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Title:	Cyclopropenium Ions Catalyzed Organic Transformations and Their Applications in the Total Synthesis of Resveratrol-based Natural Products
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Abstract:	<p>This thesis work primarily focuses on organocatalytic transformations using cyclopropenium ions as an organocatalyst. This work is organized into four chapters. Chapter 1 discusses the general introduction to the chemistry of cyclopropenium-based organic molecules. Chapter 2 illustrates the bis(amino)cyclopropenyliene (BACs) catalyzed intramolecular cyclization of 2-(2-formylaryl)aryl-substituted p-quinone methides via umpolung of aldehyde followed by 1,6-conjugate addition leading to phenanthrols and 7-membered carbocycles. Chapter 3 involves cyclopropenium cation-catalyzed conjugate addition reactions of p-QMs. Chapter 4 describes the tris-arylcyclopropenium carbocation as a highly promising organocatalyst in fundamental organic transformation such as Nazarov cyclization and other conjugate addition reactions. Chapter 1: General introduction to the chemistry of cyclopropenium-based small molecules. In this chapter, the structure, properties, and catalytic applications (Figure 1) of cyclopropenium-based small molecules are briefly discussed. Due to the unique structural and electronic properties of cyclopropenium salts, they have been used in a wide range of applications such as organocatalysts (Figure 1.), potential materials for energy storage devices, electro-photocatalyst, ligands for catalytic metal complexes, ionic liquids, fluorescent materials, aromatic cations in hybrid halide perovskites, nanoparticles, redox-active polymers for redox flow batteries and as transfection agents. Chapter 2: Bis(amino)cyclopropenyliene catalyzed intramolecular cyclization of 2-(2-formylaryl)-phenyl-substituted p-quinone methides. This Chapter is further divided into two parts namely, Part A and Part B. Part A: Access to phenanthrols through a bis(amino)cyclopropenyliene catalyzed intramolecular cyclization of 2-(formylaryl)-aryl-substituted p-quinone methides. The organocatalytic application of bis(amino)cyclopropenyliene (BAC) was unknown until Tamm and co-workers employed it for aldehyde umpolung reactions. It has been reported that carbene can readily react with an aldehyde to form a Breslow-type intermediate, which then can react with various electrophiles such as aldehydes (Benzoin reaction), enones (Stetter reaction), imines (aza-benzoin reaction), dienones (Rauhut-Currier reaction), etc. to form the corresponding acylated products. In line with this, we have developed a BAC-catalyzed intramolecular cyclization reaction of 2-(2-formylaryl)-phenyl-substituted p-quinone methides to access 10-(4-hydroxyphenyl)phenanthren-9-ol derivatives (Scheme 1). Additionally, this method was also elaborated for the synthesis of medium-sized rings, which are proven to possess antimicrobial and anticancer properties. Scheme 1. Synthesis of 10-(4-hydroxyphenyl)phenanthren-9-ol derivatives through BACs catalyzed intramolecular cyclization reaction Part B: Total syntheses of shoreaphenol, malibatol A, & B, parviflorol, and diptoinonesin A through a BAC catalyzed intramolecular cyclization reactions of 2-(formylaryl)-aryl-substituted p-quinone methides. This part describes the synthesis of some of the recently discovered resveratrol-based natural products through BAC catalyzed intramolecular cyclization reactions of 2-(formylaryl)-aryl-substituted p-quinone methides. Resveratrol has been associated with a diverse range of biological functions including antioxidant, anticancer, anti-diabetic, anti-tumor, cardioprotective, and anti-aging characteristics. Malibatol A and B are two novel oligostilbenes that were isolated by Boyd and colleagues in 1998 and were derived from an organic extract of the leaves of Hopea malibato. Since then, several natural products in the same family have been isolated, and some articles on their total synthesis have been published. Hence, alternate methodologies for synthesizing these compounds are undoubtedly required as most previously known synthetic procedures involve multiple steps resulting in low overall yields. Scheme 2. Total synthesis of hopeafurane, malibatol A and B. After establishing the strategy for the synthesis of the crucial core structure of 10-dihydro-11H-benzo[6,7]cyclohepta[1,2,3-cd]indol-11-one in part A, we turned our attention to synthesize some of the resveratrol and found that our methodology could be successfully applied to the total syntheses of malibatol A, malibatol B, hopeafurane, parviflorol E, and its epimer diptoinonesin D (Scheme 2). Chapter 3: Bis(amino)cyclopropenium ion as a hydrogen-bond donor catalyst for 1,6-conjugate addition reactions. In this chapter, we have explored, for the first time, BAC precursor as a 'Hydrogen Bond Donor' catalyst in conjugate addition reactions of p-QMs with indoles and 2-naphthols. Deuterium isotope labeling experiments and spectroscopic investigations (^1H & ^{13}C NMR and UV-vis) were performed to prove the hypothesis; revealing that the C-H hydrogen atom in the cyclopropene ring of the catalyst is indeed responsible for the catalytic activity. This catalyst was also shown to be incredibly beneficial for the 1,6-conjugate addition of p-QMs with various nucleophiles such as 2-naphthols, phenols, and thiols. Later some of the indolyl vinyldimethanes were transformed into other valuable products to demonstrate the synthetic potential of this protocol (Scheme 3). Scheme 3. Cyclopropenium ion as a hydrogen bond donor in activation of p-QM Chapter 4: Tris-arylcyclopropenium carbocation as an organic Lewis acid catalyst in Nazarov cyclization and conjugate addition reactions. While working on the smallest aromatic Huckel moiety, widely recognized as cyclopropenium ion-based catalysis, we anticipated that it could behave as an organic Lewis acid catalyst in various organic transformations. In line with this, we have utilized, for the first time, tris-arylcyclopropenium carbocation as an organic Lewis acid catalyst in Nazarov cyclization reactions. The reactions worked very well under mild reaction conditions and the cyclopentenone derivatives could be obtained in excellent yields within a short reaction time. The same protocol was utilized for diversified reactions including 1,6/1,4 hydroolefinations and 1,2 addition of indoles to aromatic carboxaldehydes. The hypothesis was further supported by spectroscopic investigations (^1H & ^{13}C NMR and UV-vis) and the XPS technique. To show the Lewis acidity of the catalyst pK_a value of the cation was calculated using the Breslow method. Scheme 4. Tris-arylcyclopropenium carbocation catalyzed Nazarov cyclization reaction</p>
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