Synthetic Methods

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Olefin Cyclopropanation by a Sequential Atom-Transfer Radical Addition and Dechlorination in the Presence of a Ruthenium Catalyst**

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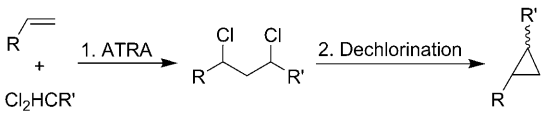
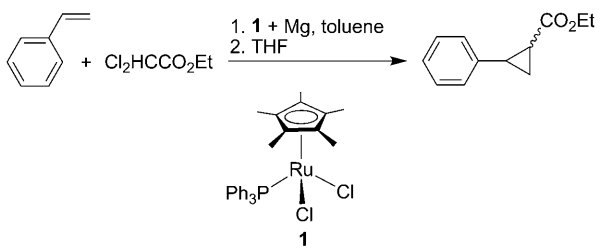
Cyclopropanes can be found in a number of biologically active compounds, and methods for the synthesis of this smallest carbocycle have been investigated extensively.[1] Most often, cyclopropanations are performed with Simmons–Smith-type reagents or by transition metal catalyzed reactions of olefins with diazo compounds.[1] Cyclopropanes can also be synthesized by reductive coupling of 1,3-dihalogen derivatives. Reagents, which can induce this transformation, include metals such as Na,[2] Mg,[3] or Zn,[4] alkyllithium,[5] and Grignard compounds,[6] and transition metal complexes,[7] among others.[8] However, dehalogenation reactions are not very popular for synthetic applications. A likely explanation for the dominance of olefin cyclopropanations is the fact that olefins are easier to access than 1,3-dihalides. Furthermore, it is possible to control the stereochemistry of the products with the help of chiral auxiliaries.[1b] Herein we describe a novel one-pot procedure for the synthesis of substituted cyclopropanes. Olefins are reacted with 1,1′-dichlorides in a ruthenium-catalyzed atom-transfer radical addition (ATRA) process. The resulting 1,3-dichlorides are directly converted into cyclopropanes by reductive coupling with magnesium (Scheme 1). This method is applicable to a wide range of substrates and the reactions can be performed in an inter- and intramolecular fashion.



Scheme 1.

In 1973, it was reported that the complex $[RuCl_2(PPh_3)_3]$ is able to catalyze the addition of CCl_4 or $CHCl_3$ to olefins ("Kharasch reaction").[9] Since then, numerous ruthenium complexes have been tested for their ability to catalyze the ATRA reaction of olefins with polyhalogenated compounds.[10,11] Copper complexes have also been used widely in this context.[12,13] One of the best procedures described so far is based on the ruthenium(III) complex $[Cp^*RuCl_2(PPh_3)]$ (**1**; Cp^* = pentamethylcyclopentadienyl), which is employed in conjunction with AIBN[14] (AIBN = azobis(isobutyronitrile)) or Mg.[15] The additives AIBN and Mg are used to generate and regenerate the catalytically active ruthenium(II) species by reduction of the ruthenium(III) complex.[16] This novel procedure allows performing intermolecular ATRA reactions as well as intramolecular atom-transfer radical cyclization (ATRC) reactions with high efficiency. Since the addition products are 1,3-dihalides, we were interested in exploring the possibility of coupling ruthenium-catalyzed ATRA and ATRC reactions with a dehalogenation step to produce cyclopropanes.[17] There were indications that reaction sequences of this kind can be realized. Baldovini et al. have reported that the ATRC products of highly activated dichloromalonamides and dichloromalonates can be converted into cyclopropanes with stoichoimetric amounts of a copper complex.[18] However, the method failed for less active substrates. In a report about the crystal structure of 2-phenyl-1-chlorocyclopropane-1-carbocyclic acid, it was mentioned that the compound was obtained by a copper-induced ATRA reaction at high temperature, but experimental details were not given.[19]

As a test reaction we used the coupling of styrene with ethyl dichloroacetate (Scheme 2). Screening of different reactions conditions revealed that magnesium in combination with THF can induce the cyclization step of the ATRA product. The radical addition, however, was best performed in a nonpolar organic solvent such as toluene. We therefore decided to employ a one-pot, two-step procedure.[17] First, ethyl dichloroacetate was coupled to styrene at 60 °C in toluene using 1 mol% of the ruthenium catalyst **1** in combination with Mg (40 equiv with respect to the styrene). After six hours the toluene solution was cooled to 0 °C,



Scheme 2.

[*] K. Thommes, G. Kiefer, Dr. R. Scopelliti, Prof. K. Severin
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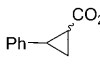
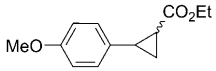
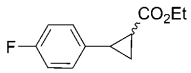
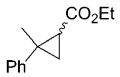
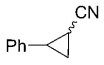
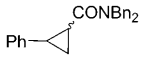
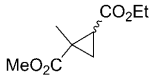
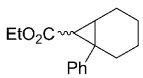
diluted with THF, and the reaction proceeded for an additional hour. 2-Phenylcyclopropane-1-carboxylic acid ethyl ester was then obtained as a mixture of isomers (*cis*/*trans* = 1:3.0) in good yield.

Encouraged by the results of the reaction between styrene and ethyl dichloroacetate, we investigated the coupling of other substrates. Under similar conditions as described above, cyclopropanes were obtained for numerous chlorinated substrates and olefins (Table 1). Styrene derivatives were successfully reacted with ethyl dichloroacetate (Table 1, entries 1–4), dichloroacetonitrile (Table 1, entries 5 and 6) and chloroform (Table 1, entry 7) to give the corresponding cyclopropanes as a mixture of *cis*/*trans* isomers. Cyclopropanecarboxamides can also be obtained by this methodology as demonstrated by the reaction of styrene with a dichloroacetamide (Table 1, entry 8). Methylmethacrylate, a substrate with a high tendency to form polymeric side products, and the internal olefin cyclohexenylbenzene could both be reacted with ethyl dichloroacetate to give the corresponding cyclopropanes in acceptable yields (Table 1, entries 9 and 10).

For the reactions listed in Table 1, the ATRA step was performed at slightly elevated temperature with reaction times between 6 and 24 hours. The dechlorination step, however, was very fast, and cooling to 0 °C turned out to beneficial for some substrates (Table 1, entries 1–3, 8, and 10). Previous studies about cyclopropanations by the reductive coupling of 1,3-dihalides had focused on either iodides or bromides, since chlorides are significantly less reactive.[4a,8a] The successful coupling of the chlorinated ATRA products under very mild reaction conditions was thus surprising. To investigate the second step of the reaction in more detail, dehalogenation reactions were performed with the isolated ATRA product of chloroform and styrene as the model compound. The reactions were carried out at room temperature in pure THF with an excess of magnesium in the presence and absence of the ruthenium catalyst **1**. The ruthenium complex was found to accelerate the dechlorination reactions substantially. With 1 mol% of the ruthenium catalyst, the reaction was finished in less than two hours, whereas in the absence of ruthenium it needed four hours to go to completion (for details see the Supporting Information). Furthermore, both reactions proceeded with a pronounced induction period. It is well-known that cross-coupling reactions, which involve Grignard reagents, can be catalyzed by iron(III) complexes.[20] The catalytically active species are assumed to be low-valent iron complexes, which are formed by reduction of the iron(III) precursors by the Grignard reagents. The cyclization of the ATRA products should proceed via magnesium–organic intermediates. It is conceivable that the C–C coupling reactions are directly promoted by a ruthenium complex in a low oxidation state (as in the case of Fe), but an indirect mode of action (e.g., activation of Mg) is plausible as well.

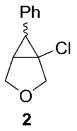
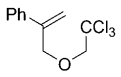
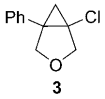
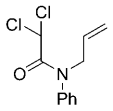
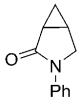
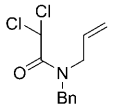
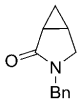
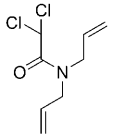
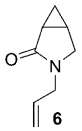
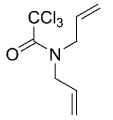
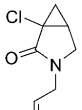
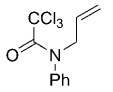
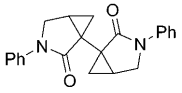
Next, we investigated the synthesis of bicyclic cyclopropanes by one-pot ATRC/dechlorination reactions. Two different classes of substrates were employed: trichlorinated allylethers and di- and trichlorinated *N*-allylacetamides. Using 1–2 mol% of the ruthenium catalyst **1**, we were able to isolate the cyclopropanes in yields between 57 and 67% (Table 2, entries 1–7). The cyclization of the ethers [(2,2,2-

Table 1: Sequential ATRA/dechlorination reactions catalyzed by complex **1** in the presence of Mg.[a]

Entry	Olefin	Cl_2HCR	Product	t_1 [h]	T_1 [°C]	t_2 [h]	T_2 [°C]	Yield [%][b]	*cis*/*trans*[c]
1	styrene	Cl_2HCCO_2Et		6	60	1	0	74 (82)	1:3.0
2	*p*-methoxystyrene	Cl_2HCCO_2Et		6	60	1	0	69 (80)	1:2.7
3	*p*-fluorostyrene	Cl_2HCCO_2Et		6	60	1	0	70 (79)	1:2.0
4	α-methylstyrene	Cl_2HCCO_2Et		6	60	1	25	61 (70)	1:3.3
5	styrene	Cl_2HCCN		24	60	2	25	70 (80)	1:2.8
6	α-methyl styrene	Cl_2HCCN		24	60	2	25	65 (75)	1:2.4
7	styrene	$CHCl_3$[d]		24	60	2	25	71 (80)	1:2.3
8	styrene	$Cl_2HCCONBn_2$		24	60	1	0	65 (72[e])	1:1.2
9	methylmethacrylate	Cl_2HCCO_2Et		8	60	3	25	60 (67)	1:2.9
10[f]	cyclohexenylbenzene	Cl_2HCCO_2Et		48	60	0.5	0	51 (62)	1:12.6

[a] The reactions were performed in toluene with [olefin] = 0.33 M, [Cl_2HCR] = 0.33 M, and [olefin]/[Mg] = 1:40. Ruthenium catalyst **1**: 1 mol% relative to the substrates. After the time t_1 at temperature T_1,the reaction mixture was diluted with 2.5 times the volume of THF an then stirred for the time t_2 at temperature T_2. [b] Yield of isolated product; the values in brackets correspond to the yield of the product in the crude reaction mixture as determined by GC/MS methods. [c] Determined by GC/MS methods, entry 8: determined by NMR analysis. [d] [styrene]/[$CHCl_3$] = 1:2. [e] Yield of product in crude reaction mixture as determined by NMR analysis. [f] The reaction was performed with 3 mol% Ru and [olefin]/[Cl_2HCR] = 1.5:1. Bn = benzyl.

Table 2: Sequential ATRC/dechlorination reactions catalyzed by complex **1** in the presence of Mg.[a]

Entry	Substrate	Product	[Ru] [mol%]	t_1 [h]	T_1 [°C]	t_2 [h]	T_2 [°C]	Yield [%][b]
1		 **2**	1	3	60	1	25	67 (77)[c]
2		 **3**	2	2	60	1	25	61 (74)
3		 **4**	1	4	60	0.5	25	65 (80)
4		 **5**	2	1	60	0.5	25	62 (72)[d]
5		 **6**	1	4	60	0.5	0	63 (72)
6		 **7**	1	2	60	0.5	0	57 (63)[d]
7		 **8**	1	2	60	24	25	61

[a] The reactions were performed in toluene with [olefin] = 0.16 M and [olefin]/[Mg] = 1:40. After the time t_1 at temperature T_1, the reaction mixture was diluted with 2.5 times the volume of THF an then stirred for the time t_2 at temperature T_2. [b] Yield of isolated product; the values in brackets correspond to the yield of the product in the crude reaction mixture as determined by GC/MS methods. [c] The *cis*/*trans* = 1:11.7 was determined by GC/MS methods. [d] Yield of product in crude reaction mixture as determined by NMR analysis.

trichloroethoxy) prop-1-enyl]benzene (Table 2, entry 1) and (3-(2,2,2-trichloroethoxy)prop-1-en-2-yl)benzene (Table 2, entry 2) gave 3-oxabicyclo[3.1.0]hexanes (**2** and **3**). Different synthetic routes have been suggested for the preparation of 3-oxabicyclo[3.1.0]hexanes.[21] Our method is interesting because the starting materials are easily accessible and because the chloro substituent in the product is a good handle for additional functionalization.

Three different *N*-allyl-2,2-dichloroacetamides were successfully cyclized to provide the corresponding 3-azabicyclo-[3.1.0]hexan-2-one derivatives **4**–**6** (Table 2, entries 3–5). There has been considerable interest in the synthesis of this bicyclic lactam/cyclopropane framework.[22] Importantly, 3-azabicyclo[3.1.0]hexan-2-one is a precursor of *cis*-2-aminomethylcyclopropanecarboxylic acid (CAMP), a pharmacologically active analogue of γ-amino butyric acid (GABA).[23]

When the corresponding trichloroacetamides were subjected to our reaction conditions, the product was found to depend on the nature of the substituents. For *N*,*N*-diallyl-2,2,2-trichloroacetamide, the expected chlorinated 3-azabicyclo[3.1.0]hexan-2-one **7** was obtained as the main product (Table 2, entry 6). However, the cyclization of *N*-allyl-2,2,2-trichloro-*N*-phenylacetamide resulted in the formation of a more complex product (Table 2, entry 7). The structure of the latter was established by NMR spectroscopy, mass spectrometry, and crystallographic analysis (see the Supporting Information). It consists of the dimer **8**, in which two 3-phenyl-3-azabicyclo[3.1.0]hexan-2-one fragments are joined through the C1 carbon atom. The reaction sequence had thus provided a completely dechlorinated product. The dimer **8** was formed in a diastereoselective fashion as a racemic mixture of the *R*,*R*- and the *S*,*S*-isomer, as evidenced by the NMR data and the crystallographic analysis. We have not been able to detect the *meso* isomer, but small amounts of the monomeric bicycles 1-chloro-3-phenyl-3-azabicyclo[3.1.0]hexan-2-one and 3-phenyl-3-azabicyclo-[3.1.0]hexan-2-one were observed as side products (ca. 10% each). At present, we have no explanation for the difference in reactivity of the *N*-allyl- (Table 2, entry 6) and the *N*-phenyl-acetamide (Table 2, entry 7). It is remarkable, however, that a complex product such as **8** can be obtained with high diastereoselectivity in a simple one-pot reaction.

In summary, we have described a novel method for the synthesis of substituted cyclopropanes by sequential ATRA/dechlorination reactions. The one-pot procedure is applicable to a variety of substrates, and the reactions can be performed in an inter- or intramolecular fashion. The required ruthenium catalyst is air-stable and its synthesis is facile.[24] The yields for this new cyclopropanation reaction are lower than for some of the optimized procedures described previously.[1] Furthermore, it is not easy to envision an enantioselective version. However, a key advantage of our methodology is the fact that functionalized cyclopropanes can be obtained without the utilization of potentially problematic diazo compounds. Instead, stable and readily accessible chlorinated compounds are employed. Future work will include studies

about the mechanism of the reaction, in particular the role of the ruthenium complex in the dechlorination step. Furthermore, the scope of this one-pot transformation will be explored in more detail.

Experimental Section

General: The ruthenium catalyst **1** was prepared as described in the literature.[24] The substrates were either commercially available or they were prepared following published procedures (for details see the Supporting Information). Mg powder (>99%) was purchased from Fluka. To activate its surface, it was agitated by a stirring bar under an atmosphere of dry dinitrogen for five days before use. All reactions were performed under an atmosphere of dry nitrogen. The solvents and the commercially available substrates were distilled from appropriate drying agents and stored under nitrogen before use.

General procedure for sequential ATRA or ATRC/dechlorination reactions: Mg powder (40 equiv) and toluene were added to a flask containing the desired amount of catalyst **1**. The olefin (1 equiv) and the chlorinated substrate (1 equiv) were added ([substrates ATRA] = 0.33 M, [substrates ATRC] = 0.16 M) and the mixture was stirred at 60 °C. After the time t_1, the solution was cooled to RT (or cooled to 0 °C) and about 2.5 times the volume of THF was added to the reaction mixture in one portion. For all entries of Table 1 and for the entries 1–3 of Table 2: when the reaction was finished, *n*-hexane was added and the mixture was filtered. The solvent was removed under reduced pressure and the product was purified by flash chromatography on silica gel. For the entries 3–7 of Table 2: when the reaction was finished, H_2O was added and the mixture was extracted with CH_2Cl_2. The organic phase was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the products were purified by flash chromatography on silica gel. The yields of the crude products were determined by GC/MS using a Varian 3800 spectrometer coupled to a Varian 2200 mass spectrometer. Mesitylene or 1,4-bis(trifluoromethyl)benzene was used as internal standard.

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[1] For selected reviews, see: a) G. Maas, *Chem. Soc. Rev.* **2004**, *33*, 183–190; b) H. Lebel, J.-F. Marcoux, C. Molinaro, A. B. Charette, *Chem. Rev.* **2003**, *103*, 977–1050; c) W. A. Donaldson, *Tetrahedron* **2001**, *57*, 8589–8627; d) A. F. Noels, A. Demonceau in *Applied Homogenous Catalysis with Organometallic Compounds* (Eds.: B. Cornils, W. A. Hermann), Wiley-VCH, Weinheim, **2000**, pp. 733–747; e) A. Pfaltz in *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, p. 100–113.

[2] a) M. S. Newman, J. R. LeBlanc, H. A. Karnes, G. Axelrad, *J. Am. Chem. Soc.* **1964**, *86*, 868–872; b) K. B. Wiberg, G. M. Lampman, *Tetrahedron Lett.* **1963**, *4*, 2173–2175; c) A. Freund, *J. Prakt. Chem.* **1882**, *26*, 367–377.

[3] J. T. Gragson, K. W. Greenlee, J. M. Derfer, C. E. Boord, *J. Am. Chem. Soc.* **1953**, *75*, 3344–3347.

[4] a) D. Sakuma, H. Togo, *Tetrahedron* **2005**, *61*, 10138–10145; b) A. A. Kamyshova, E. T. Chukovskaya, R. K. Freidlina, *Izv. Akad. Nauk SSSR* **1979**, *7*, 161–1612; c) R. G. Kelso, K. W. Greelees, J. M. Derfer, C. E. Boord, *J. Am. Chem. Soc.* **1955**, *77*, 1751–1755; d) R. G. Kelso, K. W. Greelees, J. M. Derfer, C. E. Boord, *J. Am. Chem. Soc.* **1952**, *74*, 287–292; e) R. W. Shortridge, R. A. Craig, K. W. Greenlees, J. M. Derfer, C. E. Boord, *J. Am. Chem. Soc.* **1948**, *70*, 946–949; f) G. Gustavson, *J. Prakt. Chem.* **1887**, *36*, 300–303.

[5] a) K. B. Wiberg, J. V. McClusky, *Tetrahedron Lett.* **1987**, *28*, 5411–5414; b) W. F. Bailey, R. P. Gagnier, J. J. Patricia, *J. Org. Chem.* **1984**, *49*, 2098–2107; c) W. F. Bailey, R. P. Gangnier, *Tetrahedron Lett.* **1982**, *23*, 5123–5126.

[6] a) C. H. DePuy, G. M. Dappen, K. L. Eilers, R. A. Klein, *J. Org. Chem.* **1964**, *29*, 2813–2815; b) M. S. Kharasch, M. Weiner, W. Nudenberg, A. Bhattacharya, T.-I. Wang, N. C. Yang, *J. Am. Chem. Soc.* **1961**, *83*, 3232–3234.

[7] a) T. Takeda, K. Shimane, T. Fujiwara, A. Tsubouchi, *Chem. Lett.* **2002**, 290–291; b) S. Takahashi, Y. Suzuki, N. Hagiara, *Chem. Lett.* **1974**, 1363–1366; c) P. B. Chock, J. Halpern, *J. Am. Chem. Soc.* **1969**, *91*, 582–588; d) J. K. Kochi, D. M. Singleton, *J. Org. Chem.* **1968**, *33*, 1027–1034.

[8] a) T. Ohkita, Y. Tsuchiya, H. Togo, *Tetrahedron* **2008**, *64*, 7247–7251; b) D. P. Curran, A. E. Gabarda, *Tetrahedron* **1999**, *55*, 3327–3336; c) M. S. Newman, G. S. Cohen, R. F. Cunico, L. W. Dauernheim, *J. Org. Chem.* **1973**, *38*, 2760–2763; d) L. Kaplan, *J. Am. Chem. Soc.* **1967**, *89*, 1753.

[9] H. Matsumoto, T. Nakano, Y. Nagai, *Tetrahedron Lett.* **1973**, *14*, 5147–5150.

[10] Reviews: a) L. Delaude, A. Demonceau, A. F. Noels, *Top. Organomet. Chem.* **2004**, *11*, 155–171; b) K. Severin, *Curr. Org. Chem.* **2006**, *10*, 217–224.

[11] Selected recent examples: a) R. P. Nair, T. H. Kim, B. J. Frost, *Organometallics* **2009**, *28*, 4681–4688; b) J. Wolf, K. Thommes, O. Briel, R. Scopelliti, K. Severin, *Organometallics* **2008**, *27*, 4464–4474; c) R. J. Lundgren, M. A. Rankin, R. McDonald, M. Stradiotto, *Organometallics* **2008**, *27*, 254–258; d) B. Dutta, E. Solari, R. Scopelliti, K. Severin, *Organometallics* **2008**, *27*, 423–429; e) Y. Borguet, A. Richel, S. Delfosse, A. Leclerc, L. Delaude, A. Demonceau, *Tetrahedron Lett.* **2007**, *48*, 6334–6338; f) Y. Motoyama, S. Hanada, K. Shimamoto, H. Nagashima, *Tetrahedron* **2006**, *62*, 2779–2788; g) L. Quebatte, E. Solari, R. Scopelliti, K. Severin, *Organometallics* **2005**, *24*, 1404–1406; h) Y. Motoyama, S. Hanada, S. Niibayashi, K. Shimamoto, N. Takaoka, H. Nagashima, *Tetrahedron* **2005**, *61*, 10216–10226; i) L. Quebatte, M. Haas, E. Solari, R. Scopelliti, Q. T. Nguyen, K. Severin, *Angew. Chem.* **2005**, *117*, 1108–1112; *Angew. Chem. Int. Ed.* **2005**, *44*, 1084–1088.

[12] Reviews: a) T. Pintauer, K. Matyjaszewski, *Chem. Soc. Rev.* **2008**, *37*, 1087–1097; b) A. J. Clark, *Chem. Soc. Rev.* **2002**, *31*, 1–11.

[13] Selected recent examples: a) C. Ricardo, T. Pintauer, *Chem. Commun.* **2009**, 3029–3031; b) T. Pintauer, W. T. Eckenhoff, C. Ricardo, M. N. C. Balili, A. B. Biernesser, S. J. Noonan, M. J. W. Taylor, *Chem. Eur. J.* **2009**, *15*, 38–41; c) J. M. Muñoz-Molina, T. R. Belderraín, P. J. Pérez, *Adv. Synth. Catal.* **2008**, *350*, 2365–2372; d) J. A. Bull, M. G. Hutchings, C. Luján, P. Quayle, *Tetrahedron Lett.* **2008**, *49*, 1352–1356; e) W. T. Eckenhoff, S. T. Garrity, T. Pintauer, *Eur. J. Inorg. Chem.* **2008**, 563–571; f) R. N. Ram, N. Kumar, *Tetrahedron Lett.* **2008**, *49*, 799–802; g) J. A. Bull, M. G. Hutchings, P. Quayle, *Angew. Chem.* **2007**, *119*, 1901–1904; *Angew. Chem. Int. Ed.* **2007**, *46*, 1869–1872; h) W. T. Eckenhoff, T. Pintauer, *Inorg. Chem.* **2007**, *46*, 5844–5846; i) J. M. Muñoz-Molina, A. Caballero, M. M. Díaz-Requejo, S. Trofimenko, T. R. Belderraín, P. J. Pérez, *Inorg. Chem.* **2007**, *46*, 6858–6863.

[14] L. Quebatte, K. Thommes, K. Severin, *J. Am. Chem. Soc.* **2006**, *128*, 7440–7441.

[15] K. Thommes, B. Içli, R. Scopelliti, K. Severin, *Chem. Eur. J.* **2007**, *13*, 6899–6907.

[16] M. A. Fernández-Zúmel, K. Thommes, G. Kiefer, A. Sienkiewicz, K. Pierzchala, K. Severin, *Chem. Eur. J.* **2009**, DOI: 10.1002/chem.chem.200901396.

[17] For sequential reactions with Ru catalysts see: C. Bruneau, S. Dérien, P. H. Dixneuf, *Top. Organomet. Chem.* **2006**, *19*, 295 – 326.
[18] N. Baldovini, M.-P. Bertrand, A. Carrire, R. Nouguier, J.-M. Plancher, *J. Org. Chem.* **1996**, *61*, 3205 – 3208.
[19] A. A. Karapetyan, R. A. Tamazyan, A. R. Mikaelyan, N. P. Raganyan, *J. Struct. Chem.* **2004**, *45*, 352 – 355.
[20] B. D. Sherry, A. Fürstner, *Acc. Chem. Res.* **2008**, *41*, 1500 – 1511.
[21] a) G.-Q. Tian, M. Shi, *Org. Lett.* **2007**, *9*, 4917 – 4920; b) M. S. Baird, V. M. Boitsov, A. V. Stepakov, A. P. Molchanov, J. Kopf, M. Rajaratnam, R. R. Kostikov, *Tetrahedron* **2007**, *63*, 7717 – 7726; c) M. Lautens, P. H. M. Delanghe, *J. Am. Chem. Soc.* **1994**, *116*, 8526 – 8535; d) H. Maskill, *J. Chem. Soc. Perkin Trans. 2* **1995**, 197 – 204; e) M. S. Baird, *Chem. Commun.* **1971**, 1145 – 1146.
[22] Selected recent examples: a) T. W. Lyons, M. S. Sanford, *Tetrahedron* **2009**, *65*, 3211 – 3221; b) K. Asahi, H. Nishino, *Synthesis* **2009**, 409 – 423; c) M. Zhang, F. Jovic, T. Vickers, B. Dyck, J. Tamiya, J. Grey, J. A. Tran, B. A. Fleck, R. Pick, A. C. Foster, C. Chen, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3682 – 3686; d) V. Rodríguez-Soria, L. Quintero, F. Sartillo-Piscil, *Tetrahedron* **2008**, *64*, 2750 – 2754; e) Á. Mallagaray, G. Domínguez, A. Gradillas, J. Pérez-Castells, *Org. Lett.* **2008**, *10*, 597 – 600; f) L. L. Welbes, T. W. Lyons, K. A. Cychosz, M. S. Sanford, *J. Am. Chem. Soc.* **2007**, *129*, 5836 – 5837.
[23] a) D. L. Crittenden, A. Park, J. Qiu, R. B. Silverman, R. K. Duke, G. A. R. Johnston, M. J. T. Jordan, M. Chebib, *Bioorg. Med. Chem.* **2006**, *14*, 447 – 455; b) J. E. Carland, A. J. Moorhouse, P. H. Barry, G. A. R. Johnston, M. Chebib, *J. Biol. Chem.* **2004**, *279*, 54153 – 54160; c) R. K. Duke, M. Chebib, V. J. Balcar, R. D. Allan, K. N. Mewett, G. A. R. Johnston, *J. Neurochem.* **2000**, *75*, 2602 – 2610; d) R. D. Allan, D. R. Curtis, P. M. Headley, G. A. R. Jonston, D. Lodge, B. Twitchin, *J. Neurochem.* **1980**, *34*, 652 – 654.
[24] T. Arliguie, C. Border, B. Chaudret, J. Devillers, R. Poilblanc, *Organometallics* **1989**, *8*, 1308 – 1314.

