

# Asymmetric Transfer of Carbenes with Phenyliodonium Ylides

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## ABSTRACT

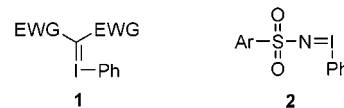
Phenyliodonium ylides, readily available upon treatment of C–H acidic compounds such as 1,3-dicarbonyl derivatives with iodobenzene diacetate, react in the presence of rhodium(II) or copper catalysts to afford products derived from carbenoid pathways. Chemo- and enantioselectivity of the reactions are identical to those of the corresponding diazocompounds, indicating metalcarbene intermediates with both precursors. An exception to this occurs in the intramolecular cyclopropanation of phenyliodonium ylides, where a competing uncatalyzed pathway intervenes at room temperature. When phenyliodonium ylides are generated in the presence of Rh(II) catalysts and olefins, they react in situ to afford cyclopropanes.

## I. Introduction

The reaction of C–H acidic compounds such as 1,3-dioxo derivatives with trivalent aryl iodine reagents affords aryl iodonium ylides (**1**, Scheme 1).<sup>1</sup> Arylsulfonamides, in turn, under the same conditions, are converted to phenyliodonium imides (**2**), also called iminophenyliodanes or iminophenyl- $\lambda^3$ -iodanes.<sup>2</sup> Upon heating, both **1** and **2** may participate in formal transfer of the carbene<sup>3</sup> or nitrene<sup>2</sup> moiety, respectively, to acceptors having lone pairs, such as thioanisole, dimethyl sulfoxide, and triphenylphosphine. The formal carbene transfer usually requires the presence of a catalyst, although there are a few exceptions.<sup>4</sup>

The enantioselective transfer of nitrenes from imino phenyliodonium imides of type **2** is well developed, mainly with Cu(I) or Rh(II) catalysts, and comprehensive reviews are available.<sup>5</sup> In contrast, catalytic carbene transfer with ylides of type **1** is much less established and is partially controversial for mechanistic reasons. In view of the remarkable progress that has recently been achieved in transition metal-catalyzed, asymmetric carbene transfer starting from diazoprecursors,<sup>6</sup> it appeared of interest to examine the potential of phenyliodonium ylides to serve as substitutes for diazocompounds in these reactions. Since the transition metal-catalyzed carbene transfer proceeds via metalcarbene intermediates, the primary

Scheme 1



objective of our research was to establish the intermediacy of such metalcarbenes upon decomposition of phenyliodonium ylides. In the affirmative case, we hoped to develop and extend the synthetic methodology for asymmetric carbene transfer with phenyliodonium ylides.

## II. Background

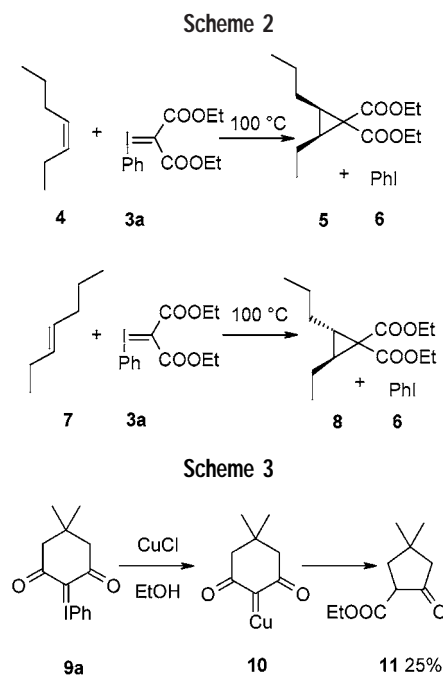
The enantioselective transfer of carbenes via transition metal-catalyzed decomposition of diazo compounds has seen impressive developments since the seminal report of Nozaki et al. in 1966.<sup>7</sup> A large number of efficient and selective catalysts, mostly based on Cu(I) or Rh(II), are now available for carbenoid reactions, such as cyclopropanation of olefins, cyclopropanation of acetylenes, insertion into CH or SiH bonds, and for formation of ylides generated upon reaction of the carbenes with heteroatoms with lone pairs.<sup>6</sup> The reaction mechanism involves interaction of the catalyst with the diazo precursor to afford a metalcarbene intermediate with concomitant release of nitrogen and subsequent transfer of the carbene to an appropriate substrate. Enantiocontrol in the carbene transfer step may be achieved by chiral ligands surrounding the metal center of the catalyst.

Asymmetric carbene transfer involving diazo decomposition is almost exclusively restricted to the research laboratory, and only a few large scale processes are known.<sup>8</sup> A possible reason for this lack of applications may be the often unjustified prejudice with regard to diazocompounds and the reagents used to prepare them: they are believed to be toxic, carcinogenic, and potentially explosive.<sup>9</sup> Several approaches to circumvent isolation of these carbene precursors have been proposed, such as thermolysis of tosylhydrazone salts of carbonyl compounds<sup>10</sup> and in situ diazotization/decomposition of amino compounds in the presence of transition metal catalysts.<sup>11</sup> However, these methods have as yet not found general application. Phenyliodonium ylides<sup>1,12</sup> could provide an alternative to diazo precursors in the carbene transfer reaction. They are readily accessible by reaction of C–H acidic compounds with iodobenzene diacetate,  $\text{PhI}(\text{OAc})_2$ .<sup>13</sup> They occur as amorphous solids or oils. Often, their decomposition occurs at temperatures well below those required for diazo decomposition. On the other hand, they are sometimes unstable and difficult to purify.

Heating of phenyliodonium bis(ethoxycarbonyl)methanide (**3a**, Scheme 2) in *cis*-hept-3-ene (**4**) at 100 °C afforded the *cis*-cyclopropane **5**, iodobenzene (**6**), and several minor products, while in the presence of *trans*-hept-2-ene (**7**), the *trans*-cyclopropane **8** was formed. The

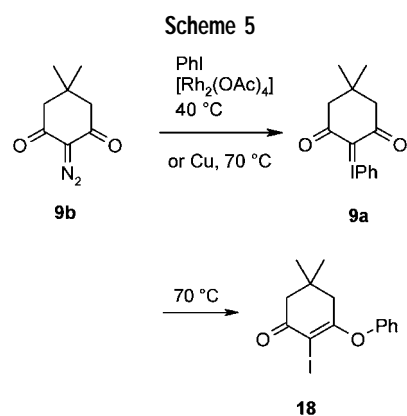
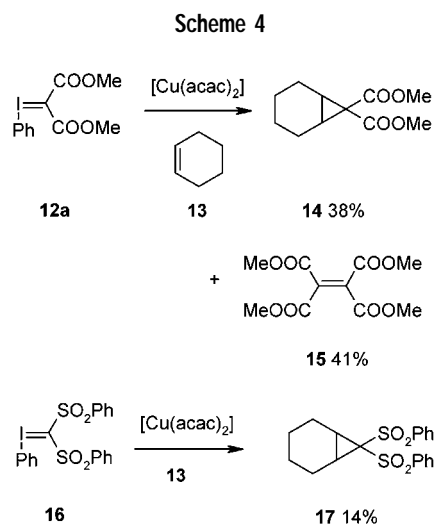
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Paul Müller received his Ph.D. in chemistry at the Swiss Federal Institute of Technology, Zürich (ETHZ), in 1966. Subsequently, he spent three years as research associate at the University of Illinois at Chicago and at the University of Chicago. He joined the University of Geneva as "Chef de Travaux" in 1969 and was promoted to the rank of full professor in 1982. He is author or coauthor of close to 200 publications in the fields of asymmetric catalytic transfer of carbenes and nitrenes, desymmetrizations of small ring compounds with nucleophiles and bases, reactive intermediates, and strained hydrocarbons.



high stereospecificity of the reaction suggests cyclopropanation of the double bond by a singlet carbene, cyclopropanation being faster than intersystem crossing. Photolysis of **3a** in the presence of *cis*-hept-2-ene, in turn, afforded a 34:66 mixture of *cis* and *trans* cyclopropanes **5** and **8**, respectively, in low yield, while photolysis in the presence of *trans*-hept-2-ene resulted in a 22:78 ratio of **5** and **8**.<sup>14</sup>

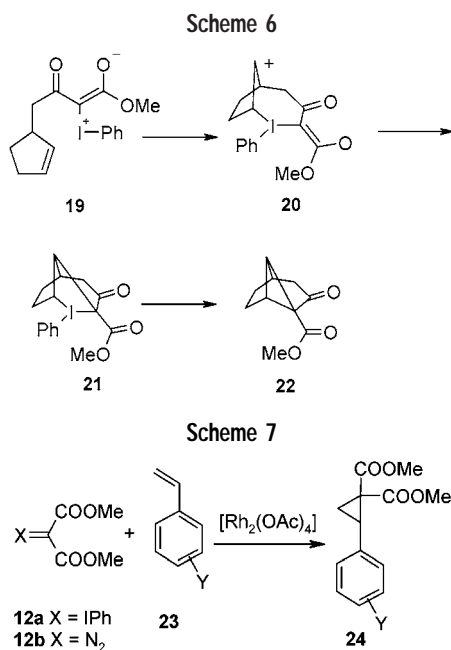
Several reports in the literature suggest the involvement of carbenes or carbenoids upon exposure of phenyliodonium ylides to Cu catalysts:<sup>15</sup> Hayasi et al. observed formation of ethyl 4,4-dimethyl-2-oxocyclopentane-1-carboxylate (**11**) when the ylide (**9a**) derived from dimedone was heated in EtOH in the presence of [CuCl]. The formation of **11** was attributed to Wolff rearrangement of a Cu-complexed carbene **10** followed by reaction of the resulting ketene with EtOH (Scheme 3).<sup>16</sup> It should be noted, however, that the occurrence of products derived from Wolff rearrangement of carbenes is not typical for Cu- or Rh(II)-catalyzed carbenoid reactions of diazo compounds<sup>17</sup> and the involvement of a free carbene appears more likely. Similarly, the formation of cyclopropane **14** (Scheme 4) and formal carbene dimer **15** upon exposure of phenyliodonium bis(methoxycarbonyl)methanide (**12a**) to [Cu(acac)<sub>2</sub>] in the presence of cyclohexene (**13**) was attributed to the intermediate formation of a carbene or carbenoid species.<sup>3</sup> A carbene mechanism was also proposed for the [Cu(acac)<sub>2</sub>]-catalyzed reaction of phenyliodonium bis(phenylsulfonyl)methanide (**16**) with cyclohexene (**13**) to afford the cyclopropane **17**.<sup>4</sup> The role of the catalyst in these reactions remained obscure, and it was not established whether it was limited to the decomposition of the ylide to afford a free carbene and iodobenzene or whether a metallocarbene was formed as reactive intermediate.



Interestingly, the reverse reaction, that is, transition metal-catalyzed transfer of a carbene moiety to iodobenzene, has been observed. Heating of 2-diazodimedone (**9b**) in iodobenzene (**6**) in the presence of [Rh<sub>2</sub>(OAc)<sub>4</sub>] to 40 °C afforded the ylide **9a** (Scheme 5). Copper catalysts required higher reaction temperatures (70 °C), and under these conditions, the ylide **9a** rearranged to **18**.<sup>18</sup>

The intermediacy of metallocarbenes in the Cu-catalyzed reactions of phenyliodonium ylides was questioned. Moriarty et al. investigated a series of intramolecular cyclopropanations of phenyliodonium ylides such as **19** to afford **22** with [CuCl] as catalyst.<sup>19</sup> Surprisingly, although [CuCl] had a catalytic effect, the reaction also proceeded in the absence of catalyst. For the uncatalyzed reaction, Moriarty proposed a mechanism in which the ylide **19** acts as a dipolarophile and adds to the double bond with the iodonium center to afford a zwitterionic intermediate **20**, which then cyclizes to **21** (Scheme 6). Extrusion of iodobenzene (**6**) affords **22**. Alternatively, a mechanism proceeding via a free carbene appears feasible, while the Cu-catalyzed reaction may be formulated involving radical, biradical, or free carbene intermediates.

The ionic mechanism of Moriarty is clearly incompatible with an asymmetric synthesis. Whether the radical or biradical mechanisms may lead to enantioselection depends on the mechanistic details, that is, whether the reaction occurs in the coordination sphere of the metal.

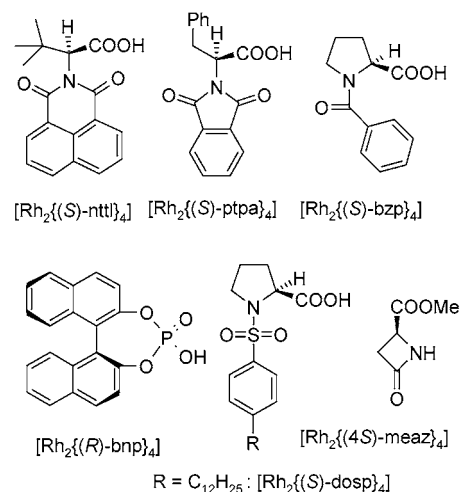


Our approach to establish metalcarbene intermediates upon decomposition of phenyliodonium ylides uses comparative selectivity studies: the observation of identical selectivities for reactions starting with diazocompounds and the corresponding phenyliodonium ylides under the same reaction conditions would provide conclusive evidence for the same reaction intermediate. Rh(II) catalysts were studied first because of our past experience with Rh(II)-catalyzed enantioselective carbene transfer<sup>20</sup> and because Rh(II) catalysts, contrary to their Cu counterparts, are not known to participate in electron-transfer reactions.

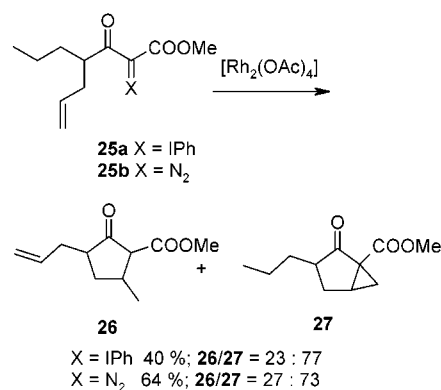
### III. Rh(II)-Catalyzed Carbene Transfer

The sensitivity of the carbene transfer toward electronic effects was examined by competitive cyclopropanation of pairs of substituted styrenes **23** with phenyliodonium bis(dimethoxycarbonyl)methanide (**12a**), in the presence of [Rh<sub>2</sub>(OAc)<sub>4</sub>] (Scheme 7). The Hammett plot had a slope of  $\rho = -0.47$  (vs  $\sigma^+$ ,  $r = 0.990$ ). The slope of the corresponding plot with dimethyl 2-diazomalonate (**12b**) was practically identical ( $\rho = -0.49$ ,  $r = 0.999$ ).<sup>21</sup> In addition, the selectivity constants ( $\log k_{\text{rel}}$  relative to styrene) for cyclopropanation of allylbenzene and phenylacetylene with **12a** using [Rh<sub>2</sub>(OAc)<sub>4</sub>] as catalyst are  $-0.96$  and  $-0.25$ , respectively, in good agreement with the  $\log k_{\text{rel}}$  values of  $-0.91$  and  $-0.43$  recorded for **12b**. The magnitude of the slope of the Hammett plots is in the range typical for carbene additions: Davies et al. reported  $\rho$ -values of  $-0.2$  for cyclopropanation of styrene with diazomalonate and  $-1.0$  with phenyldiazoacetate esters with [Rh<sub>2</sub>{(S)-dosp}<sub>4</sub>] (Chart 1).<sup>22</sup> The value of  $-0.47$  for **12a** is not compatible with the ionic mechanism of Moriarty. However, it does not provide conclusive evidence for the involvement of a metalcarbene, since a radical mechanism could give a similar reaction constant.

**Chart 1. Ligands L\*H and Abbreviations for Rh(II)-Catalyzed Reactions**

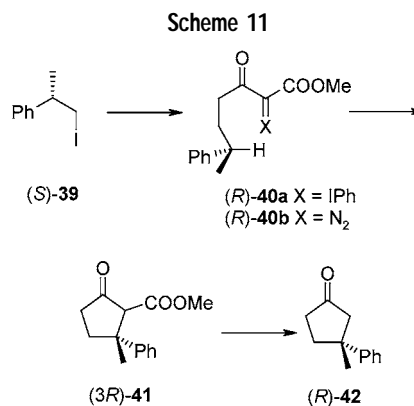
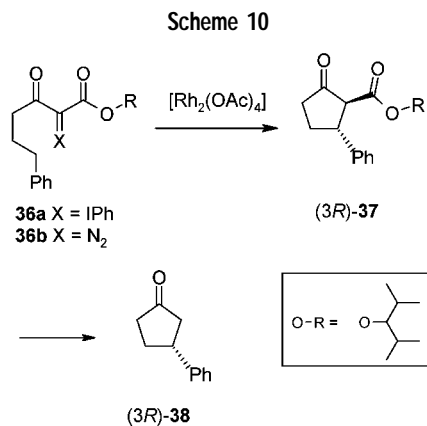
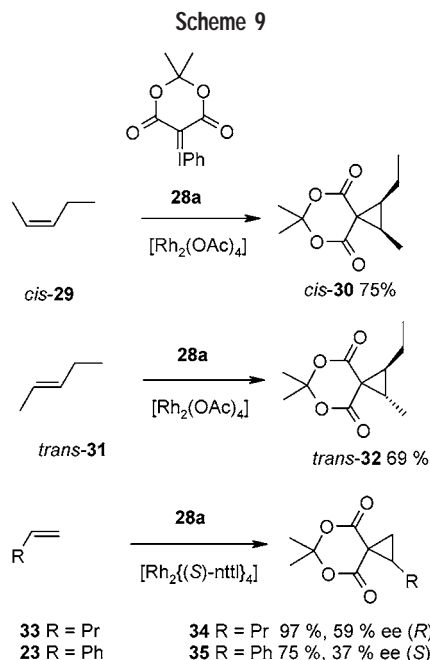


**Scheme 8**



The chemoselectivity of the ylide decomposition was investigated by exposure of the phenyliodonium ylide **25a** to [Rh<sub>2</sub>(OAc)<sub>4</sub>]. The reaction afforded a mixture of the insertion product **26** and the cyclopropane **27** in a 23:77 ratio with a total yield of 40% (Scheme 8). Under the same conditions, the diazoacetate **25b** gave a 27:73 ratio of **26** and **27** with a total yield of 64%. The formation of the insertion product **26** upon decomposition of the ylide **25a** is particularly significant, because insertion products are typical for carbenoid reactions. Their formation is incompatible with the ionic mechanism proposed by Moriarty.

However, surprisingly, the insertion/cyclopropanation ratio changed to 10:90 when the ylide had been stored ( $-18$  °C, 8 days) before use. This was ascribed to spontaneous intramolecular cyclopropanation of the ylide upon standing, consistent with other uncatalyzed cyclopropanations of ylides, as reported by Moriarty.<sup>19</sup> Thus the evidence is conflicting; the insertion reaction suggests a carbene mechanism, but the intramolecular cyclopropanation may proceed without catalyst, and a carbene intermediate is clearly not required. In contrast, no cyclopropanation product **26** was formed from the diazo precursor **25b** in the absence of catalyst. The nature of the uncatalyzed cyclopropanation was not investigated; however, the phenomenon seems to be restricted to



intramolecular reactions. Indeed, the intermolecular reaction of ylide **3a** in Scheme 2 requires heating to 100 °C,<sup>14</sup> but no reaction was observed between Meldrum's ylide **28a** and styrene (**23**) in the absence of catalyst at room temperature. The [Rh<sub>2</sub>(OAc)<sub>4</sub>]-catalyzed cyclopropanation of *cis*- and *trans*-pent-2-ene (**29** and **31**) with **28a** was stereospecific and yielded the cyclopropanes **30** and **32**, respectively, as expected for a carbene mechanism, but inconsistent with an addition-elimination reaction (Scheme 9).<sup>23</sup> In the presence of [Rh<sub>2</sub>{(S)-nttl}<sub>4</sub>] (Chart 1) pentene (**33**) and styrene (**23**) reacted with **28a** to afford the cyclopropanes **34** and **35** with 59% and 37% ee, respectively (Scheme 9).<sup>23</sup> Although this is not satisfactory for synthetic applications, it should be noted that the highest enantioselectivity for cyclopropanation of a substituted styrene with diazomalonate esters reported so far is 50%.<sup>24,25</sup> The diazo derivative of Meldrum's acid **28b** failed to undergo diazo decomposition when exposed to Rh(II) carboxylate catalysts even at elevated temperatures, so direct comparison of **28a** and **28b** was impossible.

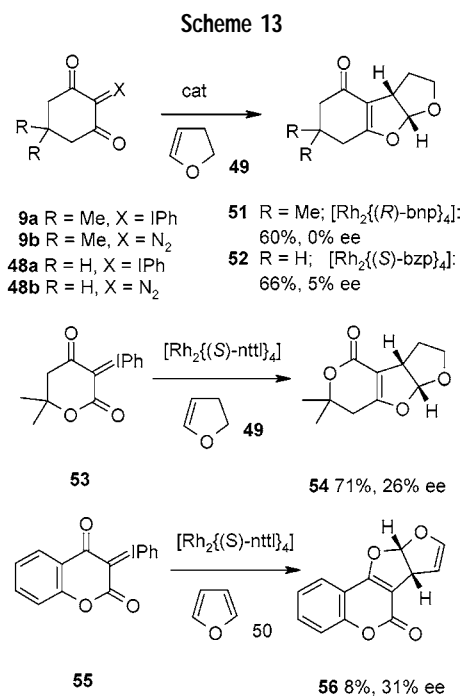
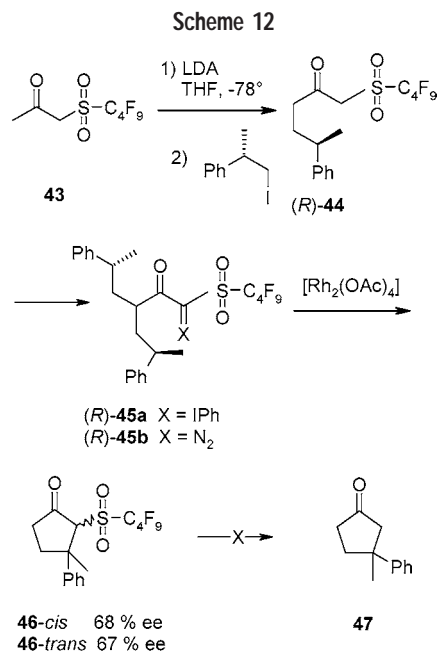
The enantioselectivity of the intramolecular CH insertion was investigated via decomposition of ylide **36a** and diazo compound **36b** (Scheme 10) in the presence of the chiral [Rh<sub>2</sub>{(S)-ptpa}<sub>4</sub>]-catalyst (Chart 1) developed by Hashimoto and Ikegami.<sup>26</sup> Both precursors afforded the cyclopentanone **37** with identical yield and enantioselectivity. The absolute configuration of **37** was determined by decarboxylation to **38**, as described by Hashimoto et al.<sup>26</sup>

The stereochemical course of the CH insertion was established with a precursor **40** having a chiral tertiary center but with an achiral catalyst (Scheme 11). The optically pure ylide **40a** and diazoacetate **40b** were synthesized from the iodide **39**. Both cyclized to **41** upon exposure to [Rh<sub>2</sub>(OAc)<sub>4</sub>]. The absolute configuration of **41** was determined via conversion to known **42**. Both reactions proceeded with >98% retention of configuration.<sup>27</sup>

The results presented so far indicate a reaction mechanism involving a metalcarbene intermediate. However, we also made some observations that led to ambiguous or no mechanistic conclusions. Thus, owing to difficulties encountered during purification of the ylide **36a**, we turned our attention to the (perfluoroalkyl)sulfonyl-substituted ylide (*R*)-**45a**, which on the grounds of literature reports was expected to be more easy to handle.<sup>28</sup> Such ylides are known to undergo decomposition in the presence of transition metal catalysts.<sup>28,29</sup> The ylide (*R*)-**45a** was prepared from the sulfone **43** via alkylation to **44** and subsequent reaction with Et<sub>3</sub>N, followed by PhI(OAc)<sub>2</sub> (Scheme 12). It was remarkably stable and could be purified by column chromatography. Upon exposure to [Rh<sub>2</sub>(OAc)<sub>4</sub>], it reacted to a *cis*/*trans* mixture of **46** with 68% (*cis*) and 67% (*trans*) ee. Desulfonation of **46** to **47** was attempted under a variety of conditions but failed, so the absolute configuration could not be determined.<sup>27</sup> The reasons for this partial loss of enantiopurity are not clear; however, the ee of **46** remained unchanged after several weeks, so the loss of stereochemical integrity must be attributed to the insertion process itself. Since it is known that the Rh(II)-catalyzed intramolecular CH insertion of a diazoketosulfone proceeds with full retention of configuration,<sup>30</sup> the partial racemization observed here cannot be attributed to the presence of the sulfonyl group but rather to the perfluorinated substituent of the sulfone. Unfortunately, we were unable to effect diazo transfer with (*R*)-**44**, so comparison of the reaction of the ylide **45a** with that of the diazo compound (*R*)-**45b** could not be realized.

The transition metal-catalyzed decomposition of diazo





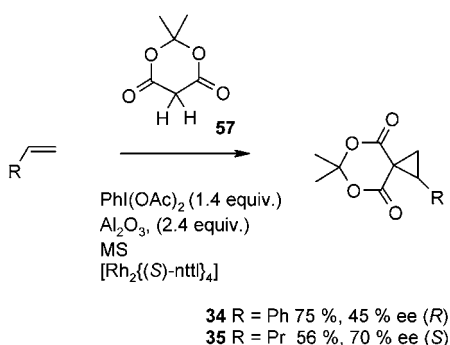
ketones or esters in the presence of olefins affords usually cyclopropanation products. However, with 2-diazopyruvates or 2-diazocyclohexane-1,3-diones, products formally derived from 1,3-cycloaddition of an intermediate oxocarbene may be isolated. A typical example is the cycloaddition of 2-diazocyclohexane-1,3-dione (**48b**) or 2-diazodimedone (**9b**) with dihydrofuran (**49**) or furan (**50**) (Scheme 13). The reaction was investigated in 1992 with Rh(II) catalysts. Pirrung and Zhang reported an ee of 44% for cycloaddition of **48b** to dihydrofuran (**49**) with [Rh<sub>2</sub>{(R)-bnp}<sub>4</sub>] (Chart 1), and ee's of 49% and 50% for cycloaddition of **9b** and **48b**, respectively, to furan (**50**).<sup>31</sup> More recently, Ishitani and Achiwa found ee's of up to 93% for addition of **48b** to **49** with Rh(II) catalysts having *N*-benzoylated proline ligands, that is, [Rh<sub>2</sub>{(S)-bzip}<sub>4</sub>]

(Chart 1).<sup>32</sup> We became interested in these reactions because, since the time of their first publication, no other asymmetric reactions of 2-diazo-1,3-diones had been reported except one<sup>33</sup> and that one was not reproducible, as we found out later.<sup>34</sup> The reactions appeared ideally suited for our purpose; however, we were unable to reproduce the results reported in the literature for the diazo precursors **9b** and **48b** with [Rh<sub>2</sub>{(R)-bnp}<sub>4</sub>] and [Rh<sub>2</sub>{(S)-bzip}<sub>4</sub>], respectively. A large number of catalysts of various structure were tried, but in no case could enantioselectivities above 10% be achieved. The reactions with the corresponding ylides **9a** and **48a** proceeded in the same manner with respect to both yield and enantioselectivity; in view of the low enantioselectivities in both reactions, no mechanistic conclusions could be drawn from the results.<sup>35</sup> Slightly higher enantioselectivities resulted with reactions of the modified ylides **53** and **55**, which gave up to 26% and 31% ee upon cycloaddition to furan and dihydrofuran, respectively (Scheme 13). The improved enantioselectivities of the modified ylides may be ascribed to the presence of the oxygen atom in the ring. Ethoxycarbonyl carbenes having electron-attracting substituents exhibit low enantioselectivity, and their transition state for carbene transfer occurs early on the reaction coordinate. In contrast, ethoxycarbonyl carbenes with electron-donating substituents have later transition states and, therefore, are more selective.<sup>22</sup> Since the ester substituent is less electron-attracting than the ketone, the carbene derived from **53** or **55** is stabilized relative to that derived from the phenyliodonium ylide **48a** or the diazoprecursor **48b**.<sup>35</sup> The observation of substantial enantioselectivity upon cyclopropanation of olefins with the ylide **28a** derived from Meldrum's acid, which has two stabilizing oxygens, is consistent with this interpretation. In contrast, the enantioselectivity of carbene transfer reactions with diazo ketones is more difficult to control,<sup>36</sup> and successful systems have been found only recently.<sup>37</sup>

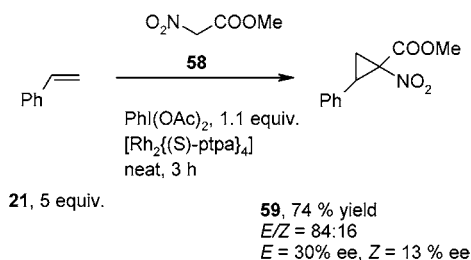
The yields of the cycloadditions of the diazo compounds corresponding to the stabilized ylides **30** and **55**, were poor, and in view of these disappointing results the research was discontinued. Although the results for the cycloaddition provide no arguments for the intermediacy of a metalcarbene, we note that the quasi-absence of enantioselectivity is observed for both diazo compounds and ylides, so that the results are mechanistically inconclusive.

Recently, Dauban et al. proposed a system for in situ generation and transition metal-catalyzed decomposition of phenyliodonium ylides by reaction of dimethyl malonate with iodosylbenzene in the presence of a Cu catalyst. Thus styrene was cyclopropanated in 55% yield.<sup>38</sup> We have optimized a system similar to that proposed by Du Bois for Rh(II)-catalyzed transfer of nitrenes with in situ prepared phenyliodonium imides.<sup>39</sup> Our reagent combination uses Meldrum's acid (**57**, 1.0 mmol), PhI(OAc)<sub>2</sub> (1.4 equiv), Al<sub>2</sub>O<sub>3</sub> (2.4 equiv), 4 Å molecular sieves (250 mg), and a [Rh<sub>2</sub>(OAc)<sub>4</sub>] catalyst (5 mol %) (Scheme 14). Yields of up to 80% were obtained when the olefin was used in 10-fold excess. The system is compatible with

Scheme 14



Scheme 15



asymmetric catalysis. Thus yields and enantioselectivity are comparable for cyclopropanation using the isolated ylide **28a** derived from Meldrum's acid or the in situ prepared ylide.<sup>40</sup>

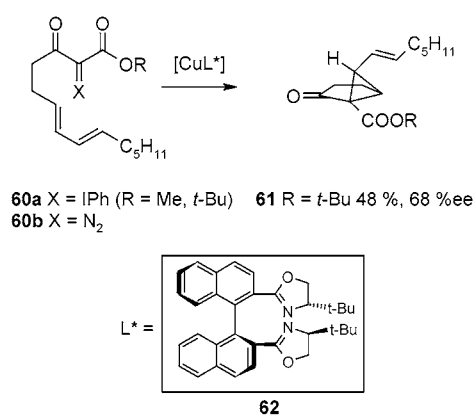
While this work was in progress, a communication appeared by Charette describing the synthesis of 1-nitro-1-carbonyl cyclopropanes **59** via in situ generated ylides, which are prepared from  $\alpha$ -nitro esters or ketones **58** with  $\text{PhI(OAc)}_2$  in the presence of  $[\text{Rh}_2(\text{OPiv})_4]$  (OPiv = pivalate).<sup>41</sup> Styrene was cyclopropanated with methyl nitroacetate and  $\text{PhI(OAc)}_2$  in the presence of  $[\text{Rh}_2\{\text{(S)-ptpa}\}_4]$  in 74% yield and with 30% ee (for *E*-isomer) (Scheme 15). The remarkable aspect of the system of Charette is the low catalyst loading of 0.5 mol %, which still affords high yields of cyclopropanes.

The synthetic application of carbene transfer of phenyliodonium ylides is limited to ylides carrying two electron-attracting substituents, such as carbonyl, sulfonyl, or cyano groups. Monocarbonyl iodonium ylides, in contrast, are not isolable, although they may be generated and intercepted.<sup>42</sup> To overcome these limitations, the use of diphenylsulfonium ylides for enantioselective carbene transfer was examined.<sup>43</sup> Chiral, nonracemic Rh(II) and Cu(I) catalysts exhibited similar diastereo- and enantioselectivities for carbene transfer of diphenylsulfonium ylides as the corresponding diazoacetates; however, the product yield of the reactions using sulfonium ylides was poor. Apparently, the metalcarbenes react faster with sulfonium ylides to afford formal carbene dimers than with the olefin to yield a cyclopropane.

#### IV. Cu(I)-Catalyzed Carbene Transfer

Although Cu(I) salts have been used by Moriarty<sup>19</sup> for decomposition of phenyliodonium ylides,  $[\text{Cu}(\text{acac})_2]$  is also effective.<sup>3,4</sup> In diazo decompositions, Cu(II) catalysts

Scheme 16

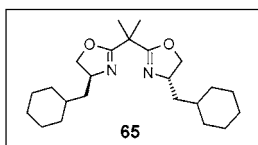
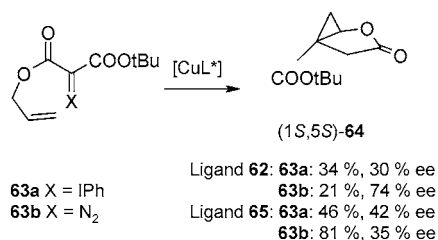


are reduced to Cu(I).<sup>7</sup> Similarly, Cu(II) and Cu(I) catalysts are equally effective for nitrene transfer with phenyliodonium imides.<sup>5</sup> For convenience, we have used either  $[\text{Cu}(\text{acac})_2]$  or  $[\text{Cu}(\text{OTf})_2]$  in conjunction with a chiral ligand in our work.

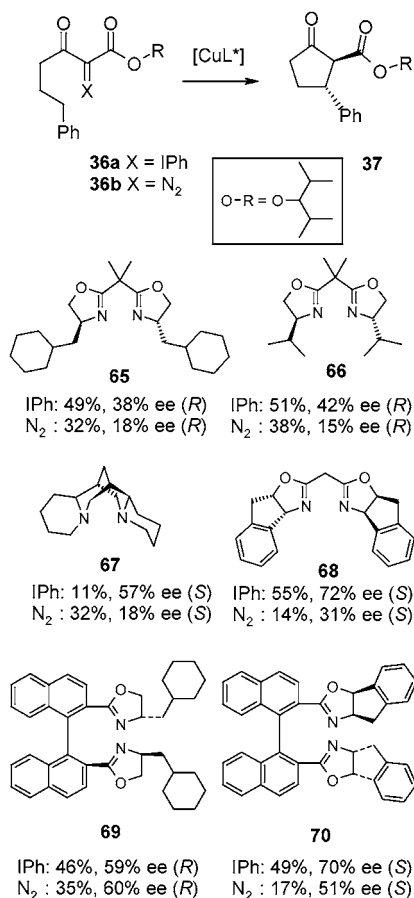
Competition experiments for cyclopropanation of substituted styrenes with  $[\text{Cu}(\text{acac})_2]$  lead to a Hammett plot with  $\rho = -1.12$  (vs  $\sigma^+$ ), about twice the value for the Rh(II)-catalyzed reaction.<sup>21</sup> A comparison of the enantioselectivity of reactions of phenyliodonium ylides and the corresponding diazo compounds was attempted for the intramolecular cyclopropanation of the ylide **60a** (R = Me) described by Moriarty.<sup>44</sup> The system was optimized with a selection of Cu(I) catalysts. Reactions proceeded to **61** in  $\text{CH}_2\text{Cl}_2$  at 0 °C in yields of 48–61%. The highest enantioselectivity (68%) was observed with the *tert*-butyl ester **60a** (R = *t*-Bu) in conjunction with the bis(oxazoline) ligand **62** (Scheme 16). Unfortunately, the diazo compound **60b** could not be decomposed with Cu(I) catalysts, even at elevated temperatures,<sup>45</sup> so comparison of the enantioselectivities of **60a** and **60b** was impossible. However, irrespective of the reaction mechanism, the observation of significant levels of enantioselectivity implies that the reaction must proceed in the coordination sphere of the metal and that the ionic mechanism proposed by Moriarty cannot apply.

In view of the low reactivity of diazo compound **60b**, we turned our attention to the allylic malonate ester **63b** for which diazo decomposition with chiral Cu(I) catalysts had been described.<sup>46</sup> The system was affected by two complications. First, diazo decomposition of **63b** with chiral Cu catalysts required elevated temperatures in the range of 65–100 °C. Second, the ylide **63a** was an unstable oil and decomposed at room temperature, mainly to form carbene dimers. The cyclopropanation with **63a** was therefore carried out at 0 °C. It was expected that these different reaction temperatures would lead to higher ee's in the reactions of the ylide **63a**. However, this was not always the case. Out of five catalysts, two gave a higher ee with the ylide **63a** and three gave the higher ee with the diazo malonate **63b**. Representative examples are shown in Scheme 17. These irregularities may be attributed to a competing nonselective pathway for intramolecular cyclopropanation of the ylide **63a** analogous

Scheme 17



Scheme 18



to that reported in the Rh(II)-catalyzed intramolecular cyclopropanation of **25a**. For comparison, Doyle has reported an ee of 57% for diazo decomposition of **63b** with [Rh<sub>2</sub>{(4*S*)-meaz<sub>4</sub>}] (Chart 1).<sup>25</sup>

Since no uncatalyzed CH insertions of phenyliodonium ylides at room temperature have ever been reported, we returned to the intramolecular reaction already investigated with Rh(II) (Scheme 10).<sup>47</sup> Cu(I) complexes are not the catalysts of choice for CH insertions, but they may also catalyze these reactions in the absence of alternatives. As before, reactions with the ylide **36a** were carried out at 0 °C and those with the diazo compound **36b** at 65 °C (Scheme 18). The enantioselectivity of the reactions was examined with six catalysts. In five cases, it was higher

with the ylide than with the diazo precursor, and in one, it was equal within experimental error.

When the decomposition of the chiral, nonracemic precursors **40a** and **40b** (Scheme 11) was carried out with an achiral copper catalyst, [Cu(hfa)<sub>2</sub>] (hfa = 1,1,1,5,5,5-hexafluoropentane-2,4-dione), the reactions proceeded with >98% retention of configuration, as observed with [Rh<sub>2</sub>(OAc)<sub>4</sub>]. The Cu-catalyzed decomposition of the fluorinated ylide **42a**, in turn, afforded again a mixture of *cis* and *trans* isomers in 56% yield (*trans/cis* ratio 81:19) with 67% (*cis*) and 56% (*trans*) ee, respectively.

## V. Conclusion

In the majority of the reactions investigated in this study, we find identical selectivities for reactions of Rh(II)- and Cu(I)-catalyzed decomposition of diazo compounds and phenyliodonium ylides. This parallel compartment strongly suggests the intermediacy of metalcarbenes in both reactions. However, in the intramolecular cyclopropanation, a competing uncatalyzed and unselective secondary reaction may intervene. We hope to be able to suppress this secondary reaction of phenyliodonium ylides by using the *in situ* procedure. Further research will be directed to the *in situ* generation and decomposition of phenyliodonium ylides that are not isolable and to improve the enantioselectivity of the reactions to reach levels of induction comparable to those possible in diazo decompositions.

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