Macrocyclic Cyclopropenes by Highly Enantioselective Intramolecular Addition of Metal Carbenes to Alkynes**

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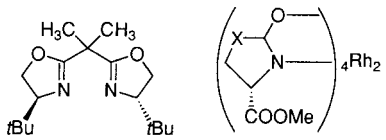
Cyclopropenes that are formed by intermolecular carbene addition to a carbon–carbon triple bond are generally stable to self-decomposition,[1] and many of these compounds have well-defined biological effects.[2] Intramolecular cyclopropenation has been investigated with similar intensity,[3] but, in those cases where ring strain is further increased, the cyclopropene products are unstable and, in the presence of transition metal catalysts employed for their formation, rapidly decompose to vinyl carbenes which have their own characteristic chemistry.[3, 4] We have previously reported that $[Cu(MeCN)_4]PF_6$ in combination with chiral bis-oxazoline **1** was an effective catalyst for enantioselective (87–91% *ee*) intramolecular cyclopropanation that resulted in the formation of 10- to 15-membered ring cyclopropane-fused lactones; chiral dirhodium(II) carboxamidate catalysts of the type **2** were appreciably less effective for enantioselective synthesis (<50% *ee*).[5] We now report that macrocyclic cyclopropenation occurs in even higher yields and enantiocontrol, but that selectivity in these processes is highly dependent on the catalyst.



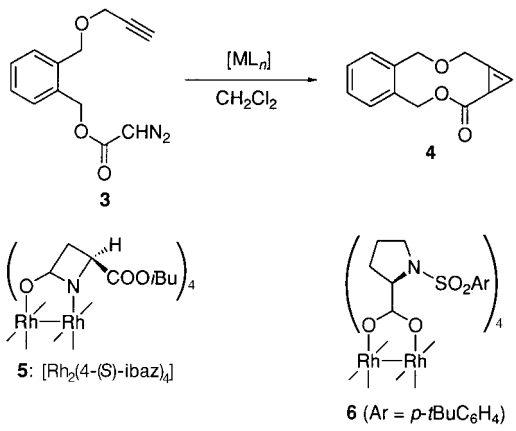
1 **2**

a, X = CH_2 : $[Rh_2(5\text{-}(S)\text{-mepy})_4]$

b, X = O : $[Rh_2(4\text{-}(S)\text{-meox})_4]$

c, X = $NCOCH_2CH_2Ph$: $[Rh_2(4\text{-}(S)\text{-mppim})_4]$

Catalytic diazo decomposition of **3** in CH_2Cl_2 caused by the action of a broad array of chiral catalysts resulted in the formation of **4** as the sole product, which was isolated in yields ranging from 62 to 92%. The X-ray crystal structure of **4** was determined, and an ORTEP diagram of the structure is provided in Figure 1.[6] Of the catalysts employed, $[Rh_2(4\text{-}(S)\text{-ibaz})_4]$ (**5**)[7] exhibited the highest enantiocontrol at 92% *ee*, the next best catalyst was $CuPF_6$/**1** at 80% *ee*. Other chiral



3 **4**

5: $[Rh_2(4\text{-}(S)\text{-ibaz})_4]$

6 (Ar = *p*-*t*BuC$_6$H$_4$)

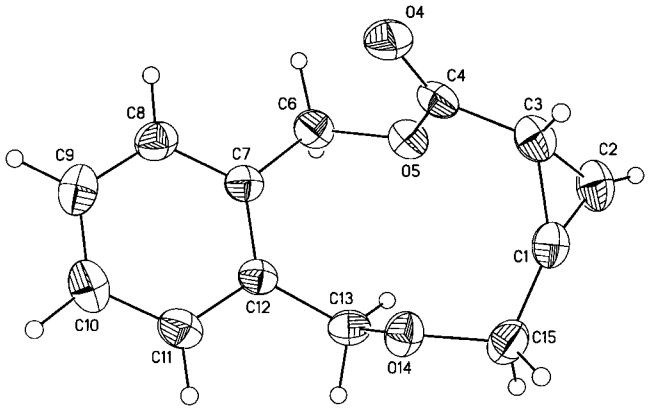


Figure 1. Crystal structure of (*S*)-**4** with selected bond lengths [Å] and angles [°]: C1–C3 1.514(3), C2–C3 1.506(3), C1–C2 1.265(3), C3–H3 0.88(2), C2–H2 0.93(3); C2-C3-C1 49.5(2), C1-C2-C3 65.5(2), C2-C1-C3 64.9(2), O5-C4-C3 111.0(2).

dirhodium carboxamidates showed a lower degree of enantiocontrol, but the chiral dirhodium prolinate (**6**)[8] was basically unselective. The absolute configuration of **4** formed by the *S*-configured dirhodium(II) catalyst **5** was established by hydrogenolysis/hydrogenation catalyzed by 5% $Pd(OH)_2$/C in ethanol to the known (1*R*,5*S*)-3-oxabicyclo[3.1.0]hexan-2-one.[9] Thus, in the presence of catalytic amounts of **5**, **3** yielded (1*R*)-**4** in 92% *ee*.

Since dirhodium(II) carboxamidates exhibited a high selectivity for allylic cyclopropanation,[9] compared with addition to a remote double bond, while $CuPF_6$/**1** favored addition to the terminal site,[5] we expected the same outcome for the propargyl analogue **7**. Instead we found that, although with dirhodium carboxamidates of type **2** compound **9** was formed highly selectively, $[Rh_2(4\text{-}(S)\text{-ibaz})_4]$ (**5**) had the inverse selectivity along with exceptional enantiocontrol. In contrast, use of $CuPF_6$/**1** gave a 1:2 mixture of **8** and **9** with unexpectedly unimpressive enantiocontrol.

That macrocyclic cyclopropenation of **3** and **7** is not merely a function of the geometry of the reactants is evident in results obtained with the propargyl diazoacetate **10** having a 1,4-

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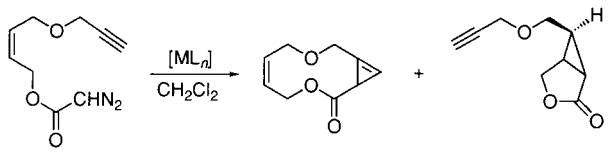
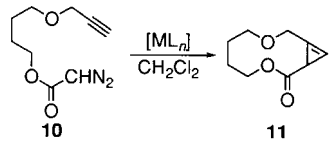
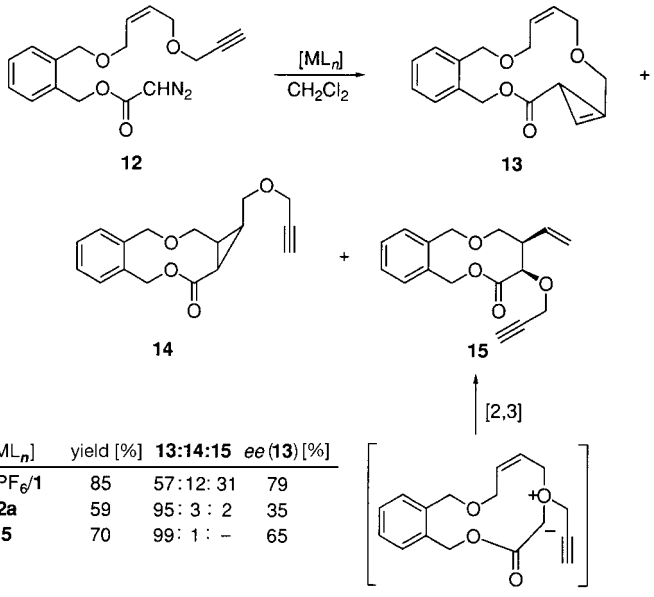


[ML$_n$]	yield [%]	**8**:**9**	*ee* (**8**)[%]	*ee* (**9**)[%]
CuPF$_6$/**1**	54	31:69	75	46
2a	76	4:96	–	96
5	80	84:16	97	88
6	87	96:4	12	20

butanediol linker. With yields of isolated products in the range 73–92%, [Rh$_2$(4-(*S*)-ibaz)$_4$] gave **11** with ≥99% *ee*, whereas enantioselectivities with other catalysts were: 82% *ee* (CuPF$_6$/**1**), 78% *ee* (**2a**), and 17% *ee* (**2c**). Once again [Rh$_2$(4*S*-ibaz)$_4$] exhibited exceptional enantiocontrol.



A defining test of chemoselectivity/enantiocontrol is found in the diazo decomposition of **12** from which three reaction pathways are possible: cyclopropenation yielding the 15-membered ring **13**, cyclopropanation yielding the 10-membered ring **14**, and ylide generation/[2,3]-sigmatropic rearrangement[10] forming **15**. All three products were obtained with CuPF$_6$/**1** as the catalyst, but the formation of **13** was virtually the exclusive outcome of reactions with chiral dirhodium carboxamidates, although with diminished enantiocontrol from that obtained for the formation of **4**, **8**, or **11**. Cyclopropene **13** was relatively unstable and, therefore, was treated with 1,3-diphenylisobenzofuran to form its stable *exo*-Diels–Alder adduct;[11] the % ee of **13** was obtained following selective hydrogenation of the cyclopropene with diimide.[12] The ylide derived product **15** that was a major outcome of the CuPF$_6$/**1** catalyzed reaction was formed in only 18% *ee*.



[ML$_n$]	yield [%]	**13**:**14**:**15**	*ee* (**13**) [%]
CuPF$_6$/**1**	85	57:12:31	79
2a	59	95:3:2	35
5	70	99:1:–	65

The chiral dirhodium(II) azetidinone-carboxylate **5** is clearly superior to all other catalysts examined for enantio- and chemoselective cyclopropenation. In contrast to prior results from intermolecular cyclopropenation,[12] the CuPF$_6$/**1** combination is an effective catalyst,[13] although not sufficiently selective to be of synthetic value. With product yields averaging 80% for the formation of 10-membered ring-fused cyclopropenes, without the need for high-dilution techniques, this methodology is one of the most effective for the enantioselective synthesis of large ring compounds.

Experimental Section

In a typical procedure, [Rh$_2$(4*S*-ibaz)$_4$] (8.8 mg, 10 μmol, 1.0 mol%) was added to an oven-dried two-neck round-bottom flask fitted with a reflux condenser and a rubber septum. To this flask was added freshly distilled CH_2Cl_2 (5 mL), and the homogeneous solution was stirred at reflux for 5 min. Diazoacetate **3** (244 mg, 1.00 mmol) dissolved in anhydrous CH_2Cl_2 (10 mL) was added to the refluxing solution of catalyst through a syringe pump at a rate of 1.0 mL h^{-1}. Upon completion of addition, the reaction solution was passed through a plug of silica gel, and the solvent was removed under reduced pressure. The resulting solid material was purified by flash chromatography on silica gel (8:1 CH_2Cl_2:ethyl acetate) to provide pure **4** (119 mg; 62%) as a white solid, m.p. 98–100 °C. The product mixture was hydrogenolyzed in the presence of 5% Pd(OH)$_2$/C in ethanol to (1*R*,5*S*)-3-oxabicyclo[3.1.0]hexan-2-one in 93% yield: 92% *ee* by GC analysis (Chiraldex G-TA, 90 °C; Altech and Assoc., Inc.). $[\alpha]_D^{23} = -84.0$ ($c = 1.07$ in CH_2Cl_2).

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[6] Crystal data for **4**: $C_{13}H_{12}O_3$, $M_r = 216.23$, tetragonal, space group $P4_12_12$ with $a = 8.388(1)$, $c = 31.804(2)$ Å, $V = 2237.7(7)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.28$ g cm^{-3}, $F(000) = 912$. Colorless triangular prism (0.24 × 0.42 × 0.78 mm) cut from larger crystal. Data were collected out to $2\theta = 55°$ by the ω-scan technique (1.2°ωscan) on a Siemens P4 diffractometer at 25 °C using graphite-monochromatized Mo$_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). A total of 6225 reflections were measured, of which 2578 reflections were unique [$R_{int}(F^2) = 0.049$]. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-hydrogen atoms. The hydrogen atom positions were observed in a ΔF map and refined with isotropic displacement parameters. The final $R_\omega(F^2) = 0.0856$ with a goodness of fit = 1.032 for refining 194 parameters. The conventional $R(F) = 0.0454$ for 1540 reflections with $F_o > 4(\sigma(F_o))$. Data reduction, decay correction, structure solution, and refinement were done using the SHELXTL/PC software package (G. M. Shel-

drick, SHELXTL/PC, Version 5.03, Siemens Analytical X-ray Instruments, Inc., Madison, WI, (USA)). b) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-103167. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[13] In the presence of $CuPF_6$/**1**, addition of ethyl diazoacetate to propargyl methyl ether formed the product from cyclopropenation in 81% *ee* (60% yield).

A Novel Method for the Demetalation of Tricarbonyliron–Diene Complexes by a Photolytically Induced Ligand Exchange Reaction with Acetonitrile**

Hans-Joachim Knölker,* Helmut Goesmann, and Rüdiger Klauss

Tricarbonyl(η^4-1,3-diene)iron complexes are a useful class of organometallic compounds with versatile applications to organic synthesis.[1] The coordination of the conjugated diene to the transition metal fragment leads to a significant alteration of its reactivity. Therefore, the tricarbonyliron fragment has been used for the stabilization of labile hydrocarbons and as a protecting group for dienes.[1] After the desired transformations at the ligand of the tricarbonyl(η^4-1,3-diene)iron complex a demetalation is required to provide the free diene. This decomplexation of tricarbonyliron complexes is usually achieved under strong oxidizing reaction conditions, for example with ferric chloride,[2] ceric ammonium nitrate,[3] trimethylamine *N*-oxide (TMANO),[4] cupric chloride,[5] or hydrogen peroxide/sodium hydroxide.[6] In connection with investigations of the iron-mediated [2+2+1] cycloaddition[7, 8] and our studies directed towards the application of tricarbonyliron complexes to the synthesis of alkaloids[9] we required a method for demetalation of tricarbonyliron complexes by using extremely mild reaction conditions. Herein we describe a novel procedure for the demetalation of tricarbonyliron–diene complexes using a photolytically induced exchange of the carbonyl ligands by acetonitrile at low temperature and subsequent demetalation in the air.

Although the iron-mediated [2+2+1] cycloaddition has been known for four decades,[10] only a few very limited applications were reported because of the difficulties associated with the demetalation of the resulting tricarbonyl(η^4-cyclopentadienone)iron complexes. We recently demonstrated that selective demetalation is feasible using trimethylamine *N*-oxide by careful control of the reaction conditions.[7a,b] However, the yields in some cases were only moderate. Therefore, we set out to develop a novel demetalation procedure in which the bonding of the metal fragment to the diene becomes labile by exchange of the carbon monoxide ligands. Acetonitrile ligands appeared to be promising candidates for such a transformation in the coordination sphere of the metal since they are rather poor acceptors. Thus, their introduction should result in a decreased back donation of electrons from the filled iron d orbitals to the ligand and the resulting complexes should be more easily oxidized.

The tricarbonyliron complex **1a**[7a] is stable at room temperature in the air. No acetonitrile complexes are observed on refluxing a solution of **1a** in acetonitrile for 29 h in the dark. However, exposure to daylight at room temperature results in a very slow formation of the monoacetonitrile complex **2a** along with the demetalated cyclopentadienone **5a**. Irradiation of a solution of complex **1a** in acetonitrile under argon atmosphere using a medium-pressure mercury lamp accelerates the ligand exchange dramatically and leads to a stepwise exchange of all three carbonyl ligands (Scheme 1, Table 1).

Photolysis of **1a** in acetonitrile at $-30\,^{\circ}C$ afforded after 1 h the diacetonitrile complex **3a** in 76% as dark red crystals. Injection of argon into the solution during the photolysis provided a purple solution of the triacetonitrile complex **4a**. The addition of the third acetonitrile ligand is reversible even at $-30\,^{\circ}C$. Therefore, the complexes **3a** or **4a** can be prepared selectively. In order to prove the reversibility of the ligand exchange carbon monoxide was injected at $-30\,^{\circ}C$ into the purple solution of complex **4a** in acetonitrile. Within 30 min the color changed to red and the diacetonitrile complex **3a** was isolated in 65% yield based on **1a**. On warming the mixture, the exchange of the second acetonitrile ligand becomes reversible too. By injection of carbon monoxide at room temperature the red solution turned orange and the monoacetonitrile complex **2a** was obtained in 61% yield based on **1a**. Related ligand exchange reactions at the cationic complex $[\eta^5\text{-CpFe(CO)}_3]^+PF_6^-$ were previously described by Astruc et al.[11] However, the cationic CpFe complexes with acetonitrile ligands reported therein are fairly stable compared to those of cyclopentadienones.

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