



Scheme 12.1 Bohlmann's dimeric copper acetylides in the Glaser coupling reaction.

12.2 COPPER-CATALYZED SYNTHESIS OF SYMMETRICAL AND UNSYMMETRICAL 1,3-DIYNES

The homo- and heterocoupling **reactions** of alkynes is the most efficient and direct route to symmetrical and unsymmetrical 1,3-diynes. The oxidative homocoupling of terminal alkynes is an efficient reaction allowing the synthesis of symmetrical 1,3-diynes, and the first example of such type of coupling reaction was reported by Glaser in 1869 with the use of cuprous chloride as catalyst and aqueous ammonia as the base under an oxygen atmosphere.^[5] A very stimulating historical perspective on this venerable reaction, including a discussion on the different mechanisms, can be found in a 2000 review by Diederich and coworkers.^[1a] Although several mechanisms have been proposed, the most currently accepted one has been reported by Bohlmann and coworkers in 1964 and relies on dimeric copper acetylides as intermediates in the oxidative acetylenic coupling (Scheme 12.1).^[6]

A similar catalytic system for the oxidative homocoupling of terminal alkynes was reported by Hay in 1960 with the use of an atmosphere of oxygen and CuCl·TMEDA (tetramethylethylenediamine [TMEDA]) as the catalyst, which is soluble in a range of organic solvents, resulting in a much more practical coupling reaction (Scheme 12.2, Eq. 1).^[7] Recent density functional theory (DFT) calculations have demonstrated that a bimetallic process relying on copper(I), (II), and (III) oxidation states was operating (Scheme 12.2, Eq.