

Review Commentary

Metal-catalyzed carbenoid reactions with iodonium and sulfonium ylides

Paul Müller,* Daniel Fernandez, Patrice Nury, Jean-Claude Rossier

Département de Chimie Organique, Université de Genève, 30 Quai Ernest Ansermet, CH-1211 Geneva, Switzerland

Received 22 July 1997; revised 16 September 1997; accepted 18 September 1997

ABSTRACT: Transition metal-catalyzed decomposition of phenyliodonium and diphenylsulfonium ylides was investigated with regard to application in asymmetric carbenoid reactions. Phenyliodonium ylides react in the presence of Rh(II) catalysts with the same selectivity in inter- and intramolecular cyclopropanations as the corresponding diazo compounds, and intramolecular CH insertions proceed with identical enantioselectivities. With diphenylsulfonium ethoxycarbonylmethylide the Cu(I)-catalyzed cyclopropanation of olefins affords *trans/cis* ratios and asymmetric inductions identical with those of diazo compounds, but with Rh(II) catalysts some small, although significant, selectivity variations occur, which are ascribed to coordination of diphenyl sulfide to one of the coordination sites of the catalyst. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: metal-catalyzed carbenoid reactions; Iodonium ylides; Sulfonium ylides

INTRODUCTION

The thermal and photochemical decomposition of diazo compounds affords carbenes.¹ Diazo compounds are also decomposed in the presence of certain transition metal catalysts based on Cu,² Rh,³ Ru,⁴ Pd⁵ or Co.⁶ Under these reaction conditions, metal carbenoids are formed as reactive intermediates, which are capable of transferring the carbene moiety to appropriate acceptors. These metallocarbenes are not, in general, isolable, but convincing evidence for their occurrence in transition metal-catalyzed carbenoid reactions of diazo compounds is available.⁷

If the transition metal carries chiral ligands, the carbene transfer may become enantioselective. Over recent years efficient methods for high-yield cyclopropanations,⁸ cyclopropanations⁹ and CH insertions¹⁰ proceeding with almost perfect enantioselectivities have been developed. Despite this progress, large-scale applications of metal-catalyzed carbene transfer reactions are limited. Among the known examples are pyrethroid synthesis (Cu-catalyzed cyclopropanation of 2,5-dimethylhexa-2,4-diene)¹¹, the cyclopropanation of iso-

butylene (synthesis of cilastatin)¹² and an Rh(II)-catalyzed intramolecular NH insertion (Merck synthesis of thienamycin).¹³ One of the reasons for this short list of applications is the requirement for diazo compounds as carbenoid precursors, which are potentially explosive, toxic and/or carcinogenic.¹⁴ For this reason we have investigated ways to generate metal-complexed carbenes from precursors other than diazo compounds. The systems investigated are phenyliodonium and diphenylsulfonium ylides. For both precursors the possibility of metal-catalyzed carbenoid transfer has been suggested, although not demonstrated, previously in the literature.

CARBENOID REACTIONS WITH PHENYLIODONIUM YLIDES

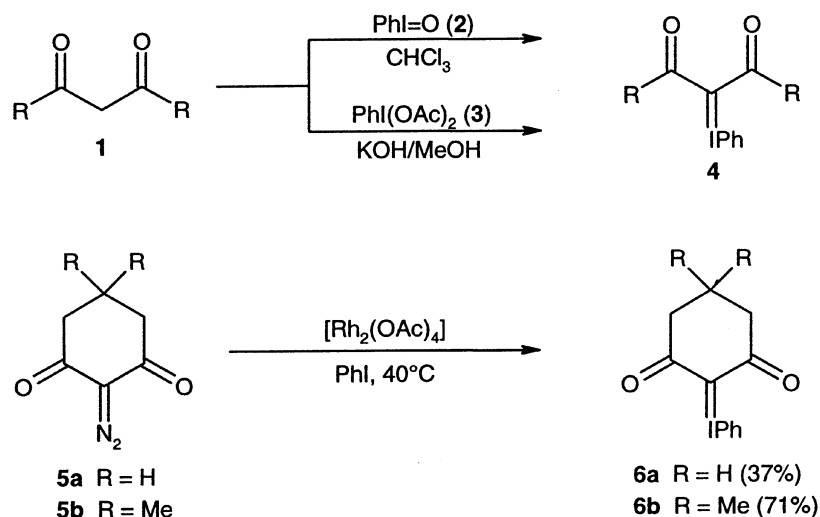
Synthesis and thermal, and photochemical decomposition of phenyliodonium ylides

The chemistry of phenyliodonium ylides has been pioneered by Neilands.¹⁵ The ylides (**4**) are synthesized by heating activated methylene compounds (**1**) with iodosylbenzene (**2**) in chloroform. Other procedures use iodosylbenzene and acetic anhydride¹⁶ or diacetoxyiodosylbenzene (**3**) in MeOH in the presence of KOH at –5 to 0°C.¹⁷ This latter method of Schank¹⁷ is the method of choice. It is, however, limited to ylides such as **4** carrying two electron-withdrawing substituents, such as carbonyl,

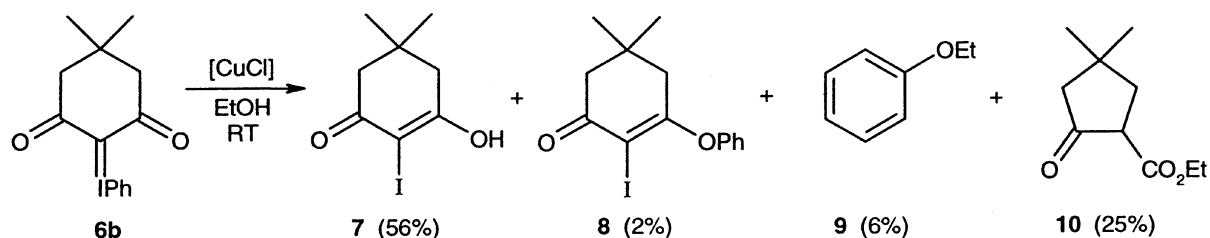
*Correspondence to: P. Müller, Département de Chimie Organique, Université de Genève, 30 Quai Ernest Ansermet, CH-1211 Geneva, Switzerland.

Contract/grant sponsor: Swiss National Science Foundation; contract grant number: 20-45255.95, 20-48156.96.

Contract/grant sponsor: Société Académique de Genève.



Scheme 1.



Scheme 2.

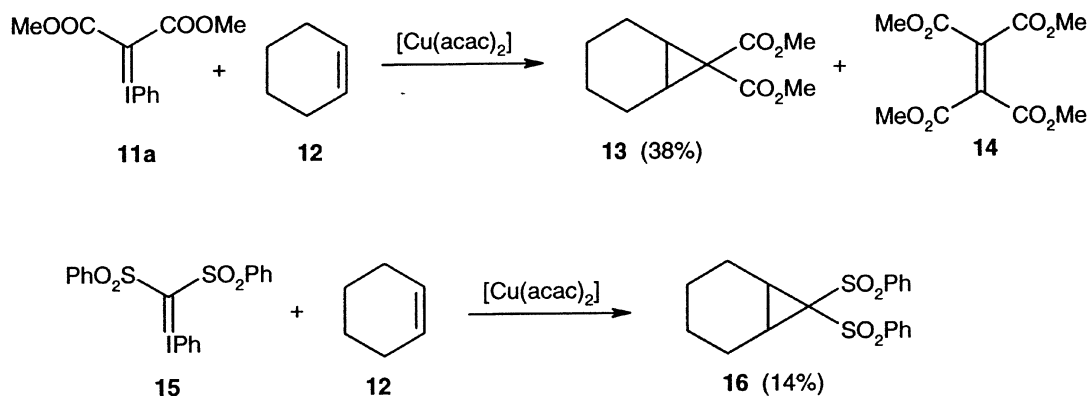
alkoxycarbonyl or sulfonyl. Phenyliodonium ylides having only one such substituent are not isolable. Alternatively, phenyliodonium ylides have been generated *via* $[\text{Rh}_2(\text{OAc})_4]$ -catalyzed decomposition of diazo compounds at 40–45 °C in the presence of iodobenzene.¹⁸ Thus, decomposition of 2-diazocyclohexane-1,3-dione (**5a**) or its 5,5-dimethyl derivative **5b** afforded the ylides **6a** and **6b** in yields of 37 and 71%, respectively. A plausible interpretation of this reaction involves transfer of the carbene from the diazo compound to the iodine *via* a rhodium–carbenoid intermediate. However, the procedure is not of interest within the context of our objective, which consists of avoiding the use of diazo compounds in the generation of metal-complexed carbenes.

The photochemical and Cu-catalyzed decomposition of phenyliodonium ylides, and the reactions of the corresponding diazo compounds, were investigated under a variety of reaction conditions by Hayasi *et al.*¹⁶ The products **7–10** resulted from the Cu-catalyzed reaction of the ylide **6b** in EtOH at 25 °C. The occurrence of a ring-contracted product **10** (25%), presumably derived from Wolff-type rearrangement of an intermediate carbene, is noteworthy. Compound **10** is also formed in 39% yield together with other products upon Cu(I)-catalyzed decomposition of diazodimedone in refluxing ethanol

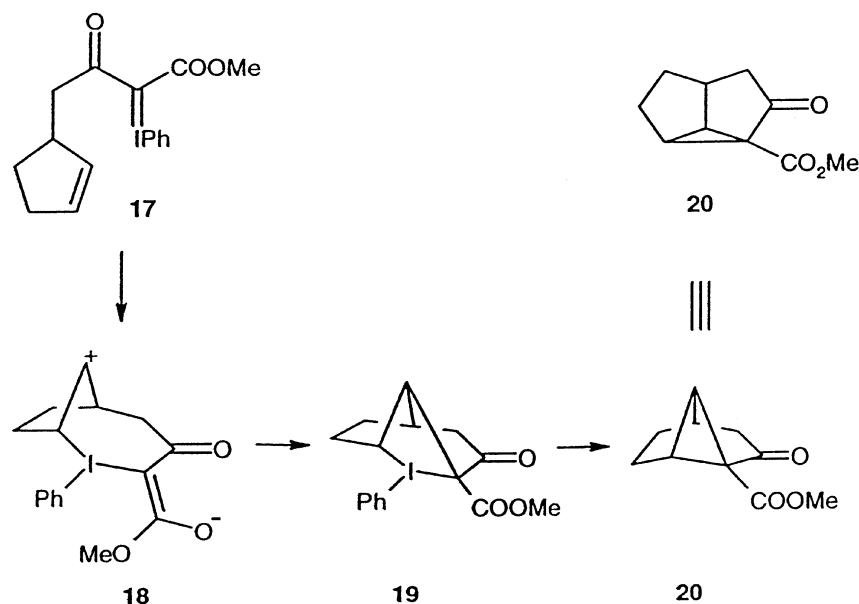
(**5b**). Hayasi *et al.*¹⁶ were the first to invoke a Cu-complexed carbene in the metal-catalyzed reactions and free carbenes in different spin states in the photochemical transformations to account for the variation of product distribution with differing reaction conditions in the decomposition of iodonium ylides.

Nicholas *et al.*¹⁹ reacted several diazo compounds and phenyliodonium ylides in the presence of triphenylarsine and Cu(I) or Cu(II) catalysts to generate arsonium ylides. In addition, the $[\text{Cu}(\text{acac})_2]$ -catalyzed reaction of the iodonium ylide **11a** derived from malonic ester afforded a sulfonium ylide with thioanisole and a sulfoxonium ylide with dimethyl sulfoxide. When **11a** was decomposed using $[\text{Cu}(\text{acac})_2]$ in cyclohexene (**12**), cyclopropanation to **13** occurred in 38% yield. The formal carbene dimer **14** (41%) was isolated in addition. Similarly, the $[\text{Cu}(\text{acac})_2]$ -catalyzed decomposition of phenyliodonium bis(phenylsulfonyl)methylide (**15**), first described by Varvoglis and co-workers,²⁰ afforded the cyclopropanation product **16** with **12** (14%). Photochemical decomposition of **15** in acetonitrile–cyclohexene afforded the adduct **16** in 31% yield. Photolysis in benzene, in turn, resulted in a 65% yield of formal insertion into the aromatic CH bond.

Although the mechanism of these reactions was not



Scheme 3.

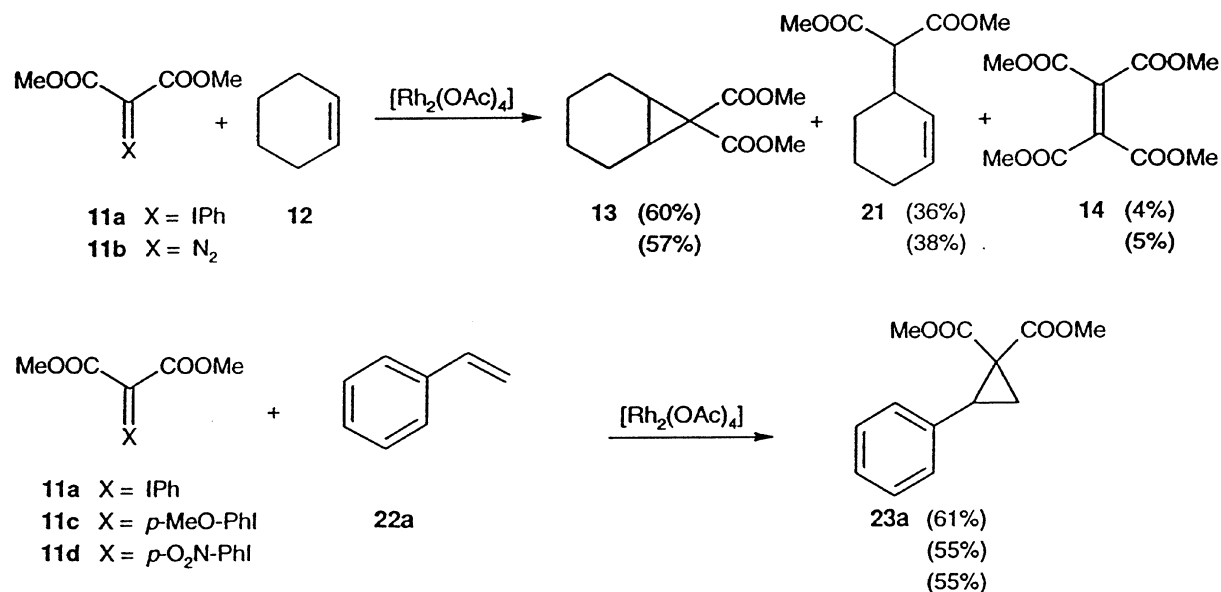


Scheme 4.

investigated in detail, further studies by Moriarty and co-workers²¹ showed that the situation was complicated. Several phenyliodonium ylides derived from β -keto esters and β -keto sulfones such as **17** underwent intramolecular cyclopropanation at 25 °C in the presence of a catalytic amount of CuCl in yields ranging from 76 to 90%. The reaction also occurred in the absence of catalyst, although in lower yield. The proposed mechanism of the uncatalyzed intramolecular cyclopropanation involves an electrophilic attack on the double bond by the iodonium center of **17**, followed by intramolecular trapping of the resulting cationic center of the zwitterionic intermediate **18**. The sequence is terminated by reductive elimination of PhI from the hypervalent intermediate **19** to afford **20**. An analogous mechanism involving radical intermediates was also envisaged. The role of the catalyst was considered to consist in electron transfer to the proposed iodonium center of the ylide. It is

noteworthy that photochemical reaction of **17** afforded none of the expected **20**.

A carbene mechanism was ruled out for the metal-catalyzed reaction on two grounds. First, iodonium ylides underwent a number of cycloaddition reactions leading to five-membered heterocyclic rather than cyclopropane products with polarized double bonds, and even with alkenes.^{22,23} In addition, no cyclopropanes are formed from 2,4-dinitro-6-phenyliodonium phenoxide with alkenes, alkynes and aromatics.²⁴ Second, no Wolff-type rearrangement products were formed in the reactions of the iodonium ylides which would be expected if ketocarbenes were involved as reactive intermediates.²⁵ However, heterocyclic rather than cyclopropane products have also been reported in carbenoid reactions of diazo compounds with a variety of multiple bonds including nitriles, acetylenes, carbodiimides, aldehydes and isothiocyanates^{1a,26} and even with certain olefins.²⁷ In



Scheme 5.

addition, the reactions of 2-diazonium phenoxides show remarkable similarities to those of the analogous phenyliodonium compounds.²⁸ Furthermore, ketocarbenes, when generated in the presence of Cu or Rh catalysts, do not, in general, undergo Wolff rearrangement.²⁹

Although the observations of Moriarty and co-workers do not definitely rule out a carbene mechanism for the metal-catalyzed decomposition of phenyliodonium ylides, they are pertinent with respect to the prospect of realizing enantioselective reactions with these reagents. The occurrence of a non-catalytic competitive reaction pathway in the intramolecular cyclopropanation of olefins could be detrimental to the enantioselectivity of the overall process. In addition, if the role of the catalyst is limited to reversible electron transfer, then the possibility of realizing enantioselective reactions is unlikely. It should be noted, on the other hand, that a radical pathway does not, *per se*, preclude asymmetric induction. As recently demonstrated in the asymmetric version of the [CuCl]-catalyzed allylic acetoxylation (Kharasch reaction), asymmetric induction is compatible with a radical pathway, provided that the reaction proceeds in or near the coordination sphere of the metal.³⁰

We considered that phenyliodonium ylides would be an attractive extension of our previously examined Rh(II)-catalyzed asymmetric carbenoid reactions of diazo compounds. Rh(II) was preferred over Cu(I) as a catalyst because of our past experience with Rh-based catalysts, and because Rh(II) is not known to participate in electron transfer.³¹ If the Rh(II)-catalyzed decompositions of diazo compounds and that of the corresponding phenyliodonium ylides proceed *via* metal-complexed carbenes, then the product distribution and the selectivity

exhibited from these carbene precursors must be identical.

Rh(II)-catalyzed carbenoid reactions of iodonium ylides

Intermolecular cyclopropanation and cyclopropanation. The reaction conditions for [Rh₂(OAc)₄]-catalyzed cyclopropanation of olefins with the ylide **11a** were optimized with cyclohexene (**12**). In CH₂Cl₂ at 20°C, both **11a** and the corresponding diazo compound **11b** afforded virtually identical product mixtures consisting of products of cyclopropanation (**13**), insertion (**21**) and carbene dimer **14** in a ratio of 57:38:5. No intermolecular cyclopropanation occurred upon heating the ylide **11a** (1 equiv.) in cyclohexene (20 equiv.) for 3 h at reflux without a catalyst.³² The only products isolated were unreacted ylide and a trace of **14**. Under the same reaction conditions styrene (**22**) was cyclopropanated to give **23** in 61% yield. The *p*-methoxy- and *p*-nitro-substituted phenyliodonium ylides **11c** and **11d** both afforded a 55% yield of cyclopropanation product **23**.

Allylbenzene (**24**), representing monosubstituted non-conjugated olefins, reacted similarly to **25**. With phenylacetylene (**26**) the corresponding cyclopropene (**27**) was isolated in 37% yield (56% with ethyl diazomalonnate³³). Although this yield is low, it is remarkable in view of the fact that no cyclopropene can be isolated upon Rh(II)-catalyzed cyclopropanation of **26** with ethyl diazoacetate.³⁴

The relative reactivities (*k*_{rel}) of substituted styrenes towards the ylide **11a** and diazomalonnate **11b** under [Rh₂(OAc)₄] catalysis were determined from the product

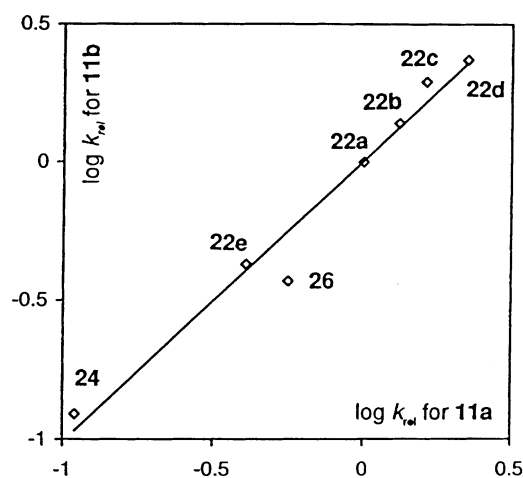
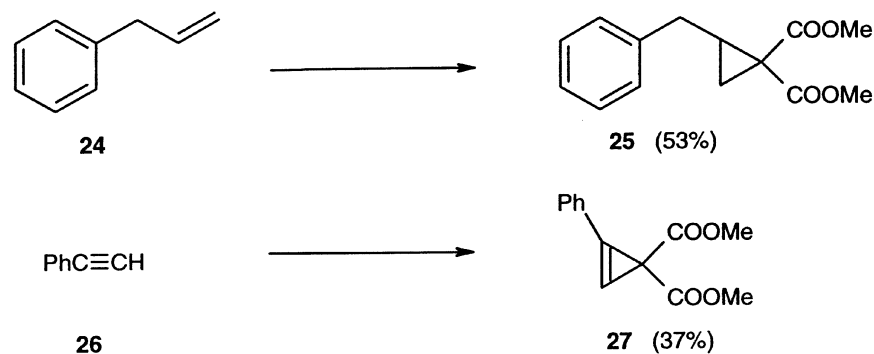


Figure 1. Plot of $\log k_{rel}$ for $[\text{Rh}_2(\text{OAc})_4]$ -catalyzed reaction of olefins **22** (**22a**, styrene; **22b**, 4-methylstyrene; **22c**, 3,4-dimethoxystyrene; **22d**, 4-methoxystyrene; **22e**, 4-nitrostyrene) and **24**, and phenylacetylene (**26**) with dimethyl diazomalonate (**11b**) vs $\log k_{rel}$ with phenyliodonium ylide (**11a**).

ratios of competition experiments using equimolar amounts of two olefins in a tenfold excess over the diazo compound or the ylide, respectively.

The correlation of the selectivity of the cyclopropanation of styrenes (**22**), allylbenzene (**24**) and phenylacetylene (**26**) with the ylide **11a** vs that of diazomalonate **11b** exhibits a slope of 1.01 (Fig. 1). A slight deviation, probably due to instability of the cyclopropane, is found for the cyclopropanation of phenylacetylene (**26**), but otherwise the selectivities are identical, which suggests that the reactions of both reagents may proceed *via* the same intermediate.

The Hammett plot of the relative reactivities of the substituted styrenes vs σ^+ (Fig. 2) has a slope -0.47 , which is in the same range as the values obtained for cyclopropanation with free carbenes ($\rho = -0.62$ for addition of dichlorocarbene to styrene at 80°C).³⁵ This weak selectivity is characteristic of carbene additions, and is generally attributed to an early transition state.^{5a,36} For the analogous $[\text{Cu}(\text{acac})_2]$ -catalyzed reaction the ρ -value is -1.12 . Although this latter value is considerably

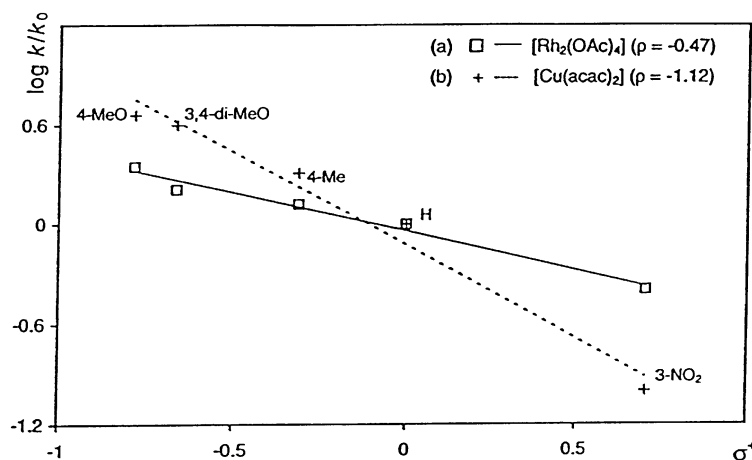
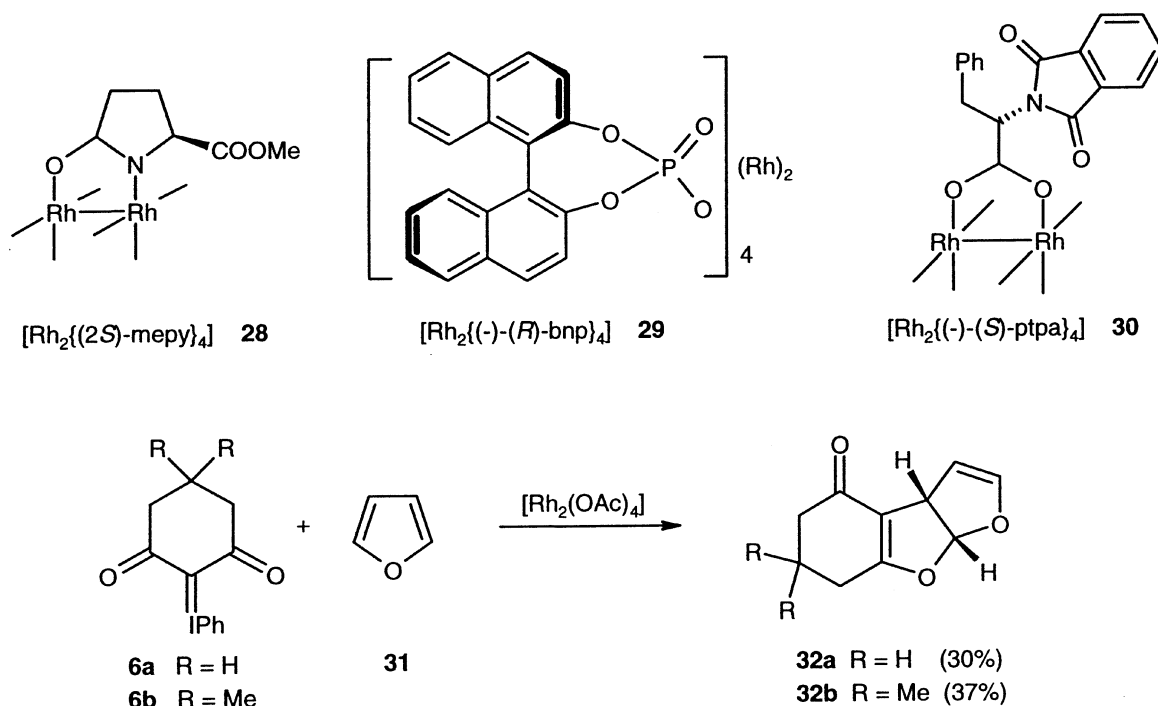


Figure 2. Hammett plot (vs σ^+) for cyclopropanation of substituted styrenes (**22a–e**) with phenyliodonium ylide (**11a**) catalyzed by $[\text{Rh}_2(\text{OAc})_4]$ ($\rho = -0.47$) or $[\text{Cu}(\text{acac})_2]$ ($\rho = -1.12$).



Scheme 7.

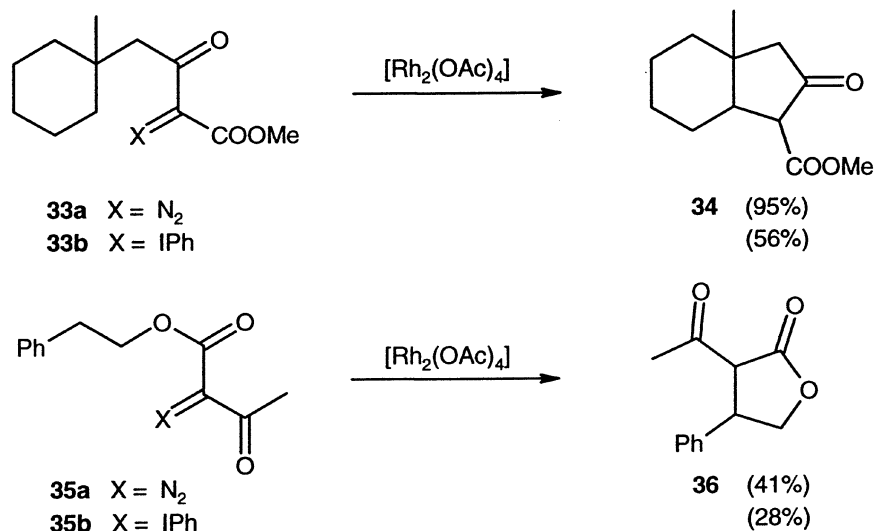
higher than that observed for $[Rh_2(OAc)_4]$, its significance is questionable. It could be simply indicative of a more polar transition state, but could also be indicative of a mechanistic change. At present, there are no experimental data which would allow a distinction to be made between these possibilities.

No reaction took place when dimethyl diazomalonate (**11b**) was exposed to Doyle *et al.*'s $[Rh_2\{(2S)\text{-mepy}\}_4]$ ³⁷ catalyst **28**. In contrast, the phenyliodonium ylide **11a** and its *p*-nitro- and the *p*-methoxy derivatives **11c** and **11d**, respectively, decomposed slowly within 3 h to afford the cyclopropane **23** in yields ranging from 12 to 20%. However, no optical induction occurred with this catalyst.

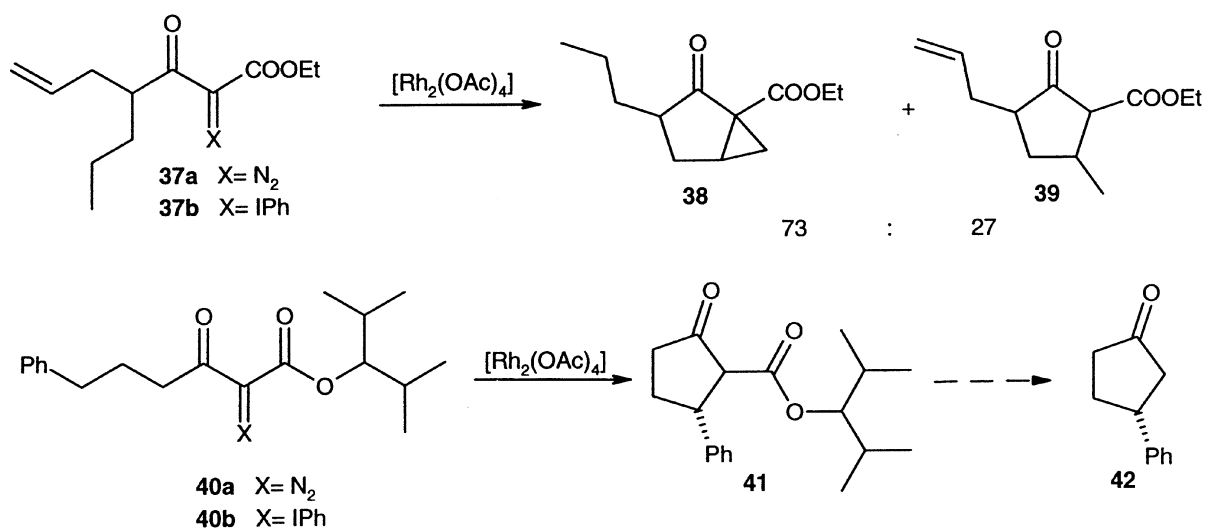
Cycloaddition of cyclic phenyliodonium ylides to furans. In 1991, Pirrung and co-workers^{7b,38} reported Rh(II)-catalyzed formal 1,3-dipolar cycloadditions between cyclic 2-diazo-1,3-diketones **5a** and **b** and furan (**31**), dihydrofurans and enol ethers. The reaction proceeds *via* cyclopropanation of the double bond by the carbenoid, followed by rearrangement. With the chiral $[Rh_2\{(R)\text{-bnp}\}_4]$ catalyst³⁹ (**29**) the adducts **32a** and **b** were isolated in 44–50% yield with an *ee* of *ca* 50%. In our hands, the diazoketones **5a** and **b** prepared according to the procedure of Moriarty *et al.*¹⁸ reacted as expected with $[Rh_2(OAc)_4]$, but other catalysts such as $[Cu(acac)_2]$ and $[Rh_2\{(2S)\text{-mepy}\}_4]$ were ineffective. The iodonium ylides **6a** and **b**, in turn, afforded **32a** and **b** with $[Rh_2(OAc)_4]$ in 30 and 37% yield, respectively, but no

reaction occurred with $[Rh_2\{(R)\text{-bnp}\}_4]$. Use of Ikegami and co-workers' $[Rh_2\{(S)\text{-ptpa}\}_4]$ ⁴⁰ catalyst **30** resulted in a yield of 21% and an *ee* at the limits of credibility (6%).

Intramolecular CH insertion. Carbon–hydrogen bond insertions are characteristic carbene reactions. CH insertions are particularly favored when carbenes are generated in the presence of Rh(II) catalysts. The reaction then proceeds with retention of configuration⁴¹ and, in the presence of suitable chiral catalysts, with high enantioselectivity.¹⁰ The observation of enantioselective CH insertion upon Rh(II)-catalyzed decomposition of phenyliodonium ylides was therefore considered to provide conclusive evidence for the intermediacy of rhodium carbenoids. The choice of compounds to be investigated was limited, however, since the ylide had to be stabilized by two electron-attracting substituents in order to be isolable. Unfortunately, this structural necessity rules out the use of the rhodium(II) carboxamidate catalysts which lead to the highest enantioselectivities in the insertions. At the same time, the use of secondary *meso* alcohols with which the highest induction has been achieved is problematic, because their acetodiazoacetates often give rise preferentially to achiral β -lactones.⁴² The diazo ketoester **33a** underwent cyclization upon decomposition with $[Rh_2(OAc)_4]$ to afford **34** in 95% yield.⁴³ Under comparable conditions, the corresponding iodonium ylide **33b** afforded a 56% yield of **34**. Similarly, the diazo-acetoacetate **35a** of 2-phenyl-



Scheme 8.



Scheme 9.

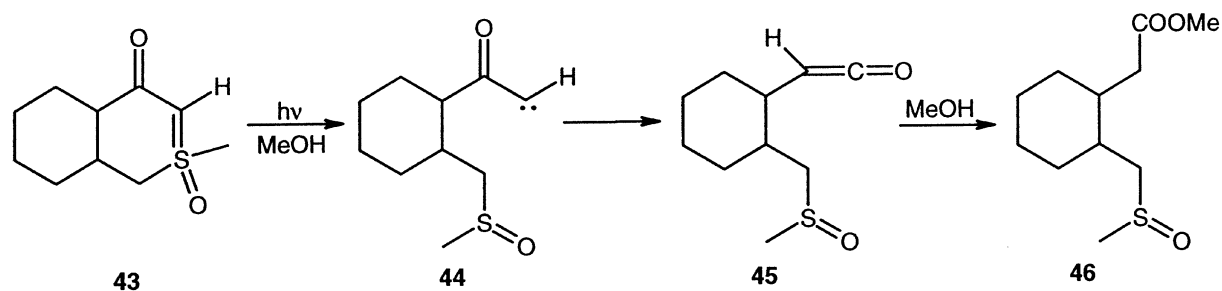
ethanol afforded the lactone **36** in 41% yield in CH₂Cl₂ at 20°C (85% in refluxing benzene).⁴⁴ In this case, the presence of the phenyl group activates the benzylic position and formation of the γ -lactone takes preference over that of the β -isomer. The iodonium ylide **35b**, in turn, afforded the γ -lactone **36** in 28% yield.

The diazoester **37a** may react *via* two different pathways. Intramolecular cyclopropanation of the double bond to **38** may compete with intramolecular CH insertion into the saturated side-chain affording **39**.⁴⁰ The decomposition of **37a** with [Rh₂(OAc)₄] afforded a 73:27 mixture of **38** and **39** (mixture of stereoisomers) in a total yield of 64%. When the reaction was carried out using freshly prepared iodonium ylide **37b** the product ratio was 77:23. However, the ratio changed to 90:10 when **37b** was stored (−18°C, 8 days) before the

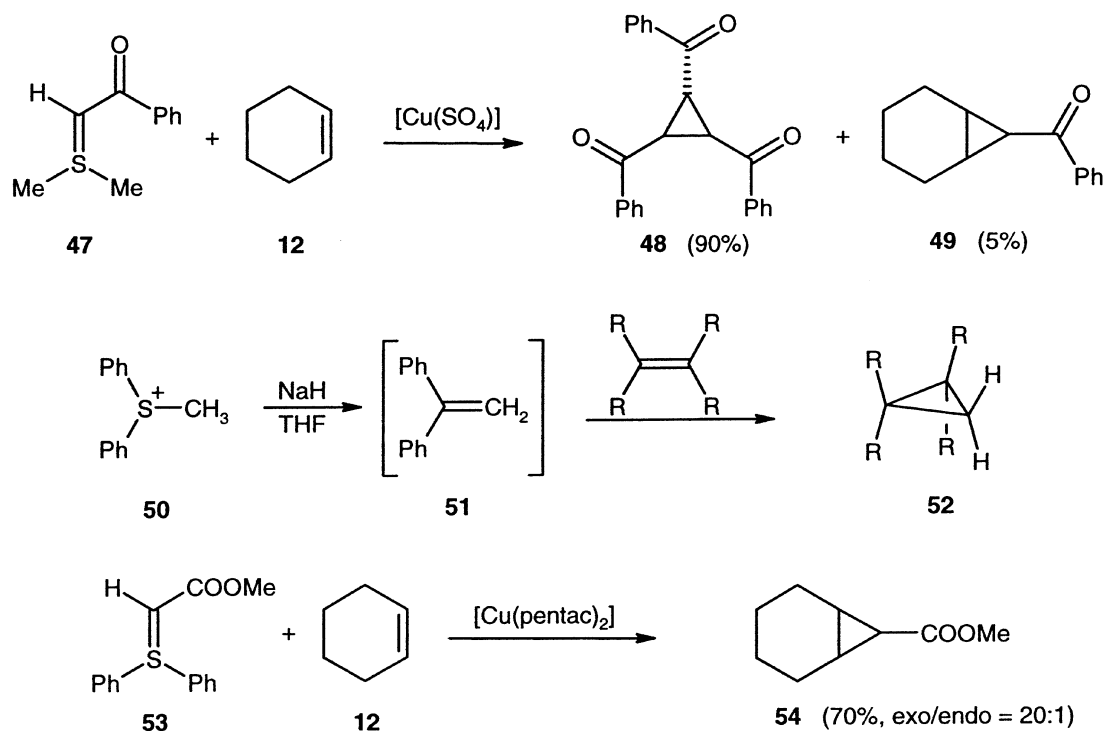
reaction. This change in product composition is ascribed to a non-catalyzed spontaneous intramolecular cyclopropanation of the ylide, entirely consistent with the proposition of Moriarty et al.¹⁸ However, it is noteworthy that no uncatalyzed intermolecular cyclopropanation or uncatalyzed intramolecular CH insertion has ever been reported.

The intramolecular CH insertion of the keto ester **40a** catalyzed by [Rh₂{(*S*)-(−)-ptpa}₄]⁴⁰ proceeds to **41** in 89% yield with 69% *ee* [*R*-configuration at C-3], [determined after conversion to 3-phenylcyclopentanone (**42**)]. Under the same reaction conditions, the phenyliodonium ylide **40b** afforded **41** in 78% yield with 67% *ee*.

In all cases investigated so far, the product composition for the Rh(II)-catalyzed decomposition of diazo compounds and that of the corresponding phenyliodo-



Scheme 10.



Scheme 11.

anium ylides is identical within experimental error. Since the intermediacy of rhodium-complexed carbenes in the decomposition of diazo compounds is firmly established,⁵ the same must hold for the ylides. This is not necessarily the case for the Cu-catalyzed reactions, where a different mechanism might apply.⁴⁵

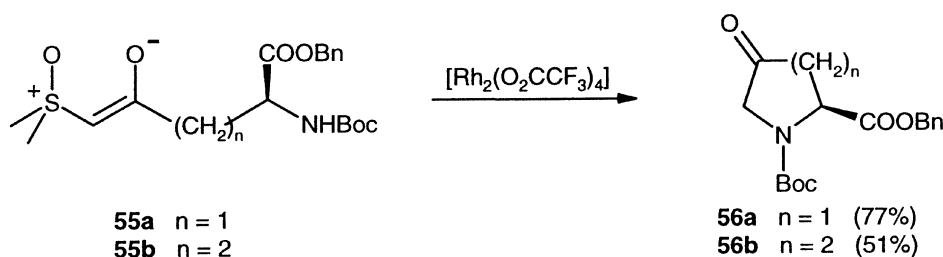
Despite the mechanistic analogy between diazo compounds and phenyliodonium ylides, the synthetic applicability of the ylide methodology appears to be limited. As mentioned above, the ylides are only isolable when stabilized by two electron-attracting substituents (alkoxycarbonyl, carbonyl or sulfonyl). They are often more difficult to purify than diazo compounds, and their Rh(II)-catalyzed decomposition requires relatively electrophilic catalysts such as Rh(II) carboxylates. Unfortunately, the Rh(II) carboxamides which have been shown to be the most efficient catalysts for asymmetric

diazo decomposition are not sufficiently reactive also to induce decomposition of phenyliodonium ylides.

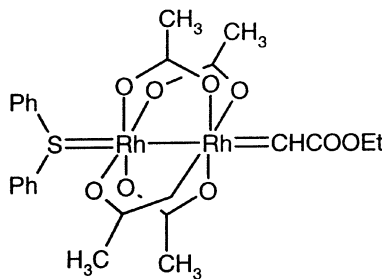
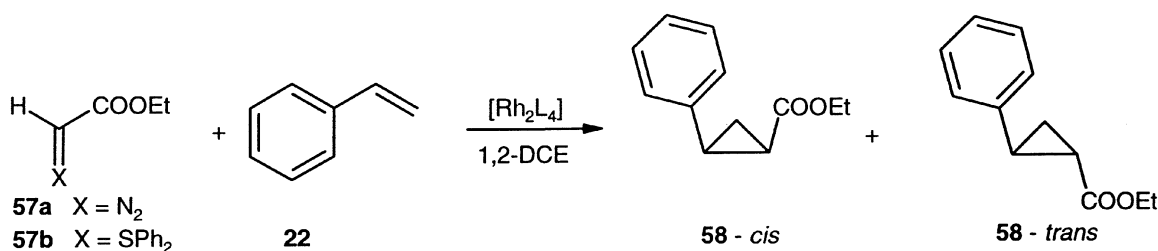
CARBENOID REACTIONS OF SULFONIUM YLIDES

Background

Sulfonium and sulfoxonium ylides are reagents for the cyclopropanation of electron-deficient carbon-carbon double bonds or of carbonyl groups.⁴⁶ The reaction mechanism proceeds stepwise *via* zwitterionic intermediates and does not involve carbenes. The possibility of generating carbenes from sulfoxonium ylides was first recognized by Corey and Chaykovsky.⁴⁷ Photolysis of **43** in MeOH afforded **46**, the formation of which was



Scheme 12.



Scheme 13.

rationalized by formation of an acylcarbene **44** with subsequent Wolff rearrangement to a ketene **45** and capture of the latter by the solvent.

Trost,⁴⁸ in turn, postulated a metalcarbene intermediate in order to rationalize the formation of cyclopropanes **48** (90%) and **49** (5%) upon decomposition of the sulfonium ylide **47** with anhydrous $[\text{Cu}(\text{SO}_4)]$ in cyclohexene (**12**). The same products, although in different proportions and accompanied by acetophenone, were formed upon photolysis of **47** in cyclohexene.⁴⁹ Diphenylsulfonium methylide (**51**) generated *in situ* from the sulfonium salt **50** using NaH in THF reacted under $[\text{Cu}(\text{acac})_2]$ catalysis with simple olefins to afford cyclopropanes **52** in 31–48% yield. Metalcarbenes were proposed as reaction intermediates.⁵⁰ The system was further improved by Cimetière and Julia,⁵¹ who employed copper (II) 3-pentylacetylacetonate ($[\text{Cu}(\text{pentac})_2]$) instead of $[\text{Cu}(\text{acac})_2]$, which resulted in an increase in yields to up to 92%. Decomposition of the ylide **53** in cyclohexene with $[\text{Cu}(\text{acac})_2]$ or $[\text{Cu}(\text{pentac})_2]$ afforded the cyclopropane **54** in 70% yield with an *exo/endo* product ratio of 20:1. Ylide **53** is therefore a synthetic substitute for methyl diazoacetate.

The formal Rh(II)-catalyzed intramolecular NH in-

sertion of two sulfoxonium ylides **55a** and **b** to give lactams **56a** and **b** was reported by Baldwin *et al.*⁵² Reaction took place in refluxing 1,2-dichloroethane with $[\text{Rh}_2(\text{O}_2\text{CCF}_3)_4]$. Other Rh(II)- or Cu-based catalysts did not decompose the ylides or provided only decomposition products.⁵²

In contrast to the phenyliodonium ylides, which require two stabilizing substituents at the carbanionic center in order to be isolable, one (or even no) such substituent is sufficient in the case of sulfonium and sulfoxonium ylides. Accordingly, these species could find complementary applications in enantioselective carbenoid reactions. Although other mechanisms for metal-catalyzed reactions of such ylides may be possible,⁵³ the intervention of metal carbenoids is usually suggested or implicitly assumed.

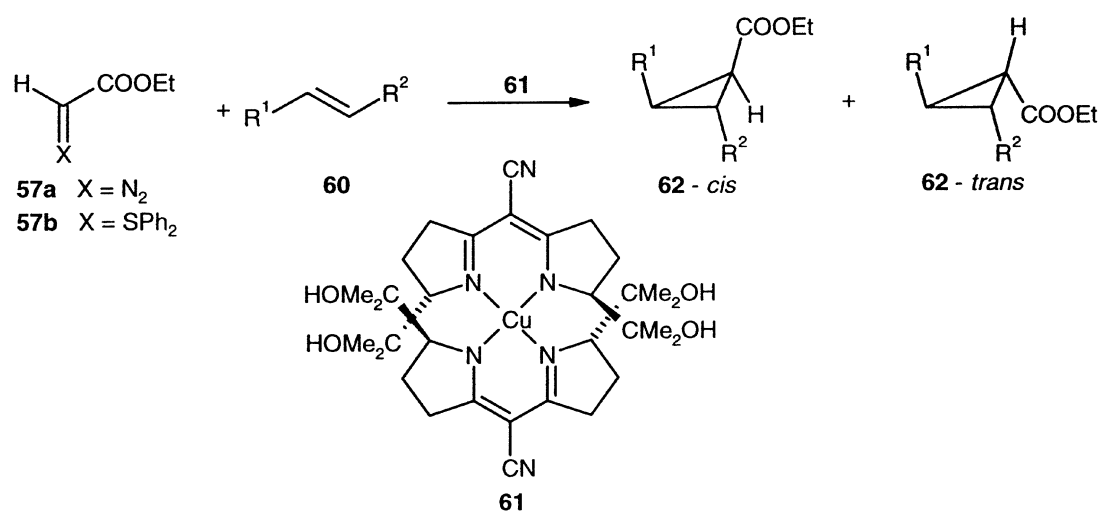
Metal-catalyzed reactions of sulfonium ylides

The metal catalyzed cyclopropanation of olefins was investigated with ethyl diazoacetate (EDA, **57a**) and diphenylsulfonium ethoxycarbonylmethylide (**57b**) with Rh and Cu catalysts. As in the case of phenyliodonium

Table 1. Rh(II)-catalyzed cyclopropanation of styrene (**22**) with ethyl diazoacetate (**57a**) and Ph₂S=CHCOOEt (**57b**)^a

Catalyst	X	Yield 58 (%)	<i>trans/cis</i> ratio	<i>ee</i> (<i>trans</i>) (%)	<i>ee</i> (<i>cis</i>) (%)
[Rh ₂ (OAc) ₄]	N ₂	62	60:40	–	–
	SPh ₂	44	50:50	–	–
[Rh ₂ { <i>R</i> -(–)-bnp} ₄]	45	50:50	5	3	–
	SPh ₂	47	60:40	0	2
[Rh ₂ { <i>S</i> -(–)-ptpa} ₄]	N ₂	57	47:53	2	2
	SPh ₂	35	52:48	0	2
[Rh ₂ { <i>2S</i> -mepy} ₄]	N ₂	20	52:48	54 (1 <i>S</i> ,2 <i>S</i>)	38 (1 <i>S</i> ,2 <i>R</i>)
	SPh ₂	34	65:35	48 (1 <i>S</i> ,2 <i>S</i>)	34 (1 <i>S</i> ,2 <i>R</i>)

^a Conditions: syringe-pump addition (15 h) of **57a** or **57b** (1.0 equiv.) in DCE (5.0 ml) to [Rh₂L₄] (2 mol%) and styrene (10 equiv.) in refluxing DCE (10 ml).

**Scheme 14.**

ylides, the observation of identical di- and enantioselectivity of the cyclopropanation was expected to provide evidence for the same reaction intermediate when starting from either of the carbene precursors. The ylide **57b** was prepared according to a procedure developed by Nozaki *et al.*⁵⁴

The ylide was surprisingly stable and remained unchanged when dissolved in CDCl₃ at 20 °C for 24 h, although decomposition products started to appear after 4 days. No reaction occurred with the ylide in the presence of [Cu(acac)₂] or [Rh₂(OAc)₄] in CH₂Cl₂ at 20 °C or at reflux, but cyclopropanation of olefins took place in refluxing 1,2-dichloroethane (DCE). Slow addition of the ylide to styrene (**22**) (10 equiv.) in refluxing DCE containing [Rh₂(OAc)₄] (2%) afforded the cyclopropane **58** in 44% yield and with a *trans/cis* ratio of 1:1. When the reaction was repeated under the same conditions with EDA (**57a**) the *trans/cis* ratio changed 60:40. Experiments with other Rh(II) catalysts, such as [Rh₂{(*R*)-(–)-bnp}₄] (**29**) or [Rh₂{(*S*)-(–)-ptpa}₄] (**30**) afforded similar differences in the *trans/cis* ratios for **58a** and **58b** (Table 1). The asymmetric inductions of the reactions with these latter catalysts were insignificant, however.⁵⁵ Inductions

consistent with results published under comparable conditions with EDA (**57a**)⁵⁶ were realized with [Rh₂{(*2S*-mepy)₄] (**28**), but again, the *trans/cis* ratios for **57a** and **b** were different, changing from 52:48 to 67:33. When diphenyl sulfide was added simultaneously with EDA to the cyclopropanation reaction of **22**, the ratio was 58:42, intermediate between that for EDA and ylide. This suggests that diphenylsulfide intervenes in the reaction, affecting slightly the *trans/cis* ratios and the enantioselectivities. A plausible rationalization of this observation consists in the occupation of one of the axial coordination sites of the catalyst by the sulfide to form a complex of type **59**, where the other axial site is occupied by the carbene.

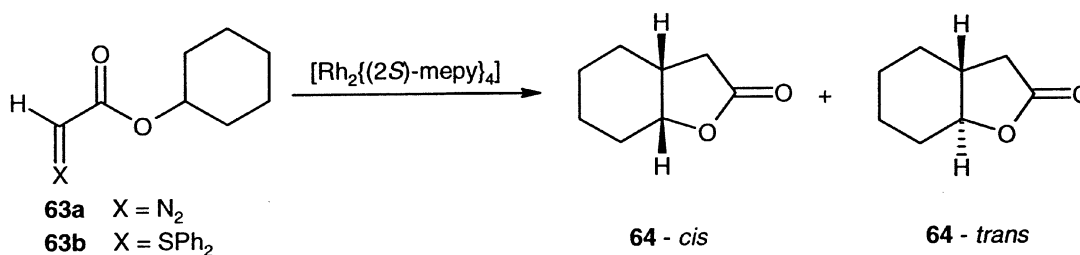
In order to verify whether **57a** and **57b** would exhibit similar variations in the *cis/trans* ratios of cyclopropanes with Cu catalysts, several olefins were cyclopropanated with the Cu–semicorrin complex **61** of Pfaltz and co-workers.^{8b,57} As before, the cyclopropanations with the ylide **57b** were effected in refluxing DCE. However, under these reaction conditions, the cyclopropanations with EDA (**57a**) proceeded without asymmetric induction. When the cyclopropanation of styrene was carried

Table 2. Selectivity for cyclopropanation of olefins **60** with ethyl diazoacetate (**57a**) and Ph₂S=CHCOOEt (**57b**) with Cu-semicorrin Complex **61**^a

Olefin	R ¹	R ²	X	Yield of 62 (%)	<i>trans/cis</i> ratio	<i>ee</i> (<i>trans</i>) (%)	<i>ee</i> (<i>cis</i>) (%)
22	Ph	H	N ₂	75	75:25	78	54
22	Ph	H	SPh ₂	31	77:23	71	59
60a	C ₅ H ₁₁	H	N ₂	20	72:28	63	70
60a	C ₅ H ₁₁	H	SPh ₂	20	73:27	72	74
60b	H ₂ C=CH	H	N ₂	50	61:39	70	77
60b	H ₂ C=CH	H	SPh ₂	24	60:40	76	80
60c	Me ₂ C=CH	H	N ₂	50	59:41	nd ^b	nd
60c	Me ₂ C=CH	H	SPh ₂	36	57:43	nd	nd
60d	Ph	Me	N ₂	42	70:30	5	48
60d	Ph	Me	SPh ₂	20	65:35	7	50

^a Conditions: syringe-pump addition (16 h) of EDA (**57a**) or ylide (**57b**) (1.0 mmol) in DCE (4.0 ml) to olefin **60** (10.0 mmol) and catalyst **61** (0.02 mmol) in DCE, 20 °C for **57a**, at reflux for **57b**.

^b nd = Not determined.

**Scheme 15.**

out at 60 °C with addition of EDA over 16 h, the *ee* decreased drastically with increasing reaction time. Some irregularities occurred also at 50 °C. This indicates partial decomposition of the catalyst, a phenomenon not observed in the cyclopropanations using the ylide **57b**. In order to avoid all complications, the reactions with EDA were carried out at room temperature (see Table 2).

Although the reaction conditions for cyclopropanation with **57a** and **b** are not exactly identical, some general conclusions may be drawn from comparison of the data. Yields of cyclopropanes **62** resulting from the reaction with the ylide **57b** are below those resulting from reaction with EDA. The *trans/cis* ratios of the cyclopropanes are constant within 1–5%. The enantioselectivities change slightly more (2–9%), but the variations are considerably below those observed in the Rh(II)-catalyzed reaction.⁵⁸ It appears justified, therefore, to invoke the same intermediate for the cyclopropanation starting from both carbene precursors in the case of Cu catalysis. Although the presence of Ph₂S in the Rh(II)-catalyzed ylide decomposition has some influence on the reacting species, it does not fundamentally change its carbenoid nature. This was demonstrated by the intramolecular CH insertion of cyclohexyl diazoacetate (**63a**) and the corresponding diphenylsulfonium ylide **63b**. The diazo compound reacted with [Rh₂{(2*S*)-mepy}₄] in CH₂Cl₂ at 20 °C to afford a 34% yield of *cis* (97% *ee*) and *trans*

(93% *ee*) lactones **64** in a 75:25 ratio.⁸ In refluxing DCE the yield decreased to 11% and the isomer ratio was 68:32, with *ees* of 88 and 77%, respectively. The ylide **63b**, in turn, afforded **64** with a yield of 8.5%, a 73:27 isomer ratio and *ees* of 93 and 85%. Although the reaction is, at present, not synthetically applicable, the occurrence of insertion products from a sulfonium ylide, the nearly constant *cis/trans* ratios and degrees of asymmetric induction support the mechanistic hypothesis of a metal-complexed carbene intermediate. As in the Rh(II)-catalyzed cyclopropanations, we note again small variations in the results which should be attributed to coordination of the Ph₂S with the chiral Rh(II) complex.

CONCLUSIONS

This research was started with the objective of establishing iodonium and sulfonium ylides as substitutes for diazo compounds in transition metal-catalyzed carbenoid reactions. The prerequisite is that the reactions proceed by the same mechanism, involving metal-complexed carbenes as intermediates. Our results show that this requirement is clearly met in the Rh(II)-catalyzed reactions of iodonium ylides. In the case of diphenylsulfonium ylides, both Rh(II)- and Cu(II)-catalyzed reactions also proceed *via* metal-complexed carbenes,

but there are some complications arising from the presence of the diphenyl sulfide. As far as the Cu-catalyzed reactions of phenyliodonium ylides are concerned, the data currently available are contradictory and insufficient to draw a definite conclusion.

In order to be of practical interest, the ylides should be readily accessible in high yield, easy to purify and stable upon storage. In this respect, much has to be improved to make them truly competitive with diazo compounds. The synthetic potential of sulfoxonium ylides in carbenoid reactions is currently under investigation in our laboratory.

Acknowledgments

The authors are indebted to the Swiss National Science Foundation (Projects No. 20-45255.95 and 20-48156.96) and to the Société Académique de Genève (Fonds Frédéric Firmenich et Philippe Chuit) for financial support.

REFERENCES

- (a) W. Kirmse. *Carbene Chemistry*, 2nd ed. Academic Press, New York (1971); (b) M. Jones and R. A. Moss. *Carbenes*. Wiley-Interscience, New York (1972).
- (a) H. Nozaki, S. Moriuti, M. Yamabe and R. Noyori. *Tetrahedron Lett.* **59** (1966); (b) W. R. Moser. *J. Am. Chem. Soc.* **91**, 1135, 1141 (1969).
- (a) R. Paulissen, H. Reimlinger, E. Hayez, A. J. Hubert and Ph. Teyssié. *Tetrahedron Lett.* 2223 (1973); A. J. Hubert, A. F. Noels, A. J. Anciaux and Ph. Teyssié. *Synthesis* 600 (1976); (b) M. P. Doyle. *Recl. Trav. Chim. Pays-Bas* **110**, 305 (1991); M. P. Doyle. *Chem. Rev.* **86**, 919 (1986); M. P. Doyle. in *Catalytic Asymmetric Synthesis*, edited by I. Ojima, Chapt. 3, p. 68. VCH, Weinheim (1993).
- H. Nishiyama, Y. Itoh, H. Matsumoto, S.-B. Park and K. Itoh. *J. Am. Chem. Soc.* **116**, 2223 (1994); H. Nishiyama, S.-B. Park and K. Itoh. *Chem. Lett.* 599 (1995).
- (a) A. J. Anciaux, A. J. Hubert, A. F. Noels, N. Petiniot and P. Teyssié. *J. Org. Chem.* **45**, 695 (1980); (b) S. E. Denmark, R. A. Stavenger, A.-M. Faucher and J. P. Edwaerds. *J. Org. Chem.* **62**, 3375 (1997).
- A. Nakamura, A. Konishi, Y. Tatsunoto and S. Otsuka. *J. Am. Chem. Soc.* **100**, 3443 (1978).
- (a) M. P. Doyle, J. H. Griffin, V. Bagheri and R. L. Dorow. *Organometallics* **3**, 53 (1984); (b) M. C. Pirrung and A. T. Morehead. *J. Am. Chem. Soc.* **118**, 8162 (1996); S. B. Park, N. Nakata and H. Nishiyama. *Chem. Eur. J.* **2**, 303 (1996).
- (a) D. A. Evans, K. A. Woerpel, M. M. Hinman and M. M. Faul. *J. Am. Chem. Soc.* **113**, 726 (1991); D. A. Evans, K. A. Woerpel and M. J. Scott. *Angew. Chem. Int. Ed. Engl.* **31**, 430 (1992); (b) H. Fritschi, U. Leutenegger and A. Pfaltz. *Helv. Chim. Acta* **71**, 1553 (1988); D. Müller, G. Umbricht, B. Weber and A. Pfaltz. *Helv. Chim. Acta* **74**, 232 (1991); A. Pfaltz. *Acc. Chem. Res.* **26**, 339 (1993); (c) R. E. Lowenthal, A. Abiko and S. Masamune. *Tetrahedron Lett.* **31**, 6005 (1990); R. E. Lowenthal and S. Masamune. *Tetrahedron Lett.* **32**, 7373 (1991); (d) M. P. Doyle, R. J. Pieters, S. F. Martin, R. E. Austin, C. J. Oalman and P. Mueller. *J. Am. Chem. Soc.* **113**, 1423 (1991); M. P. Doyle, R. E. Austin, A. S. Bailey, M. P. Dwyer, A. B. Dyatkin, A. V. Kalinin, M. M. Y. Kwan, S. Liras, C. J. Oalman, R. J. Pieters, M. N. Propopopova, C. E. Raab, G. H. P. Roos, Q. L. Zhou and S. F. Martin. *J. Am. Chem. Soc.* **117**, 5763 (1995).
- M. P. Doyle, M. N. Protopopova, P. Mueller, D. Ene and E. A. Shapiro. *J. Am. Chem. Soc.* **116**, 8492 (1994); M. N. Protopopova, M. P. Doyle, P. Mueller and D. Ene. *J. Am. Chem. Soc.* **114**, 2755 (1994).
- P. Müller and P. Polleux. *Helv. Chim. Acta* **77**, 645 (1994); M. P. Doyle, A. B. Dyatkin, G. H. P. Roos, F. Cañas, D. A. Pierson, A. van Basten, P. Müller and P. Polleux. *J. Am. Chem. Soc.* **116**, 4507 (1994).
- G. M. Ramos-Tombo and D. Bellus. *Angew. Chem. Int. Ed. Engl.* **30**, 1193 (1991); G. W. Parshal and S. Ittel. *Homogeneous Catalysis*, 2nd ed. Wiley-Interscience, New York (1992).
- A. Aratani. *Pure Appl. Chem.* **57**, 1839 (1995); R. Noyori. *Science* **248**, 1194 (1990).
- T. N. Salzmann, R. W. Ratcliffe, B. G. Christensen and F. A. Bouffard. *J. Am. Chem. Soc.* **102**, 6161 (1980); D. G. Mellilo, I. Shinkai, T. Liu, K. Ryan and M. Sletzing. *Tetrahedron Lett.* **21**, 2783 (1980); B. G. Christensen. *Chem. Br.* 371 (1989).
- B. Eistert, M. Regitz, G. Heck and H. Schwab. in *Houben-Weyl, Methoden der Organischen Chemie*, Vol X/4, p. 473. Georg Thieme, Stuttgart (1968); N. I. Sax. *Dangerous Properties of Industrial Materials*, 5th ed., p. 544. Van Nostrand Reinhold, New York (1979); L. Bretherick. *Handbook of Reactive Chemical Hazards*, 2nd ed., p. 589. Butterworth, London (1979).
- B. Karele and O. Neilands. *Zh. Org. Khim.* **4**, 1818 (1968).
- Y. Hayasi, T. Okada and M. Kawanisi. *Bull. Chem. Soc. Jpn.* **43**, 2506 (1970).
- K. Schank and C. Lick. *Synthesis* 392 (1983).
- R. M. Moriarty, B. R. Bailey, III, O. Prakash and I. Prakash. *J. Am. Chem. Soc.* **107**, 1375 (1985).
- J. Nicholas, C. Hood, D. Lloyd, W. A. McDonald and T. M. Shepherd. *Tetrahedron* **38**, 3355 (1982).
- L. Hadjarapoglou, S. Spyroudis and A. Varvoglis. *J. Am. Chem. Soc.*, **107**, 7178 (1985); L. Hadjarapoglou, A. Varvoglis, N. W. Alcock and G. A. Pike. *J. Chem. Soc. Perkin Trans. 1* 2839 (1988).
- R. M. Moriarty, O. Prakash, R. K. Vaid and L. Zhao. *J. Am. Chem. Soc.* **111**, 6443 (1989); R. M. Moriarty, O. Prakash, R. K. Vaid and L. Zhao. *J. Am. Chem. Soc.* **112**, 1297 (1990); R. M. Moriarty, J. Kim and L. Guo. *Tetrahedron Lett.* **34**, 4129 (1993).
- I. Hadjarapoglou. *Tetrahedron Lett.* **28**, 4449 (1987); M. Papadopoulou, S. Spyroudis and A. Varvoglis. *J. Org. Chem.* **50**, 1509 (1985).
- G. F. Koser and S. M. Yu. *J. Org. Chem.* **40**, 1166 (1975).
- S. P. Spyroudis. *J. Org. Chem.* **51**, 3453 (1986).
- G. Stork and R. P. Szajewski. *J. Am. Chem. Soc.* **96**, 5787 (1974).
- (a) R. Huisgen, S. S. Sturm and G. Binsch. *Chem. Ber.* **97**, 2864 (1964); (b) J. Drapier, A. Feron, R. Warin, A. J. Hubert and Ph. Teyssié. *Tetrahedron Lett.* **20**, 559 (1975); (c) M. E. Alonso and A. W. Chitty. *Tetrahedron Lett.* **22**, 4181 (1981); (d) G. l'Abbé, A. Francis, W. Deahen and S. Toppet. *J. Chem. Soc., Chem. Commun.* 67 (1995).
- M. C. Pirrung, J. Zhang, K. Lackey, D. D. Sternbach and F. Brown. *J. Org. Chem.* **60**, 2112 (1995).
- R. Huisgen, G. Binsch and H. König. *Chem. Ber.* **97**, 2868 (1964); R. Huisgen and V. Weberndörfer. *Experientia*, **17**, 566 (1961).
- K.-P. Zeller. *Angew. Chem., Int. Ed. Engl.* **14**, 32 (1975).
- M. B. Andrus, A. B. Argade, X. Chen and M. G. Pamment. *Tetrahedron Lett.* **36**, 2945 (1995); A. S. Gokhale, A. B. E. Minidis and A. Pfaltz. *Tetrahedron Lett.* **36**, 1831 (1995).
- M. P. Doyle. *Acc. Chem. Res.* **19**, 348 (1986).
- D. Fernandez. PhD Thesis, University of Geneva (1997).
- (a) Ch. Gränicher. PhD Thesis, University of Geneva (1994); (b) H. M. L. Davies and K. R. Romines. *Tetrahedron* **44**, 3343 (1988).
- N. Petiniot, A. J. Anciaux, A. F. Noels, A. J. Hubert and Ph. Teyssié. *Tetrahedron Lett.* 1239 (1978).
- D. Seyferth, J. Yick-Pui Mui and R. Damraner. *J. Am. Chem. Soc.* **90**, 6182 (1968).
- M. P. Doyle, L. C. Wang and K.-L. Loh. *Tetrahedron Lett.* **25**, 4087 (1984).
- M. P. Doyle, W. R. Winchester, J. A. A. Hoorn, V. Lynch, S. H. Simonsen and R. Gosh. *J. Am. Chem. Soc.* **115**, 958 (1993).
- M. C. Pirrung, J. Zhang and A. T. McPhail. *J. Org. Chem.* **56**, 6269 (1991); M. C. Pirrung, J. Zhang and A. T. Morehead, Jr. *Tetrahedron Lett.* **35**, 6229 (1994); M. C. Pirrung and Y. R. Lee. *Tetrahedron Lett.* **34**, 6231 (1994).

39. M. C. Pirrung and J. Zhang. *Tetrahedron Lett.* **33**, 5987 (1992).
40. S. Hashimoto, N. Watanabe, T. Sato, M. Shiro and S. Ikegami. *Tetrahedron Lett.* **34**, 5109 (1993); S.-I. Hashimoto, N. Watanabe and S. Ikegami. *Synlett* 353 (1994); N. Watanabe, M. Tanada, S. Hashimoto and S. Ikegami. *Synlett* 1031 (1994).
41. D. F. Taber, E. H. Petty and K. Raman. *J. Am. Chem. Soc.* **107**, 196 (1985).
42. E. Lee, K. W. Jung and Y. S. Kim. *Tetrahedron Lett.* **31**, 1023 (1990).
43. D. F. Taber and R. E. Ruckle. *J. Am. Chem. Soc.* **108**, 7686 (1986).
44. M. P. Doyle, L. J. Westrum, W. N. E. Wolthuis, M. M. See, W. P. Boone and V. Bagheri. *J. Am. Chem. Soc.* **115**, 958 (1993).
45. R. M. Moriarty. University of Illinois, Chicago, personal communication (1997).
46. B. M. Trost and L. S. Melvin, Jr. in *Sulfur Ylides in Organic Chemistry*, edited by A. T. Blomquist, H. H. Wasseman, pp. 77–107. Academic Press, New York (1963); E. J. Corey and M. Chaykovsky. *J. Am. Chem. Soc.* **87**, 1353 (1965).
47. E. J. Corey and M. Chaykovsky. *J. Am. Chem. Soc.* **86**, 1640 (1964).
48. B. M. Trost. *J. Am. Chem. Soc.* **89**, 138 (1967).
49. B. M. Trost. *J. Am. Chem. Soc.* **88**, 1587 (1966).
50. T. Cohen, G. Herman, T. M. Chapman and D. Kuhn. *J. Am. Chem. Soc.* **96**, 5627 (1974).
51. B. Cimetière and M. Julia. *Synlett* 271 (1991).
52. J. E. Baldwin, R. M. Adlington, C. R. A. Godfrey, D. W. Gollins and J. G. Vaughan. *J. Chem. Soc. Chem. Commun.* 1434 (1993).
53. J.-J. Zhang and G. B. Schuster. *J. Am. Chem. Soc.* **111**, 7149 (1989).
54. H. Nozaki, D. Tunemoto, S. Matubara and K. Kondo. *Tetrahedron* **23**, 545 (1967).
55. P. Müller, D. Fernandez, P. Nury and J.-C. Rossier. to be published.
56. M. P. Doyle, B. D. Brandes, A. P. Kazala, R. J. Pieters, M. B. Jarstfer, L. M. Watkins and C. T. Eagle. *Tetrahedron Lett.* **31**, 6613 (1990).
57. A. Pfaltz, in *Modern Synthetic Methods 1989*, edited by R. Scheffold, p. 199. Springer, Berlin (1989); H. Fritschi, U. Leutenegger, K. Siegmann, A. Pfaltz, W. Keller and C. Kratzky. *Helv. Chim. Acta* **71**, 1541 (1988).
58. P. Nury. Diploma Thesis, University of Geneva (1996), unpublished results.