389.44, monoclinic, *Pc*, final *R* indices [I >  $2\sigma(I)$ ], *R*1 = 0.0549, *wR*2 = 0.1248, *R* indices (all data): *R*1 = 0.0633, *wR*2 = 0.1299, *a* = 13.7051 (13) Å, *b* = 11.8187 (11) Å, *c* = 12.9999 (12) Å, *β* = 103.869 (2)°, *V* = 2044.3 (3) Å<sup>3</sup>, *T* = 293 (2) K, *Z* = 4, reflections collected/unique: 11758/4448 (*R*<sub>int</sub> = 0.1361), number of observations [> $2\sigma(I)$ ] 3626, parameters, 531. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre: CCDC 635123.

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#### (10) Crystal Data for 4e

C<sub>23</sub>H<sub>25</sub>N<sub>3</sub>O<sub>6</sub>, *MW* = 439.46, triclinic, *P*-*1*, final *R* indices [I > 2σ(*I*)], *R*1 = 0.0394, *wR*2 = 0.1111, *R* indices (all data): *R*1 = 0.0498, *wR*2 = 0.1212, *a* = 8.4388 (4) Å, *b* = 8.5666 (4) Å, *c* = 16.3077 (7) Å, *a* = 99.1060 (10)°, β = 100.0250 (10)°, γ = 105.3230 (10)°, V = 1093.44 (9) Å<sup>3</sup>, *T* = 296 (2) K, *Z* = 2. Reflections collected/unique: 12810/ 3839 (*R*<sub>int</sub> = 0.0204), number of observations [>2σ(*I*)] 3118, parameters, 289. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre: CCDC 750106.

- (11) Crystal Data for 7
  - C<sub>33</sub>H<sub>34</sub>Cl<sub>4</sub>N<sub>6</sub>O<sub>8</sub> (M + 2CH<sub>2</sub>Cl<sub>2</sub>), *MW* = 784.46, monoclinic, *P*2 (1)/*c*, final *R* indices [I > 2*σ*(*I*)], *R*1 = 0.0827, *wR*2 = 0.2345, *R* indices (all data): *R*1 = 0.1191, *wR*2 = 0.2521, *a* = 15.8125 (15) Å, *b* = 11.7056 (11) Å, *c* = 19.5084 (18) Å, β = 93.543 (2)°, V = 3604.0(6) Å<sup>3</sup>, *T* = 293 (2) K, *Z* = 4. Reflections collected/unique: 18430/ 6687 (*R*<sub>int</sub> = 0.1120), number of observations [>2*σ*(*I*)] 3630, parameters, 464. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre: CCDC 738018.

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