

Metal-Catalyzed Ylide Formation and [2,3] Sigmatropic Rearrangement of Allyl Sulfides with Trimethylsilyldiazomethane

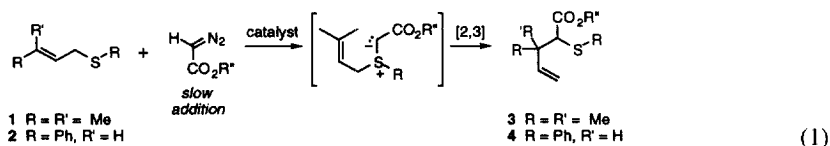
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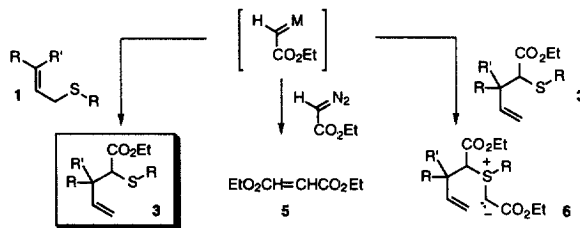
Abstract: Trimethylsilyldiazomethane is compared with ethyl diazoacetate for the rhodium, copper, and cobalt catalyzed formation and [2,3] rearrangement of allylsulfonium ylides. At room temperature, the reaction can be carried out using the allyl sulfide as the limiting reagent by slow addition of 3 equivalents of the diazo compound. Slightly better yields were obtained with trimethylsilyldiazomethane than with ethyl diazoacetate. © 1999 Elsevier Science Ltd. All rights reserved.

Catalytic reactions involving metal carbenoids provide a valuable method for cyclopropanation and ylide formation.¹⁻³ The greatest success has been shown with diazo compounds,⁴ especially commercially available ethyl diazoacetate (EDA). A variety of metals catalyze the formation of allylsulfonium ylides from ethyl diazoacetate, notably, rhodium, copper, cobalt, and palladium. This process is useful because allylsulfonium ylides undergo a rapid [2,3] sigmatropic rearrangement (eq 1).⁵⁻⁸



Optimization of the intermolecular ylide formation/rearrangement reaction is challenging because three different species compete for addition to the metal carbenoid intermediate (Scheme 1): the allyl sulfide starting material, the diazo precursor, and the homoallylic sulfide product.⁹ To tip the balance in favor of allyl sulfide addition, the diazo precursor can be added slowly and the allyl sulfide can be used in excess.⁵ However, Uemura¹⁰ has shown that excess sulfide is not always required for good yields, and Katsuki¹¹ has shown that slow addition is not necessary for the addition of *t*-butyl diazoacetate to phenyl cinnamyl sulfide using a cobalt(III)-salen catalyst.

Scheme 1



In a recent review, Doyle proposed the use of commercially available trimethylsilyldiazomethane (TDM) for the formation of allylsulfonium ylides.² The attraction of silyl-stabilized diazo precursors is that silicon should allow for more effective variation of the sterics and electronics than is possible with esters. Such

variation might be used to inhibit further reaction of the product (due to hindrance) or to enhance the rate of rearrangement in cases where the π system is unreactive¹² (e.g., the thia-Sommelet rearrangement). In addition, α -silyl sulfides are useful carbonyl equivalents via a sila-Pummerer reaction.¹³ We initiated a comparison of trimethylsilyldiazomethane¹⁴ and ethyl diazoacetate in the formation and rearrangement of allylsulfonium ylides. In this study we investigated the importance of catalyst and stoichiometry, as well as the effect of adventitious water and acids.

Copper and rhodium are the two most common catalysts used in the generation of sulfonium ylides. We chose to examine the copper-catalyzed and rhodium-catalyzed reactions separately, starting with copper. Since TDM (2.0 M in hexanes) and EDA are commercially available all of our experiments were carried out using the allyl sulfide as the limiting reagent according to eq 2. Excess diazo compound was required for effective conversion of starting material because the diazoester is depleted by reacting with the carbenoid intermediate. Our initial attempt to catalyze the addition of TDM to allylic sulfides in refluxing dichloroethane led to numerous unidentifiable products. In order to control reactivity and maintain mild conditions, all further experiments were carried out at room temperature. In Tables 1 and 2 we account for the neutral components: homoallyl sulfide and starting material. We assume that most of the remaining mass balance is lost due to formation of homoallylic sulfonium ylide **6**, or the silyl analog.

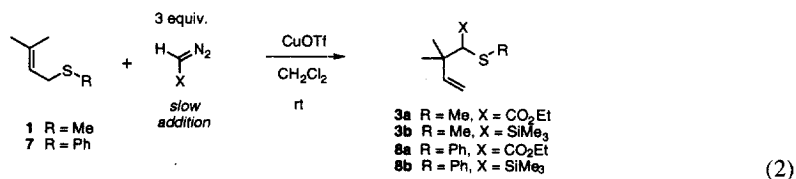
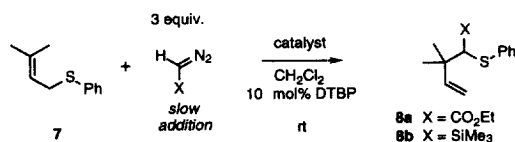


Table 1. Copper-Catalyzed Ylide Formation/Rearrangement (Eq 2)

Entry	% cat.	catalyst	DTBP	R	X	[2,3] ^a	S.M. ^a
1	10	CuOTf	-	Ph	CO ₂ Et	41%	2%
2	10	CuOTf	-	Me	CO ₂ Et	36%	+ ^b
3	10	CuOTf	-	Ph	TMS	64%	6%
4	10	CuOTf	-	Me	TMS	4%	++ ^b
5	10	CuOTf	10%	Ph	CO ₂ Et	53%	10%
6	10	CuOTf	10%	Ph	TMS	76%	18%
7	5	CuOTf	10%	Ph	TMS	25%	60%
8	1	CuOTf	10%	Ph	TMS	6%	74%
9	5	Cu(BOX)OTf	10%	Ph	TMS	37%	34%

^a isolated yield, ^b yield not determined due to volatility

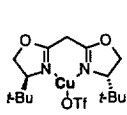
In contrast to copper(II) bis(acetylacetonate), we found copper(I) triflate was an effective catalyst for ylide formation. Using this catalyst, methyl sulfide **1** led to poorer conversion than the corresponding phenyl sulfide **7** (Table 1, entries 1-4). We suspected that triflic acid, a common culprit in metal triflate reactions, might be reducing the yield of [2,3] product by protonating the ylide. Consistent with this suspicion, inclusion of 10% 4-methyl-2,6-di-*tert*-butyl pyridine (DTBP) increased the yield of the [2,3] product by about 10% (entries 1, 3, 5, and 6). The catalyst loading was important. When catalyst loading was reduced to 5 and then 1 mol%, the degree of conversion dropped accordingly. We interpret this effect in terms of low catalyst turnover. Use of the Evans-Woerpel bis-oxazoline ligand¹⁵ led to an increase in yield, but the mass balance was compromised.



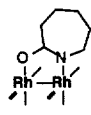
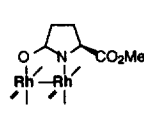
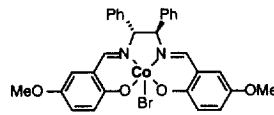
(3)

Table 2. Catalysis of Ylide Formation/Rearrangement by Other Metals

entry	catalyst	mol %	MS 4 Å	X	[2,3]	s.m.
1	PdCl ₂	5	-	TMS	4%	89%
2	Rh ₂ OAc ₄	5	-	TMS	52%	38%
3	Rh ₂ OAc ₄	5	-	CO ₂ Et	41%	2%
4	Rh₂OAc₄	5	+	TMS	86%	1%
5	Rh ₂ OAc ₄	5	+	CO ₂ Et	32%	1%
6	Rh ₂ OAc ₄	2.5	+	TMS	59%	41%
7	Rh₂(CAP)₄	5	+	TMS	83%	2%
8	Rh ₂ (MEPY) ₄	5	+	TMS	63%	17%
9	Co(III)salen	5	-	TMS	0%	79%
10	Co(III)salen	5	-	CO ₂ Et	22%	56%



Cu(BOX)OTf

Rh₂(CAP)₄Rh₂(MEPY)₄

CoBr*salen

While copper(I) triflate was an effective catalyst for allylsulfonium ylide formation, the air and moisture sensitivity of this reagent led us to explore other metals which could be handled without the need for a glove box. Having obtained consistently better results with the phenyl sulfide **7**, we chose to use this as the substrate for subsequent reactions (eq 3, Table 2). Palladium chloride showed only marginal catalytic activity (entry 1), but rhodium(II) acetate dimer proved to be a worthy catalyst. At equal catalyst loading, Rh₂(OAc)₄ was more active than copper(I) triflate giving higher yields and higher mass balance. The addition of 4 Å mol sieves improved the reaction with TMD (entries 2 and 4), but not the reaction with EDA (entries 3 and 5). All subsequent reactions with TMD were performed in the presence of 4 Å mol sieves. Like the copper-catalyzed reaction, a reduction in the amount of rhodium(II) acetate comes at the expense of conversion, however, the rhodium is much less sensitive to this effect (entry 6) than cuprous triflate.

Switching from carboxylate to lactamate ligands should decrease the electrophilicity of the metal carbenoid while increasing the bulk. When sulfide **7** was treated with TDM and Rh₂(CAP)₄, **8b** was isolated in 83 % yield. Rh₂(MEPY)₄ was not as active as Rh₂(CAP)₄ possibly due to the increased steric bulk of the MEPY ligand (entry 8). The cobalt(III)-salen catalyst, which can be effective with *t*-butyl diazoacetate, gives no rearrangement product with TDM and only marginal results with EDA (entries 9 and 10).

Overall, trimethylsilyldiazomethane is an effective partner for the generation of allylsulfonium ylides which can subsequently undergo [2,3] sigmatropic rearrangements. The increased reactivity of α -silyl sulfonium ylides may allow catalysis of reactions where diazoesters fail. In addition, α -silyl thioethers provide a useful functional handle for subsequent manipulations.

Typical Procedure:

To a flame dried round bottom flask equipped with a magnetic stir-bar was added DTBP (0.230 g, 0.11 mmol), Rh₂(OAc)₄ (0.025 g, 0.06 mmol), and 4Å mol sieves (0.15 g) under nitrogen. The sulfide **7** was dissolved in 1.1 mL CH₂Cl₂ and introduced via syringe. The purple solution was allowed to stir for 15 min. Trimethylsilyldiazomethane (1.70 mL, 2.0 M in hexanes, 3.39 mmol) was added via syringe pump over 20 h. The solution was decanted. The mol sieves were triturated with CH₂Cl₂ until the solvent was colorless. The solvent was removed *in vacuo* to give a brown oil. The crude oil was purified via preparative thin layer chromatography (pentane) to afford **8b** (0.257 g, 86%) and starting material **7** (0.002 g, 1%).

3b: ¹H NMR (400 MHz, CDCl₃) δ 5.93 (dd, *J* = 17.5, 10.7 Hz, 1H), 4.99 (dd, *J* = 17.5, 1.3 Hz, 1H), 4.94 (dd, *J* = 10.7, 1.3 Hz, 1H), 2.16 (s, 3H), 1.47 (s, 1H), 1.16 (2, 3H) 1.13 (s, 3H), 0.14 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 148.3, 100.5, 49.3, 42.2, 27.6, 26.1, 21.9, 0.6; HRMS(Cl) Calcd for C₁₀H₂₂SSi [M]⁺ 202.1211, Found: 202.1206; Anal calcd for C₁₀H₂₂SSi: C, 59.33; H, 10.95; Found: C, 59.61; H, 10.87.
8b: ¹H NMR (500, MHz, CDCl₃) δ 7.44 (m, 2H), 7.31-7.27 (m, 2H), 7.19-7.15 (m, 1H), 5.98 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.03 (dd, *J* = 17.4, 1.2 Hz, 1H), 4.97 (dd, *J* = 10.7, 1.2 Hz, 1H), 2.50 (s, 1H), 1.20 (s, 3H), 1.17 (s, 3H), 0.24 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 147.9, 140.7, 128.8, 128.6, 125.3, 110.9, 47.6, 44.4, 28.1, 26.1, 0.8; HRMS(Cl) Calcd for C₁₅H₂₄SSi [M]⁺ 264.1368, Found: 264.1369; Anal calcd for C₁₅H₂₄SSi: C, 68.12; H, 9.15; Found: C, 68.17; H, 9.16.

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