

DEUTERATION OF CYCLOALKYNES

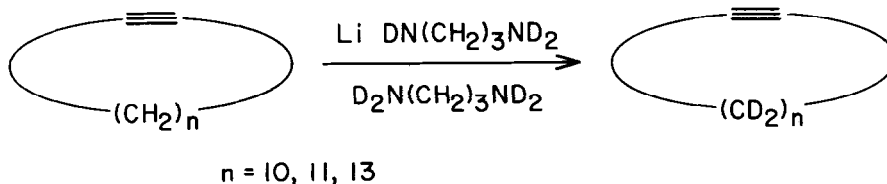
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Abstract: When treated with the lithium salt of 1,3-diaminopropane, triple bonds in cyclic alkynes undergo multiple degenerate rearrangements. By employing the N,N,N',N'-d₄ reagent, the course of the isomerization is followed as the triple bond circumnavigates the ring. Cycloalkynes are readily perdeuterated with this novel methodology.

As part of our program on synthetic methodology employing acetylenes, we have been interested in base mediated rearrangement of triple bonds as a means of preparing terminal alkynes that can be employed as intermediates in syntheses of long chain compounds such as insect sex pheromones and fatty acids¹. We have recently reported² a procedure that is an improvement over that originally described by Brown and Yamashita³. Addition of potassium t-butoxide to the lithium salt of 1,3-diaminopropane in 1,3-diaminopropane affords a reagent which cleanly isomerizes triple bonds along a long methylene chain to the free terminus. Yields are high, and preparations can safely be carried out on large scale. Substitution of the solvent by its N,N,N',N'-d₄ analog affords a reagent that can be used to deuterate methylene chains⁴.

We now report that multiple isomerizations of a triple bond in cyclic alkynes are effected with our reagents, and that perdeuterated cycloalkynes are readily prepared with this methodology.



Our studies⁵ have concentrated on the readily available 12, 13 and 15 carbon cyclic acetylenes⁶. Cyclododecyne is reversibly isomerized at 0°C by the relatively mild isomerization reagent, the lithium salt of 1,3-diaminopropane, to the allene. At equilibrium, the ratio of allene to acetylene is 2 to 3. Employing more vigorous conditions, either higher temperature or stronger base such as the sodium salt, results in the formation of 1,3-dienes. Cyclotridecyne and cyclopentadecyne can be recovered after rearrangement with the lithium salt at ambient temperature in about 40% yield. In these cases no allenes are observed.

Cyclooctyne is unstable under the reaction conditions.

By using the lithium salt of 1,3-diaminopropane-N,N,N',N'-d₄⁴ the multiple isomerizations are no longer degenerate, and the course of the migration around the ring can be followed. After 2 hours the triple bond of the 15 membered carbocycle has circumnavigated the entire ring, and cyclopentadecyne has incorporated an average of 24 deuterons into the possible 26 positions⁷. In preparative scale reactions, cyclopentadecyne and cyclotridecyne are both deuterated to the extent of 94% in one isomerization reaction, and to greater than 98% on resubjection to the deuterated reagent⁸. In the twelve membered ring both the allene and acetylene are equally deuterated to the extent of 90% on the first reaction and 95% on the second rearrangement. Isolated yields of labelled compounds are in the range of 40-60%. The cyclic systems are effectively perdeuterated after only two treatments.

Standard techniques for deuteration of long chain compounds give fully reduced products⁹. This new procedure preserves the triple bond so that it can be employed for further manipulations.

References

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2. S.R. Abrams, *Can. J. Chem.* **62** (1984) 1333.
3. C.A. Brown, A. Yamashita, *J. Am. Chem. Soc.* **97** (1975) 891.
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5. Previous studies of base mediated rearrangements of allenes and acetylenes in cyclic systems have been reported by a) W.R. Moore, H.R. Ward, *J. Am. Chem. Soc.* **85** (1963) 86; b) R. Vaidyanathaswamy, D. Devaprabhakara, *Ind. J. Chem.* **44** (1966) 1021; c) W. Ziegenbein, W.M. Schneider, *Chem. Ber.* **98** (1968) 824.
6. The cyclic acetylenes were prepared by the method of E.V. Dehmlow, M. Lissel, *Ann.* (1980) 1. 1) Cyclododecyne, obtained from cyclododecene, gave a molecular ion in the MS (25 eV) 164(8.62), 165(1.01); V. Prelog, M. Speck, *Helv. Chim. Acta* **38** (1955) 1786; 2) cyclotridecyne, obtained from cyclotridecanone, gave a molecular ion in the MS (30 eV) 178(8.52), 179(1.18); H. Nozaki, S. Kato, R. Noyori, *Can. J. Chem.* **44** (1966) 1021; and 3) cyclopentadecyne obtained from cyclopentadecanone, gave a molecular ion in the MS (40 eV) 206(2.81), 207(0.44); J. Schreiber, D. Felix, A. Eschenmoser, M. Winter, F. Gautschi, K.H. Schulte-Elte, A. Sundt, G. Ohloff, J. Kalvoda, H. Kaufmann, P. Wieland, G. Anner, *Helv. Chim. Acta* **50** (1967) 2101.
7. The isomerization was performed using 12 equivalents of the deuterated reagent at ambient temperature.
8. For the preparative reactions, 1,3-diaminopropane-N,N,N',N'-d₄ (min. 97% D) obtained from Merck, Sharpe and Dohme Isotopes was employed. The cyclic acetylenes (0.50 mmol) were isomerized using 12 equivalents of the lithium salt in 5.0 mL of the deuterated solvent for 4.0 h, at RT for the cyclotridecyne and cyclopentadecyne, and at 0°C for cyclododecyne. The reactions were worked up with D₂O and chromatographed. Cyclododecyne afforded deuterated 1,2-cyclododecadiene (15%, MS 25 eV, 180(0.47), 181(1.06), 182(2.26), 183(2.84), and 184(1.72)) 90.5% D and deuterated cyclododecyne (53%, MS 25 eV, 180(0.35), 181(0.67), 182(1.21), 183(1.49), and 184(0.83)) 91.8% D. Cyclotridecyne gave deuterated cyclotridecyne (41%, MS 30 eV, 196(0.20), 197(0.71), 198(1.72), 199(2.78), 200(2.19), 201(0.26)) 93.8% D. Cyclopentadecyne afforded deuterated cyclopentadecyne (57%, MS 40 eV, 228(0.86), 229(2.17), 230(3.80), 231(4.16), 232(2.38) and 233(0.23)) 93.0% D. Resubmission of the deuterated cyclic acetylenes to the procedure afforded deuterated cyclododecyne (MS 25 eV, 181(0.44), 182(1.33), 183(2.52), 184(2.69), and 185(0.25)) 94.8% D; and deuterated 1,2-cyclododecadiene (MS 25 eV, 181(0.99), 182(4.91), 183(12.28), 184(17.02), and 185(1.86)) 96.2% D; deuterated cyclotridecyne (MS 30 eV, 197(0.13), 198(0.61), 199(1.83), 200(5.25), and 201(0.69)) 97.8% D; and deuterated cyclopentadecyne (MS 40 eV, 229(0.14), 230(0.95), 231(3.50), 232(6.39), and 233(0.93)) 97.9% D.
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