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**Abstract:**

2-Bromo-3,4-dicyanopyridine 2 was obtained in moderate yield by reacting 1,1,2,2-tetracyano-3-trimethylsiloxyoctane 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.
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Abstract

2-Bromo-3,4-dicyanopyridine 2 was obtained in moderate yield by reacting 1,1,2,2-tetracyano-3-trimethylsiloxy-cyclobutane 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.
In the course of our study of the synthesis of multicyanocyclopropanes,\textsuperscript{1,2} we found a facile synthetic route to 2-halo-3,4-dicyanopyridines.

1,1,2,2-Tetracyano-3-trimethylsiloxycyclobutane \(1\) was prepared by \(2+2\) cycloaddition reaction of tetracyanoethylene and trimethylsilyl vinyl ether.\textsuperscript{3} The latter was available according to a literature procedure from lithium enolate\textsuperscript{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-trimethylsiloxycyclopropane with phosphorus tribromide.\textsuperscript{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-trimethylsiloxycyclobutane \(1\) with chlorinating reagents, such as thionyl chloride and oxalyl chloride, led to the corresponding 2-chloro-3,4-dicyanopyridine \(3\) in 40\% yield.

The chemical structure of \(2\) and \(3\) was assigned on the basis of their IR, \(^1\text{H}-\text{NMR}, \quad ^{13}\text{C}-\text{NMR}, \quad \text{and elemental analyses data. The } \quad ^1\text{H}-\text{NMR spectra of compound } 2 \quad \text{and } 3 \text{ show only two doublets in aromatic region. The IR spectra confirmed the}\) chemical structure, exhibiting all the absorption bands corresponding to the functional groups in the products. The \(^{13}\text{C}-\text{NMR spectra showed a five different}\) 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*C and 96*-97*C, 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 PBr₃. Elimination of a β-cyano group is facilitated by complexation with PBr₃. Analogous reactions have been described previously, for example for 3,3-dicyanovinyl chloride⁷. Attack of bromide anion on a nitrile function allows ring-closure and aromatization by expulsion of trimethylsilanol.

Experimental Section

General. Tetracyanoethylene was purified by two successive recrystallizations from chlorobenzene and sublimations (125°C, 0.4 mmHg). Chlorotrimethylsilane was distilled under nitrogen, collecting the middle fraction, followed by drying over 4Å molecular sieves. Tetrahydrofuran was dried over 4Å molecular sieves activated by heating to 220°C for 20 hr under vacuum. Tetra-n-butylammonium chloride was recrystallized from acetone in a drybox. IR spectra were taken on a Perkin-Elmer 983 spectrometer. 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.

Trimethylsilyl vinyl ether was prepared according to a literature procedure⁴ from the lithium enolate of acetaldehyde and chlorotrimethylsilane. Dry tetrahydrofuran (50 ml, 0.61 mol) was placed in a dry three-neck, round-bottomed flask under nitrogen. n-Butyllithium in n-hexane solution (2.5M, 32.4 ml, 0.08 mol) was added using a syringe. After 3 hr 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 mol) was added dropwise at 0°C during 20 min. After a further 2 hr stirring at room tem-
perature, the diethyl ether was evaporated. Two successive fractional distillation with a Vigreux column gave a 40% solution of trimethylsilyl vinyl ether in tetrahydrofuran (24.0 g, 53% yield). Bp 67-71°C (760 mmHg) (lit. 71-73°C).

H-NMR (CDCl$_3$) 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-trimethylsiloxy cyclobutane (1). To a solution of 0.43 g (3.3 mmol) of tetracyanoethylene (TCNE) in 4 ml of tetrahydrofuran was added a solution of 0.58 g (5.0 mmol) of trimethylsilyl vinyl ether in 3 ml of tetrahydrofuran under nitrogen. The reaction mixture was stirred for 5 hr 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 (KBr) 2962 (C-H), 2253 (C-N), 1255, 847, 754 (all Me$_3$Si) cm$^{-1}$; $^1$H NMR (CDCl$_3$) 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 C$_{13}$H$_{12}$N$_4$OSi: 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 mmol) of 1,1,2,2-tetracyano-3-trimethylsiloxy cyclobutane and 10 ml of 1,2-dichloroethane under nitrogen. The solution was stirred for 20 min at room temperature. Phosphorus tribromide (2.12 g, 7.84 mmol) was added with brisk stirring, followed by a catalytic amount of 48% aqueous hydrobromic acid. The resulting solution was stirred for 5 hr at room temperature. The brown precipitate was filtered off and rinsed with 10 ml of 1,2-dichloroethane. The filtrate was chilled to -20°C 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, 60Å, ethyl acetate/n-hexane: 50/50, v/v) and sublimation (90°C, 0.3 mmHg). Yield = 0.94 g (45%). Mp = 100°-101°C. IR (KBr) 3067 (aromatic C-H), 2245 (C=N), 1561, 1534, 1443 (all C-C and C-N), 840 (C-Br) cm⁻¹; ¹H-NMR (CDCl₃) δ 7.64-7.66 (d, 1H), 8.78-8.79 (d, 1H); ¹³C-NMR (CDCl₃) 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-trimethylsiloxycyclobutane (2.44 g, 10 mmol) was added to freshly distilled thionyl chloride (11.88 g, 0.1 mol) under nitrogen. A catalytic amount of tetra-n-butylammonium chloride was added under nitrogen atmosphere. The reaction mixture was gently refluxed for 2 hr. 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°C 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 mmHg) to give white crystals. Yield = 0.71 g (40%). Mp 96°C. IR (KBr) 3084 (aromatic C-H), 2246 (C=N), 1571, 1548, 1454 (all C=C and C=N), 858 (C-Cl) cm⁻¹; ¹H-NMR (CDCl₃) δ 7.67-7.69 (d, 1H), 8.80-8.83 (d, 1H); ¹³C-NMR (CDCl₃) 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.
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References

Scheme 1
Scheme 2