

Ju-Yeon Lee and H. K. Hall, Jr.*

C. S. Marvel Laboratories, Department of Chemistry, University of Arizona,
Tucson, AZ 85721

Received April 23, 1990

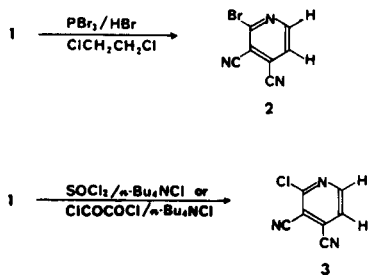
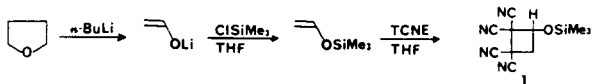
2-Bromo-3,4-dicyanopyridine **2** was obtained in moderate yield by reacting 1,1,2,2-tetracyano-3-trimethylsilyloxycyclobutane **1** with phosphorus tribromide. Similarly, reaction of **1** with chlorinating reagents such as thionyl chloride and oxalyl chloride led to the corresponding 2-chloro-3,4-dicyanopyridine **3** in 40% yield. A reaction mechanism is suggested.

J. Heterocyclic Chem., **27**, 1653 (1990).

In the course of our study of the synthesis of multi-cyanocyclopropanes [1,2], we found a facile synthetic route to 2-halo-3,4-dicyanopyridines.

1,1,2,2-Tetracyano-3-trimethylsilyloxycyclobutane **1** was prepared by [2 + 2] cycloaddition reaction of tetracyanoethylene and trimethylsilyl vinyl ether [3]. The latter was available according to a literature procedure from acetaldehyde lithium enolate [5] and chlorotrimethylsilane (Scheme 1). The reaction of **1** with phosphorus tribromide gave none of the expected 3-bromo-1,1,2,2-tetracyanocyclobutane, even though there is a literature report describing the synthesis of 1-bromo-1-ethoxycyclopropane from reaction of 1-ethoxy-1-trimethylsilyloxycyclopropane with phosphorus tribromide [6]. Instead, 2-bromo-3,4-dicyanopyridine **2** was obtained in the reaction of **1** with phosphorus tribromide in 45% yield, (Scheme 1). Similarly, the reaction of 1,1,2,2-tetracyano-3-trimethylsilyloxycyclobutane (**1**) with chlorinating reagents, such as thionyl chloride and oxalyl chloride, led to the corresponding 2-chloro-3,4-dicyanopyridine (**3**) in 40% yield.

Scheme 1

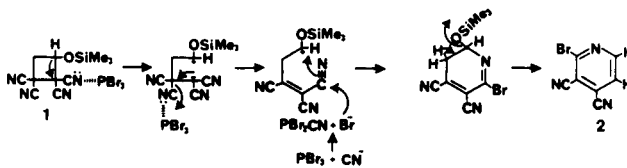


The chemical structure of **2** and **3** was assigned on the basis of their ir, ¹H-nmr, ¹³C-nmr, and elemental analyses data. The ¹H-nmr spectra of compound **2** and **3** show only two doublets in aromatic region. The ir spectra confirmed the chemical structure, exhibiting all the absorption bands

corresponding to the functional groups in the products. The ¹³C-nmr spectra showed five different pyridine ring carbon signals in the range of 112-155 ppm. Pyridine derivatives **2** and **3** are soluble in common solvents such as chloroform and acetone. They are weak bases and soluble in dilute aqueous hydrochloric acid. They were purified by sublimation and their melting points are 100-101° and 96-97°, respectively.

The proposed mechanism, depicted in Scheme 2, involves ring-opening of cyclobutane **1** to form a tetramethylene zwitterion under the influence of the Lewis acid phosphorus tribromide. Elimination of a β-cyano group is facilitated by complexation with phosphorus tribromide. Analogous reactions have been described previously, for example for β,β-dicyanovinyl chloride [7]. Attack of bromide anion on a nitrile function allows ring-closure and aromatization by expulsion of trimethylsilanol.

Scheme 2



EXPERIMENTAL

General.

Tetracyanoethylene was purified by two successive recrystallizations from chlorobenzene and sublimations (125°, 0.4 mm Hg). Chlorotrimethylsilane was distilled under nitrogen, collecting the middle fraction, followed by drying over 4 Å molecular sieves. Tetrahydrofuran was dried over 4 Å molecular sieves activated by heating to 220° for 20 hours under vacuum. Tetra-*n*-butylammonium chloride was recrystallized from acetone in a drybox. The ir spectra were taken on a Perkin-Elmer 983 spectrometer. The ¹H-nmr and ¹³C-nmr spectra were obtained on a Bruker WM 250 nuclear magnetic resonance spectrometer at 250 MHz. Elemental analyses were performed by Desert Analytics, Tucson, AZ. Melting points were measured in a Thomas-Hoover melting point apparatus.

Lithium enolate of acetaldehyde was prepared according to the literature [5].

Trimethylsilyl vinyl ether was prepared according to a literature procedure [4] from the lithium enolate of acetaldehyde and chlorotrimethylsilane. Dry tetrahydrofuran (50 ml, 0.61 mole) was placed in a dry three-neck, round-bottomed flask under nitrogen. *n*-Butyllithium in *n*-hexane solution (2.5*M*, 32.4 ml, 0.08 mole) was added using a syringe. After 3 hours stirring at room temperature under nitrogen, 40 ml of the solvent was distilled off under vacuum. Dry diethyl ether (70 ml) was added to the resulting concentrated lithium enolate of acetaldehyde solution. Chlorotrimethylsilane (8.0 g, 0.074 mole) was added dropwise at 0° during 20 minutes. After a further 2 hours stirring at room temperature, the diethyl ether was evaporated. Two successive fractional distillations with a Vigreux column gave a 40% solution of trimethylsilyl vinyl ether in tetrahydrofuran (24.0 g, 53% yield), pp 67-71° (760 mm Hg) (lit [1] 71-73°); ¹H-nmr (deuteriochloroform): δ 0.13 (s, 9H), 4.08 (d, 1H), 4.39 (d, 1H), 6.29-6.36 (q, 1H).

1,1,2,2-Tetracyano-3-trimethylsiloxycyclobutane (1).

To a solution of 0.43 g (3.3 mmoles) of tetracyanoethylene (TCNE) in 4 ml of tetrahydrofuran was added a solution of 0.58 g (5.0 mmoles) of trimethylsilyl vinyl ether in 3 ml of tetrahydrofuran under nitrogen. The reaction mixture was stirred for 5 hours at room temperature. Excess trimethylsilyl vinyl ether and tetrahydrofuran solvent were evaporated by rotary evaporator. The last traces were removed under high vacuum and pure product obtained, yield, 0.78 g (96%); ir (potassium bromide): 2962 (C-H), 2253 (C≡N), 1255, 847, 754 (all TMS) cm⁻¹; ¹H-nmr (deuteriochloroform): δ 0.28 (s, 9H), 3.06-3.15 (q, 1H), 3.29-3.37 (q, 1H), 4.90-4.97 (q, 1H).

Anal. Calcd. for C₁₁H₁₂N₄O₂Si: C, 54.08; H, 4.92; N, 22.94. Found: C, 53.99; H, 4.94; N, 22.86.

2-Bromo-3,4-dicyanopyridine (2).

A 50 ml round-bottomed flask equipped with a magnetic stirring bar is charged with 2.44 g (10 mmoles) of 1,1,2,2-tetracyano-3-trimethylsiloxycyclobutane and 10 ml of 1,2-dichloroethane under nitrogen. The solution was stirred for 20 minutes at room temperature. Phosphorus tribromide (2.12 g, 7.84 mmoles) was added with brisk stirring, followed by a catalytic amount of 48% aqueous hydrobromic acid. The resulting solution was stirred for 5 hours at room temperature. The brown precipitate was filtered off and rinsed with 10 ml of 1,2-dichloroethane. The filtrate was chilled to -20° in a dry ice-ethanol-water bath and 15 ml of saturated, aqueous sodium carbonate solution was added slowly. The resulting solution was carefully shaken and separated. The aqueous phase was extracted with 10 ml of 1,2-dichloroethane. The organic layer was dried over anhydrous magnesium sulfate, filtered and solvent was removed by rotary evaporator. The crude product was purified by column chromatography (Silica gel, 70-270 mesh, 60 Å, ethyl acetate/*n*-hexane: 50/50, v/v) and sublimation (90°, 0.3 mm Hg), yield = 0.94 g (45%), mp =

100-101°; ir (potassium bromide): 3067 (aromatic C-H), 2245 (C≡N), 1561, 1534, 1443 (all C=C and C=N), 840 (C-Br) cm⁻¹; ¹H-nmr (deuteriochloroform): δ 7.64-7.66 (d, 1H), 8.78-8.79 (d, 1H); ¹³C-nmr (deuteriochloroform): δ 113.1 (s, C≡N), 113.5 (s, C≡N), (s, C-3), 124.8 (s, C-4), 126.6 (s, C-5), 145.6 (s, C-2), 153.8 (s, C-6).

Anal. Calcd. for C₇H₂BrN₃: C, 40.40; H, 0.96; Br, 38.43; N, 20.20. Found: C, 40.39; H, 0.92; Br, 38.50; N, 20.25.

2-Chloro-3,4-dicyanopyridine (3).

1,1,2,2-Tetracyano-3-trimethyl-siloxycyclobutane (2.44 g, 10 mmoles) was added to freshly distilled thionyl chloride (11.88 g, 0.1 mole) under nitrogen. A catalytic amount of tetra-*n*-butylammonium chloride was added under nitrogen atmosphere. The reaction mixture was gently refluxed for 2 hours. Excess thionyl chloride was distilled off and the residue was dissolved in 30 ml of 1,2-dichloroethane. The resulting solution was chilled to -20° in dry ice-ethanol-water bath and saturated, aqueous sodium carbonate solution (20 ml) was added carefully with stirring. The aqueous phase was extracted with 15 ml of 1,2-dichloroethane. The organic layer was washed with 15 ml of water and separated. The organic layer was dried over anhydrous potassium carbonate and concentrated by rotary evaporator. The crude product was purified by column chromatography and sublimation (88°C, 0.3 mm Hg) to give white crystals, yield = 0.71 g (40%), mp 96°; ir (potassium bromide): 3084 (aromatic C-H), 2246 (C≡N), 1571, 1548, 1454 (all C=C and C=N), 858 (C-Cl) cm⁻¹; ¹H-nmr (deuteriochloroform): δ 7.67-7.69 (d, 1H), 8.80-8.83 (d, 1H); ¹³C-nmr (deuteriochloroform): δ 111.7 (s, C≡N), 112.2 (s, C≡N), 112.7 (s, C-3), 124.4 (s, C-4), 126.4 (s, C-5), 153.3 (s, C-2), 154.2 (s, C-6).

Anal. Calcd. for C₇H₂ClN₃: C, 47.34; H, 1.13; Cl, 19.98; N, 23.67. Found: C, 47.27; H, 1.10; Cl, 19.89; N, 23.76.

Acknowledgment.

We are deeply indebted to the Office of Naval Research for partial financial support of this work and to Dr. Anne Padias for helpful discussions.

REFERENCES AND NOTES

- [1] J. Y. Lee and H. K. Hall, Jr., *Macromolecules* (submitted).
- [2] A. B. Padias and H. K. Hall, Jr., (in preparation).
- [3] H. K. Hall, Jr. and P. Ykman, *J. Am. Chem. Soc.*, **97**, 800 (1975).
- [4] Y. Kawakami, T. Aoki, and Y. Yamashita, *Polym. Bull.*, **18**, 473 (1987).
- [5] R. B. Bates, L. M. Kroposki and D. E. Potter, *J. Org. Chem.*, **37**, 560 (1972).
- [6] R. C. Gadwood, *Tetrahedron Letters*, **25**, 5851 (1984).
- [7] H. K. Hall, Jr. and H. A. A. Rasoul, in *Contemporary Topics of Polymer Science*, Vol 4, W. J. Bailey and T. Tsuruta, eds, Plenum, 1984, p 295.