Palladium(0), Copper(I) Catalysed Synthesis of Conjugated Alkynyl α-Allenols from Alkynyl Cyclic Carbonates and Terminal Alkynes

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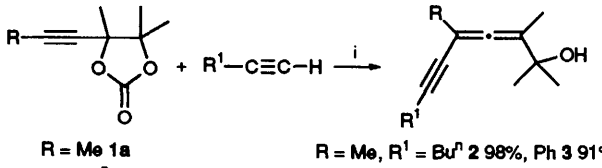
Alkynyl cyclic carbonates react with terminal alkynes and prop-2-ynylic alcohols in the presence of catalytic amounts of $Pd(PPh_3)_4$ and CuI to selectively afford functional conjugated alkynyl α-allenols in good yields.

The conjugated allenyne system is found in many allenes isolated from microorganisms and their metabolites,[1] and has potential as an unsaturated building block in organic synthesis. Initial syntheses of allenyne derivatives were based on reduction of diynenols with $LiAlH_4$[2] or copper(I)-catalysed coupling of terminal alkynes with allenyl[3] or prop-2-ynyl[4] halides in the presence of a base. Recently, profit has been taken of the easy formation of allenyl palladium intermediates from allenic halides or prop-2-ynylic halides,[5–7] epoxides[8] and carbonates[9] to produce alkynyl allenes *via* C–C bond formation on reaction with alkynyl zinc halides[6,8] or *in situ* generated copper acetylides.[5,7,9] The selective synthesis of α-allenols from alkynyl epoxides and organocopper derivatives is known,[10] but to our knowledge, the only transformation of cyclic alkynyl carbonates involving C–C bond formation generating allenols has been performed with alkyl magnesium halides in the presence of $BF_3{\cdot}Et_2O$ and CuI catalyst.[11] Alkynyl α-allenols, analogues of metabolites of fungi,[1] have previously been obtained by stoichiometric reaction of alkynyl zinc chlorides with alkynyl epoxides.[8] We now report that a variety of alkynyl α-allenols, the functional 1,2-dimethylhepta-3,4-dien-5-yn-2-ol derivatives, can be selectively obtained from the easily accessible alkynyl cyclic carbonates **1a–b** and terminal alkynes in the presence of catalytic amounts of Pd^0 and Cu^I derivatives, and we show that this reaction can be used for the modification of steroids.

The alkynyl cyclic carbonates **1a–b**, obtained in one step from 1,1-dimethyl-2-oxopropyl ethyl carbonate ($MeCOCMe_2OCO_2Et$) and lithium acetylides,[12] were expected to react with palladium(0) complexes to afford reactive α-allenyl palladium(II) intermediates. Thus, from 3 mmol of terminal alkyne $R^1C{\equiv}CH$ (R^1 = Bu^n, Ph, Me_3Si) in 10 ml of THF, alkynyl copper(I) species generated in the presence of 10 mol% of CuI and 6 mmol of triethylamine, reacted with carbonate **1a** in the presence of 5 mol% of $Pd(PPh_3)_4$ at room temp. The conjugated alkynyl α-allenols **2** (98%), **3** (91%) and **4** (92%) resulting from opening of the cyclic carbonate and C–C bond formation were readily obtained after 30, 18 and 8.5 h of reaction, respectively (Scheme 1).

This carbonate transformation allows the generation of an allene functionality, the introduction of an alkynyl group and the liberation of the hydroxy group. It requires the use of a palladium(0) complex as catalyst precursor; $Pd(PPh_3)_4$ and $Pd(dba)_2$/dppe were shown to provide efficient catalytic systems. Similarly, carbonate **1b** reacted with hex-1-yne and trimethylsilylacetylene to afford **5** (97%) and **6** (76%) but longer reaction times were necessary (46 h at room temp. and 18 h at 80 °C, respectively).

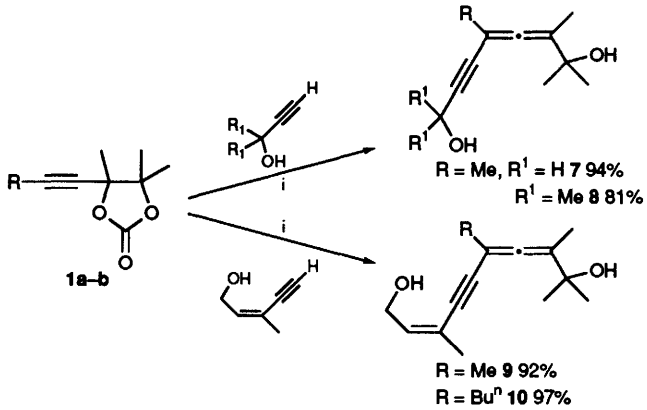


Scheme 1 *Reagents and conditions*: i, alkyne (3 mmol), carbonate **1a** or **1b** (3 mmol) in THF (10 ml), $Pd(PPh_3)_4$ (0.15 mmol, 5 mol%), CuI (0.3 mmol, 10 mol%), NEt_3 (6 mmol)

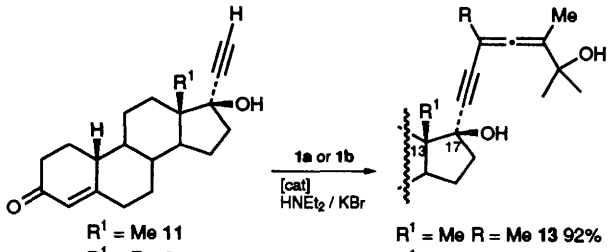
The reaction took place under mild conditions without using basic alkynyl organometallics, which made possible the use of unprotected acetylenic alcohols for the direct access to conjugated unsaturated diols **7** (94%) and **8** (81%) at room temp. (Scheme 2). However, the rate of the reaction was increased by using Et_2NH instead of triethylamine, and KBr as additive. Under similar conditions, unsaturated diols **9** (92%) and **10** (97%) were obtained by respective coupling of **1a** and **1b** with (*Z*)-3-methylpent-2-en-4-yn-1-ol, which contains the α-hydroxy enyne structure required to build furan rings[13] (Scheme 2).

The efficiency of the coupling of prop-2-ynylic alcohols under mild conditions offers a new possibility to modify steroids containing the ethynyl and hydroxy group at C(17). Thus, norethindrone **11** reacted with carbonate **1a** to give the steroid **13** containing the hydroxy allenynyl group at C(17) in 92% isolated yield. Analogously, levonorgestrel **12** afforded steroid derivatives **14** (88%) and **15** (80%) on reaction with carbonates **1a** and **1b**, respectively (Scheme 3).

Two singlets of equal intensities were detected by ^1H NMR for the methyl group directly attached to the allenyl moiety of compounds **13–15** (Scheme 3) indicating the presence of two stereoisomers. The single signals and the chemical shifts of the alkyl substituents R^1 at C(13) [Me (**13**) and Et (**14**, **15**)]



Scheme 2 *Reagents and conditions*: i, $Pd(PPh_3)_4$ (5 mol%), CuI (10 mol%), $HNEt_2$ (20 equiv.), KBr (2 equiv.) in THF (10 ml)



Scheme 3

suggested that the reaction proceeded with retention of configuration at C(17).

The above selective reaction results from three successive transformations of alkynes as 1,1-dimethyl-2-oxopropyl ethyl carbonate is obtained in two steps from 1-methylbut-3-yn-1-ol and CO_2.[14] It tolerates the presence of hydroxy groups and represents a one-step synthesis of functional conjugated allenynols and unsaturated diols from alkynyl cyclic carbonates under mild catalytic conditions.

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