A New Synthesis of Phenylalkynes from the *p*-Toluenesulfonylhydrazone of α-Methylthioacetophenone

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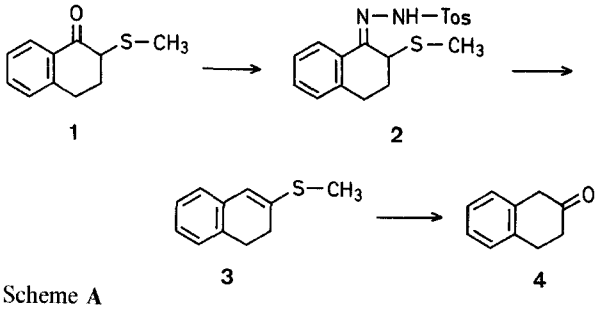
The reaction of *p*-toluenesulfonylhydrazones of ketones with alkyllithium reagents has been an important route to olefins[1]. The reaction of *p*-toluenesulfonylhydrazones of β-ketosulfides with alkyllithium should lead to a thioenol ether[2], which would provide a new method for the transposition of the carbonyl group[2]. The reaction of the *p*-toluenesulfonylhydrazone of 2-methylthio-1-tetralone (**2**) with methyllithium in ether at room temperature afforded 2-methylthio-3,4-dihydronaphthalene (**3**), which was converted to 2-tetralone (**4**) in quantitative yield[3].



1 2 3 4

Scheme A

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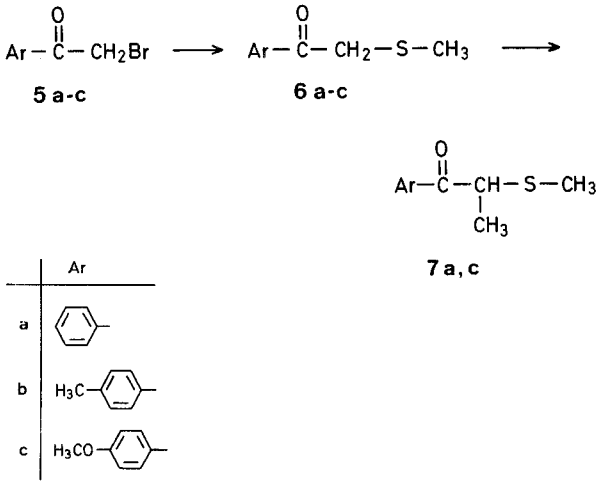
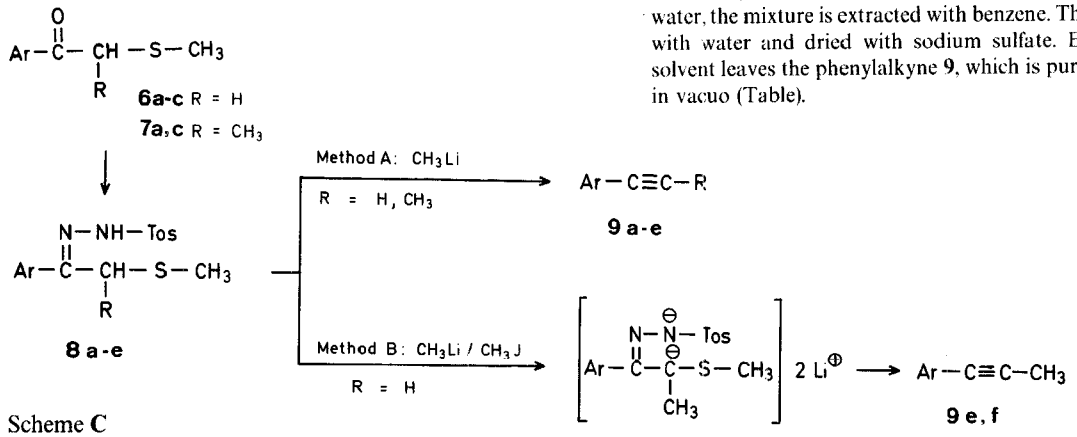
From this point of view, we have investigated the reactions of *p*-toluenesulfonylhydrazones of β-ketosulfides with methyllithium and we now wish to report a novel synthesis of phenylalkynes via the vinyl anion of a thioenol ether generated from the *p*-toluenesulfonylhydrazone of α-methylthioacetophenones. α-Methylthioacetophenones (**6a–c**) were prepared from the corresponding α-bromoacetophenones (**5a–c**), respectively. Methylation of **6a** and **6c** with methyl iodide in benzene in the presence of sodium hydride gave the α-methylthiopropiophenones (**7a** and **7c**), respectively (Scheme **B**).



Scheme **B**

The *p*-toluenesulfonylhydrazone (**8a**), obtained from **6a**, was treated with methyllithium (6 mol-eq) in ether at room temperature to yield phenylacetylene (**9a**)[4] in 97% yield. In a similar fashion, *p*-tolylacetylene (**9b**)[5], *p*-methoxyphenylacetylene (**9c**)[6] were obtained from **6b** and **6c**, respectively, through the corresponding *p*-toluenesulfonylhydrazones. Furthermore, 1-phenyl-1-propyne (**9d**)[7] and 1-*p*-methoxyphenyl-1-propyne (**9e**)[8] were also synthesized from the respective *p*-toluenesulfonylhydrazones **8**. In addition, we investigated an application of this method to the one-pot synthesis of phenylalkynes through alkylation of *p*-toluenesulfonylhydrazone[1]. The *p*-toluenesulfonylhydrazone (**8c**) was treated with methyllithium (6 mol-eq) at −78° for 10 min. After addition of methyl iodide (1 mol-eq) to the mixture at the same temperature, the mixture was allowed to stand at room temperature for 1 h under stirring to give 1-*p*-methoxyphenyl-1-propyne (**9e**)[8] in 53% yield. These results are listed the Table (see Scheme **C**).

These methods would be applicable to the formation of a variety of carbon-carbon triple bonds.



Scheme **C**

Preparation of α-Methylthioacetophenones (6a–c); General Procedure:

To a solution of the α-bromoacetophenone **5** (25 g) in ether (200 ml) is added a 20% aqueous solution of the sodium salt of methyl mercaptan (1 mol-eq.) at room temperature. The mixture is allowed to stand at room temperature for 14 h under stirring. The solvent is evaporated and the resulting residue is extracted with benzene. The extract is washed with water, dried over sodium sulfate, and evaporated. The residual oil is distilled in vacuo.

Product	Yield	b.p./torr	Molecular formula[a]
6a	18 g (86%)	100–104°/2	$C_9H_{10}OS$ (166.2)
6b	19.5 g (92%)	120–125°/2	$C_{10}H_{12}OS$ (180.2)
6c	19 g (89%)	132–136°/1	$C_{10}H_{12}O_2S$ (196.2)

[a] Satisfactory microanalyses obtained (C ± 0.28%, H ± 0.21%).

Preparation of α-Methylthiopropiophenones (7a, c); General Procedure:

To a stirred solution of the α-methylthioacetophenone **6** (10.0 g, 0.06 mol for **6a**, 0.051 mol for **6c**) in benzene (120 ml) is added methyl iodide (1.2 mol-eq.) in the presence of sodium hydride (50% dispersion in oil is used after washing with petroleum ether). The mixture is stirred for 14 h at room temperature, then washed with water, and dried over sodium sulfate. The solvent is evaporated and the residual oil distilled.

Product	Yield	b.p./torr	Molecular formula[a]
7a	8.0 g (70%)	118–124°/2	$C_{10}H_{12}OS$ (180.2)
7c	7.8 g (73%)	140–145°/2	$C_{11}H_{14}O_2S$ (210.2)

[a] Satisfactory microanalyses obtained (C ± 0.26%, H ± 0.27%).

Preparation of *p*-Toluenesulfonylhydrazones (8a–e); General Procedure:

A mixture of product **6** (5 g), *p*-toluenesulfonylhydrazide (1 mol-eq.), and ethanol (50 ml) is refluxed for 24 h. The solvent is evaporated and the resultant residue is recrystallized from ethanol to give **8a–e**; yield: 80–85% (Table).

Preparation of Phenylalkynes (9a–e); General Procedures:

Method A: To a stirred suspension of **8** (0.1 mol) in ether (50 ml) is added an ethereal solution of methyllithium (prepared from 8.46 g, 0.06 mol of freshly distilled methyl iodide and 700 mg of lithium in ether) at room temperature under stirring. The mixture is allowed to stand under stirring until evolution of nitrogen ceases (about 1 h). After excess methyllithium has been decomposed with water, the mixture is extracted with benzene. The extract is washed with water and dried with sodium sulfate. Evaporation of the solvent leaves the phenylalkyne **9**, which is purified by distillation in vacuo (Table).

Table. Preparation of Tosylhydrazones **8a–e** and Phenylalkynes **9a–f**

Product	R	Ar	Yield [%]	m.p. or b.p./torr	Molecular formula[a] or Lit. m.p. or b.p./torr
8a	H	C_6H_5	83	103–105°	$C_{16}H_{18}N_2O_2S_2$ (334.3)
8b	H	4-H_3C—C_6H_4	82	124–125°	$C_{17}H_{20}N_2O_2S_2$ (348.4)
8c	H	4-H_3CO—C_6H_4	85	101–103°	$C_{17}H_{20}N_2O_3S_2$ (364.4)
8d	CH_3	C_6H_5	80	142–143°	$C_{17}H_{20}N_2O_3S_2$ (348.4)
8e	CH_3	4-H_3CO—C_6H_4	85	95–97°	$C_{18}H_{22}N_2O_3S_2$ (378.4)
9a	H	C_6H_5	97[b]	140–144°/760	142–144°/760[4]
9b	H	4-H_3C—C_6H_4	95[b]	75–77°/30	79–82°/31–35[5]
9c	H	4-H_3CO—C_6H_4	95[b]	85–88°/17	86–87°/16[6]
9d	CH_3	C_6H_5	90[b]	73–75°/20	185°/760[7]
9e	CH_3	4-H_3CO—C_6H_4	93[b], 53[c]	116–118°/20	115–117°/9[8]
9f	CH_3	4-H_3C—C_6H_4	57[c]	70–75°/2	70°/1[9]

[a] All hydrazones gave satisfactory microanalyses (C ±0.28 %, H ±0.11 %).
[b] Method A.
[c] Method B.

Method B: To a stirred suspension of hydrazone **8e** (3.46 g, 0.01 mol) in ether (50 ml) is added an ethereal solution of methyllithium (prepared from 8.46 g, 0.06 mol, of freshly distilled methyl iodide and 700 mg of lithium) at −78°. After 10 min, feshly distilled methyl iodide (1.45 g, 0.01 mol) is added. The mixture is allowed to stand at the same temperature for 30 min under stirring, and then the stirring is continued at room temperature until evolution of nitrogen ceases (about 1 h). Work-up as above affords **9e**; yield: 830 mg (53 %).

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