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Sambasivarao Kotha, Rama Gunta

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Graphical Abstract

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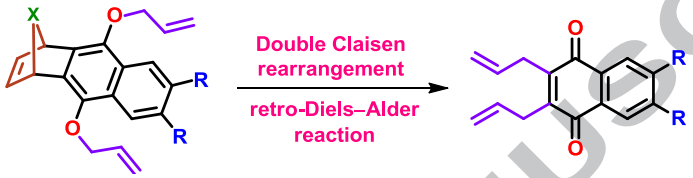

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A new synthetic strategy to 2,3-diallyl-1,4-quinones via one-pot double Claisen rearrangement and retro Diels–Alder reaction

Sambasivarao Kotha[a,]* and Rama Gunta[a]

[a]*Department of Chemistry, Indian Institute of Technology-Bombay, Powai, Mumbai-400 076, India*

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ABSTRACT

A simple and an efficient synthetic strategy to 2,3-diallyl-1,4-quinone derivatives via a highly reliable and 100% atom economic reactions such as Diels–Alder (DA) reaction, Claisen rearrangement (CR) and retro Diels–Alder (rDA) reaction as key steps is reported.

* Corresponding author. Tel.: +91-22-25767160; fax: *022-25767152*; e-mail: srk@chem.iitb.ac.in

Introduction

Functionalized quinones are useful building blocks to design medicinally important targets and they are also present in many natural product frame works.[1] Biologically active isoprenoid quinones such as vitamin K, coenzyme Q and plastoquinones play an important role in several biological processes like blood clotting, oxidative phosphorylation and respiratory systems.[2] In addition, electron transport in photosynthetic process involve quinone's role. Functionalized quinones are used to signal the presence of anions[3] and they act as good fluorophores as well.[4] Several strategies have been developed to functionalize quinones involving C-C bond formation sequence.[5-8] To this end, allylindium reagents,[9] cross-coupling of vinylalanes with benzyl chlorides mediated by Ni(0)[10] and coupling of benzylic zincs with alkenyl halides provide a direct route to allylated quinones.[11] Claisen rearrangement (CR)[12-14] has proved to be a gold mine for C-C bond formation processes in organic synthesis.[15] It has become one of the most widely used methods of stereoselective C-C bond formation and, moreover, various aromatics were assembled via CR in combination with ring-closing metathesis (RCM).[16-26] Since quinones are reactive substrates their direct functionalization is a difficult task. To avoid this problem, initially, we have used Diels–Alder (DA) reaction to mask the reactivity of quinone moitey and then functionalized the DA adduct via CR and retro Diels–Alder (rDA) reaction sequence. Recently, rDA reaction[27] has become an attractive tool when cyclopropyl substituent is present at 7-position of norbornene system. To this end, experimental and theoretical studies on rDA reaction showed that cyclopropyl substituent aids to realize the rDA reaction under mild rection conditions[28-31] and thus prevents decomposition of sensitive substrates formed during the rDA reaction sequence.

Results and Discussion

Retrosynthetic approach to 2,3-diallyl-1,4-quinones is shown in Figure 1. Here, the desired diallyl quinone **1** would be derived from *O*-allyl compound **2** via double CR followed by rDA reaction. Further, *O*-allyl compound **2** can be obtained from a known DA adduct **3** through *O*-allylation, which in turn could readily be prepared from different dienes and dienophiles using DA reaction.

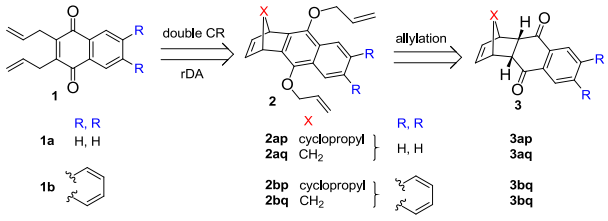
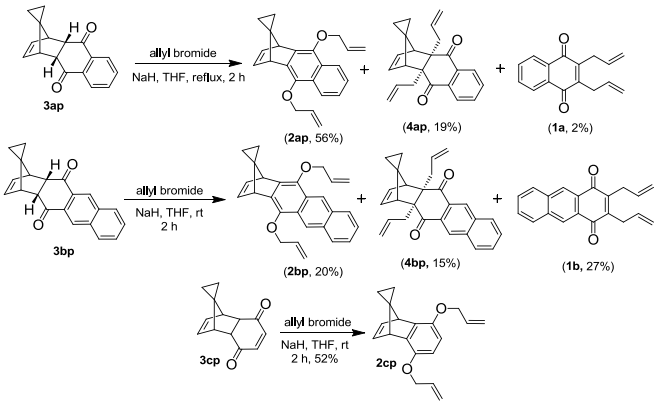


Figure 1. Retrosynthetic approach to 2,3-diallyl-1,4-quinone derivatives.

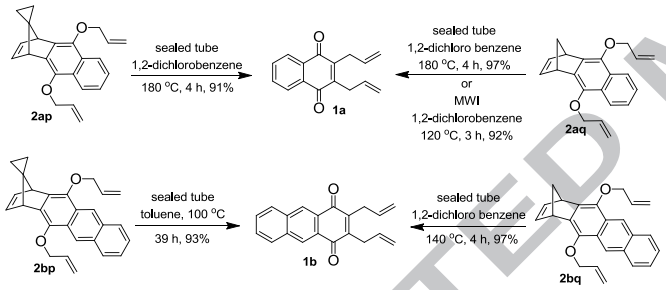
To realize the strategy shown in Figure 1, we begin our journey with the preparation of various known DA adducts **3ap**, **3bp** and **3cp** by following the literature procedures.[32] In this regard, DA adducts **3ap** and **3cp** were prepared by utilizing the micellar conditions, whereas **3bp** was obtained via conventional procedure. To this end, the DA adduct **3ap** was allylated with allyl bromide using NaH in THF reflux conditions to generate *O*-allyl derivative **2ap** in 56% yield and *C*-allyl compound **4ap** in 19% yield along with a minor amount of **1a** (2%) (Scheme 1). Later, the other DA adduct **3bp** was treated with allyl bromide using the same base at room temperature (rt) for 2 h to obtain a mixture of *O*-allyl compound **2bp** (20%) and *C*-allyl compound **4bp** (15%) along with 2,3-diallyl-1,4-anthraquinone **1b** (27%). To expand this strategy, another DA adduct **3cp** was subjected to allylation under similar reaction conditions and in this regard only *O*-allyl compound **2cp** was delivered in 52% yield (based on 4% of the starting material recovered) (Scheme 1). The structures of all new compounds were confirmed on the basis of ^{1}H and ^{13}C NMR spectral data and further supported by HRMS data. Recently reported[33] *O*-allylated compounds **2aq** and **2bq** from the corresponding DA adducts **3aq** and **3bq** were also used in this strategy.



Scheme 1. Synthesis of *O*-allylated compounds **2ap**, **2bp** and **2cp**.

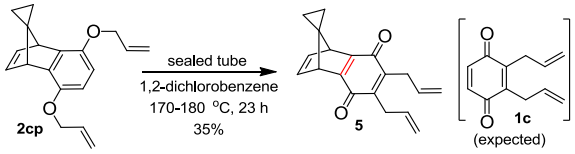
Having *O*-allyl compounds **2ap**, **2bp**, **2cp**, **2aq** and **2bq** in hand, our next goal is to synthesize the desired 2,3-diallyl-1,4-quinone derivatives. To this end, De Kimpe and his co-workers reported the synthesis of 2,3-diallyl-1,4-naphthoquinone using 3-butenoic acid in the presence of diammonium persulfate and a catalytic

amount of silver nitrate.[8] Here, we report an alternative route to prepare 2,3-diallyl-1,4-quinones from readily available starting materials. In this connection, **2aq** was heated in a sealed tube using 1,2-dichlorobenzene at 180 °C for 4 h to deliver 2,3-diallyl-1,4-naphthoquinone (**1a**) in 97% yield. The generation of diallyl quinone **1a** can be explained on the basis of double CR followed by rDA reaction of the substrate **2aq**. Next, other compound **2ap** on double CR-rDA sequence gave the compound **1a** in 92% yield under identical reaction conditions. However, the diallyl quinone **1a** was also prepared by an alternative route involving microwave irradiation (MWI) at 120 °C for 3 h (92%). Later, *O*-allylated substrate **2bq** was treated under similar reaction conditions (except 140 °C temperature) to generate the 2,3-diallyl-1,4-anthraquinone (**1b**) in 97% yield. It should be noted that the substrate **2bp** was heated in a sealed tube under toluene reflux conditions for 39 h to furnish the compound **1b** (93%) (Scheme 2). As compared to 1,2-dichlorobenzene conditions, under toluene reflux conditions the rate of reaction is slow hence it require longer time for completion.



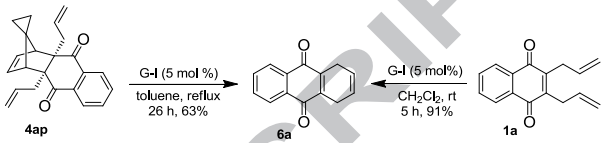
Scheme 2. Synthesis of compounds **1a-b** by a one-pot double CR and rDA reaction.

Surprisingly, when the *O*-allyl compound **2cp** was heated at 170 °C under similar reaction conditions for 23 h we did not get the expected diallyl quinone **1c**, instead the rearranged compound **5** was obtained. Formation of the tetracyclic compound **5** can be explained as follows. When the *O*-allyl compounds **2ap**, **2bp**, **2aq** and **2bq** were subjected to double CR the allyl groups migrated to norbornene ring junctions[34] and hence the subsequent rDA reaction was feasible. In contrast, the substrate **2cp** underwent double CR to generate a double bond (red in colour) at ring junctions as shown in the compound **5** (Scheme 3) and thus prevents its subsequent rDA reaction due to benzyne generation. The compound **5** has been characterized based on the spectroscopic data (^{1}H and ^{13}C NMR, DEPT 135) and further supported by HRMS data.



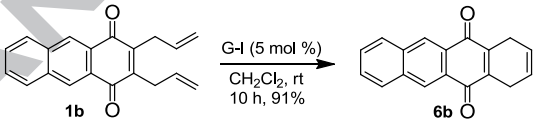
Scheme 3. Double CR of compound **2cp**.

Later, the substrate **4ap** was subjected to RCM using Grubbs first generation (G-I) catalyst under toluene reflux conditions. Interestingly, the diallyl compound **4ap** not only underwent RCM but also rDA reaction in a one-pot sequence to furnish the quinone derivative **6a** in 63% yield. Also, the quinone derivative **6a** was prepared from **1a** via RCM using G-I catalyst in CH_2Cl_2 at rt (Scheme 4). Spectral data (e.g. ^{1}H and ^{13}C NMR) of **6a** matched with the literature values.[19]



Scheme 4. One-pot RCM-rDA approach to known compound **6a**.

Likewise, RCM of the compound **1b** under similar reaction conditions gave the quinone derivative **6b** in 91% yield (Scheme 5).



Scheme 5. RCM of 2,3-diallyl-1,4-anthraquinone (**1b**).

Conclusions

In conclusion, we have developed a simple and an alternative method to 2,3-diallyl-1,4-quinone derivatives **1a** and **1b** via a one-pot double CR and rDA sequence involving readily available starting materials. This method may be extended to the synthesis of functionalized quinone derivatives suitable for material science and drug discovery. A well-conceived design involving DA reaction, CR and rDA reaction in a timely manner gave allylated quinones. Allyl group is useful starting point and it can be converted into various other functional groups (e.g. aldehyde, ketone, diol and alcohol etc.) by judicious selection of various functional group transformations. The allyl group introduced by CR is masked until the time when that functionality is required.

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Supplementary data

Supplementary data (detailed experimental procedures,

characterization data and copies of NMR (^{1}H and ^{13}C) spectra for all new compounds) associated with this article can be found, in the online version.

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34. **Note:** Our mechanistic explanation is based on the following observation. When we monitored the reaction progress of the conversion of **2bp** to **1b** by thin-layer chromatography (TLC), we observed a new spot whose R_f value was matched with that of the authentic C-allyl compound **4bp** on the TLC plate and then it was disappeared to give another new spot whose R_f value was same as that of **1b**.

Highlights

- An efficient synthetic strategy to 2,3-diallyl-1,4-quinone derivatives has been developed.
- Strategy includes one-pot Claisen rearrangement and retro Diels–Alder reaction.
- 100% atom economic reactions were used.
- This strategy embraces redox economy.