

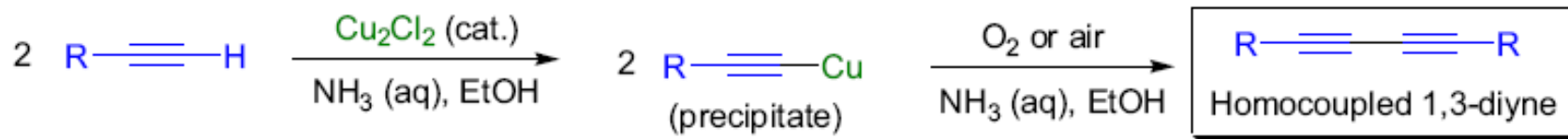
GLASER COUPLING

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Definition

The oldest alkyne coupling reaction

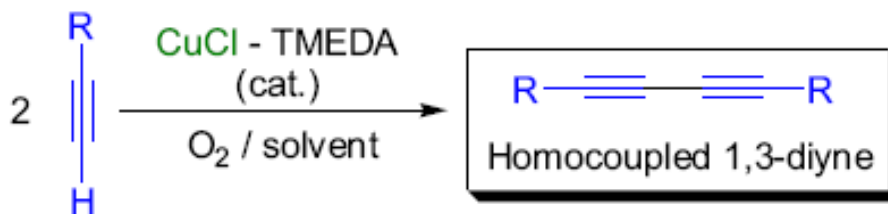


The preparation of symmetrical conjugated diynes and polyynes (linear or cyclic) by the oxidative homocoupling of terminal alkynes in the presence of copper salts is known as the *Glaser coupling*.

Numerous Versions

- Besides oxygen and air, CuCl_2 and $\text{K}_3\text{Fe}(\text{CN})_6$ are used most often as oxidizing agents.

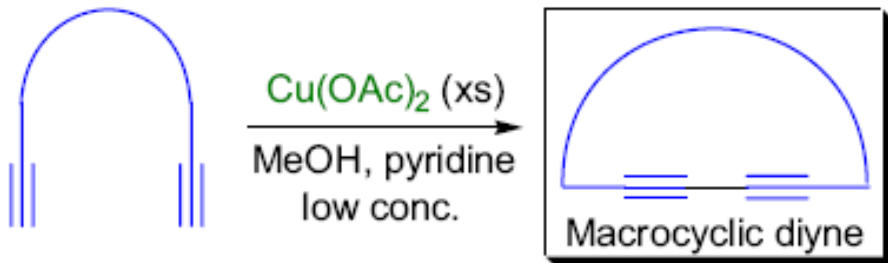
Hay's conditions:



- Glaser: heterogeneous and Galbraith: using $\text{Cu}(\text{OAc})_2$ homogeneous and fast synthesis of macrocyclic

- A.S. Hay: tertiary amines such as pyridine or the bidentate ligand TMEDA solubilize the $\text{Cu}(\text{I})$ -salt. through this solution to in a few minutes at room quantitative yield (Hay coupling conditions)

Eglinton procedure:

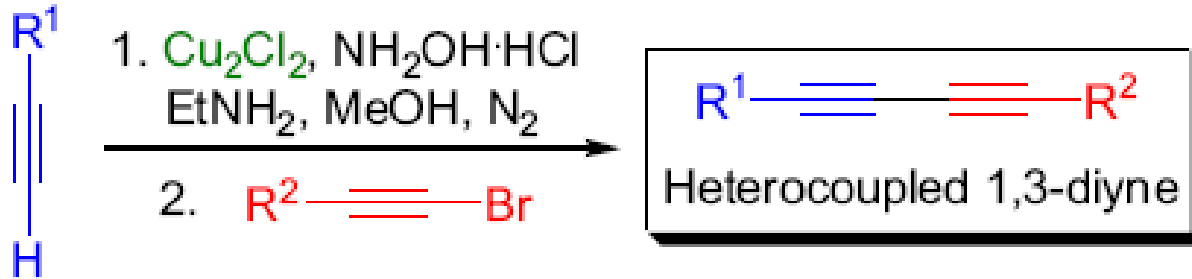


General Features

- It works well for acidic terminal alkynes, but the yield tends to drop when the alkyne is less acidic (e.g., alkyl- or silicon-substituted terminal alkynes);
- The reaction rate is often increased when a small amount of DBU, which most likely serves as a strong base to deprotonate the alkyne, is added to the reaction mixture;
- The reaction conditions tolerate a wide range of functional groups as the oxidation is mostly restricted to the triple bond;
- If the reactants or the product is oxygen sensitive, side reactions can be minimized by either running the reaction for shorter periods of time or applying an inert atmosphere and using large amounts of the Cu(II)-salt;

General Features

- The Chodkiewitz-Cadiot heterocoupling:



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DME

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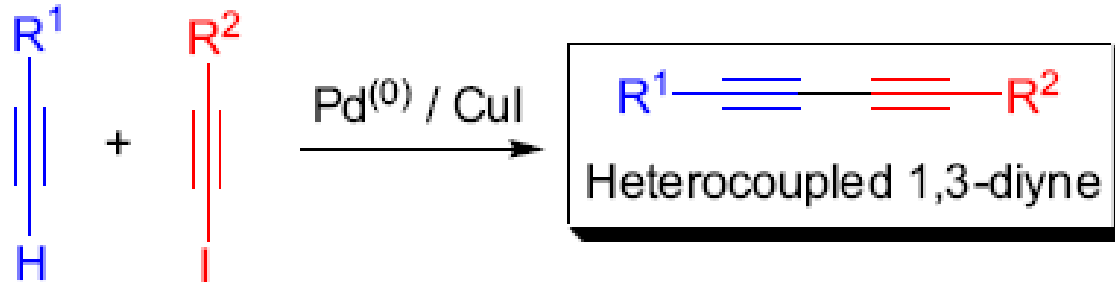
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Pd-catalyzed heterocoupling:

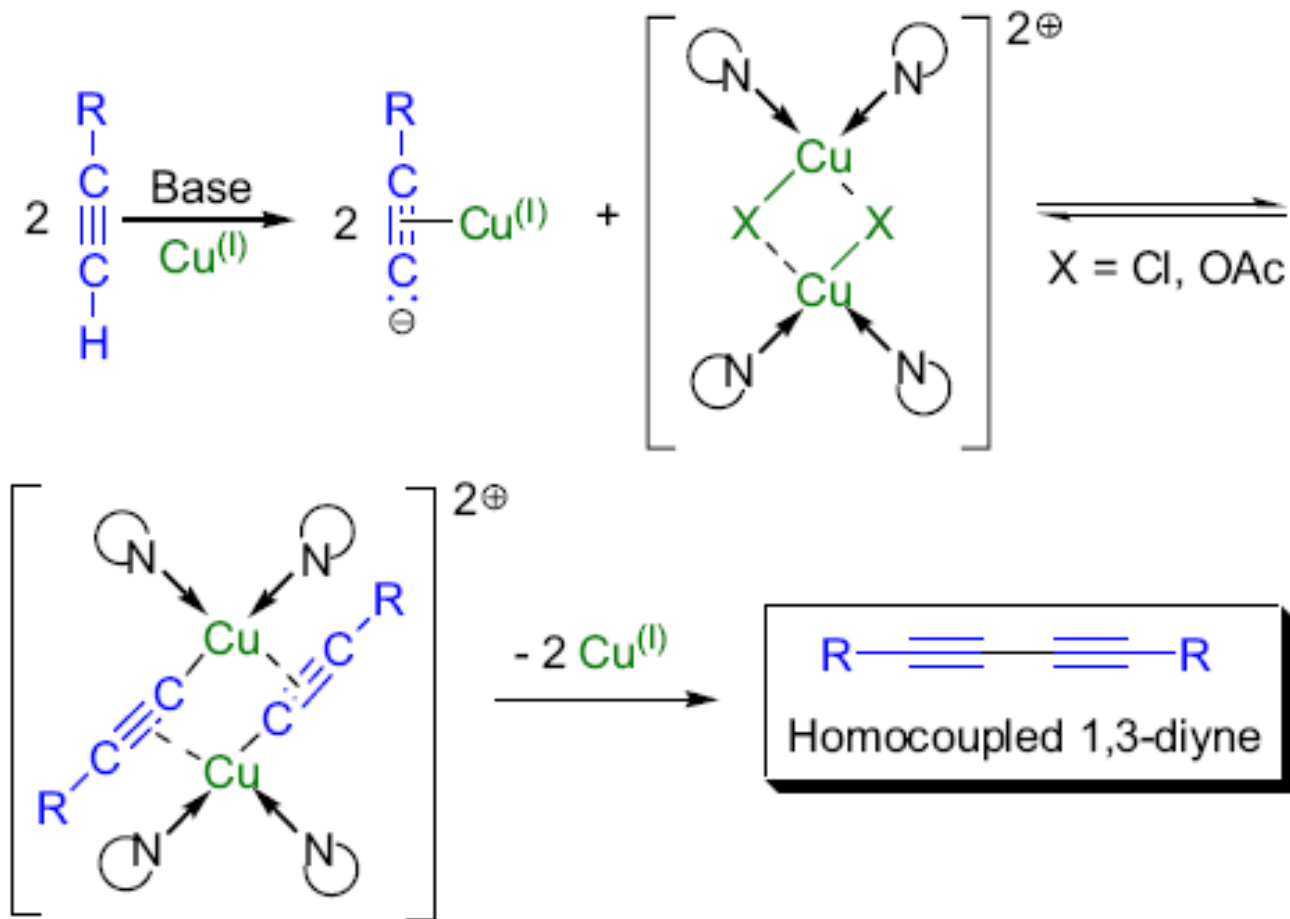
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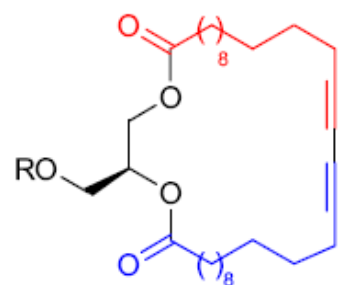
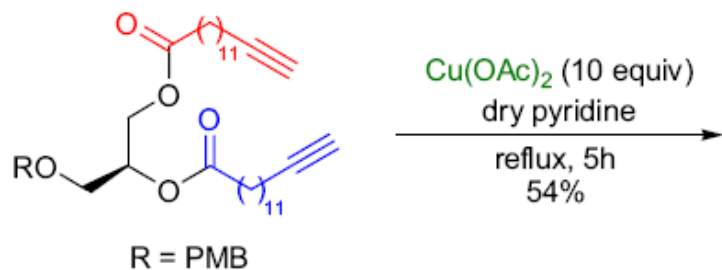
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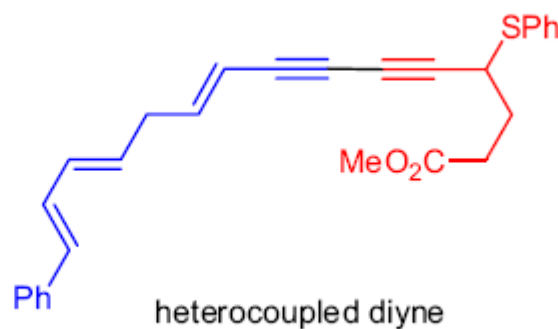
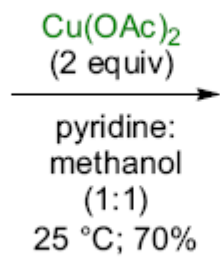
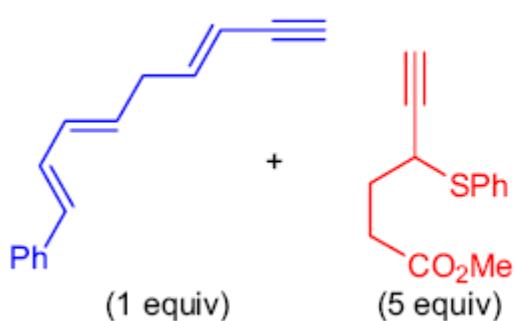
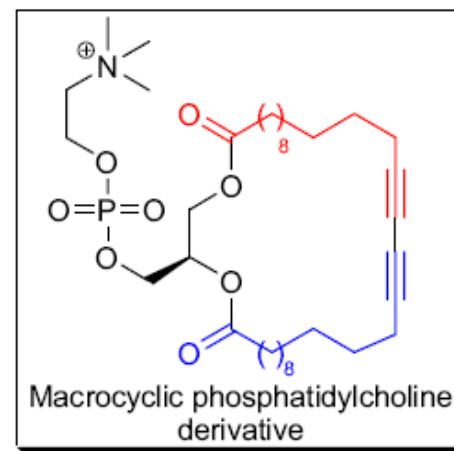
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Synthetic Applications

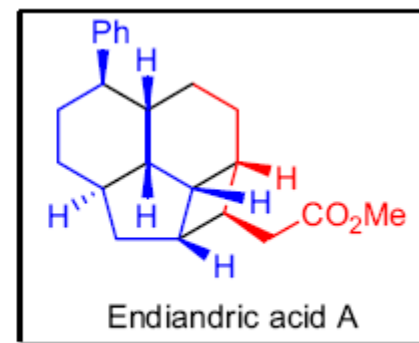


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steps



steps



K.C. Nicolaou, et al.

Synthetic Applications

