ORGANIC LETTERS

1999
Vol. 1, No. 2
219−221

(ω-Ammonioalkyl)cyclopentadienides by Rhodium-Catalyzed Vinylcarbene Transfer to Semicyclic Enaminocarbonyl Compounds

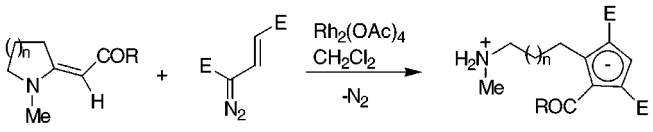
Gerhard Maas* and Andreas Müller

Division of Organic Chemistry I, University of Ulm, Albert-Einstein-Allee 11, D-89081 Ulm, Germany

gerhard.maas@chemie.uni-ulm.de

Received March 31, 1999

ABSTRACT



1 **2** **3**

R = aryl, hetaryl, OMe, O^{t}Bu
n = 1, 2, 3
E = COOMe

The rhodium(II)-catalyzed reaction of vinyldiazoacetate 2 with semicyclic β-enaminocarbonyl compounds 1 provides (ω-(methylammonio)-alkyl)cyclopentadienides 3. This transformation represents a novel reaction cascade which combines carbenoid addition at a C═C bond with ring-chain transformation. In some cases, products resulting from vinylcarbene insertion into the enaminic C–H bond of 1 are also isolated. These dienamines undergo subsequent isomerization to furnish betaines 3.

In the past few years, transition-metal-catalyzed carbene transfer from diazocarbonyl compounds onto appropriate substrates has emerged as a valuable method for the efficient and selective construction of multiply functionalized molecular frameworks.[1] Besides one-step transformations, such as cyclopropanation and insertion into C−H and X−H bonds, cascade reactions have been developed in which the carbene transfer step is followed by cycloaddition, rearrangement, and other reactions.[2] Cascade reactions beginning with carbenoid ylide formation[2,3] or acyl(vinyl)carbene transfer onto unsaturated substrates[4] have received particular attention. Herein, we report on a novel reaction sequence, in which the carbenoid reaction between a vinyldiazoacetate and a semicyclic enaminocarbonyl compound is followed by a ring-chain transformation.

Rhodium(II)-catalyzed decomposition of vinyldiazoacetate **2** in the presence of semicyclic β-enamino ketones **1a**−**e**,**h**−**l** provides in mostly good yield (ω-(methylammonio)alkyl)-cyclopentadienides **3**, some of which crystallize already from the reaction mixture (Scheme 1 and Table 1). Analogously, the carbenoid reaction of diazoacetate **2** with β-enaminoesters

(1) (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998. (b) Padwa, A.; Austin, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1797. (c) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091. (d) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Elsevier Science: Oxford, U.K., 1995; Vol. 12, pp 387, 421. (e) Cox, G. G.; Moody, C. J. *Tetrahedron* **1993**, *49*, 5109. (f) Padwa, A. Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385. (g) Davies, H. M. L. In *Comprehensive Organic Synthesis*; Semmelhack, M., Ed.; Pergamon Press: Oxford, U.K., 1991; Vol. 4, p 1031. (h) Adams, J. Spero, D. M. *Tetrahedron* **1991**, *47*, 1765. (i) Maas, G. In *Methoden der organischen Chemie (Houben-Weyl)*; Regitz, M., Ed.; Thieme: Stuttgart, Germany, 1989; Vol. E19b, p 1022.

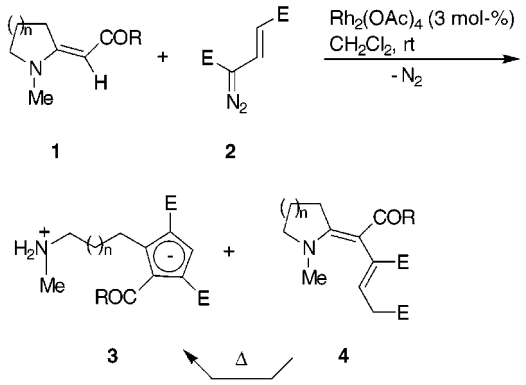
(2) (a) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. (b) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.

(3) Padwa, A. *Acc. Chem. Res.* **1991**, *24*, 22.

(4) (a) Sequential cyclopropanation/Cope rearrangement: Davies, H. M. L. *Tetrahedron* **1993**, *49*, 5203. (b) Intramolecular [3 + 4] annulation at a pyrrole ring: Davies, H. M. L.; Matasi, J. J. Ahmed, G. *J. Org. Chem.* **1996**, *61*, 2305.

10.1021/ol990546u CCC: $18.00
Published on Web 05/27/1999

Scheme 1



1f,**g** affords the betaines **3f**,**g**. In a few cases, mixtures of betaines **3** and dienamines **4** were formed which could be separated by column chromatography. It is not obvious why **4f** was obtained only as a minor byproduct and **4g,j** were

Table 1. Rh(II)-Catalyzed Reaction of Vinyldiazoacetate **2** with β-Enaminocarbonyl Compounds **1** (Scheme 1)

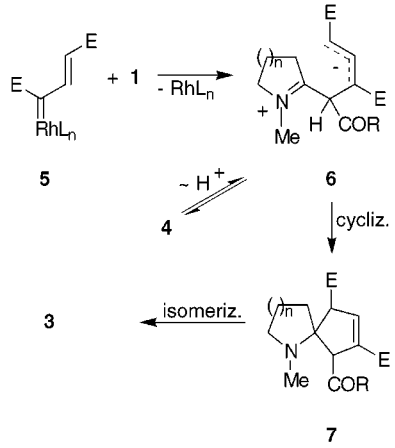
1, **3**, **4**	n	R	yield of **3** (%)	yield of **4** (%)
a	1	Ph	23	
b	1	C_6H_4-4-OMe	72	
c	1	C_6H_4-4-Cl	35	
d	1	2-furyl	91	
e	1	2-thienyl	94	
f	1	OMe	73	4[a]
g	1	O^{t}Bu	37	50[a]
h	2	C_6H_4-4-Cl	85	
i	2	2-thienyl	57	
j	3	Ph	5	72[b]
k	3	C_6H_4-4-OMe	75	
l	3	2-thienyl	65	

[a] Isomerization to the corresponding betaine **3** at 150 °C/10 min. [b] Two diastereoisomers (1:1); isomerization to betaine **3j** at 200 °C/5 min.

the major components in the product mixture.[5] Complete isomerization **4** → **3** took place in the liquid phase (CH_2Cl_2 solution or neat) within 7 days at room temperature or when the dienamine was heated at 150−200 °C for a few minutes. In the solid state, however, crystalline **4g** remained unchanged for at least 1 month. Structural identification of compounds **3** and **4** was based mainly on 2D NMR spectroscopy (^{13}C,^1H correlation and gradient-selected HMBC spectra). Although the double-bond configuration of dienamines **4** could not be established beyond doubt, a weak nOe effect between the NMe protons and the olefinic proton suggested the *E* configuration for the enaminic bond and the *Z* configuration for the other C=C bond of **4f**,**g**.

We assume (Scheme 2) that the electrophilic rhodium carbene complex **5** derived from diazoacetate **2** reacts with

Scheme 2



the enaminocarbonyl compound to form the dipolar species **6** which may isomerize by a proton shift to give the formal insertion product **4** or by cyclization to form the spiro compound **7**. Spontaneous ring-chain isomerization of the latter is initiated by a proton transfer onto the amine nitrogen atom and profits energetically from the formation of a tris-(acceptor)-substituted cyclopentadienide system. The intermediary formation of **7** would correspond to the [3 + 2] annulation of carbenoids such as **5** at the electron-rich double bond of enol ethers.[7] The observation that dienamines **4** undergo isomerization to form betaines **3** indicates the reversibility of the proton-transfer step **6** → **4**.

Reactions of enamino ketone **1e** with other vinyldiazoacetates were also investigated. The thermally rather unstable

(5) **Typical Procedure for the Preparation of Betaines 3.** Enamino ketone **1e**[15a] (0.500 g, 2.44 mmol) and rhodium(II) acetate dimer ($Rh_2(OAc)_4$, 39 mg, 0.09 mmol) were dissolved in dichloromethane (10 mL). A solution of vinyldiazoacetate **2**[6] (0.538 g, 2.92 mmol) in dichloromethane (5 mL) was added over 10 h via an infusion pump. After 2 h more, the solvent was replaced by ethyl acetate. After the mixture was stirred for 10 h, most of the betaine **3e** had crystallized from the solution and was isolated by filtration. An additional small amount of product was obtained from the mother liquor by column chromatography (silica gel, elution with ethyl acetate). Recrystallization of the combined crops from ethyl acetate gave yellow crystals (0.828 g, 94%): mp 177 °C; IR (KBr) 3436 (br, w) and 3150−2250 (w, NH_2^+), 1680 (s), 1657 (vs), 1484 (s), 1440 (s), 1393 (s), 1231 (vs) cm^{-1}; ^1H NMR (500.14 MHz, $CDCl_3$) δ 2.18 (m_c, 2H), 2.50 (br s, 3H), 2.85 (m_c, 2H), 2.97 (mc, 2H), 3.45 (s, 3H), 3.71 (s, 3H), 7.01 (dd, J = 5.0, J = 3.5, 1H), 7.28 (s, 1H), 7.45 (dd, J = 3.5, J = 1.0, 1H), 7.50 (dd, J = 5.0, J = 1.0, 1H), 9.15 (br s, 2H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 22.99, 24.49, 32.18, 48.11, 50.29, 50.64, 113.91, 116.57, 123.92, 125.02, 127.69, 131.68, 134.05, 135.47, 147.88, 167.25, 167.83, 187.36. Anal. Calcd for $C_{18}H_{21}NO_5S$ (363.4): C, 59.49; H, 5.82; N, 3.85. Found: C, 59.35; H, 5.91; N, 3.86.

(6) Dimethyl ester **2** was prepared by analogy with the corresponding diethyl ester; see: Davies, H. M. L.; Clark, D. M.; Alligood, D. B.; Eiband, G. R. *Tetrahedron* **1987**, *19*, 4265.

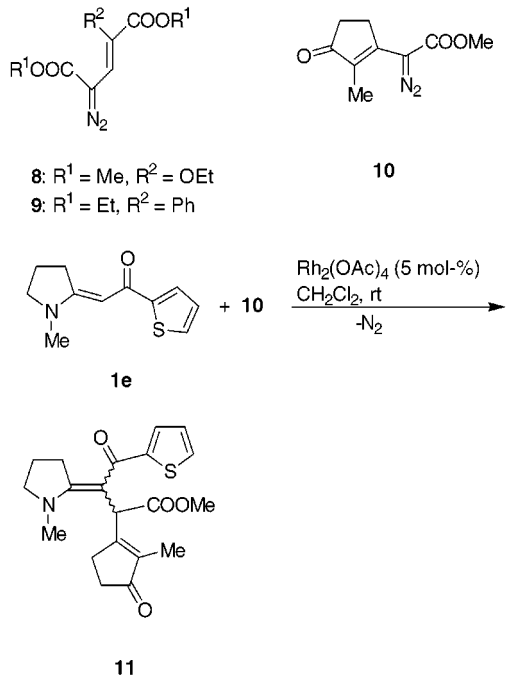
(7) Davies, H. M. L.; Hu, B. *Tetrahedron Lett.* **1992**, *33*, 453.

(8) Diazo compound **8** was prepared by analogy with the corresponding diethyl ester:[9] yellow oil (yield 46%; 5:1 mixture of diastereomers) which loses N_2 slowly at room temperature.

(9) Davies, H. M. L.; Clark, T. J.; Smith, H. D. *J. Org. Chem.* **1991**, *56*, 3817.

(10) Padwa, A.; Kulkarni, Y. S.; Zhang, Z. *J. Org. Chem.* **1990**, *55*, 4144.

Scheme 3



diazoacetates **8**[8] and **9**[10] did not deliver a vinylcarbene to **1e** in the presence of $Rh_2(OAc)_4$ or copper(I) triflate as catalysts, but rather underwent unspecific decomposition (Scheme 3). On the other hand, rhodium-catalyzed reaction of diazoester **10**[11] with **1e** in dichloromethane provides the formal carbene insertion product **11** in 48% yield. Only a single diastereoisomer of this enamino ketone was isolated, but the configuration at the double bond was not established. Interestingly, the high-field NMR spectra indicate some kind of a dynamic process. From the ^{13}C and ^{1}H signals affected by coalescence between 243 and 303 K (NCH_3, NC═C, CH_2C═C), it may be concluded that this process is caused by a configurational change at the polarized enaminic double bond. Compound **11** undergoes unspecific decomposition at 150−200 °C rather than isomerization to a cyclopentadiene derivative.

(11) Cantrell, W. R., Jr.; Davies, H. M. L. *J. Org. Chem.* **1991**, *56*, 723.

The reported results demonstrate that vinyldiazoacetate **2** is uniquely suited for the synthesis of betaines **3**. As far as the formation of dienamines **4** and **11** is concerned, it should be noted that they represent insertion products of the vinylcarbene moiety into the enaminic β-CH bond, whereas methyl diazoacetate reacts with the same enaminocarbonyl compounds by cyclopropanation/ring opening to form β-enamino esters which formally represent the products of carbene insertion into the enaminic double bond.[12]

In conclusion, we have developed an easy synthesis of (ω-(methylammonio)alkyl)cyclopentadienides which, due to their unusual combination of functional groups, hold promise for further synthetic transformations. Simple ammonio-[13] and sulfonio(tetramethoxycarbonyl)cyclopentadienides[14] are already known. With regard to the separation of the amino group and the ring moiety by a flexible spacer, betaines **3** structurally resemble the (aminoalkyl)cyclopentadienides, which recently have received attention as ligands in metal complexes.[15] The synthetic method described here represents a carbocyclic counterpart to the versatile transformation of enaminocarbonyl compounds such as **1** into ω-aminoalkyl heterocycles.[16]

Acknowledgment. We thank the Fonds der Chemischen Industrie for financial support of this work.

Supporting Information Available: Experimental details and full characterization data for compounds **2**, **3a**−**d**,**f**−**l**, **4f**,**g**,**j**, and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL990546U

(12) Müller, A.; Maier, A.; Neumann, R.; Maas, G. *Eur. J. Org. Chem.* **1998**, 1177.
(13) Hoffmann, R. W.; Backes, J. *Chem. Ber.* **1975**, *109*, 1928.
(14) Seitz, G. *Chem. Ber.* **1968**, *101*, 585.
(15) (a) Jutzi, P.; Siemeling, U. *J. Organomet. Chem.* **1995**, *500*, 175. (b) Jutzi, P.; Redeker, T.; Neumann, B.; Stammler, H.-G. *J. Organomet. Chem.* **1995**, *498*, 127.
(16) Selected examples: (a) Virmani, V.; Nigam, M. B.; Jain, P. C.; Anand, N. *Indian J. Chem.* **1979**, *17B*, 472. (b) Dannhardt, G.; Geyer, Y.; Mayer, K. K.; Obergrusberger, R. *Arch. Pharm. (Weinheim)* **1988**, *321*, 17. (c) Dannhardt, G.; Grobe, A. Gussmann, S.; Obergrusberger, R.; Ziereis, K. *Arch. Pharm. (Weinheim)* **1988**, *321*, 163. (d) Bohrisch, J.; Pätzel, M.; Mügge, C.; Liebscher, J. *Synthesis* **1991**, 1153. (e) Bohrisch, J.; Pätzel, M.; Liebscher, J.; Jones, P. G.; Chrapkowski, A. *Heterocycles* **1994**, *38*, 1333.