Asymmetric Cyclopropanations and Cycloadditions of Dioxocarbenes

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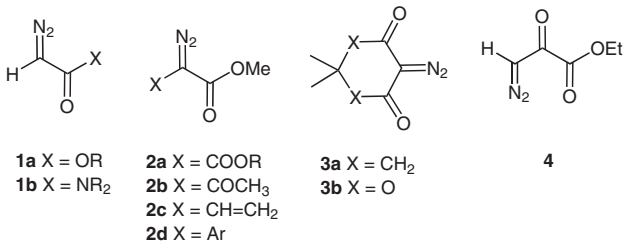
Abstract: Methods for enantioselective transfer of carbenes starting from precursors carrying two carbonyl groups have been elaborated. A one-pot procedure for olefin cyclopropanation with CH-acidic precursors via intermediate phenyliodonium ylides has been developed. The structure of the [Rh_2{(*S*)-nttl}$_4$] catalyst was optimized to produce up to 98% ee in olefin cyclopropanations with dimethyl malonate or Meldrum's acid. Highly selective Rh(II)-catalyzed olefin cyclopropanations could be observed upon replacement of methyl diazoacetoacetate by methyl (silyloxyvinyl)diazoacetate. Enantioselective dipolar cycloadditions of diazopyruvate to polar olefins have been realized with Ru(II)-pybox catalysts.

Key words: carbenoids, catalysis, diazo decomposition, phenyliodonium ylides, rhodium

Asymmetric carbene transfer has seen spectacular development during the recent years thanks to the development of highly efficient and selective catalysts.[1] The reaction involves the transition-metal-induced decomposition of a diazo compound[2] to afford an intermediate metallocarbene, which subsequently transfers the carbene moiety to an appropriate substrate. The enantioselectivity of the reaction may be controlled by the chiral ligands surrounding the metal. Exceptional enantioselectivities have been reported for asymmetric transfer of diazoacetate esters **1a** and amides **1b**, having a single substituent on the diazo group. In contrast, the enantioselectivity of diazo compounds carrying two substituents of type **2** and **3** is more difficult to control (Figure 1). A notable exception to this is provided by vinyl- and aryl-substituted diazo esters **2c** and **2d**, respectively, with which impressive selectivities have been achieved.[3] Davies proposed that the unusual selectivity of the metallocarbenes derived from these latter precursors should be ascribed to a transition state occurring late on the reaction coordinate, as evidenced by the high negative ρ-value of –1.0 for cyclopropanation of styrene with Rh(II) catalysts.[4]

In contrast, diazo esters having a second electron-withdrawing substituent such as diazomalonate (**2a**) or 2-diazodimedone (**3a**) exhibit low selectivity. The corresponding metallocarbenes are highly electrophilic, and the transition state for carbene transfer occurs early on the reaction coordinate. Typically, a ρ-value of –0.3 has been reported for cyclopropanation of styrene with diazomalonate **2a**. In addition, the steric requirements of disubstituted carbenes differ obviously from those of their mono-substituted counterparts, so that the need for different catalysts is not surprising.



1a X = OR
1b X = NR_2

2a X = COOR
2b X = $COCH_3$
2c X = $CH{=}CH_2$
2d X = Ar

3a X = CH_2
3b X = O

4

Figure 1 Diazo compounds **1–4**

This paper summarizes efforts which we have carried out during the past years with the objective to tune Rh(II) catalysts in order to achieve enantioselective carbene transfer with diazo esters carrying a second electron-attracting substituent **2a**, **2b**, **3** and **4** (Figure 1) or the corresponding phenyl iodonium ylides. Alternatively, vinyl diazoacetates were used as synthetic equivalents of diazo acetoacetates in cyclopropanations and formal cycloadditions.

A One-Pot Carbene Transfer with in situ Generated Phenyliodonium Ylides

The transition-metal-catalyzed decomposition of dimethyl diazomalonate (2a, X = CO_2Me) and of the diazo derivative of Meldrum's acid **3b** presents difficulties owing to the high stability of the diazo precursors. In addition, the carbene transfer is characterized by disappointingly low enantioselectivities.[5] Phenyliodonium ylides derived from CH-acidic compounds may be used as substitutes for diazo compounds in catalytic carbene-transfer reactions,[6] in analogy to phenyliodonium ylides derived from carbamates, sulfonamides, and sulfamates (iminophenyliodanes) which may be applied to catalytic nitrene transfer.[7] The ylide **5** derived from Meldrum's acid is isolable and decomposes under mild conditions in the presence of Rh(II) catalysts, but the reactions proceed with only modest enantioselectivity.[8] In general, however, such ylides are amorphous, often unstable and difficult to purify. Protocols for in situ generation and decomposition of iminophenyliodanes have been developed which offer significant improvement over procedures using isolable ylides.[9] Based on previous work of Dauban,[10] and in parallel with Charette,[11] we have adapted the in situ procedure for carbene transfer with dimethyl malonate (**7**) and

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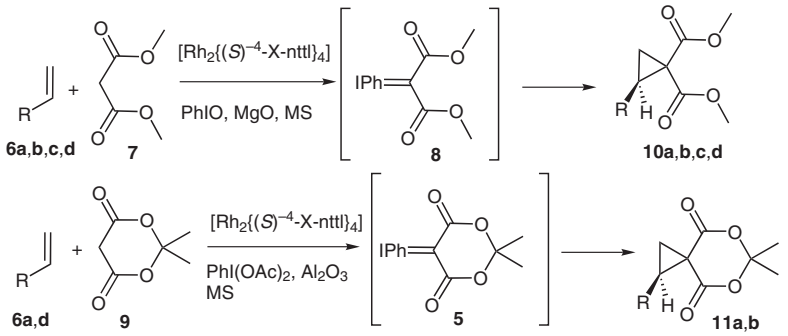


Scheme 1

Meldrum's acid **9**.[12] The intermediate ylides **8** and **5**, respectively, were generated either with iodosylbenzene (PhI=O) in the presence of MgO and molecular sieves (for **7**), or with diacetoxyiodobenzene [$PhI(OAc)_2$] in the presence of aluminum oxide and molecular sieves (for **9**). Good yields of cyclopropanes **11** were obtained when the reaction was carried out with a tenfold excess of olefin (Scheme 1). In addition, an unexpected substituent effect on the enantioselectivity was observed when Rh(II)-based catalysts (Figure 2) with 4-substituted 1,8-napthanoyl-derivatized *tert*-leucine ligands were screened. The ee for cyclopropanation of styrene (**6a**) with **7** increased from 37% with [Rh_2{(*S*)-nttl}$_4$] to 82% with [Rh_2{4-Br-(*S*)-nttl}$_4$] (Table 1). This compares favorably with the 40% ee reported for cyclopropanation of styrene with dimethyl diazomalonate in the presence of Doyle's [Rh_2{(*S*)-bnaz}$_4$] catalyst.[5] [Rh_2{4-Br-(*S*)-nttl}$_4$] led to 98% ee in the cyclopropanation of pentene (**6d**) with **7**. A similar trend was observed in cyclopropanations starting with Meldrum's acid (**9**), where enantioselectivities of up to 92% were achieved.

Cyclopropanation with Methyl (Silyloxyvinyl)diazoacetate 13

The decomposition of diazoacetoacetates (**2b**) results in the formation of carbenes which are destabilized by two electron withdrawing carbonyl substituents and which are, therefore, unselective. (Silyloxyvinyl)diazoacetates, their synthetic equivalents, have been used with some success by Davies for enantioselective carbene transfer with [Rh_2{(*S*)-dosp}$_4$] as catalyst.[13] We observed that the [Rh_2(*S*)-nttl}$_4$]-catalyst[8] is particularly adapted for diazo transfer with the TIPS-enol ether **13** derived from methyl diazoacetoacetate (**2b**).

Cyclopropanation of Styrene[14]

The cyclopropanation of styrene (**6a**) with methyl diazoacetoacetate (**2b**) in the presence of [Rh_2{(*S*)-nttl}$_4$] proceeded in 68% yield to a mixture of racemic *trans*-adduct **12** and enantio-enriched *cis*-**12** of 16% ee in a 1:8 ratio (Scheme 2). Replacement of **2b** by its silyl enol ether **13** resulted in a dramatic increase in selectivity. Under optimized conditions [Rh_2{(*S*)-nttl}$_4$] afforded the *cis* isomer of the adduct **14a** with 95% diastereoselectivity and 95%

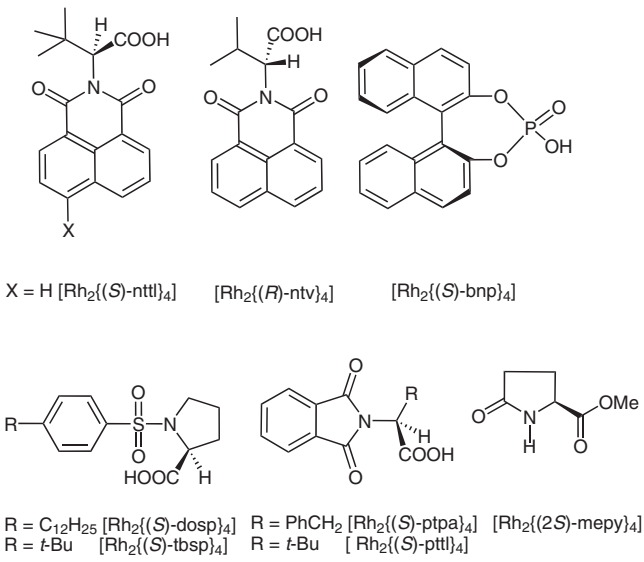


Figure 2 Structures of some rhodium catalysts

Table 1 One-Pot Asymmetric Cyclopropanations with in situ Generated Phenyliodonium Ylides[a]

Olefin	R	Precursor	Catalyst	Product, yield (%)	ee (%)
6a	Ph	**7**	$[Rh_2\{(S)\text{-nttl}\}_4]$	**10a**, 72	37
6a	Ph	**7**	$[Rh_2\{(S)\text{-4-Cl-nttl}\}_4]$	**10a**, 77	66
6a	Ph	**7**	$[Rh_2\{(S)\text{-4-Cl-nttl}\}_4]$	**10a**, 75	82
6a	Ph	**7**	$[Rh_2\{(S)\text{-4-Br-nttl}\}_4]$	**10a**, 75	82
6a	Ph	**7**	$[Rh_2\{(S)\text{-4-NO}_2\text{-nttl}\}_4]$	**10a**, 60	66
6b	4-BrC_6H_4	**7**	$[Rh_2\{(S)\text{-4-Br-nttl}\}_4]$	**10b**, 65	90
6c	4-MeC_6H_4	**7**	$[Rh_2\{(S)\text{-4-Br-nttl}\}_4]$	**10c**, 62	87
6d	C_3H_7	**7**	$[Rh_2\{(S)\text{-4-Br-nttl}\}_4]$	**10d**, 56	98
6a	Ph	**9**[b]	$[Rh_2\{(S)\text{-nttl}\}_4]$	**11a**, 90	43
6d	C_3H_7	**9**[b]	$[Rh_2\{(S)\text{-nttl}\}_4]$	**11d**, 70	72
6a	Ph	**9**[b]	$[Rh_2\{(S)\text{-4-Br-nttl}\}_4]$	**11a**, 76	92
6d	C_3H_7	**9**[b]	$[Rh_2\{(S)\text{-4-Br-nttl}\}_4]$	**11d**, 65	87

[a] Conditions: In CH_2Cl_2 (5.0 mL), **7** (10 mmol), PhI=O (1.4 equiv), MgO (2.3 equiv), molecular sieves (250 mg), olefin (10 equiv), and catalyst (5 mol%), at r.t.
[b] In CH_2Cl_2 (10 mL), **9** (10 mmol), $PhI(OAc)_2$ (1.4 equiv), Al_2O_3 (2.3 equiv molecular sieves (250 mg), and catalyst (5 mol%), 30 °C.

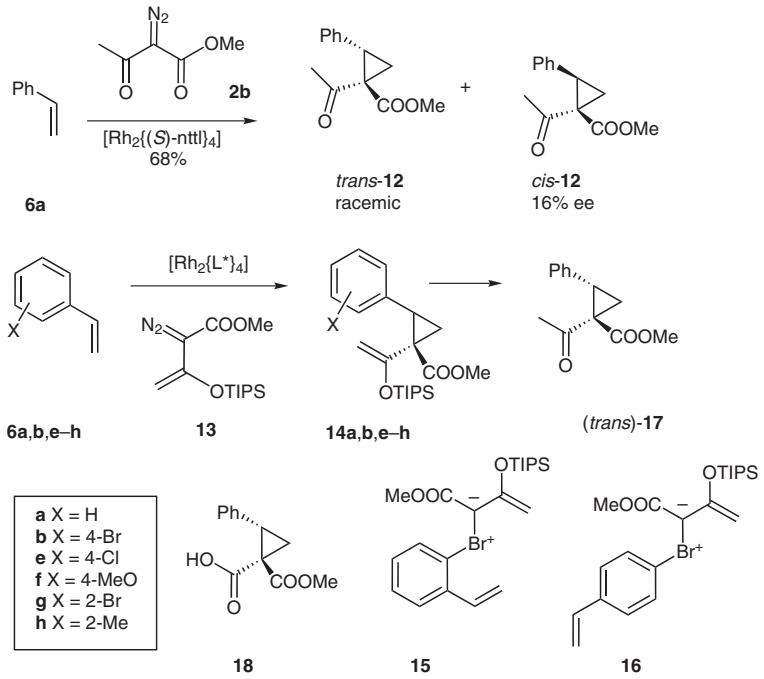
enantioselectivity at –78 °C in toluene (Table 2). The absolute configuration of **14a** was determined to be 1*R*,2*S* by X-ray crystallography. Lower selectivities were observed, when the TIPS group was replaced by the sterically less demanding TBDMS.

Table 2 Cyclopropanation of Substituted Styrenes with (Silyloxyvinyl)diazoacetate **13** in the Presence of Rh(II) Catalysts[a]

Olefin	X	Catalyst	Solvent	Product, yield (%)	ee (%)	de (%)
6a	H	$[Rh_2\{(S)\text{-nttl}\}_4]$	toluene	**14a**, 77	94	91
6a	H	$[Rh_2\{(S)\text{-nttl}\}_4]$	styrene[b]	**14a**, 72	94	nd
6a	H	$[Rh_2\{(S)\text{-nttl}\}_4]$	toluene[c]	**14a**, 76	98	95
6a	H	$[Rh_2\{(S)\text{-nttl}\}_4]$	CH_2Cl_2	**14a**, 84	95	nd
6a	H	$[Rh_2\{(S)\text{-ntv}\}_4]$	styrene[b]	**14a**, 77	94[d]	92[d]
6a	H	$[Rh_2\{(S)\text{-pttl}\}_4]$	toluene	**14a**, 86	94	93
6a	H	$[Rh_2\{(S)\text{-ptpa}\}_4]$	toluene	**14a**, 86	88	95
6a	H	$[Rh_2\{(S)\text{-dosp}\}_4]$	toluene	**14a**, 84	81	98.5
6b	4-Br	$[Rh_2\{(S)\text{-nttl}\}_4]$	toluene	**14b**, 70	92	nd
6e	4-Cl	$[Rh_2\{(S)\text{-nttl}\}_4]$	toluene	**14e**, 77	94	nd
6f	4-MeO	$[Rh_2\{(S)\text{-nttl}\}_4]$	toluene	**14f**, 80	89	nd
6g	2-Br	$[Rh_2\{(S)\text{-nttl}\}_4]$	toluene	**14g**, 71	11	nd
6h	2-Me	$[Rh_2\{(S)\text{-nttl}\}_4]$	toluene	**14h**, 84	91	nd

[a] Conditions: **6** (8.7 mmol), **13** (0.6 mmol) in the appropriate solvent (5.0 mL), and catalyst (2 mol%), 0 °C. nd = not detected.
[b] In neat styrene (**6a**).
[c] At –78 °C.
[d] *ent*-**14a**.

Surprisingly, when 2-bromostyrene (**6g**) was cyclopropanated with **13** and $[Rh_2\{(S)\text{-nttl}\}_4]$ as catalyst, the resulting cyclopropane **14g** had an ee of only 11%. In contrast, the 2-methyl derivative **6h** reacted normally with



Scheme 2

91% ee. The 4-bromo substituted styrene **6b**, in turn, reacted with an enantioselectivity of 92%, while the selectivity of the 4-chloro and the 4-methoxy derivatives were found in the same range with 94% and 89%, respectively. These observations may be rationalized by formation of a (achiral) intermediate bromonium ylide **15**, which transfers the carbene moiety intramolecularly to the *ortho*-double bond without intervention of the chiral catalyst. In contrast, the high enantioselectivity of the cyclopropane **14b** derived from 4-bromostyrene suggests the intervention of the catalyst in the transfer of the carbene moiety of the (hypothetical) ylide **16**.

Treatment of **14a** with TBAF afforded the methyl ketone *trans*-**17** (61%), while its ozonolysis led to the half-ester **18** (16%). Thus, the two-step procedure allows the stereospecific introduction of a cyclopropane carrying two different carbonyl substituent with high enantioselectivity.

Intramolecular Cyclopropanation of Allyl 2-Diazo-3-silyloxybut-3-enoates 19[15]

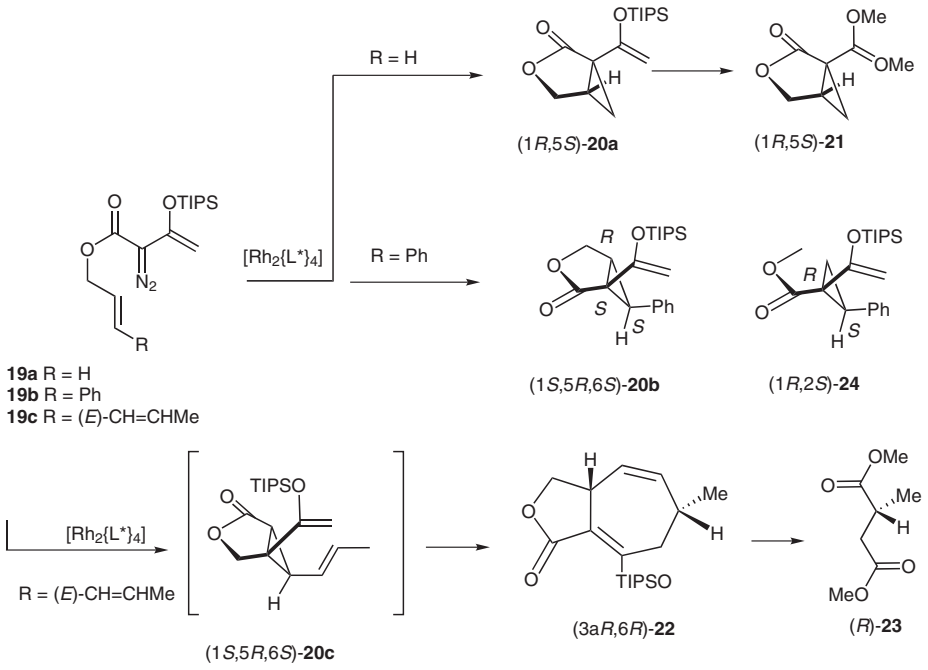
The intramolecular cyclopropanation of (silyloxyvinyl) diazoacetates, i.e. allyl 2-diazo-3-silyloxybut-3-enoates **19** was somewhat less successful. The diazo precursors **19a–c** were synthesized by conventional procedures and subjected to diazo decomposition with a limited selection of catalysts (Scheme 3 and Table 3). The cyclopropanation product of **19c** underwent Cope rearrangement under the reaction conditions to afford **22**. The enantioselectivities of all these reactions were below those achieved with styrene. $[Rh_2\{(S)\text{-nttl}\}_4]$ and $[Rh_2\{(S)\text{-pttl}\}_4]$ provided the best selectivities, although even at –78 °C the highest ee was only 89%. Surprisingly, Davies' $[Rh_2\{(S)\text{-dosp}\}_4]$ catalyst was less suitable for these transformations, although it has been found to be the catalyst of choice in other intramolecular cyclopropanations of allyl diazoacetates.[16]

Table 3 Intramolecular Cyclopropanation of Allyl 2-Diazo-3-silyloxybut-3-enoates **19a–c** in Toluene[a]

Precursor	R	Catalyst	Product, yield (%)	ee (%)
19a	H	$[Rh_2\{(S)\text{-nttl}\}_4]$	**20a**, 81	47[c]
19a	H	$[Rh_2\{(S)\text{-pttl}\}_4]$	**20a**, 75	50[c]
19a	H	$[Rh_2\{(S)\text{-pttl}\}_4]$[b]	**20a**, 50	70[c]
19b	Ph	$[Rh_2\{(S)\text{-nttl}\}_4]$	**20b**, 77	73[d]
19b	Ph	$[Rh_2\{(S)\text{-pttl}\}_4]$	**20b**, 93	77[d]
19b	Ph	$[Rh_2\{(S)\text{-pttl}\}_4]$[b]	**20b**, 66	89[d]
19c	(*E*)-CH=CHMe	$[Rh_2\{(S)\text{-nttl}\}_4]$	**22**, 77	67[e]
19c	(*E*)-CH=CHMe	$[Rh_2\{(S)\text{-pttl}\}_4]$	**22**, 81	60[e]
19c	(*E*)-CH=CHMe	$[Rh_2\{(S)\text{-pttl}\}_4]$[b]	**22**, 71	68[e]

[a] At 0 °C.
[b] At –78 °C.
[c] 1*R*,5*S*.
[d] 1*S*,5*R*,6*S*.
[e] 3a*R*,6*R*.

The absolute configurations of **20a** and **22**, were determined by degradation with O_3 to afford **21** and **23**, respectively, of known absolute configuration. The absolute configuration of **20b**, in turn, was tentatively assigned on



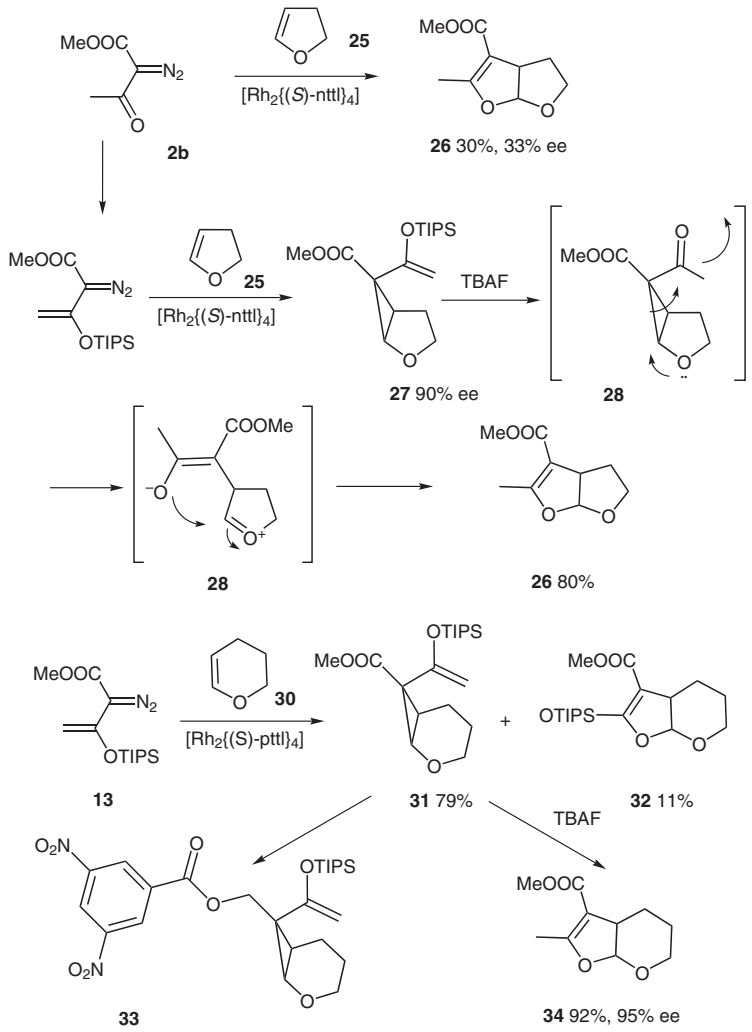
Scheme 3

the grounds of its CD in comparison to that of **24**. The results indicate an inversion of the sense of absolute configuration between **20a** as opposed to that of **20b** and **20c**. Precedents for such inversions upon change of substituents have been reported, however, for other intramolecular cyclopropanations of diazoacetates.[16,17]

A Formal Cycloaddition of 2,3-Dihydrofuran (25) via Cyclopropanation with Methyl (Silyloxyvinyl)diazoacetate (13)[18]

Diazo compounds, when exposed to transition-metal catalysts react with olefins usually via cyclopropanation. However, some oxocarbenes, when exposed to polar or polarizable olefins, undergo dipolar cycloadditions. For example, methyl diazoacetoacetate (**2b**), in the presence of $[Rh_2\{(S)\text{-nttl}\}_4]$ reacts with 2,3-dihydrofuran (**25**) to afford the cycloadduct **26** in 30% yield and 33% ee (Scheme 4). The result is as unsatisfactory as the cyclopropanation of styrene with **2b** mentioned above. However, if **2b** is replaced by the vinyl diazoacetate **13**, the cyclopropane **27** may be obtained with high enantioselectivity and yield. Treatment of the cyclopropane **27** with TBAF affords the formal cycloadduct **26**.[13]

The cyclopropanation of 2,3-dihydrofuran (**25**) with **13** in the presence of $[Rh_2\{(S)\text{-nttl}\}_4]$ afforded **27** as a single diastereoisomer (Scheme 4). The enantiomers of **27** were not separable; however, upon treatment with TBAF the silyloxy group of **27** was cleaved off, and the resulting ketone **28** underwent spontaneous ring-opening to **29** and recyclization to afford **26**, on which the enantioselectivity could be determined by GC. In general, **27** was not isolated, and the yields reported in Table 4 refer to the two-step sequence. The yield for transformation of isolated **27** to **26** was in the order of 80%. Other catalysts were examined, but led to lower selectivities, except $[Rh_2\{(S)\text{-pttl}\}_4]$. The analogous reaction of 3,4-dihydro-2*H*-pyran (**30**) yielded the corresponding adduct **31** in 79% yield and 95% ee in the presence of $[Rh_2\{(S)\text{-pttl}\}_4]$, as determined on **34** after treatment with TBAF (Scheme 4, Table 4). In view of these satisfactory results, no extensive screening with other catalysts was carried out. A secondary product **32** resulting from direct cycloaddition of **13** to **30** was also isolated in ca. 10% yield, but the enantioselectivity of the secondary process was not investigated.



Scheme 4

The racemic cyclopropane **31** was reduced with $LiAlH_4$ to afford the corresponding alcohol, which was derivatized with 3,5-dinitrobenzoyl chloride to afford **33**. The structure of **33** was unambiguously confirmed by X-ray structure analysis. Unfortunately, no suitable crystals could be obtained from enantiopure derivatives from any compound in this series, and the absolute configuration of the products could not be established.

Cycloadditions with Dioxocarbenes

If the transition-metal-catalyzed diazo decomposition of diazo esters carrying a second carbonyl substituent is carried out in the presence of polar olefins, products of formal [2+3] dipolar cycloadditions may be formed. This is typically the case with ethyl diazoacetoacetate (**2d**)[19] and 2-diazodimedone (**3**)[20] but also with ethyl diazopyruvate (**4**).[21] There is evidence that some of these cycloadditions are concerted; however, the occurrence of two-step additions involving intermediate cyclopropanes or dipolar species may not be definitely ruled out.

Cycloaddition of 2-Diazo-5,5-dimethylcyclohexane-1,3-dione (3a) to 2,3-Dihydrofuran (25)

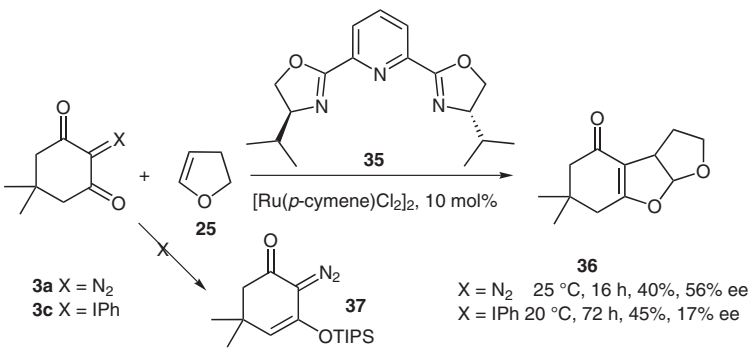
2-Diazodimedone (**3a**) undergoes cycloaddition to 2,3-dihydrofuran (**25**) upon diazo decomposition to afford the adduct **36** (Scheme 5). Contrary to previous claims in the literature,[22] these cycloadditions are not enantioselective when catalyzed by Rh(II).[23] In light of our observations with diazo acetoacetate presented above, we tried to circumvent the problem by preparing the silyl enol derivative **37** of diazodimedone; however, we were unable to isolate the desired product. Subsequently, we turned our attention to Ru catalysts. Recently, Mezzetti has reported highly diastereo- and enantioselective cyclopropanations of styrene with Ru catalysts. These cyclopropanations have exceptionally high (negative) ρ-values of –2.3.[24] By extending the reasoning of Davies mentioned above, we hypothesized that the Ru-catalyzed cycloadditions might exhibit higher enantioselectivities than the Rh-catalyzed reactions.

Table 4 Cyclopropanation–Rearrangement of 2,3-Dihydrofuran (**25**) and 3,4-Dihydro-2*H*-pyran (**30**) with **13**[a]

Olefin	Catalyst	Solvent	Product, yield (%)	ee (%)	**33** (%)
25	$[Rh_2\{(S)\text{-nttl}\}_4]$	**25**	**26**, 44	84	–
25	$[Rh_2\{(S)\text{-nttl}\}_4]$	CH_2Cl_2	**26**, 63	76	–
25	$[Rh_2\{(S)\text{-nttl}\}_4]$	pentane	**26**, 58	86	–
25	$[Rh_2\{(S)\text{-nttl}\}_4]$	PhF	**26**, 77	82	–
25	$[Rh_2\{(S)\text{-nttl}\}_4]$	$toluene_3$	**26**, 68	90	–
25	$[Rh_2\{(S)\text{-ptpa}\}_4]$	toluene	**26**, 75	64	–
25	$[Rh_2\{(S)\text{-pttl}\}_4]$	toluene	**26**, 95	85	–
25	$[Rh_2\{(S)\text{-tbsp}\}_4]$	toluene	**26**, 59	60	–
25	$[Rh_2\{(S)\text{-dosp}\}_4]$	toluene	**26**, 50	59	–
25	$[Rh_2\{(S)\text{-bnp}\}_4]$	toluene	**26**, 35	40	–
25	$[Rh_2\{(S)\text{-mepy}\}_4]$	toluene	**26**, 43	44	–
30	$[Rh_2\{(S)\text{-nttl}\}_4]$	toluene	**31**, 78	82[b]	7
30	$[Rh_2\{(S)\text{-pttl}\}_4]$	toluene	**31**, 79	95[b]	11
30	$[Rh_2\{(S)\text{-dosp}\}_4]$	toluene	**31**, 68	53[b]	not detected

[a] Conditions: At 0 °C, **13** (0.3 mmol) was reacted with **25** or **30** (10–15 equiv), respectively, in the appropriate solvent (3.0 mL), and catalyst (3 %).
[b] Determined based on **32** by GC.

Our expectations were only partially satisfied.[25] Under optimized conditions the Ru-catalyzed cycloaddition of 2-diazodimedone (**3a**) to **25** in the presence of the pybox ligand **35** (10 mol%) produced the adduct **36** in only 40% yield although with 56% ee. With 5 mol% of catalyst, the yield was 22% (in CH_2Cl_2). The yield increased to 70% when the reaction time was increased to 72 hours, and to 76% when the reaction was carried out at 45 °C with 5 mol% of catalyst. In this latter case, the ee decreased slightly to 52%. A large selection of Ru catalysts was screened, but the enantioselectivity of the reaction could not be improved. In the hope of speeding up the reaction, the diazo precursor **3a** was replaced by the corresponding phenyliodonium ylide **3c**. However, the results with ylide

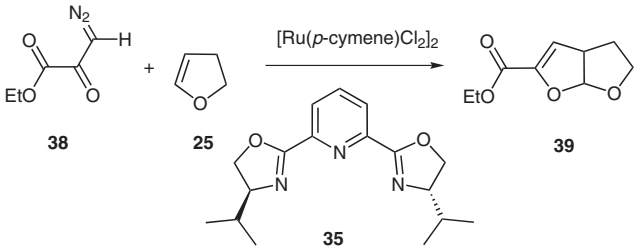


Scheme 5

3c under similar reaction conditions were even more disappointing. The reaction proceeded even more sluggishly than that of **3a** and the enantioselectivity decreased to 17%. This suggests that the postulated metallocarbene intermediate was not formed between **3c** and the Ru catalyst. The residual enantioselectivity which was observed in the adduct **36** may be ascribed to a loose association between the catalyst and the ylide **1c** or to a complex of unknown structure derived from **1b**.

Cycloaddition of Ethyl Diazopyruvate (38) to 2,3-Dihydrofuran (25)[25]

The diazo decomposition of ethyl diazopyruvate (**38**) in the presence Rh(II) carboxylate catalysts afforded good yields of adduct **39**, but the reactions were not enantioselective (Scheme 6, Table 5). With Ru–pybox catalysts, the cycloadditions of **38** contrary to those of **3a** proceeded conveniently at room temperature, although the Ru-catalyzed reactions afforded lower yields of **39** than the Rh(II)-catalyzed ones.



Scheme 6

Table 5 Cycloaddition of Ethyl Diazopyruvate (**38**) and 2,3-Dihydrofuran (**25**)[a]

Catalyst[b]	Solvent	Yield of **39** (%)	ee (%)
$[Rh_2(OAc)_4]$	toluene	85	–
$[Rh_2\{(S)\text{-tbsp}\}_4]$	toluene	70	0
$[Rh_2\{(R)\text{-ntv}\}_4]$	toluene	80	12
$[RuCl_2(\mathbf{35})]$	neat	65	62
$[RuCl_2(\mathbf{35})]$	toluene	65	68
$[RuCl_2(\mathbf{35})]$[c]	toluene	68	74
$[RuCl_2(\mathbf{35})]$	CH_2Cl_2	55	56
$[RuCl_2(\mathbf{35})]$	hexane	20	66
$[RuCl_2(\mathbf{35})]$	$PhCF_3$	50	58

[a] Conditions: catalyst (10 mol%) and 30-fold excess of **25** over **38** at 25 °C.
[b] Threefold excess of **35** over $[Ru(p\text{-cymene})Cl_2]_2$.
[c] At 0 °C.

At 25 °C, the highest enantioselectivity of 68% was obtained with $[Ru(p\text{-cymene})Cl_2]_2$ in conjunction with ligand **35** in toluene, and this improved to 74% when the temperature was lowered to 0 °C. Other pybox ligands were examined, but afforded lower enantioselectivities. In addition, the cycloaddition to other olefins, such as ethyl vinyl ether, *tert*-butyl vinyl ether and dihydropyran proceeded with lower yields and enantioselectivities.

The presence of a second carbonyl substituent of a diazo carbonyl precursor results in a more electron-deficient carbene which exhibits intrinsically lower selectivities in carbene transfer reactions. Nevertheless, high selectivities in such reactions have been achieved. With dimethyl malonate and Meldrum's acid as precursor, optimization of the carboxylate ligand of the Rh(II) carboxylate catalyst led to substantial enhancement of selectivity. In the case of diazo acetoacetate, the problem was solved by its transformation to the silyl enol ether, which is a synthetic equivalent. Encouraging results were obtained for dipolar cycloadditions of diazopyruvates to dihydrofuran by the use of chiral Ru catalysts, although further optimization is necessary.

The catalysts were prepared according to published procedures: $[Rh_2\{(S)\text{-nttl}\}_4]$;[8] $[Rh_2\{(R)\text{-ntv}\}_4]$;[14] $[Rh_2\{(S)\text{-4-X-nttl}\}_4]$;[12b] $[Rh_2\{(S)\text{-dosp}\}_4]$;[26] $[Rh_2\{(S)\text{-tbsp}\}_4]$;[27] $[Rh_2\{(S)\text{-ptpa}\}_4]$;[28] $[Rh_2\{(S)\text{-pttl}\}_4]$;[29] $[Rh_2\{(S)\text{-mepy}\}_4]$;[30] $[Rh_2\{(S)\text{-bnp}\}_4]$;[22a] $[RuCl_2(\mathbf{35})]$.[31]

One-Pot Cyclopropanation of Olefins with Dimethyl Malonate; General Procedure

Dimethyl malonate (**7**; 1.32 g. 0.01 mol, 1 equiv) was added to a mixture of iodosylbenzene (1.4 equiv), olefin **6** (10 equiv), MgO (2.3 equiv), rhodium(II) catalyst (5 mol%) and molecular sieves 4 Å (250 mg) in CH_2Cl_2 (10 mL). The mixture was stirred under argon for 24 h. Samples (100 μL) were taken after several time intervals. The samples were filtered using a syringe filter holder (0.2 μm pore size) and the organic layer was diluted with CH_2Cl_2 (100 μL) and analyzed by GC. The reaction progress was monitored qualitatively by TLC using heptane–EtOAc (5:1) as eluent. An aliquot of the supernatant was used for GC analysis. When maximum conversion was reached, the reaction was terminated by filtration through Celite. The Celite pad was washed with CH_2Cl_2 (2 ×). Evaporation of the combined filtrates under reduced pressure followed by chromatography on silica gel with heptane–EtOAc (5:1) as eluent afforded the desired cyclopropane derivatives **10**.

Cyclopropanation of Styrene with Methyl (Triisopropylsilyloxyvinyl)diazoacetate (13); (1*R*,2*S*)-1-[Tri(isopropyl)silyloxyvinyl]-2-phenylcyclopropanecarboxylate (14a)

The catalyst $[Rh_2\{(S)\text{-nttl}\}_4]$ (11.6 mg, 0.008 mmol) was activated by heating in vacuo, and dissolved in toluene (3.0 mL). After addition of styrene (**6a**; 730 mg, 7.0 mmol) the mixture was cooled to 0 °C, and **13** (208 mg, 0.70 mmol) in toluene (2.0 mL) was added dropwise. After the addition, stirring was continued for 1 h. The solvent was evaporated and the residue was purified by flash chromatography (SiO_2, Et_2O–pentane, 5:95) to afford **14a** (194 mg, 77%) as a colorless solid. For data, see ref. 7.

Intramolecular Cyclopropanation of Allyl 2-Diazo-3-silyloxybut-3-enoate (19a); (1*R*,5*S*)-1-[1-Tri(isopropyl)silyloxyvinyl]-3-oxabicyclo[3.2.0]hexan-2-one (20a); Typical Procedure

$[Rh_2\{(S)\text{-nttl}\}_4]$ (13.9 mg, 0.01 mmol) was activated by heating in vacuo, dissolved in toluene and cooled to 0 °C. The diazoacetate **19a** (152.4 mg, 0.47 mmol) in toluene (1.0 mL) was added dropwise. After stirring for 1 h, the solvent was evaporated and the res-

idue was purified by flash chromatography (SiO_2, Et_2O–pentane 15:85) to afford **20a** as a colorless oil in 81% yield. For data, see ref. 15.

Cyclopropanation–Rearrangement of 2,3-Dihydrofuran (25) with Methyl (Triisopropylsilyloxyvinyl)diazoacetate (13); Methyl *cis*-2-Methyl-3*a*,4,5,6*a*-tetrahydrofuro[2,3-*b*]furan-3-carboxylate (26)

The catalyst (1.0 mol%) was activated by heating in vacuo and dissolved in toluene (2.0 mL). 2,3-Dihydrofuran (**25**, 10 equiv) was added and the mixture was cooled to 0 °C. The diazoacetate **13** (0.30 mmol) in toluene (1.5 mL) was added dropwise with stirring. After the addition, stirring was continued for 1 h. The solvent was evaporated and the residue was dissolved in Et_2O (5.0 mL). After cooling to –78 °C, TBAF (0.5 mL, 1 M in THF, 0.5 mmol) was added. After 1 h, the reaction was quenched by addition of 5% aq NH_4Cl (1.0 mL). The mixture was diluted with H_2O (4.0 mL), the aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was evaporated and the residue was purified by flash chromatography to afford **26** (77%) as a colorless oil. For data, see ref. 18.

Cycloaddition of Ethyl 2-Diazopyruvate (38) to 2,3-Dihydrofuran (25); Ethyl 4,5-Dihydro-3a*H*-furo[2,3-*b*]furan-2-carboxylate (39)

(*S*,*S*)-2,6-Bis(4-isopropyl-2-oxazolin-2-yl)pyridine (86 mg, 0.294 mmol) was added to a solution of $[RuCl_2(p\text{-cymene})]_2$ (58 mg, 0.095 mmol) in CH_2Cl_2. The dark-red mixture was stirred at r.t. for 1 h under argon. The solvent was removed under reduced pressure. 2,3-Dihydrofuran (**25**; 1.4 mL) and a solution of ethyl diazopyruvate (**38**; 100 mg, 0.95 mmol) in toluene (3.0 mL) was added. The resulting suspension was stirred until complete consumption of starting material (TLC). The mixture was concentrated, and the residue was purified by column chromatography on silica gel using EtOAc–pentane (60:40) as eluent to afford **39** as pale-yellow solid.

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