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# Ruthenium-catalyzed addition of sulfenamides to alkynes leading to selective synthesis of polyfunctional alkenes

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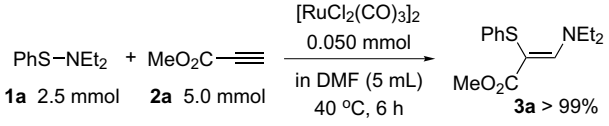
**Abstract**—Sulfenamides smoothly add to alkynes by $[RuCl_2(CO)_3]_2$ or $Ru_3(CO)_{12}$ catalyst to give the corresponding polyfunctional alkenes in high yield with high regio- and stereoselectivity (*Z* 100%).


Sulfenamides are interesting and synthetically useful compounds, which have a unique $S^{\delta+}$–$N^{\delta-}$ bond.[1] If sulfenamides add to alkynes by the use of transition-metal catalysts, a variety of polysubstituted alkenes, which are expected as novel functional monomers can be obtained. However, the widespread belief that organosulfur compounds including sulfenamides are catalyst poisons may have precluded intensive research in this area.[2] Only palladium-catalyzed azathiolation of carbon monoxide with sulfenamides was reported as the transition-metal complex-catalyzed transformation of sulfenamides.[3]

Recently, we found the first example of the transition-metal complex-catalyzed addition of organic disulfides to *alkenes*[4,5] as well as S-allylation[6] and S-propargylation[7] of thiols, all of which are realized by the use of ruthenium catalysts. Therefore, the ruthenium complex seems to be one of the most promising catalysts for developing novel transformations of sulfenamides. After many trials, we finally found the first ruthenium-catalyzed addition of sulfenamides to alkynes under mild reaction conditions. We report here the development of this new ruthenium-catalyzed reaction, which enables a simple and general synthesis of polysubstituted alkenes.

Treatment of *N*,*N*-diethylbenzenesulfenamide (**1a**) with methyl propiolate (**2a**) in the presence of 2 mol% of $[RuCl_2(CO)_3]_2$ in *N*,*N*-dimethylformamide at 40 °C for 6 h under an argon atmosphere gave the corresponding adduct (**3a**) in quantitative yield (GLC yield, >99%; isolated yield, 84%) with high regio- and stereoselectivity (*Z* 100%) (Eq. 1).[8]




(1)

First, the catalytic activity of several ruthenium complexes was examined in the reaction of **1a** with **2a**. Among the catalysts examined, $RuCl_2(PPh_3)_3$ (**3a**, 78%) and $RuCl_3{\cdot}3H_2O$ (**3a**, 90%) as well as $[RuCl_2(CO)_3]_2$ showed high catalytic activity. The catalytic activities of other zero- and divalent ruthenium complexes, such as $Ru(\eta^4\text{-cod})(\eta^6\text{-cot})$ [cod = 1,5-cyclooctadiene, cot = 1,3,5-cyclooctatriene] (**3a**, 12%), $Ru_3(CO)_{12}$ (**3a**, 8%), $Ru(\eta^6\text{-cot})(\eta^2\text{-dmfm})_2$ [dmfm = dimethyl fumarate] (**3a**, trace), and $Cp^*RuCl(cod)$ [$Cp^*$ = pentamethylcyclopentadienyl] (**3a**, trace), were quite low. Besides ruthenium, $PdCl_2(PPh_3)_2$ (**3a**, 84%) and $RhCl_3{\cdot}3H_2O$ (**3a**, 93%) also showed high catalytic activity. As for the solvent, propionitrile (**3a**, 85%), 1,4-dioxane (**3a**, 82%), and toluene (**3a**, 77%) can be used for the present reaction, but no reaction occurred in a basic solvent, *N*-methylpiperidine, which is a suitable solvent for several ruthenium-catalyzed reactions.[7,9] Since methyl propiolate (**2a**) is

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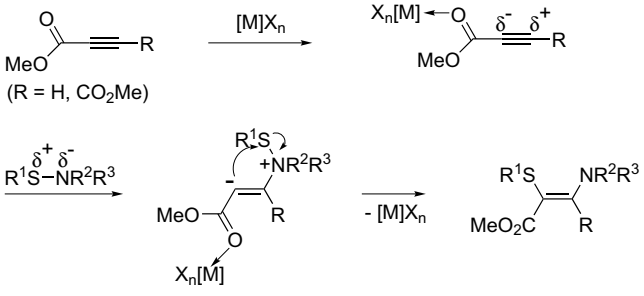
**Table 1.** Ruthenium-catalyzed addition of sulfenamides to alkynes[a]

| Entry | Sulfenamide | Alkyne | Catalyst[b] | Product | Yield (%)[c] |
|---|---|---|---|---|---|
| 1 | $PhS–NEt_2$ **1a** | $MeO_2C$—≡ **2a** | $[RuCl_2(CO)_3]_2$ | PhS, $NEt_2$, $MeO_2C$ **3a** | 84 (>99) |
| 2 | $PhCH_2S–NEt_2$ **1b** | **2a** | $[RuCl_2(CO)_3]_2$ | $PhCH_2S$, $NEt_2$, $MeO_2C$ **3b** | 77 |
| 3 | $C_7H_{15}S–NEt_2$ **1c** | **2a** | $[RuCl_2(CO)_3]_2$ | $C_7H_{15}S$, $NEt_2$, $MeO_2C$ **3c** | 75 |
| 4[d] | PhS–N⟨⟩ **1d** | **2a** | $[RuCl_2(CO)_3]_2$ | PhS, N⟨⟩, $MeO_2C$ **3d** | 77 |
| 5[d] | $PhS–NHC_4H_9$ **1e** | **2a** | $[RuCl_2(CO)_3]_2$ | PhS, $NHC_4H_9$, $MeO_2C$ **3e** | 77 |
| 6 | $PhS–NEt_2$ **1a** | $MeO_2C$—≡—$CO_2Me$ **2b** | $[RuCl_2(CO)_3]_2$ | PhS, $NEt_2$, $MeO_2C$, $CO_2Me$ **3f** | 87 (>99) |
| 7[e] | $PhS–NEt_2$ **1a** | Ph—≡ **2c** | $Ru_3(CO)_{12}$ | PhS, $NEt_2$, Ph **3g** | (29) |
| 8[e] | $PhS–NEt_2$ **1a** | F—C$_6$H$_4$—≡ **2d** | $Ru_3(CO)_{12}$ | PhS, $NEt_2$, *p*-F-$C_6H_4$ **3h** | (83) |

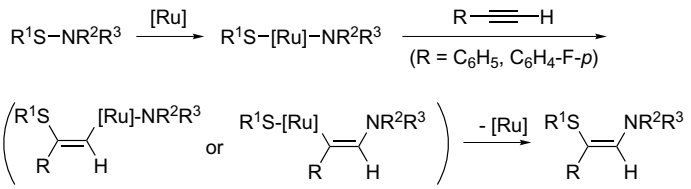
[a] **1** (2.5 mmol), **2** (5.0 mmol), and DMF (5.0 mL) at 40 °C for 6 h under an argon atmosphere.
[b] $[RuCl_2(CO)_3]_2$ (0.050 mmol) and $Ru_3(CO)_{12}$(0.066 mmol).
[c] Isolated yield (GLC yield).
[d] At 80 °C.
[e] **1a** (2.5 mmol), **2** (7.5 mmol), and mesitylene (5.0 mL) at 130 °C for 9 h.

an electron-deficient alkyne, ruthenium and other transition-metal complexes bearing two or more chloride ligands may work as an effective Lewis acid for promoting Michael-type addition reaction of **1a** to **2a**.[10] As expected, since dimethyl acetylenedicarboxylate (**2b**) is also a good Michael acceptor, the reaction of **1a** with **2b** catalyzed by $[RuCl_2(CO)_3]_2$ smoothly proceeded to give **3f** in quantitative yield (GLC yield, >99%; isolated yield, 87%) with high stereoselectivity (*Z* 100%).[11]

The results obtained from the reactions of several sulfenamides with alkynes were summarized in Table 1. The reaction using S-benzylsulfenamide **1b** and S-alkylsulfenamide **1c** smoothly proceeded under mild reaction conditions, while the reactions using N-cyclic sulfenamide **1d** and N-monoalkylsulfenamide **1e** proceeded at




**Scheme 1.**




**Scheme 2.**

slightly elevated reaction temperature (80 °C) due to their low reactivity.

On the other hand, only zero-valent ruthenium complexes, especially $Ru_3(CO)_{12}$, showed catalytic activity in the addition of sulfenamide **1a** to *phenylacetylenes* **2c**, and **2d**. Since these alkynes are not good Michael acceptor, the reactions required more forcing reaction conditions (at 130 °C for 9 h), and a different mechanism should be considered (vide infra).

It was noted that the catalytic activity of $[RuCl_2(CO)_3]_2$, was quite low (**3h**, 25%), and no reaction occurred with catalysts, such as $PdCl_2(PPh_3)_2$, and $RhCl_3{\cdot}3H_2O$, which were highly active catalyst for addition of sulfenamides to electron-deficient alkynes.

A possible mechanism for the reactions using methyl plopiolate **2a** and dimethyl acetylenedicarboxylate **2b** is illustrated in Scheme 1. In these reactions, the catalyst would play an important role as an effective Lewis acid, which first coordinates to carbonyl oxygen to facilitate the nucleophilic attack of nitrogen in sulfenamide to alkyne's $\delta^+$ carbon. Subsequent 1,3-shift of sulfur atom would give the adducts in high yields with high regio- and stereoselectivity.

On the other hand, $Ru_3(CO)_{12}$-catalyzed addition of sulfenamide to phenylacetylenes can be rationalized by assuming the mechanism involving oxidative addition of sulfenamide to a low-valent ruthenium catalyst, followed by insertion of phenylacetylenes into either an S-[Ru] or an N-[Ru] bond, and reductive elimination (Scheme 2).

The scope, mechanism including isolation of $R^1S$-[Ru]-$NR^2R^3$ species, and further synthetic application of this reaction are now under investigation.

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## References and notes

1. Craine, L.; Raban, M. *Chem. Rev.* **1989**, *89*, 689–712.
2. (a) Hegedus, L. L.; McCabe, R. W. *Catalyst Poisoning*; Marcel Dekker: New York, 1984; (b) Hutton, A. T. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon: Oxford, UK, 1987; Vol. 5, pp 1131–1155; (c) Kondo, T.; Mitsudo, T. *Chem. Rev.* **2000**, *100*, 3205–3220.
3. Kuniyasu, H.; Hiraike, H.; Morita, M.; Tanaka, A.; Sugoh, K.; Kurosawa, H. *J. Org. Chem.* **1999**, *64*, 7305–7308.
4. Kondo, T.; Uenoyama, S.; Fujita, K.; Mitsudo, T. *J. Am. Chem. Soc.* **1999**, *121*, 482–483.
5. In a pioneering study by Ogawa and Sonoda et al., the first transition-metal complex-catalyzed addition and carbonylative addition reactions of organic disulfides to terminal *alkynes* have already been reported. (a) Kuniyasu, H.; Ogawa, A.; Miyazaki, S.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 9796–9803; (b) Ogawa, A.; Kuniyasu, H.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1997**, *62*, 8361–8365.
6. Kondo, T.; Morisaki, Y.; Uenoyama, S.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **1999**, *121*, 8657–8658.
7. Kondo, T.; Kanda, Y.; Baba, A.; Fukuda, K.; Nakamura, A.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **2002**, *124*, 12960–12961.
8. The regio- and stereochemistry of the products, **3a** and **3f**, were completely determined by X-ray crystallography. The structures of other products were deduced by differential NOE measurement ($^1H$ NMR) as well as comparing their $^1H$ and $^{13}C$ NMR data with those of **3a** and **3f**. The details will be reported in a full paper.
9. (a) Mitsudo, T.; Zhang, S.-W.; Satake, N.; Kondo, T.; Watanabe, Y. *Tetrahedron Lett.* **1992**, *33*, 5533–5536; (b) Zhang, S.-W.; Mitsudo, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem.* **1995**, *485*, 55–62; (c) Kondo, T.; Okada, T.; Mitsudo, T. *J. Am. Chem. Soc.* **2002**, *124*, 186–187.
10. Kundig, E. P.; Saudan, C. M. In *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; Wiley-VCH: New York, 2000; Vol. 2, pp 597–652.
11. Selenenamides instead of sulfenamides smoothly reacted with good Michael acceptors such as enones *in chloroform without metal catalysts* to form α-seleno-β-amino carbonyl compounds. For example, see: (a) Reich, H. J.; Renga, J. M. *J. Org. Chem.* **1975**, *40*, 3313–3314; (b) Reich, H. J.; Renga, J. M.; Trend, J. E. *Tetrahedron Lett.* **1976**, 2217–2220.