Sulfonoketenimides as Key Intermediates for the Synthesis of *N*-Tosylacetoyloxy Alkanimines

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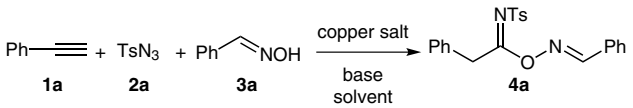
Abstract: A copper-catalyzed multicomponent reaction between terminal alkynes, sulfonyl azides, and oximes for the synthesis of *N*-tosylacetoyloxy alkanimines is reported. This one-pot procedure is carried out in the presence of copper(I) iodide in acetonitrile at room temperature.

Key words: alkanimines, terminal alkyne, sulfonyl azide, oxime, copper iodide

Copper-catalyzed multicomponent reactions involving a ketenimines have served as an effective approach for the synthesis of compounds with various functional groups.[1–5] This intermediate has attracted much attention due to its easy formation, relative reactivity, tolerance of procedure, and its diversity of products.[6–8] Recently, we have disclosed a novel reactivity of sulfonoketenimides in reactions with amines to give *N*-sulfonylamidine derivatives.[9]

As part of our current studies on the development of new applications of sulfonoketenimides in organic synthesis,[10–12] we report a novel pathway for the synthesis of *N*-tosylacetoyloxy alkanimines via a copper(I) iodide catalyzed reaction between sulfonyl azides, 1-alkynes, and oximes (Scheme 1). Chang and co-workers reported a facile access to *N*-sulfonylimidates via the reaction of sulfonoketenimides and alcohols.[13,14]



Scheme 1

Initially, the reaction of phenylacetylene, toluenesulfonyl azide, and benzaldoxime in the presence of triethylamine and copper(I) iodide (10 mol%) in tetrahydrofuran (2 mL) at room temperature under argon was studied. After four hours, product **4a** was obtained in 25% yield (Table 1). To optimize the reaction conditions, a variety of solvents, copper sources, and bases were considered. The best results were obtained with triethylamine and copper(I) iodide in acetonitrile.

Table 1 Optimization of the Reaction Conditions for the Preparation of **4a**[a]

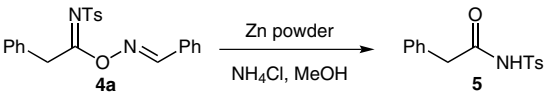
Catalyst	Base	Solvent	Yield (%)[b]
CuI	Et_3N	DMF	81
CuI	Et_3N	MeCN	93
CuI	Et_3N	$CHCl_3$	32
CuI	Et_3N	THF	25
CuI	Et_2NH	MeCN	79
CuI	DABCO	MeCN	–
CuCl	Et_3N	MeCN	70
CuBr	Et_3N	MeCN	47

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.0 mmol), **3a** (1.2 mmol), CuI (10 mol%), and Et_3N (1.5 mmol) were stirred at 25 °C for 4 h under argon.
[b] Isolated yields.

With the optimized reaction conditions in hand a series of substituted sulfonyl azides, terminal alkynes, and oximes were subjected to the reaction conditions (Table 2).[15]

When carbonyl azides were used as the azide source, no alkanimine was detected in the reaction mixture.

N-Tosylacetoyloxy alkanimines **4** can be transformed to the corresponding *N*-tosylacetamide derivatives. Thus, efficient conversion of product **4a** into 2-phenyl-*N*-tosylacetamide (**5**) was achieved by zinc dust and ammonium chloride in methanol (Scheme 2).[16]



Scheme 2

In summary, it is shown that *N*-tosylacetoyloxy alkanimines can be prepared by the coupling of terminal alkynes, sulfonyl azides, and oximes in the presence of copper(I) iodide and triethylamine. The advantages of this procedure are the use of air-stable, inexpensive copper(I) iodide catalyst and mild reaction conditions. Transformation of alkanimine **4a** into 2-phenyl-*N*-tosylacetamide (**5**) was achieved by zinc dust and ammonium chloride in methanol.

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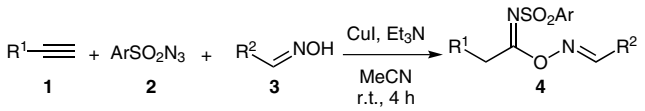
Table 2 Synthesis of *N*-Tosylacetoyloxy-alkanimines **4**



Entry	**1–4**	R^1	Ar	R^2	Yield of **4** (%)
1	**a**	Ph	Tol	Ph	87
2	**b**	Ph	Tol	py	84
3	**c**	Ph	Tol	Me	83
4	**d**	*n*-Bu	Tol	Ph	79
5	**e**	*n*-Bu	Tol	py	78
6	**f**	*n*-Bu	Tol	Me	75
7	**g**	*n*-Pr	Tol	Ph	76
8	**h**	Tol	Ph	py	82
9	**i**	Tol	Ph	Me	84

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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(15) **Typical Procedure for the Preparation of Products 4a–i**
To a stirred solution of alkyne (**1**, 1.0 mmol), sulfonylazide (**2**, 1.0 mmol), and CuI (19 mg, 0.10 mmol) in MeCN (2 mL) was added Et_3N (1.5 mL) under argon at r.t. After 10 min, oxime (**3**, 1.2 mmol) was added, and the mixture was stirred for 4 h. The solvent was removed, the residue treated with of sat. aq NH_4Cl (3 mL) and extracted with EtOAc (3 × 5 mL). Organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified by chromatography (silica gel, hexane–EtOAc = 2:1) to give **4**.
4-Methyl-*N*-[(-phenylmethyleneaminooxy)phenyl-ethylidene]benzenesulfonamide (4a)
Colorless solid, mp 156–158 °C; yield 0.34 g (87%). IR (KBr): ν_{max} = 3020, 2972, 1569, 1528, 1335, 1128 cm^{-1}. ^1H NMR (500.1 MHz, $CDCl_3$): δ = 2.44 (3 H, s, CH_3), 3.60 (2 H, s, CH_2), 7.14 (2 H, d, ^3J = 8.9 Hz, 2 CH), 7.31–7.48 (8 H, m, 8 CH), 7.82 (2 H, ^3J = 8.5 Hz, 2 CH), 7.88 (2 H, d, ^3J = 8.2 Hz, 2 CH), 7.97 (1 H, s, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.7 (CH_3), 43.8 (CH_2), 126.1 (2 CH), 128.1 (CH), 128.5 (2 CH), 128.8 (2 CH), 129.0 (2 CH), 129.3 (CH), 129.4 (2 CH), 129.6 (2 CH), 133.7 (C), 137.5 (C), 141.0 (C), 143.2 (CH), 154.5 (CH), 165.9 (C). MS (EI): *m/z* (%) = 392 (5) [M^+], 271 (13), 251 (100), 140 (10), 104 (14), 77 (60), 76 (42), 64 (44). Anal. Calcd (%) for $C_{22}H_{20}N_2O_3S$ (392.47): C, 67.33; H, 5.14; N, 7.14. Found: C, 67.75; H, 5.19; N, 7.21.
(16) (a) **Conversion of 4a into 2-Phenyl-*N*-tosylacetamide (5)**
To a stirred solution of **4a** (1 mmol) in MeOH (3 mL) was added NH_4Cl (1 mmol) in H_2O (1 mL). Then, Zn powder (2 mmol) was added, and the mixture was heated at 70 °C for 2 h. The mixture was cooled, filtered, and the filtrate was extracted with EtOAc. The organic layer was evaporated and purified by chromatography (silica gel, hexane–EtOAc = 3:1) to give **5**. (b) Cassidy, M. P.; Raushel, J.; Fokin, V. V. *Angew. Chem. Int. Ed.* **2006**, *45*, 3154.