Copper-Catalyzed One-Pot Synthesis of *N*-Sulfonylalkanimidoyl Thiocyanates from Sulfonyl Azides, Alkynes, and KSCN

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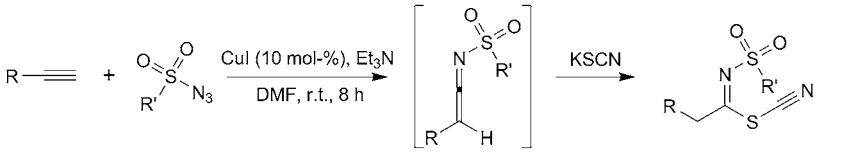
Ketenimine intermediates generated by the addition of copper acetylides to sulfonyl azides are trapped by KSCN to afford *N*-sulfonylalkanimidoyl thiocyanates in moderate-to-good yields.

Introduction. – Ketenimines [1], as useful intermediates, have attracted much attention due to their diverse chemistry and relative reactivity [2–5]. Perhaps, the most attractive method to generate ketenimines is the Cu^{I}-catalyzed azide–alkyne cycloaddition (*Scheme 1*), which was established by *Sharpless* and co-workers [6]. This method is well suited for multicomponent reactions [7]. The formation of ketenimine intermediates from terminal alkynes, sulfonyl azides, and Et_3N as the base, in the presence of CuI [8], has encouraged us to trap these intermediates using nucleophilic addition reaction [9–11].

Scheme 1



1a R = Ph
1b R = Bu

2a R = *p*-Tol
2b R = Ph
2c R = Me

	R	R'	Yield [%]
3a	Ph	*p*-Tol	
3b	Ph	Ph	
3c	Ph	Me	
3d	Bu	*p*-Tol	
3e	Bu	Ph	
3f	Bu	Me	
4a	Ph	*p*-Tol	80
4b	Ph	Ph	82
4c	Ph	Me	74
4d	Bu	*p*-Tol	62
4e	Bu	Ph	57
4f	Bu	Me	53

Herein, we report a simple and efficient procedure for the synthesis of *N*-sulfonylalkanimidoyl thiocyanates *via* the Cu-catalyzed three-component coupling reaction of sulfonyl azides, terminal alkynes, and KSCN (*Scheme 1*).

Results and Discussion. – In our initial investigations, phenylacetylene (**1a**), *p*-toluenesulfonyl azide (TsN_3; **2a**), and KSCN were selected as the model substrates. Several catalysts such as CuI, CuBr, CuCl, Cu_2O, and Cu powder were tested, with CuI giving the best results. Among several solvents screened, DMF was the best. When the

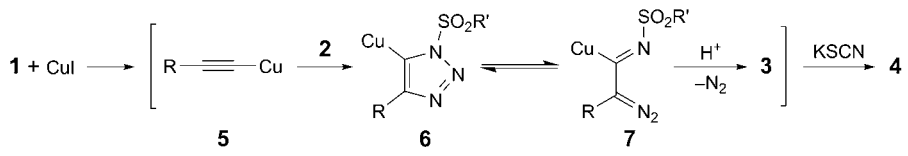
reaction was performed in DMF in the presence of 1 equiv. of Et_3N at room temperature for 8 h, *N*-sulfonyl-2-phenylethanimidoyl thiocyanate (**4a**) was obtained in 80% yield. Thus, the optimized reaction conditions used were 10 mol-% of CuI, 1 mmol of alkyne, 1.2 mmol of sulfonyl azide, and 1.5 mmol of KSCN in 3 ml of DMF at room temperature.

Aliphatic acetylenes were as low-yielding substrates compared to phenylacetylene. Aromatic and aliphatic sulfonyl azides reacted efficiently, and the corresponding products were obtained in good yields.

Structures of compounds **4a**–**4f** were assigned by IR, ^{1}H- and ^{13}C-NMR, and mass-spectral data. The ^{1}H-NMR spectrum of **4a** exhibited two *singlet*s for Me (δ(H) 2.48) and CH_2 (δ(H) 3.69) H-atoms, along with characteristic *multiplet*s for the aromatic H-atoms. The ^{13}C-NMR spectrum of **4a** displayed twelve signals in agreement with the proposed structure. The mass spectrum of **4a** showed the molecular-ion peak at *m*/*z* 330. The NMR spectra of compounds **4b**–**4f** were similar to those of **4a**, except for the substituents, which gave rise to characteristic signals in the appropriate regions of the spectra.

A plausible mechanism for the formation of compounds **4** is proposed in *Scheme 2*. The yellow copper acetylide **5**, formed from **1** and CuI, is converted to ketenimine **3** by well-documented transformations [12–14]. Nucleophilic attack of the thiocyanate ion at **3** affords **4**.

Scheme 2



In summary, ketenimine intermediates generated by the addition of copper acetylides to sulfonyl azides are trapped by KSCN to yield *N*-sulfonylalkanimidoyl thiocyanates. The potential diversity of this type of reaction, and available starting materials and catalysts are the main advantages of this methodology.

Experimental Part

General. All chemicals were obtained commercially and used without further purification. IR Spectra: *Shimadzu-IR-460* spectrometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker DRX-500 Avance* instrument at 500.1 and 125.7 MHz, resp.; δ in ppm, *J* in Hz. MS: *Finnigan-MAT-8430EI-MS* mass spectrometer; at 70 eV; in *m*/*z* (rel. %). Elemental analyses: *Vario EL III CHNOS* elemental analyzer.

General Procedure for the Synthesis of Compounds **4**. To a mixture of alkyne **1** (1 mmol), sulfonyl azide **2** (1.2 mmol), CuI (0.1 mmol), and Et_3N (1 mmol) in DMF (3 ml) was slowly added KSCN (1.5 mmol). The mixture was stirred at r.t. After completion of the reaction (*ca.* 8 h; TLC (AcOEt/hexane 1:3) monitoring), the mixture was diluted with CH_2Cl_2 (2 ml) and aq. NH_4Cl soln. (3 ml), stirred for 30 min, and the layers were separated. The aq. layer was extracted with CH_2Cl_2 (3 × 3 ml), and the combined org. fractions were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 230–400 mesh, *Merck*; AcOEt/hexane 1:3) to give the product.

N-*[(4-Methylphenyl)sulfonyl]-2-phenylethanimidoyl Thiocyanate* (**4a**). Yellow oil. Yield: 0.26 g (80%). IR (KBr): 2253, 1511, 1396, 1270, 1139, 1083. ^{1}H-NMR: 2.48 (*s*, Me); 3.69 (*s*, CH_2); 7.26 – 7.34 (*m*, 3 arom. H); 7.40 (*d*, ^3J = 7.6, 2 arom. H); 7.50 (*d*, ^3J = 7.9, 2 arom. H); 7.92 (*d*, ^3J = 7.9, 2 arom. H). ^{13}C-NMR: 32.2 (Me); 42.2 (CH_2); 115.1 (CN); 125.7 (CH); 127.5 (2 CH); 128.8 (2 CH); 129.2 (2 CH); 130.7 (2 CH); 132.5 (C); 142.1 (C); 147.3 (C); 170.3 (C). MS: 330 (2, M^+), 272 (8), 238 (12), 155 (100), 91 (70), 77 (54), 57 (35). Anal. calc. for $C_{16}H_{14}N_2O_2S_2$ (330.42): C 58.16, H 4.27, N 8.48; found: C 58.47, H 4.34, N 8.59.

2-Phenyl-N-*(phenylsulfonyl)ethanimidoyl Thiocyanate* (**4b**). Yellow oil. Yield: 0.26 g (82%). IR (KBr): 2249, 1520, 1400, 1385, 1273, 1142, 1087. ^{1}H-NMR: 3.67 (*s*, CH_2); 7.25 – 7.34 (*m*, 3 arom. H); 7.48 (*d*, ^3J = 7.6, 2 arom. H); 7.62 (*t*, ^3J = 7.6, 1 arom. H); 7.76 (*t*, ^3J = 7.9, 2 arom. H); 8.05 (*d*, ^3J = 7.9, 2 arom. H). ^{13}C-NMR: 42.5 (CH_2); 115.1 (CN); 125.6 (CH); 127.4 (2 CH); 128.7 (2 CH); 129.2 (2 CH); 130.1 (2 CH); 132.5 (CH); 135.6 (C); 144.9 (C); 170.9 (C). MS: 316 (3, M^+), 258 (12), 238 (17), 175 (31), 141 (100), 91 (45), 77 (54), 57 (46). Anal. calc. for $C_{15}H_{12}N_2O_2S_2$ (316.40): C 56.94, H 3.82, N 8.85; found: C 57.36, H 3.89, N 8.96.

N-*(Methylsulfonyl)-2-phenylethanimidoyl Thiocyanate* (**4c**). Yellow oil. Yield: 0.19 g (74%). IR (KBr): 2245, 1531, 1401, 1385, 1271, 1120. ^{1}H-NMR: 3.44 (*s*, Me); 3.64 (*s*, CH_2); 7.25 – 7.36 (*m*, 3 arom. H); 7.49 (*d*, ^3J = 7.6, 2 arom. H). ^{13}C-NMR: 33.0 (Me); 42.5 (CH_2); 115.4 (CN); 125.6 (C); 128.8 (2 CH); 129.3 (2 CH); 132.5 (CH); 170.3 (C). MS: 254 (2, M^+), 196 (10), 175 (14), 162 (30), 91 (100), 78 (88), 77 (44), 57 (34). Anal. calc. for $C_{10}H_{10}N_2O_2S_2$ (254.33): C 47.23, H 3.96, N 11.01; found: C 47.04, H 3.93, N 11.13.

N-*[(4-Methylphenyl)sulfonyl]hexanimidoyl Thiocyanate* (**4d**). Yellow oil. Yield: 0.19 g (62%). IR (KBr): 2233, 1520, 1401, 1369, 1270, 1118. ^{1}H-NMR: 0.90 (*t*, ^3J = 6.9, Me); 1.39 – 1.45 (*m*, CH_2); 1.47 – 1.53 (*m*, CH_2); 1.91 – 1.93 (*m*, CH_2); 2.17 (*t*, ^3J = 7.0, CH_2); 2.42 (*s*, Me); 7.39 (*d*, ^3J = 8.0, 2 arom. H); 7.92 (*d*, ^3J = 8.0, 2 arom. H). ^{13}C-NMR: 13.9 (Me); 18.5 (CH_2); 22.2 (CH_2); 30.9 (CH_2); 32.3 (Me); 38.4 (CH_2); 115.1 (CN); 127.5 (2 CH); 130.6 (2 CH); 142.1 (C); 147.2 (C); 171.2 (C). MS: 310 (3, M^+), 238 (16), 215 (13), 155 (100), 91 (51), 77 (41), 57 (52), 43 (49). Anal. calc. for $C_{14}H_{18}N_2O_2S_2$ (310.43): C 54.17, H 5.84, N 9.02; found: C 54.49, H 5.91, N 9.12.

N-*(Phenylsulfonyl)hexanimidoyl Thiocyanate* (**4e**). Yellow oil. Yield: 0.17 g (57%). IR (KBr): 2246, 1517, 1408, 1348, 1268, 1141, 1086. ^{1}H-NMR: 0.91 (*t*, ^3J = 6.9, Me); 1.39 – 1.46 (*m*, CH_2); 1.48 – 1.53 (*m*, CH_2); 1.91 – 1.93 (*m*, CH_2); 2.18 (*t*, ^3J = 7.0, CH_2); 7.62 (*t*, ^3J = 8.0, 2 arom. H); 7.74 (*t*, ^3J = 8.0, 1 arom. H); 8.05 (*d*, ^3J = 8.0, 2 arom. H). ^{13}C-NMR: 14.0 (Me); 18.5 (CH_2); 22.2 (CH_2); 30.9 (CH_2); 38.4 (CH_2); 115.2 (CN); 127.4 (2 CH); 130.1 (2 CH); 135.7 (CH); 147.4 (C); 170.9 (C). MS: 296 (1, M^+), 270 (12), 224 (10), 155 (34), 141 (100), 77 (35), 71 (77), 43 (50). Anal. calc. for $C_{13}H_{16}N_2O_2S_2$ (296.41): C 52.68, H 5.44, N 9.45; found: C 53.00, H 5.52, N 9.57.

N-*(Methylsulfonyl)hexanimidoyl Thiocyanate* (**4f**). Yellow oil. Yield: 0.12 g (53%). IR (KBr): 2237, 1522, 1403, 1345, 1270, 1119, 1040. ^{1}H-NMR: 0.90 (*t*, ^3J = 6.9, Me); 1.38 – 1.45 (*m*, CH_2); 1.48 – 1.52 (*m*, CH_2); 1.91 – 1.94 (*m*, CH_2); 2.16 (*t*, ^3J = 7.0, CH_2); 3.56 (*s*, Me). ^{13}C-NMR: 14.0 (Me); 18.5 (CH_2); 22.2 (CH_2); 30.9 (CH_2); 32.3 (Me); 39.4 (CH_2); 115.6 (CN); 170.7 (C). MS: 234 (1, M^+), 208 (12), 176 (10), 155 (39), 78 (100), 71 (32), 57 (46), 43 (21). Anal. calc. for $C_8H_{14}N_2O_2S_2$ (234.05): C 41.00, H 6.02, N 11.95; found: C 41.36, H 6.09, N 12.06.

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