Silver-catalysed Doyle–Kirmse reaction of allyl and propargyl sulfides†

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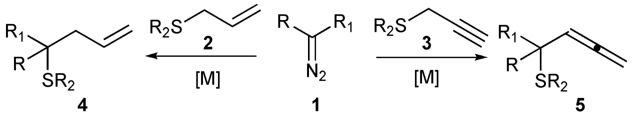
Received 16th December 2008, Accepted 3rd February 2009
First published as an Advance Article on the web 13th February 2009
DOI: 10.1039/b822584b

The silver-catalysed Doyle–Kirmse reaction of propargyl and allyl sulfides with diazo compounds is disclosed. The carbon–carbon bond forming process proceeds with a range of substituents and functionality under mild conditions.

The formation of synthetically important sulfur-ylides by reaction of a metallocarbenoid, formed by transition-metal catalysed decomposition of a diazo compound, and a sulfide is a potent tool for chemical synthesis. A range of powerful carbon–carbon and carbon–heteroatom bond forming processes are accessed by subsequent evolution or reaction of the sulfur ylides. The Doyle–Kirmse reaction involves the [2,3]-sigmatropic rearrangement of an intermediate allyl or progargyl sulfur ylide to access unsaturated products **4** and **5** respectively (Scheme 1).[1]



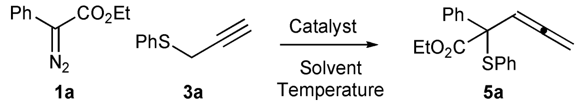
Scheme 1 Doyle–Kirmse reaction of allyl and propargyl sulfides.

We recently established a catalytic diazo-free process where a gold carbenoid species, generated *in situ* by atom-efficient rearrangement, was employed to access the sulfonium ylide intermediate.[2] Interestingly, the use of propargylic sulfides led to products containing the intact propargylic unit, rather than the allenic product expected from a [2,3]-sigmatropic rearrangement.[3]

We questioned whether this result was a peculiarity of that specific reaction system, or a more general consequence of deriving sulfur ylides from gold carbenoids. To examine this latter possibility, we reacted the donor–acceptor diazo compound **1a** with propargyl sulfide **3a** in the presence of a range of gold species known for their catalytic activity (Table 1, Entries 1–6).[4] Allene **5a** was the product in all cases, confirming that propargyl sulfonium ylides formed from gold carbenoids undergo [2,3]-sigmatropic rearrangement, and not a 1,2-shift. However, only low yields of **5a** were obtained.

With the reactivity of the gold carbenoids now established alongside previous reports of copper complexes as active catalysts for this reaction, we chose to explore the reactivity of the remaining member of this group of elements. Despite the recent uptake of interest in catalysis by coinage metals, homogeneous silver catalysis remains generally quite rare in organic synthesis, particularly in atom transfer reactions.[5] It has been questioned whether the role of silver in these processes is to form a silver carbene or if the silver simply acts as a Lewis acid to activate the carbonyl unit and generate a free carbene.[6] Pertinent recent progress in the field includes the $AgSbF_6$ catalysed cyclopropanation with aryldiazoacetates reported by Thompson and Davies,[7] and the ring expansion of cyclopropylsilver carbenoids demonstrated by Tang *et al.*[8]

Table 1 Optimisation of reaction conditions



Entry	Catalyst	Temperature/°C	Method[a]	Time/h	Yield (%)[b]
1	AuCl	70	A	18	—[c]
2	$AuCl_3$	70	A	16	—[d]
3	$AuBr_3$	70	A	18	<<5
4	PPh_3AuNTf_2	70	A	16	12
5	SMe_2AuCl	70	A	16	10
6	$(Ph_3PAu)_3OBF_4$	70	A	16	14
7	$PtCl_2$	70	A	18	<<5
8	$AgSbF_6$	70	A	16	49
9	$AgSbF_6$	23	A	17	52
10	AgOTf	23	A	17	57
11	$AgBF_4$	23	A	17	48
12	$AgPF_6$	23	A	17	45
13	AgOTf	35	B	20	85
14	AgOTf	35	C	22	60

[a] Methods: A: **1a** (1 equiv.) and **3a** (1.1 equiv.) are added to a solution of the catalyst (5 mol%) in $ClCH_2CH_2Cl$ over 15 minutes at 0 °C; B: catalyst (10 mol%) is added to a solution of **1a** (1 equiv.) and **3a** (2 equiv.) in CH_2Cl_2; C: **1a** (1 equiv.) is added *via* syringe pump over 1 h to a solution of **3a** (2 equiv.) and catalyst (12 mol%) in CH_2Cl_2. [b] Yields determined by NMR against a known quantity of durol. [c] No reaction was observed. [d] Degradation of the starting material was observed.

Our studies show that silver salts are able to catalyse the Doyle–Kirmse reaction of propargylic sulfides. Silver salts retain catalytic effectiveness in the presence of sulfides and are significantly more effective than the gold species tested (Table 1, Entries 8–12). With the diazocompound used as the limiting reagent, a good yield of **5a** was obtained by the practical approach of directly mixing **1a**, **3a** and AgOTf in dichloromethane and applying gentle heating. Slow addition of the diazo compound is unnecessary with this reaction system (Entry 13 *vs.* 14).

As the first example of the silver-catalysed Doyle–Kirmse reaction, we examined a range of different allyl and propargyl sulfides under these standard conditions (Table 2).

Despite the known proclivity of silver carbenoids to react with alkenes through cyclopropanation,[7] the silver-catalysed reaction with allyl sulfides **2** showed excellent chemoselectivity toward ylide formation, with the desired homoallyl sulfide products **4** generally formed in high yield. Both alkyl and aryl substituents on the sulfur

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† Electronic supplementary information (ESI) available: Experimental details and analytical data for new compounds. See DOI: 10.1039/b822584b

Table 2 Scope of sulfides employed in the silver-catalysed Doyle–Kirmse reaction[a]

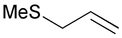
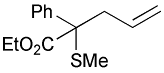
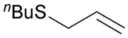
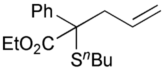
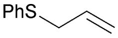
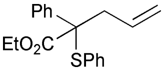
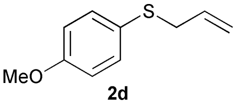
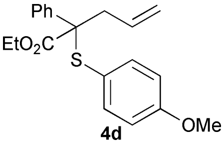
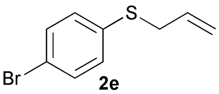
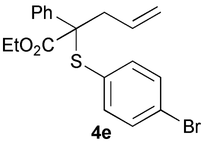
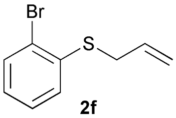
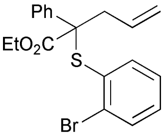
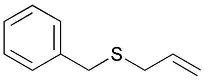
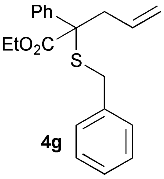
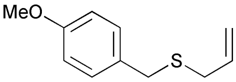
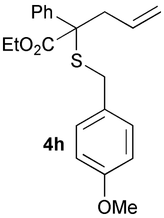
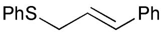
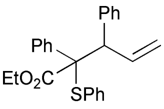
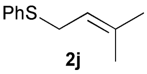
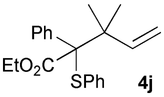
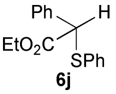
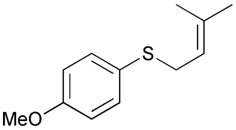
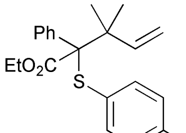
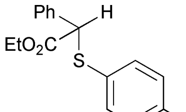
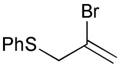
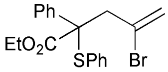
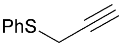
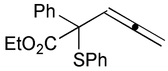
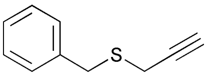
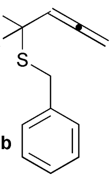
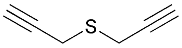
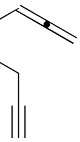
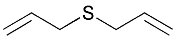
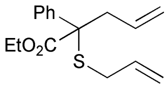
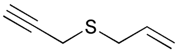
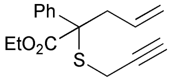
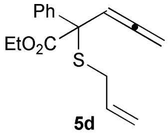
Entry	Sulfide	Time/h	Product	Yield (%)[b]
1	 **2a**	21	 **4a**	84 (95)
2	 **2b**	24	 **4b**	88 (95)
3	 **2c**	19	 **4c**	85 (93)
4	 **2d**	15	 **4d**	85 (90)
5	 **2e**	24	 **4e**	97 (98)
6	 **2f**	24	 **4f**	83 (88)
7	 **2g**	19	 **4g**	92 (96)
8	 **2h**	19	 **4h**	64 (75)
9	 **2i**	24	 **4i**	62 (75)
10	 **2j**	24	 **4j**	–(0)
			 **6j**	69 (82)

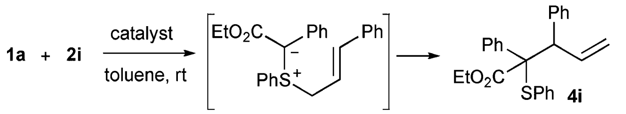
Table 2 *(Contd.)*

Entry	Sulfide	Time/h	Product	Yield (%)[b]
11	 **2k**	28	 **4k**	49[c] (55)
			 **6k**	12
12	 **2l**	33	 **4l**	89 (92)
13	 **3a**	28	 **5a**	71 (85)
14	 **3b**	18	 **5b**	90 (94)
15	 **3c**	22	 **5c**	63 (75)
16	 **2m**	21	 **4m**	84 (94)
17	 **3d**	20	 **4n**	62 (63) **4n**:**5d** = 17:83
			 **5d**	

[a] Reagents and conditions: AgOTf (10 mol%) is added to a solution of **1a** (1 equiv.) and **2** or **3** (2 equiv.) in CH_2Cl_2, the flask is sealed and heated at 35 °C overnight. [b] Refers to isolated yield after flash chromatography. Figures in parentheses are NMR yields calculated against known quantities of durol as internal standard. [c] Reaction run in the presence of 4 Å molecular sieves. In the absence of sieves **4k** was obtained in 41% alongside 21% of **6k**.

are tolerated in the reaction (Table 2, Entries 1–6). In the latter case, electron-rich and electron-deficient aryl units were employed and good results were achieved with both. The use of sulfides **2e** and **2f** demonstrates that handles for further synthetic manipulation, in the form of aryl bromides, are readily accommodated on the sulfide. Both benzyl and paramethoxylbenzyl protecting groups were employed on the sulfide; there was no evidence of competing Stevens rearrangement ([1,2]-shift) of these units in place of [2,3]-sigmatropic rearrangement of the allyl ylide (Entries 7 and 8).

The effect of substitution on the allyl unit was also studied. Cinnamylsulfide **2i** afforded a diastereomeric mixture of **4i** in a 35:65 ratio. To compare with previous results the silver, rhodium and copper promoted reactions of cinnamyl sulfide **2i** were run in aromatic solvent at room temperature (Scheme 2).[9] Each reaction gave a similar ratio of diastereomers, as determined by ^{1}H NMR, which suggests that the silver is not associated with the nucleophilic carbon on formation of the ylide.



catalyst:	Ratio of Diastereomers
AgOTf (10 mol%)	43:57
$Rh_2(OAc)_4$ (5 mol%)	37:63
$Cu(MeCN)_4BF_4$ (10 mol%)	43:57

Scheme 2 Study of metal source impact on the diastereomeric outcome.

When prenylsulfide **2j** was treated under our standard conditions, sulfide **6j** was isolated. Loss of the prenyl unit presumably occurs after formation of the sulfur ylide. The use of prenylsulfide **2k** bearing a more electron-donating substituent led to a moderate yield of the desired product **4k** incorporating the prenyl unit, alongside smaller amounts of **6k**. Activated molecular sieves were added to the reaction to further minimise the amount of adventitious water present. A slight increase in the yield of **4k** was achieved under these conditions.

Pleasingly, the 2-bromoallyl unit underwent reaction to give the desired product **4l** in high yield (Entry 12).

Both aryl and benzyl substituted propargyl sulfides gave the desired allenic products in high yield (Entries 13 and 14). The use of these types of product in furan[10] and pyrrole syntheses,[11] led us to also explore sulfide precursors bearing multiple alkene/alkyne units in the reaction. The products are potentially valuable precursors to sulfur heterocycles by further metal-promoted cyclisation processes. Bispropargyl sulfide **3c** and bisallyl sulfide **2m** afforded the 1,7-allen-yne system **5c** and the 1,7-diene **4m** respectively in good yield. Allyl propargyl sulfide was assessed and gave a mixture of products resulting from competing participation of either the allyl or propargyl unit in the sigmatropic rearrangement (Entry 17). A reasonable (4.9:1) preference was displayed for the propargylic unit to undergo this process.

To further examine the scope of the silver catalysed process, allyl ethers and amines were tested under the reaction conditions. To date, none of the products expected from oxonium or ammonium ylide formation have been observed.

In conclusion, we have shown that a simple silver salt effectively catalyses the Doyle–Kirmse reaction between diazo compounds and both allyl and propargyl sulfides. The reaction involves a straightforward procedure and tolerates a range of substituents and functionality, including vinyl and aryl bromides, allyl, propargyl, benzyl and PMB units to afford the desired products in high yields.

Acknowledgements

We thank the EPSRC (EP/E032168/1) and the University of Birmingham for their financial support of this programme.

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