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Rhenium-Catalyzed Regio- and Stereoselective Addition of Two Carbon Units to Terminal Alkynes via Carbon–Carbon Bond Cleavage of *β*-Keto Sulfones

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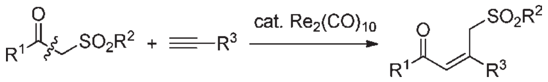
ABSTRACT



Treatment of *β*-keto sulfones with terminal alkynes gave unsaturated *δ*-keto sulfones in good to excellent yields under rhenium catalysis. In this reaction, the insertion of the alkynes into the nonstrained carbon–carbon single bond between the α- and *β*-positions of the *β*-keto sulfones proceeded smoothly, and (*Z*)-isomers were produced with high regio- and stereoselectivities.

It is important to develop efficient and powerful methods to construct new carbon–carbon bonds. As one ideal strategy, the addition of two carbon units to carbon–carbon triple or double bonds is an efficient and powerful method. To realize such reactions, the insertion of unsaturated bonds into a carbon–carbon single bond of organic molecules is a realistic method. There have been several examples of such transformations: unsaturated molecules have been inserted into carbon–carbon bonds of three- or four-membered cyclic compounds,[1] norbornenes were incorporated into the C–C single bonds of cyclobutenones and cyclobutenediones,[2] both alkynes[3] and norbornenes[4] have been inserted into C–CN bonds, and metal-free insertion of cyclohexyne into the C–C single bond of cyclic ketones.[5] We have recently reported rhenium- and manganese-catalyzed transformations via the insertion of alkynes into a nonstrained carbon–carbon single bond of cyclic and acyclic *β*-keto esters.[6] However, when using acyclic *β*-keto esters, the products were obtained as mixtures of regio- and stereoisomers.[6c,e]

Initially, theoretical calculations on four olefinic regio- and stereoisomers, the products of the reaction between 2-(methylsulfonyl)-1-phenylethanone (*β*-keto sulfone) and phenylacetylene (terminal alkyne), were carried out. It was found that one isomer [*δ*-keto sulfone: (*Z*)-4-(methylsulfonyl)-1,3-diphenyl-2-buten-1-one] was more stable

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(6) (a) Kuninobu, Y.; Kawata, A.; Takai, K. *J. Am. Chem. Soc.* **2006**, *128*, 11368. (b) Kuninobu, Y.; Takata, H.; Kawata, A.; Takai, K. *Org. Lett.* **2008**, *10*, 3133. (c) Kuninobu, Y.; Kawata, A.; Nishi, M.; Takata, H.; Takai, K. *Chem. Commun.* **2008**, 6360. (d) Kuninobu, Y.; Morita, A.; Nishi, M.; Kawata, A.; Takai, K. *Org. Lett.* **2009**, *11*, 2535. (e) Kuninobu, Y.; Kawata, A.; Nishi, M.; Yudha, S. S.; Chen, J.; Takai, K. *Chem.—Asian J.* **2009**, *4*, 1424.

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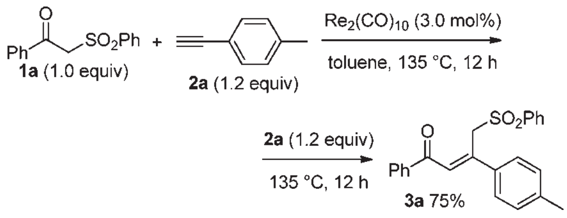
[4.2−11.2 kcal/mol, B3LYP 6-31G(d)] than the others. Therefore, we considered that single products might be obtained by the reactions between *β*-keto sulfones and alkynes. We report herein the regio- and stereoselective insertion of alkynes into a carbon−carbon single bond of *β*-keto sulfones.

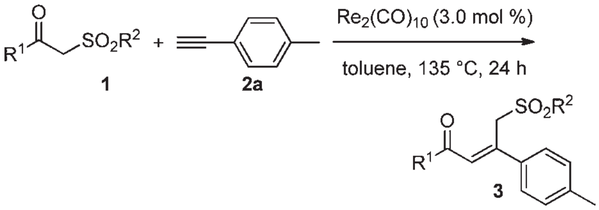
Treatment of *β*-keto sulfone **1a** with *p*-tolylacetylene (**2a**) in the presence of a catalytic amount of a rhenium complex, $Re_2(CO)_{10}$, gave unsaturated *δ*-keto sulfone **3a** in 75% yield (eq 1).[7−9] Interestingly, product **3a** was obtained regio- and stereoselectively, and no other products were formed. This selectivity is in sharp contrast to our previous report, in which unsaturated *δ*-keto esters were formed as a mixture of olefinic regio- and stereoisomers by the reactions between *β*-keto esters and alkynes.[6c,e]



(1)

Next, the reactions of several *β*-keto sulfones **1** with *p*-tolylacetylene (**2a**) were investigated (Table 1). *β*-Keto sulfones with electron-donating groups on the aromatic ring (R^1), **1b** and **1c**, gave unsaturated *δ*-keto sulfones **3b** and **3c** in 56% and 61% yields, respectively (entries 1 and 2). The yield of an unsaturated *δ*-keto sulfone decreased when the *β*-keto sulfone possessed an electron-withdrawing group on the aromatic ring (R^1), **1d** (entry 3). The corresponding *δ*-keto sulfone **3e** was generated using a *β*-keto sulfone with a bromine atom, **1e**, without loss of the bromine atom (entry 4). *β*-Keto sulfones with primary, secondary, or tertiary alkyl groups at the R^1 position, **1f**, **1g**, and **1h**, provided the corresponding unsaturated *δ*-keto sulfones **3f**−**3h** in 24−68% yields (entries 5−7). The corresponding unsaturated *δ*-keto sulfone **3i** was produced in 52% yield using the *β*-keto sulfone with a methyl group at the R^2 position, **1i** (entry 8).[10] However, when using a *β*-keto sulfone with a substituent at the active methylene moiety (1-phenyl-2-tosylpropan-1-one), the corresponding unsaturated *δ*-keto sulfone was not formed.

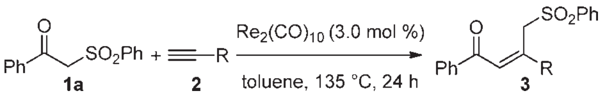
Table 1. Reactions between Several *β*-Keto Sulfones **1** and *p*-Tolylacetylene (**2a**)[a]

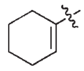


entry	R^1	R^2			yield/%
1	4-(MeO)C_6H_4	Ph	**1b**	**3b**	56
2	4-MeC_6H_4	Ph	**lc**	**3c**	61
3	4-(CF_3)C_6H_4	Ph	**1d**	**3d**	44
4	4-BrC_6H_4	Ph	**le**	**3e**	52
5	Me	Ph	**1f**	**3f**	24
6	Cy	Ph	**1g**	**3g**	68
7	^{t}Bu	Ph	**1h**	**3h**	31
8	Ph	Me	**1i**	**3i**	52

[a] **2a** (total: 2.4 equiv). At the beginning of the reaction, **2a** (1.2 equiv); additional **2a** (1.2 equiv) after 12 h.

Table 2. Reactions between *β*-Keto Sulfones **1a** and Several Alkynes **2**[a]



entry	R			yield / %
1	4-(MeO)C_6H_4	**2b**	**3j**	86
2	Ph	**2c**	**3k**	56
3	4-(CF_3)C_6H_4	**2d**	**3l**	31
4	4-BrC_6H_4	**2e**	**3m**	33
5	3-MeC_6H_4	**2f**	**3n**	73
6	2-MeC_6H_4	**2g**	**3o**	60
7		**2h**	**3p**	56
8[b]	$^nC_{10}H_{21}$	**2i**	**3q**	37[c]

[a] **2a** (total: 2.4 equiv). At the beginning of the reaction, **2a** (1.2 equiv); additional **2a** (1.2 equiv) after 12 h. [b] $Re_2(CO)_{10}$ (5.0 mol %). The product was obtained as a mixture of three compounds. The major product was **3q**. The structures of two minor products were not determined. [c] ^1H NMR yield.

Then, we investigated the scope and limitations of several alkynes (Table 2). By using an alkyne with an electron-donating group, **2b**, the insertion reactions proceeded well, and unsaturated *δ*-keto sulfone **3j** was obtained in 86% yield (entry 1). The structure of **3j** was determined by single crystal X-ray analysis (Figure 1; see also the Supporting Information).[11] This result shows that the aryl group of the alkyne was introduced at the C2 position, and **3j** has the regio- and stereochemistry as shown in Figure 1. The bond length between C1 and C2

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(7) Investigation of several catalysts: $ReBr(CO)_5$, 4%; $[HRe(CO)_4]_n$, 47%. The desired product **3a** was not formed using the following complexes: $[ReBr(CO)_3(thf)]_2$, $ReOCl_3(PPh_3)_3$, $Mn_2(CO)_{10}$, $MnBr(CO)_5$, $Mn(OAc)_2$, $Cr(CO)_6$, $W(CO)_6$, $Fe_2(CO)_9$, $Fe_3(CO)_{12}$, $Ru_3(CO)_{12}$, $Co_2(CO)_8$, and $In(OTf)_3$.

(8) Toluene, 64%; THF, 7%; CH_2ClCH_2Cl, 31%; DMF, 0%; ethanol, 0%; neat, 4%.

(9) In this reaction, while *p*-tolylacetylene (**2a**) was consumed, *β*-keto sulfone **1a** was recovered in 16% yield. However, the yield of the product **3a** was not improved by treatment with additional alkyne **2a**.

(10) In Table 1, entries 1−8, *β*-keto sulfones **1** were recovered. The total yields of the products **3** and the recovery of *β*-keto sulfones **1** were between 84 and 98%. Therefore, the yields of **3** based on the conversion were relatively high.

(11) The olefin configurations of other products were assigned by the comparison of the chemical shifts of the olefinic protons of the products with those of **3f**.

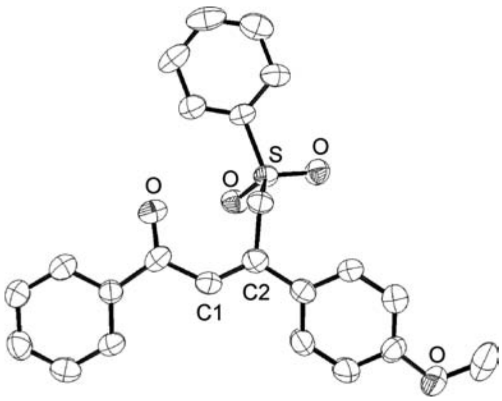


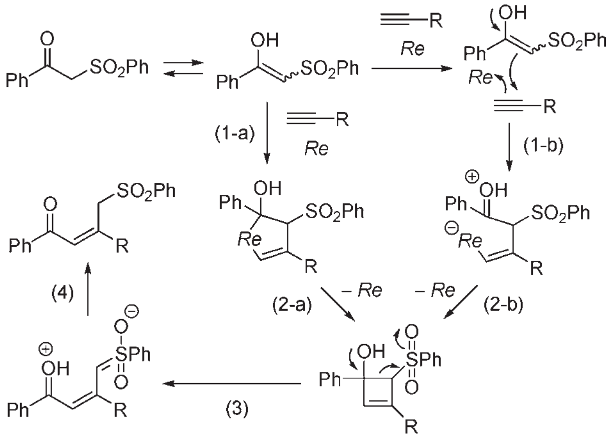
Figure 1. X-ray crystal structure of δ-keto sulfone **3j**. Thermal ellipsoids set at 50% probability. Hydrogen atoms are omitted for clarity.

is 1.351(3) Å, which is suitable for a carbon−carbon double bond. The corresponding unsaturated δ-keto sulfone **3k** was produced in 56% yield by employing phenylacetylene (**2c**) as a substrate (entry 2). The yields of unsaturated δ-keto sulfones **3l** and **3m** decreased when alkynes with electron-withdrawing groups, **2d** and **2e**, were treated with β-keto sulfone **1a** (entries 3 and 4). Aryl alkynes bearing a methyl group at the *meta*- or *ortho*-position, **2f** or **2g**, afforded unsaturated δ-keto sulfones **3n** and **3o** in 73% and 60% yields, respectively (entries 5 and 6). The corresponding δ-keto sulfone **3p** was provided in 56% yield using enyne **2h** (entry 7). An aliphatic acetylene, such as 1-dodecyne (**2j**), generated the corresponding δ-keto sulfone, but in low yield (entry 8).[12] Diphenylacetylene and 1-phenyl-1-propyne (internal alkynes) did not promote the insertion.

In order to examine the tolerance of functional groups, reactions between β-keto sulfone **1a** and *p*-tolylacetylene (**2a**) were carried out in the presence of the following compounds. Recovery of the compounds after the completion of the reactions (**3a**: 68−74% yields) are as follows: 4-methylstyrene (94%), 1-phenyl-1-propyne (96%), 5-nonanone (>99%), and methyl benzoate (>99%). In contrast, the reaction proceeded with 19% and 14% yields, respectively, when benzo- and nonanenitrile were added to the mixture.

The proposed mechanism for the insertion of an alkyne into a carbon−carbon single bond of a β-keto sulfone is as follows (Scheme 1): (1-a) oxidative cycloaddition of the enol form of the β-keto sulfone, an alkyne, and the rhenium catalyst; (2-a) reductive elimination of the rhenium catalyst from the formed rhenium cyclopentene intermediate to give a cyclobutene intermediate; (3) carbon−carbon single bond cleavage of the cyclobutene intermediate to generate an acyclic intermediate; and (4) protonation to give the product. Another possible pathway for the formation of the cyclobutene intermediate is (1-b) nucleophilic addition of the β-keto sulfone to a terminal alkyne and (2-b) intramolecular nucleophilic cyclization. We assume that the stereochemistry of the products is determined kinetically, and no isomerization of the products occurred to other regio- and stereoisomers under the reaction conditions.

Scheme 1. Proposed Mechanism for the Insertion of Alkynes **2** into a Carbon−Carbon Single Bond of β-Keto Sulfones **1**



In summary, we have succeeded in the regio- and stereoselective insertion of terminal alkynes into a non-strained carbon−carbon single bond of β-keto sulfones. Previously, insertion of unsaturated molecules into C−C single bonds was difficult to achieve regio- and stereoselectively. We hope that this reaction will serve as a useful tool for synthetic organic chemists.

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Supporting Information Available. General experimental procedure and characterization data for unsaturated δ-keto sulfones. This material is available free of charge via the Internet at http://pubs.acs.org.

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[12] In Table 2, entries 1−9, β-keto sulfones **1** were recovered. The total yields of the products **3** and the recovery of β-keto sulfones **1** were in the range 88−99%. Therefore, the yields of **3** based on the conversion were relatively high.