Alkynyl Sulfides as Dienophiles in Cobalt-Catalyzed Diels–Alder Reactions

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Dedicated to Professor Wolfgang Steglich on the occasion of his 70th birthday.

Abstract: The cobalt(I)-catalyzed cycloaddition of alkynyl sulfides with 1,3-dienes can be realized at ambient temperatures. In combination with a mild oxidation step various polysubstituted and functionalised diaryl sulfides can be synthesized in good overall yields.

Key words: alkynes, catalysis, cobalt, Diels–Alder reactions, sulfides

The thermal Diels–Alder reaction of alkynyl sulfoxides and alkynyl sulfones is well documented since both types of starting materials are activated by the electron abstracting ability of the sulfur oxide moiety for its use as an electron deficient dienophile in the Diels–Alder reaction with normal electron demand.1 In contrast, alkynyl sulfides are not activated and therefore the use of this type of dienophile is limited to very few examples where very harsh reaction conditions had to be applied.2

In continuing our investigations on cobalt(I)-catalyzed carbon–carbon bond formation processes with non-activated starting materials,3 we focussed our attention on the alkynyl sulfides as substrates. The first attempts for a cobalt(I)-catalysed Diels–Alder reaction of 1,3-butadienes with alkynyl sulfides resulted under the regular conditions used for other non-activated starting materials [ambient temperature, 1–5 mol% of CoBr2(dppe) catalyst and Bu4NBH4 as reducing agent],3 in small amounts of the desired cycloadduct and side products derived from the reaction of the alkynyl sulfide derivatives with the reducing agent.4 Under these conditions, the conversions were not complete after more than 24 hours reaction time. When the reducing agent was altered to simple zinc dust, an induction phase for the reducing step was observed, but the formation of the side products was suppressed. Furthermore, the reactivity of the catalyst was increased when 10–20 mol% of catalyst was used. However, complete conversions for alkyl alkynyl sulfides3 could not be achieved, while for aryl alkynyl sulfides6 the reactions went to completion within 20 hours reaction time. This is demonstrated in the reaction of the aryl substituted alkynyl sulfide 1, which could be converted cleanly into the dihydroaromatic intermediates and oxidized after short filtration to the corresponding diaryl sulfides 2 (Scheme 1). The dihydroaromatic primary products can be easily oxidized by air or other mild oxidizing agents.

Therefore, the separation of the dihydroaromatic compounds from air-oxidized aromatic material included in them is much more difficult than in the previous reported cases of dihydroaromatic products derived from non-activated starting materials (extensive column chromatography),3 so that we decided to oxidize the intermediates in situ to the diaryl sulfides in the further course of the investigation. Therefore, we focussed our attention on a two-step reaction sequence with aryl alkynyl sulfur derivatives as starting materials.

Scheme 1

With this modified protocol for the cobalt(I)-catalyst system we were able for the first time to convert various aryl alkynyl sulfides as dienophiles efficiently in metal catalysed cycloadditions with an acyclic 1,3-diene (2,3-dimethyl-1,3-butadiene was used as a test system) under very mild reaction conditions (Scheme 2).

Scheme 2

The catalyst system allows the conversion of neutral substituted aryl substituents (Table 1, entry 1), sterically more hindered substituents (entry 2) and shows high activity for the conversion of acceptor substituted aryl alkynyl sulfides (entries 3 and 4), while the ortho-ester derivative in entry 5 gave a slower conversion, so that higher catalyst loading was applied to reach full conversion and to obtain a good yield of the desired product. In this series of experiments we could already show that not only sterically less hindered alkyl substituted alkynes (n-hexyl in the entries 1–3), but also more bulky substituents (entries 4–6) as well as a heteroaromatic substituent (entry 7) are well accepted. Special attention should be given to the 2-thienyl substituent case (entry 7), where with rela-
tively high catalyst loadings a fast conversion can be observed. Lower catalyst loadings resulted in this case in a somewhat slower but complete conversion, while the yields were considerably lower. The rationale for the lower reactivity could be the coordination ability of the sulfur donor atoms in the product to the cobalt centre and therefore inactivation of the catalyst by chelation, so that higher amounts of catalyst have to be used, while lower catalyst loading might result in polymerised side products that could neither be detected nor isolated.

In summary, we have developed a protocol which allows for the first time the conversion of non-activated aryl alkynyl sulfides as dienophiles in cobalt(I)-catalyzed cycloadditions with a simple acyclic 1,3-diene under mild reaction conditions. The reaction conditions are superior to any other method described thus far, so that also thermally labile functionalities could be accepted. Although in some cases higher catalyst loadings have to be applied, the conversions proceed on a reasonable time scale and this preliminary investigation shows that the reaction can be used for varied sterically and electronically substituted sulfide starting materials.

**Methyl 4-[4,5-Dimethyl-2-(trimethylsilyl)phenyl]sulfanyl Benzoate (Scheme 1, Entry 6); Typical Procedure**

To a suspension of CoBr₂(dppe) (20 mg, 0.032 mmol, 10 mol%), zinc (8 mg, 0.122 mmol) and ZnI₂ (50 mg, 0.157 mmol) in anhyd CH₂Cl₂ (0.5 mL) were added methyl 4-(trimethylsilyl)ethynylsulfanyl benzoate (80 mg, 0.303 mmol) and 2,3-dimethyl-1,3-butadiene (0.20 mL, 145 mg, 1.77 mmol) under a nitrogen atmosphere. The reaction mixture was stirred at r.t. for 20 h, while after about 10–30 min a colour change from green to brown was observed. After addition of Et₂O (5.0 mL) the mixture was filtered over silica gel (pentane–Et₂O, 2:1) affording the desired product.

**Table 1** Results of the Cobalt(I)-Catalyzed Cycloaddition of 2,3-Dimethyl-1,3-butadiene with Aryl Alkynyl Sulfides.

<table>
<thead>
<tr>
<th>Entry</th>
<th>S-Ar</th>
<th>R</th>
<th>Product</th>
<th>Time (h)</th>
<th>Catalyst (mol%)</th>
<th>Yield (%)</th>
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<tr>
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<td></td>
<td>5</td>
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<tr>
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<tr>
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<td>SiMe₃</td>
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<td></td>
<td>2</td>
<td>50</td>
<td>68</td>
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</tbody>
</table>
Yield: 74 mg (0.215 mmol, 71%); colourless oil; Rf (pentane–Et2O, 20:1) 0.33.

IR (neat): 2951, 2918, 2897, 2861, 1722, 1594, 1561, 1490, 1435, 1401, 1276, 1179, 1109, 841, 761 cm⁻¹.

1H NMR (300 MHz, CDCl3): δ = 7.88–7.81 (d, 2 H, J = 8.8 Hz), 7.37 (s, 1 H), 7.29 (s, 1 H), 7.05–6.98 (d, 2 H, J = 8.8 Hz), 3.87 (s, 3 H), 2.32 (s, 3 H), 2.24 (s, 3 H), 0.27 (s, 9 H).

13C NMR (75 MHz, CDCl3): δ = 167.0, 147.5, 143.5, 139.5, 138.2, 137.6, 137.5, 134.0, 130.0, 126.5, 125.8, 52.1, 19.7, 19.6, 0.2.

MS (EI): m/z (%) = 344 (M⁺, 40), 329 (100), 313 (23), 255 (18).

HRMS: m/z calcd for C19H24O2SSi: 344.1266; found: 344.1269.

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References


(4) Small amounts of reduction products, such as alkenyl sulfides, were detected by GC-MS analysis.
