



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

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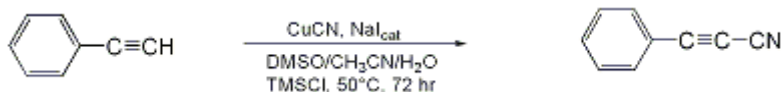
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*September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## PREPARATION OF CYANOALKYNES: 3-PHENYL-2-PROPYNENITRILE

[ 2-Propynenitrile, 3-phenyl- ]



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Checked by Christopher S. Brook, Wenqing Yao, and Amos B. Smith, III.

### 1. Procedure

**3-Phenyl-2-propynenitrile**. A 1-L, two-necked flask, fitted with a 100-mL addition funnel, 2-cm stir bar, and a thermometer, is charged with dimethyl sulfoxide (DMSO) (240 mL), acetonitrile (CH<sub>3</sub>CN) (80 mL), and water (4.3 mL, (Note 1)). To this rapidly stirring solution (Note 2) is added cuprous cyanide (CuCN) (43.0 g, 0.48 mol, (Note 3)), sodium iodide (2.4 g, 0.016 mol), and phenylacetylene (17.6 mL, 0.16 mol, (Note 4)). Chlorotrimethylsilane (TMSCl) (60.6 mL, 0.48 mol, (Note 5)) is added to the reaction mixture dropwise over a 2-hr period, via the addition funnel, and the reaction mixture is heated at 50°C (internal temperature) for 72 hr (Note 6). The mixture is cooled to room temperature, 100 mL of water is added, and it is extracted with ether (5 × 200 mL). The combined organic layers are washed with saturated sodium bicarbonate (500 mL), brine (500 mL), dried over magnesium sulfate, and concentrated (Note 7). The crude residue is dissolved in pentane (100 mL), filtered through a silica plug (50 gm), and the precipitate is washed with pentane (2 × 100 mL). The filtrate is concentrated and reduced pressure distillation (Note 8) yields 9.8 g (48% yield) of 3-phenyl-2-propynenitrile (Note 9) as a yellow solid at room temperature.

### 2. Notes

1. The optimum ratio for DMSO:CH<sub>3</sub>CN is 3:1.
2. Cuprous cyanide must be added slowly to the rapidly stirring solution in order to obtain a fine suspension and avoid clumping.
3. Cuprous cyanide was used as purchased from Aldrich Chemical Company, Inc. Trace amounts of copper(II) may cause dimerization of the phenylacetylene.
4. Phenylacetylene (98%) was used as purchased from Aldrich Chemical Company, Inc.
5. Chlorotrimethylsilane (redistilled, 99+%) was used as purchased from Aldrich Chemical Company, Inc. The optimum ratio for NaI:CuCN:phenylacetylene:TMSCl is 0.1:3:1:3.
6. The reaction was monitored by TLC using Whatman K6F 60 Å silica gel TLC plates; R<sub>f</sub> = 0.55 (hexane:chloroform = 4:1).
7. The checkers found it very important to use low boiling solvents (e.g., ether, pentane) and not to heat the rotary evaporator water bath when removing the solvent. If the bath is heated, a fair amount of the product is observed in the rotary evaporator trap.
8. The product was collected as a dark yellow liquid, bp 140-145°C at 60 mm.
9. The physical properties of 3-phenyl-2-propynenitrile are as follows: mp 37-38°C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.41 (t, 2 H, J = 7.2), 7.53 (t, 1 H, J = 7.6), 7.60 (d, 2 H, J = 7.2); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 62.9, 82.9, 105.3, 117.4, 128.7, 128.8, 131.8, 133.3, 133.4; IR (CHCl<sub>3</sub>) cm<sup>-1</sup>: (C≡N) 2272; HRMS calcd for C<sub>9</sub>H<sub>5</sub>N: 127.0422. Found 127.0417.

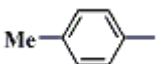
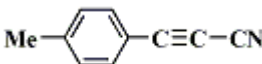
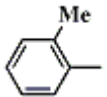
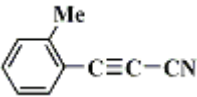
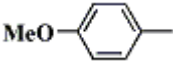
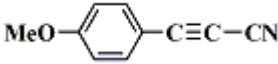
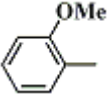
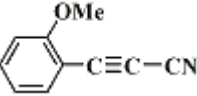
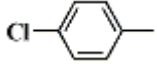
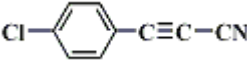
### Waste Disposal Information

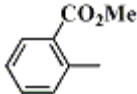
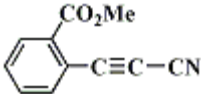
All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

### 3. Discussion

Cyanoalkynes are important in both synthetic and mechanistic studies.<sup>2 3 4 5 6 7</sup> Several synthetic methods have already been developed such as the reaction of metallated acetylides with toxic cyanogen chloride,<sup>8 9 10</sup> pyrolysis of  $\beta$ -ketoalkylidenephosphoranes,<sup>11 12</sup> dehydration of acetylenic carboxamides,<sup>13</sup> or the reaction of acetylenic bromides with cuprous cyanide.<sup>14</sup> The drawback to the last three reactions is that they require preparation of precursors:  $\beta$ -ketoalkylidenephosphoranes, acetylenic carboxamides, and acetylenic bromides, respectively. Recently, the reaction of phenylacetylene with CuCN/bis(trimethylsilyl) peroxide to give cyanoalkynes has been described by Ricci, et al.<sup>15</sup> However, the formation of acetylenic dimer in 30% yield severely limits its applicability to the preparation of other cyanoalkynes. This procedure describes the cyanation of terminal acetylenes with cuprous cyanide in the presence of chlorotrimethylsilane, water, and a catalytic amount of sodium iodide in DMSO/CH<sub>3</sub>CN to provide a general procedure for preparing cyanoalkynes in fair to good yields as shown in Table I. A wide range of terminal acetylenes bearing various kinds of functional groups can undergo this cyanation reaction. The use of DMSO with CH<sub>3</sub>CN as the co-solvent is critically important in this cyanation process. Dimerization can be minimized to less than 4% when the volume ratio of DMSO and CH<sub>3</sub>CN is 3 to 1. While increasing the amount of CH<sub>3</sub>CN in the reaction can further minimize the dimerization, yield of the desired product is sacrificed. When DMSO is used alone as the solvent, the reaction gave the desired and dimerized products in 11% and 22% yields, respectively. Under the same conditions, the use of other solvent systems such as CH<sub>3</sub>CN, THF, THF + HMPA (10%), and benzene led to recovering the starting material after 72 hr at 50°C. The addition of a catalytic amount of sodium iodide (NaI) can facilitate and accelerate the cyanation process.<sup>16</sup> On the other hand, the addition of a stoichiometric amount of NaI in the reaction gave low yields of the desired product along with one unidentified product. In the absence of iodide the desired products were formed in only low yields. For comparison with halide ion as catalyst, various salts were used in the reaction. Most iodide salts such as CuI, ZnI<sub>2</sub>, LiI and KI may also be employed as the catalyst in the cyanation reaction to give comparable results, but only low yields of the desired product were obtained when salts such as NaCl or NaBr were used in the reaction. In the absence of either TMSCl or H<sub>2</sub>O no cyanation reaction occurred.

TABLE I  
CYANOALKYNES VIA IODIDE-CATALYZED CYANATION OF TERMINAL  
ACETYLENES WITH CUPROUS CYANIDE IN THE PRESENCE OF TMSCl  
AND H<sub>2</sub>O IN DMSO/CH<sub>3</sub>CN<sup>17</sup>

Entry	R in RC≡CH	Time (hr)	Product <sup>a</sup>	Isolated Yield (%)
1	Ph	60	Ph-C≡C-CN	58
2		72		76
3		72		72
4		60		84
5		60		78
6		60		51

7		60		74
8	n-C <sub>5</sub> -	72	n-C <sub>5</sub> -C≡C-CN	56
9	n-C <sub>6</sub> -	72	n-C <sub>6</sub> -C≡C-CN	53

<sup>a</sup>All new compounds have been fully characterized by <sup>1</sup>H and <sup>13</sup>C NMR, IR or MS spectroscopy.

## References and Notes

1. Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan, ROC.
2. Ashburn, S. P.; Coates, R. M. *J. Org. Chem.* **1984**, *49*, 3127;
3. Landor, S. R.; Landor, P. D.; Williams, V. E. *J. Chem. Soc., Perkin Trans. I* **1984**, 2677;
4. Landor, S. R.; Landor, P. D.; Fomum, Z. T.; Mbafor, J. T.; Mpango, G. W. B. *Tetrahedron* **1984**, *40*, 2141;
5. Glass, R. S.; Smith, D. L. *J. Org. Chem.* **1974**, *39*, 3712;
6. Westmijze, H.; Kleijn, H.; Vermeer, P. *Tetrahedron Lett.* **1979**, 3327;
7. Westmijze, H.; Kleijn, H.; Vermeer, P. *Synthesis* **1979**, 430.
8. Van der Welle, R. A.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 667;
9. Murray, R. E.; Zweifel, G. *Synthesis* **1980**, 150;
10. Grignard, V.; Perrichon, H. *Ann. Chimie* **1926**, *5*, 5.
11. Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1962**, 2333;
12. Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1964**, 543.
13. Liso, G.; Trapani, G.; Reho, A.; Latrofa, A.; Loidodice, F. *J. Chem. Soc., Perkin Trans. I* **1983**, 567.
14. Brandsma, L. "Preparative Acetylenic Chemistry", 2nd ed.; Elsevier: New York, 1988; p. 288.
15. Casarini, A.; Dembech, P.; Reginato, G.; Ricci, A.; Seconi, G. *Tetrahedron Lett.* **1991**, *32*, 2169.
16. The addition of a catalytic amount of NaI has been shown to facilitate the conversion of alcohols into nitriles: Davis, R.; Untch, K. G. *J. Org. Chem.* **1981**, *46*, 2985.
17. Luo, F.-T.; Wang, R.-T. *Tetrahedron Lett.* **1993**, *34*, 5911.

## Appendix

### Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

3-Phenyl-2-propynenitrile:  
Propiolonitrile, phenyl- (8);  
2-Propynenitrile, 3-phenyl- (9); (935-02-4)

Dimethyl sulfoxide:  
Methyl sulfoxide (8);  
Methane, sulfinylbis- (9); (67-68-5)

Acetonitrile TOXIC (8,9); (75-05-8)

Cuprous cyanide:  
Copper cyanide (8,9); (544-92-3)

Phenylacetylene:

Benzene, ethynyl- (8,9); (536-74-3)

Chlorotrimethylsilane:  
Silane, chlorotrimethyl- (8,9); (75-77-4)