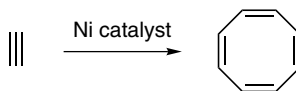


Reppe Cyclization

A. GENERAL DESCRIPTION OF THE REACTION

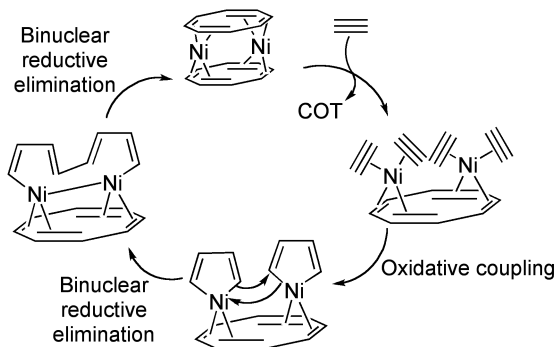
This reaction was first reported by Reppe in 1948.¹ It is a nickel complex-catalyzed $[2+2+2+2]$ cyclotetramerization of acetylene to cyclooctatetraene (COT), and is generally known as the Reppe cyclization.² Occasionally, it is also referred to as the Reppe reaction,³ Reppe synthesis,⁴ or Reppe cyclooctatetraene synthesis.⁵ The nickel catalysts used for this reaction include $\text{Ni}(\text{acac})_2$,⁶ $\text{Ni}_2(\text{COT})_2$,⁷ 1,2-diaza diene nickel complex ($\text{Ni}(\text{dad})_2$)⁸ and even vapor-deposited nickel.⁹ This reaction is the showcase of efficiency for organometallic complex-catalyzed reactions. For example, cyclooctatetraene was synthesized from pseudopelletierine by a 13-step manipulation in 1901 in very low yield,¹⁰ whereas up to 90% yield of cyclooctatetraene can be obtained by pressurizing acetylene into a warm suspension of $\text{Ni}(\text{CN})_2$ and CaC_2 in THF,^{1a,11} or $\text{NiBr}_2/\text{CaC}_2$.^{6a} In addition, it is known that the turnover number can be as high as up to 10^6 in neat propargylic alcohol, regardless of the catalyst.¹² Although it has been reported that nickel catalyst does not work for disubstituted alkynes,¹³ in a few cases, disubstituted alkynes form octa-substituted cyclooctatetraenes, as evidenced in the reaction of 1-methyl-2-phenyl-acetylene on nickel prepared by vapor deposition⁹ and cobalt complex-catalyzed cyclization of acetylenedicarboxylic acid ester.¹⁴ In general, this reaction does not hold regioselectivity,^{13c} and 1,2,4,7-tetrasubstituted cyclooctatetraene and 1,2,4,6- and 1,3,5,7-tetrasubstituted cyclooctatetraenes are often produced from monosubstituted acetylenes.^{13c} Other types of substituted cyclooctatetraenes can be produced by application of monosubstituted or disubstituted acetylene with 3 equivalents of acetylene.¹⁵ Often, this reaction is accompanied with side reactions yielding benzene derivatives.^{15d,16}

B. GENERAL REACTION SCHEME



C. PROPOSED MECHANISMS

This reaction is believed to involve a number of complex processes,¹⁷ by which four alkynes coordinate to a metal center to undergo either a stepwise coupling or a concerted “zipper-type” cyclization.^{2d,13c} However, the $\text{Ni}_2(\text{COT})_2$ -catalyzed reaction involves the formation of a bis(cyclopentadienylnickel) complex,⁷ a homobimetallic center,^{2c} as supported by the actual determination of the structure from X-ray crystallography;⁷ by the fast initiation of the reaction without an induction period when used directly for alkynes compared to other types of catalysts,¹⁸ and by kinetic studies and labeling experiments.^{2d,3,5} An illustrative mechanism catalyzed by $\text{Ni}_2(\text{COT})_2$ is given here.



D. MODIFICATION

This reaction has been modified by use of the sterically hindered 1,2-diaza diene nickel complex, $\text{Ni}(\text{dad})_2$ as catalyst to improve the regioselectivity. Under these conditions, primary propargylic alcohol is converted to 1,3,5,7-tetrasubstituted COT,⁸ whereas secondary propargylic alcohol and propargylic esters are transformed into 1,3,6,8-tetrasubstituted COTs,¹⁹ and propargylic ether is converted into 1,4,5,8-tetrasubstituted COT.²⁰ In addition, the ruthenium catalyst $[(\text{Ph}_3\text{P})_3\text{Ru}(\text{CO})\text{H}_2]$ has also been used successfully to convert diphenylbutadiyne into cyclooctatetraene.²¹ It should be mentioned that a combination of Lewis acid and base (e.g., AlBr_3 and Et_3N) has also been developed to transform terminal acetylenes into 1,3,5,7- and 1,2,5,6-tetrasubstituted *syn*-tricyclo[4.2.0.0^{2,5}]octadienes which rearrange into 1,3,5,7- and 1,2,5,6-tetrasubstituted cyclooctatetraene through thermal or photochemical ring opening.^{6b}

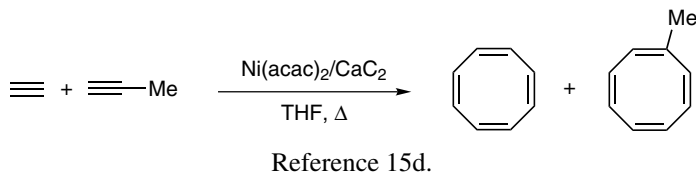
E. APPLICATIONS

This reaction has general application in the preparation of cyclooctatetraene derivatives.

F. RELATED REACTIONS

This reaction is closely related to the *Reppe Alkyne Cyclotrimerization*.

G. CITED EXPERIMENTAL EXAMPLES



To a 1-L stainless-steel autoclave cooled with dry ice and trichloroethylene were added 10 g nickel acetylacetonate, 20 g powdered calcium carbide, and 30 g propyne dissolved in 250 mL THF also cooled with dry ice and trichloroethylene. The system was sealed, and the air was evacuated and replaced by acetylene to a pressure of 150–300 psi. The mixture was stirred and heated at 70–90°C for 7–12 hours while the acetylene was maintained at same pressure by represurizing acetylene at frequent intervals. After that, the mixture was steam distilled until 2 L of distillate was collected to separate volatile material (e.g., THF, benzene, substituted benzene, and cyclooctatetraene) from a water-insoluble residue (largely cuprene from polymerization of alkyne). The water-insoluble portion of the residue was separated by filtration, and extracted in a Soxhlet apparatus for 24 h with benzene containing a small amount of hydroquinone as a polymerization inhibitor. The benzene extract was concentrated and distilled, and the crude distillate was combined with the residue obtained by fractionation of the organic portion of the steam distillate (after the benzene, and cyclooctatetraene present had been removed as low-boiling fractions). This process yielded 40 g cyclooctatetraene and 14.1 g methylcyclooctatetraene (16%). Methylcyclooctatetraene was further purified by conversion into the crystalline silver nitrate complex and regeneration by shaking with a 100% excess of concentrated NH_4OH , extraction with pentane and redistillation, b.p. 84.5°C at 67 mmHg.

Other references related to the Reppe cyclization are cited in the literature.²²

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