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Synthesis of vinyl sulfides via hydrothiolation of alkynes using Al_2O_3/KF under solvent-free conditions

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Abstract

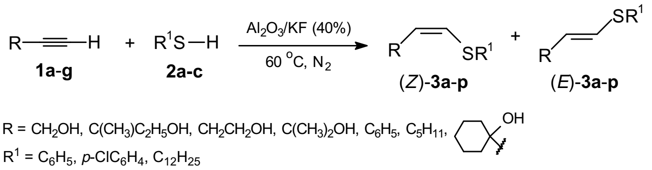
We present here a clean, solvent-free hydrothiolation of alkynes using solid supported catalyst (Al_2O_3/KF). This efficient and improved method selectively furnishes the corresponding anti-Markovnikov vinyl sulfides in good to excellent yields. The method is applicable for aliphatic and aromatic thiols and the catalytic system can be re-used up to two times without previous treatment and with comparable activity.

Keywords: Solvent-free reaction; Hydrothiolation; Vinyl sulfide

Vinyl sulfides have been found to be a very useful tool in organic synthesis, since sulfur-containing groups serve as important auxiliary function in synthetic sequences.[1] In this way, various methods are mentioned for the preparation of vinyl sulfides and the most common protocols involve the addition of thiol, or the respective anions, to terminal or internal alkynes.[2,3] Most of the described methods make use of toxic organic solvents and are catalyzed by transition-metals[2a,b] or promoted by base.[2c–e] More recently, some improvements on selective preparation of vinyl sulfides have been described.[3] These comprise the use of catalytic phenylselenenyl bromide[3a] or nickel[3b] under solvent-free conditions, β-cyclodextrin in the presence of water and acetone[3c] or under catalyst-free conditions.[3d] In recent years, the use of potassium fluoride supported on alumina (Al_2O_3/KF) as a green catalytic system for a number of transformations has been increased.[4] By using Al_2O_3/KF, the products can be easily isolated by filtration and the generation of large amounts of salts at the end of the synthesis, as well as the use of stoichiometric strong bases, can be avoided.

Our major research goal has been the development of new and cleaner protocols for the preparation and synthetic applications of organochalcogenium compounds.[5] More recently, we have described several efficient approaches using Al_2O_3/KF.[6] In continuation to these studies, we describe here the results of the hydrothiolation of alkynes **1** using Al_2O_3/KF without any solvent (Scheme 1).[7,8]

Initially, we chose propargyl alcohol (**1a**) and phenylthiol (**2a**) as standard starting materials. We examined the temperature, amount of Al_2O_3/KF (40%) and the use of N_2 atmosphere. It was found that stirring a mixture of



Scheme 1.

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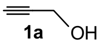
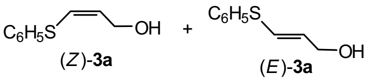
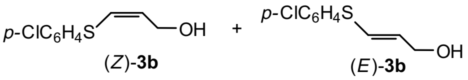
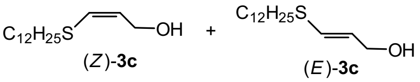
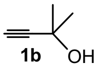
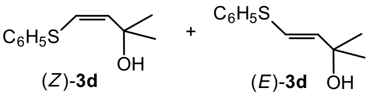
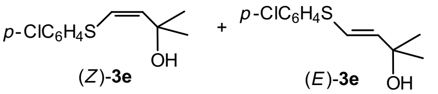
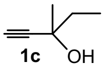
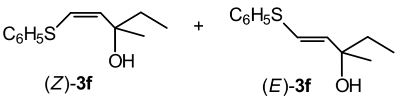
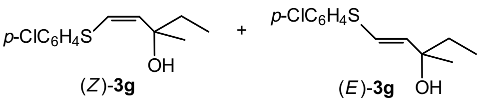
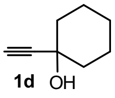
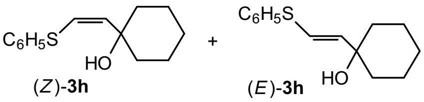
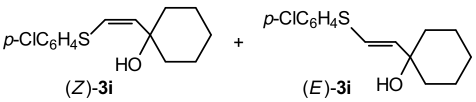
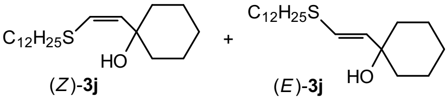
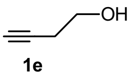
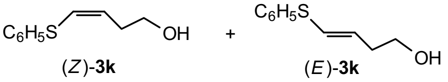
1a (2 mmol) and **2a** (1 mmol) in the presence of 0.08 g (51 mol %) of Al_2O_3/KF (40%) at room temperature, the products of hydrothiolation (**3a**) were obtained in an overall yield of 25% after 3.5 h, together with a great amount of diphenyldisulfide. On the other hand, when the same protocol was performed at gentle heating (60 °C) and under N_2 atmosphere, the yield increased to 63% yield (Table 1, entry 1). Using 0.120 g (77 mol %) of the catalyst or prolonged time (24 h) did not significantly increase the vinyl sulfides yields. It was also observed that the catalytic system can be re-used for 2 cycles, just by washing it with ethyl acetate and drying under vacuum.

Using the optimized conditions, the protocol was extended to other alkynyl alcohols and thiols (Table 1, entries 2–12).[8] Concerning the stereochemistry of products, for all the studied examples, the anti-Markovnikov adduct **3** was obtained in higher amount than the Markovnikov one. The formation of a *Z* and *E* mixture of **3** was also observed (determined by ^{1}H NMR) and the selectivity was influenced by the substituent at alkynes (see Table 1). Thus, for example, *Z*-**3a** was obtained preferentially from the reaction of propargyl alcohol (**1a**) with **2a** (63% yield, *Z*:*E* ratio = 86:14, entry 1), while *E*-**3h** was the major obtained isomer for the reaction of 1-ethynylcyclohexanol

Table 1
Hydrothiolation of alkynes using Al_2O_3/KF under solvent-free condition

Entry	Alkyne **1**	Thiol **2**	Product **3**	Time (h)	Ratio[a] (*Z*):(*E*)	Yield[b] (%)
1	 **1a**	C_6H_5SH **2a**	 (*Z*)-**3a** + (*E*)-**3a**	3.5	86:14	63 (64:36)[c]
2	**1a**	*p*-ClC_6H_4SH **2b**	 (*Z*)-**3b** + (*E*)-**3b**	1	75:25	57 (51:49)[c]
3	**1a**	$CH_3(CH_2)_{11}SH$ **2c**	 (*Z*)-**3c** + (*E*)-**3c**	4	55:45	65 (92:8)[c]
4	 **1b**	C_6H_5SH **2a**	 (*Z*)-**3d** + (*E*)-**3d**	4	31:69	90 (93:7)[c]
5	**1b**	*p*-ClC_6H_4SH **2b**	 (*Z*)-**3e** + (*E*)-**3e**	3	23:77	88 (96:4)[c]
6	 **1c**	C_6H_5SH **2a**	 (*Z*)-**3f** + (*E*)-**3f**	2.5	60:40	70 (86:14)[c]
7	**1c**	*p*-ClC_6H_4SH **2b**	 (*Z*)-**3g** + (*E*)-**3g**	3	29:71	74 (96:4)[c]
8	 **1d**	C_6H_5SH **2a**	 (*Z*)-**3h** + (*E*)-**3h**	3	13:87	56 (94:6)[c]
9	**1d**	*p*-ClC_6H_4SH **2b**	 (*Z*)-**3i** + (*E*)-**3i**	5	20:80	63 (93:7)[c]
10	**1d**	$CH_3(CH_2)_{11}SH$ **2c**	 (*Z*)-**3j** + (*E*)-**3j**	6.5	2:98	86 (92:8)[c]
11	 **1e**	C_6H_5SH **2a**	 (*Z*)-**3k** + (*E*)-**3k**	2	53:47	62 (92:8)[c]