Pergamon

Tetrahedron Letters 42 (2001) 6137–6140

TETRAHEDRON LETTERS

Ruthenium(I)-catalyzed cyclopropanation reactions with (trimethylsilyl)diazomethane and aryldiazomethanes

Gerhard Maas* and Jürgen Seitz

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

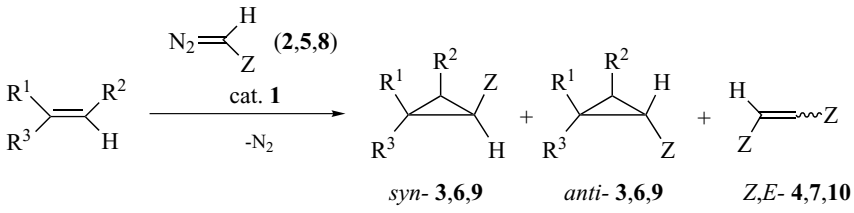
Received 8 July 2001; accepted 9 July 2001

Abstract—The polymeric ruthenium(I) complex $[Ru_2(CO)_4(\mu\text{-}OAc)_2]_n$ is a suitable catalyst for the cyclopropanation of mono-, 1,1- as well as 1,2-disubstituted, and trisubstituted alkenes with (trimethylsilyl)diazomethane, phenyl-diazomethane, and (4-cyanophenyl)diazomethane. Trisubstituted alkenes are cyclopropanated with a remarkable degree of *syn*-selectivity. © 2001 Elsevier Science Ltd. All rights reserved.

The transition-metal-catalyzed carbene transfer from diazo compounds to appropriate substrates provides an access to a variety of compounds with different structural motifs and functionalities.[1] The most efficient and versatile catalysts are based on Rh(II), Cu, and Pd(II), in that sequence. Other catalytically active metals have not arrived at general attention and use (for a survey of catalysts, see Refs. 1–4). Although it is known since 1981 that $Ru_3(CO)_{12}$ catalyzes both cyclopropanation and ylide-forming reactions with diazoacetates,[5] the potential usefulness of ruthenium catalysts for carbene transfer reactions has started to emerge only recently. Among the promising candidates for cyclopropanation and insertion reactions are $RuCl_2(PPh_3)_3$,[6] certain $[RuCl_2(PR_3)(\eta^6\text{-arene})]$[7] and [RuCl(p-cymene)(TsN-R-NH_2)][8] complexes, ruthenium porphyrins,[9] and several Ru(II) complexes with chiral ligands.[10–12] The polymeric dicarbonylruthenium(I) acetate complex $[Ru_2(CO)_4(\mu\text{-}OAc)_2]_n$ (**1**)[13] is so far the only ruthenium(I) catalyst and represents, therefore, the closest analogy to the isoelectronic rhodium(II) complex $Rh_2(OAc)_4$. In fact, **1** is similarly efficient as the rhodium complex in catalytic cyclopropanation reactions with diazoacetates[13,14] and carbonyl ylide forming reactions with (trimethylsilyl)diazoacetates.[15]

We report now that **1** is also able to catalyze the cyclopropanation of alkenes with (trimethylsilyl)diazomethane and aryldiazomethanes. In contrast to diazocarbonyl compounds, catalytic carbene-transfer reactions with these diazomethane derivatives have been studied far less frequently and their cyclopropanation reactions are in most cases less effective.

(Trimethylsilyl)diazomethane: When a hexane solution of $(Me_3Si)CHN_2$[16] (**2**) was added during 12 h to ruthenium catalyst **1** (3 mol%) suspended in CH_2Cl_2, the formal carbene dimer, 1,2-bis(trimethylsilyl)ethene (**4**), was obtained in 80% yield and with a *E*/*Z* ratio of



2-4: R = $SiMe_3$; **5-7**: Z = Ph; **8-10**: Z = C_6H_4-4-CN

Scheme 1. See Table 1 for individual compounds.

Keywords: catalysts; cyclopropanation; diazo compounds; ruthenium and compounds; silicon and compounds.

* Corresponding author. Fax: +0049 731 502 2803; e-mail: gerhard.maas@chemie.uni-ulm.de

PII: S0040-4039(01)01221-7

Table 1. Cyclopropanation of alkenes with diazo compounds **2**, **5**, and **8** catalyzed by **1** (see Scheme 1)

Entry	Alkene	R^1	R^2	R^3	Me_3SiCHN_2 (**2**)		$PhCHN_2$ (**5**)		$(4\text{-CN-}C_6H_4)CHN_2$ (**8**)	
					Yield of **3** (%)[a]	Ratio[b] (*anti*:*syn*)	Yield of **6** (%)[a]	Ratio[b] (*anti*:*syn*)	Yield of **9** (%)[a]	Ratio[b] (*anti*:*syn*)
a	Styrene	Ph	H	H	64	67.5:32.5	35	22.5:77.5	42	18:82
b	Ethyl vinyl ether	EtO	H	H	68	63:37	45	19:81	66	23:77
c	α-Methyl-styrene	Ph	H	Me	61	56:44	21	45:55		
d	Cyclohexene	$-(CH_2)_4-$		H	48	91:9	19	45:55		
e	2-Me-2-butene	Me	Me	Me	[c]		22	5:95		
f	2,5-Dimethyl-2,4-hexadiene	Me	$CH{=}CMe_2$	Me	[c]	73:27	27	8:93		

[a] Yields of isolated products are given.

[b] Determined by ^1H NMR integration; *anti*/*syn* corresponds to *E*/*Z* for entries **a**–**c**,**e**,**f** and to *exo*/*endo* for entries **d**.

[c] Cyclopropanes **3e**,**f** could not be separated from several other unidentified products and were formed in estimated yields of 30%; determination of the *anti*/*syn* ratio from the ^1H NMR spectrum of the product mixture was possible only for **3f**.

>99:1.[17] Encouraged by this efficient transformation, we carried out the same procedure in the presence of an excess of an alkene and obtained cyclopropanes **3** (Scheme 1 and Table 1). Although the stationary concentration of the diazo compound was kept low, formation of carbene dimers **4** could not be suppressed completely (yields: 20–25%).[18]

Little is known about metal-mediated cyclopropanation reactions of unactivated alkenes with **2**. The stoichiometric reaction between an isolable trimethylsilylcarbene–ruthenium(II) complex and styrene gave cyclopropane **3a** in only 34% yield.[19] CuCl was used as a catalyst for cyclopropanation of a number of alkenes; the comparison for styrene[20] (46% yield, $E/Z=4.8$) and cyclohexene[21] (72% yield, *exo*/*endo* = 9.3) with our results reveals the similar performance of catalyst **1**. The trisubstituted alkenes (entries **e** and **f**) afforded a complex mixture (NMR, GC) of highly volatile products from which the expected cyclopropanes could not be separated in pure form. It appears that some of the products are formed from cationic intermediates, and further investigations are needed to clarify this. In terms of diastereoselectivity, we note that the *E*-isomers of cyclopropanes **3** prevail in all cases and that **1** is less *E*-selective than CuCl for cyclopropanation of styrene, but shows also an expressed *exo* selectivity for cyclohexene.

Aryldiazomethanes: $Rh_2(OAc)_4$-catalyzed cyclopropanation reactions with phenyldiazomethane (**5**) give high yields only when applied to electron-rich alkenes such as enolethers.[22] The Lewis-acidic catalyst $[CpFe(CO)_2(THF)]BF_4$ performs well with styrene (80%), but not with cyclopentene (25%) and 2-methyl-2-butene (20%).[23] With ruthenium catalyst **1**, yields of cyclopropanes **6** also remained low (Table 1) and the carbene dimers, stilbenes **7**, were formed to a significant amount (yields: 30–40%) with a *Z*:*E* ratio typically between 92:8 and 96:4.[18] Cyclopropanes **6a**,**e** were formed in almost identical yield as in the $Rh_2(OAc)_4$ catalyzed reaction. We expected to achieve better yields when (4-cyanophenyl)diazomethane (**8**), giving rise to a more electrophilic metal carbene intermediate, was used. In fact, styrene and ethyl vinyl ether were cyclopropanated in somewhat higher yields than in the case of phenyldiazomethane.[18]

Metal-mediated phenylcarbene transfer to alkenes in general shows a stereochemical preference for the thermodynamically less favored *Z*- (*syn*-)cyclopropane, in contrast to analogous reactions with diazoacetates. This is not only true for reactions with $PhCHN_2$ catalyzed by $Rh_2(OAc)_4$[22] and the cationic iron complex mentioned before[23] (which provides a so far unparalleled *Z*-selectivity), but also for the stoichiometric reactions of the isolable carbene complex $(OC)_5W{=}CHPh$ with the same alkenes.[22] *Z*-selectivity is also achieved with catalyst **1**, no matter whether a monosubstituted (styrene, ethyl vinyl ether), 1,2-di-substituted (cyclohexene), or a trisubstituted C=C bond (2-methyl-2-butene, 2,5-dimethyl-2,4-hexadiene) is cyclopropanated. α-Methylstyrene is a special case, since the effective steric demand of a phenyl group in the transition state of a reaction may be not much different from that of a methyl group.

Catalyst **1** is so far the only one, which has been applied to cyclopropanation of the same set of alkenes with methyl diazoacetate (MDA),[13,14] Me_3SiCHN_2 (**2**), and $PhCHN_2$ (**5**). A comparison of the diastereoselectivities shows that cyclopropanations are *anti*-selective with **2** but *syn*-selective with **5**, while MDA gives *syn*-cyclopropanes preferentially only with trisubstituted alkenes. In other words, while catalyst **1** provides an exceptional *syn*-selectivity for cyclopropanation of trisubstituted alkenes with MDA and **5**, this is not the case with Me_3SiCHN_2. This difference may be due to a higher steric demand of the $SiMe_3$ group as compared to CO_2Me or Ph. It also shows that it may be difficult to make stereochemical predictions based on existing[1,14,22,26] mechanistic proposals.

Acknowledgements

Financial support of this work by the Fonds der Chemischen Industrie is gratefully acknowledged.

References

1. Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*: *From Cyclopropanes to Ylides*; Wiley: New York, 1998.
2. Maas, G. In *Methoden der Organischen Chemie* (*Houben-Weyl*); de Meijere, A., Ed.; Stuttgart: Georg Thieme Verlag, 1996; Vol. E17a, pp. 444–495.
3. Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon Press: New York, 1995; Vol. 12, p. 5 Chapter 1.
4. Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssié, Ph. *J. Org. Chem.* **1980**, *45*, 695–702.
5. Tamblyn, W. H.; Hoffman, S. R.; Doyle, M. P. *J. Organomet. Chem.* **1981**, *216*, C64–C68.
6. (a) Demonceau, A.; Abreu Dias, E.; Lemoine, C. A.; Stumpf, A. W.; Noels, A. F.; Pietraszuk, C.; Marciniec, B. *Tetrahedron Lett.* **1995**, *36*, 3519–3522; (b) Sengupta, S.; Das, D.; Sarma, D. S. *Tetrahedron Lett.* **1996**, *37*, 8815–8818; (c) Fujimura, O.; Honma, T. *Tetrahedron Lett.* **1998**, *39*, 625–626.
7. Simal, F.; Jan, D.; Demonceau, A.; Noels, A. F. *Tetrahedron Lett.* **1999**, *40*, 1653–1656.
8. (a) Simal, F.; Demonceau, A.; Noels, A. F. *Tetrahedron Lett.* **1998**, *39*, 3493–3496; (b) Simal, F.; Demonceau, A.; Noels, A. F. *Tetrahedron Lett.* **1999**, *40*, 63–66.
9. (a) Galardon, E.; Le Maux, P.; Simonneaux, G. *J. Chem. Soc., Chem. Commun.* **1997**, 927–928; (b) Frauenkron, M.; Berkessel, A. *Tetrahedron Lett.* **1997**, *38*, 7175–7176; (c) Galardon, E.; Le Maux, P.; Simonneaux, G. *Tetrahedron* **2000**, *56*, 615–621.
10. (a) Nishiyama, H.; Itoh, Y.; Sugawara, H.; Matsumoto, H.; Aoki, K.; Itoh, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1247–1262; (b) Park, S.-B.; Murata, K.; Matsumoto, H.; Nishiyama, H. *Tetrahedron: Asymmetry* **1995**, *6*, 2487–

2494; (c) Park, S.-B.; Sakata, N.; Nishiyama, H. *Chem. Eur. J.* **1996**, *2*, 303–306; (d) Nishiyama, H.; Soeda, N.; Naito, T.; Motoyama, Y. *Tetrahedron: Asymmetry* **1998**, *9*, 2865–2870.
11. Park, S.-W.; Son, J.-H.; Kim, S.-G.; Ahn, K. H. *Tetrahedron: Asymmetry* **1999**, *10*, 1903–1911.
12. Uchida, T.; Irie, R.; Katsuki, T. *Synlett* **1999**, 1793–1795.
13. Maas, G.; Werle, T.; Alt, M.; Mayer, D. *Tetrahedron* **1993**, *49*, 881–888.
14. Maas, G.; Werle, T. *Adv. Synth. Catal.* **2000**, *1*, 37–40.
15. Alt, M.; Maas, G. *Tetrahedron* **1994**, *50*, 7435–7444.
16. Shioiri, T.; Aoyama, T.; Mori, S. *Org. Synth., Coll. VII* **1990**, 612–615.
17. Bp 70°C/20 mbar (bulb-to-bulb distillation); ^{1}H NMR ($CDCl_3$, 200 MHz, CD_2Cl_2 as internal standard): δ 0.02 (s, $SiMe_3$, *E*), 0.10 (s, $SiMe_3$, *Z*), 6.60 (s, =CH, *E*), 6.70 (s, =CH, *Z*); ^{13}C NMR ($CDCl_3$, 50.1 MHz): δ −5.0 ($SiMe_3$, *E*), 5.0 ($SiMe_3$, *Z*), 151.0 (C=C, *E*+*Z*).
18. General procedure: A mixture of **2**[16] (5 mmol) and alkene (5 mmol) was added, by means of a syringe pump, during 12 h to a solution of alkene (45 mmol) in CH_2Cl_2 (20 ml) in which catalyst **1** (65 mg, 0.15 mmol) was suspended. Diazo compounds **5**[24] and **8**[25] were applied in CH_2Cl_2 solutions (5 mmol in 50 ml) cooled at −20°C to suppress the thermal decomposition, which is already significant at rt. When the evolution of N_2 had ceased, the solvent was distilled off at 60°C/770 mbar, and the alkene was removed by bulb-to-bulb distillation at reduced pressure. The liquid residue was separated either by fractionating bulb-to-bulb distillation or by column chromatography over silica gel. The *syn*- and *anti*-configuration of the cyclopropanes was determined from the ^3J(H,H) coupling constants of relevant cyclopropane protons ($^3J_{cis}$> $^3J_{trans}$). If this was not possible due to signal overlap, the assignment was made based on the γ-effect on ^{13}C chemical shifts of carbon atoms attached to the cyclopropane ring. NMR data of new cyclopropanes (solvent $CDCl_3$; ^{1}H: 500 MHz, CH_2Cl_2 as internal reference; ^{13}C: 125.8 MHz): compound **3b**: ^{1}H NMR: δ (*E*/*Z*) = −0.17/−0.37 (ddd, CHSi), −0.10/−0.03 (s, $SiMe_3$), 0.34/0.42 (ddd, 1H, CH_2), 0.72/0.58 (ddd, 1H, CH_2), 1.05–1.16 (m, Me), 3.08/3.41 (ddd, CH–O), 3.42–3.50 (m, OCH_2). ^{13}C NMR: δ (*E*/*Z*) = −1.7/−0.1 ($SiMe_3$), 6.3/6.1 (CHSi), 9.3/9.0 (CH_2-ring), 15.8/15.8 (CH_2*Me*), 57.3/58.3 (OCH_2), 66.6/66.4 (CH–O). Compound **3c**: ^{1}H NMR: δ (*E*/*Z*) = 0.42/−0.01 (s, $SiMe_3$), 0.35/0.26 (dd, ^3J = 7.7/7.3 and 10.7/10.1 Hz, CHSi), 1.02/1.13 (dd, 1H, ^2J = 3.7/3.7, ^3J = 10.3/7.8 Hz, CH_2), 1.50/1.30 (dd, 1H, ^3J = 10.3/7.3, ^4J = 3.6/3.6 Hz, CH_2), 1.73/1.73 (s, Me), 7.32–7.62 (m, Ph). ^{13}C NMR: δ (*E*/*Z*) = −0.8/−0.9 ($SiMe_3$), 15.5/15.6 (*C*HSi), 16.0/16.0 (*C*H_2), 25.9/24.5 (*C*MePh), 27.6/31.3 (Me), 126.1–130.0 (*o*,*m*,*p*-$C_{arom.}$), 149.2/146.0 (*i*-$C_{arom.}$). Compound **3f**: ^{1}H NMR: δ (*E*/*Z*) = −0.63/−0.28 (d, ^3J = 6.9/10.0 Hz, C*H*Si), 4.98–5.01/4.88–4.91 (m, C*H*=CMe_2). Compound **9b**: ^{1}H NMR: δ = 1.00 (t, Me, *Z*), 1.09 and 1.38–1.42 (dt and m, ring-CH_2, *E*), 1.16–1.20 and 1.26–1.32 (ddd and dt, ring-CH_2, *Z*), 1.22 (t, Me, *E*), 2.00 (dt, ArCH, *Z*), 2.12 (ddd, ArCH, *E*), 3.09 and 3.41 (two m_c, OCH_2, *Z*), 3.36–3.38 (ring-CHO, *E*), 3.54–3.67 (m, 3 H, OCH_2 (*E*), ring-CHO (*Z*)); *E*/*Z* assignment was based on Eu(fod)$_3$-induced shift of ArC*H*). ^{13}C NMR: δ (*E*/*Z*) = 15.0/14.7 (Me), 17.0 (ring-CH_2), 24.1/23.0 (*C*HAr), 62.3/59.3 (ring-*C*HO), 66.29/66.24 ((OCH_2), 147.2/144.7 (C-1 of aryl).
19. Park, S.-B.; Nishiyama, H.; Itoh, J.; Itoh, K. *J. Chem. Soc., Chem. Commun.* **1994**, 1315–1316.
20. Aoyama, T.; Iwamoto, Y.; Nishigaki, S.; Shioiri, T. *Chem. Pharm. Bull.* **1989**, *37*, 253–256.
21. (a) Seyferth, D.; Dow, A. W.; Menzel, H.; Flood, T. C. *J. Am. Chem. Soc.* **1968**, *90*, 1080–1082; (b) Seyferth, D.; Menzel, H.; Dow, A. W.; Flood, T. C. *J. Organomet. Chem.* **1972**, *44*, 279–290.
22. Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometallics* **1984**, *3*, 52–61.
23. Seitz, W. J.; Hossain, M. M. *Tetrahedron Lett.* **1994**, *35*, 7561–7564.
24. Creary, X. *Org. Synth.* **1985**, *64*, 207–216.
25. Goh, S. H. *J. Chem. Soc. C* **1971**, 2275–2277.
26. Casey, C. P.; Smith Vosejpka, L. J. *Organometallics* **1992**, *11*, 728–744.