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Donor–acceptor biaryl lactones: pH induced molecular switches with intramolecular charge transfer modulation

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ABSTRACT

The physical properties of biaryl-containing compounds are known to be highly dependent on molecular geometry. We report the syntheses and fundamental spectroscopic study of two donor–acceptor biaryl lactone (6*H*-benzo[*c*]chromen-6-one) pH-driven switches. These compounds have been determined to rapidly and efficiently switch between two geometric states upon cycling of acidic or basic stimuli. The planar lactone state exhibits enhanced intramolecular charge transfer (ICT) between the donor and acceptor units which is instantly attenuated upon addition of basic stimuli. The resulting lactone cleavage enables aryl–aryl bond rotation thus decreasing the extent of conjugation between the rings. Each state is readily identifiable by the significant changes that occur in their respective UV–vis spectra and luminescent character, indicative of the facile modulation of extended conjugation by pH.

Spectroscopic properties, such as electronic excitation, emission and non-linear optics,[1] and physical properties, such as conductance,[2] of biaryl-containing molecules are directly correlated with the geometry of the aryl–aryl bond. Efficient pi orbital overlap occurs when the biaryl moiety can adopt a planar conformation, resulting in facile electron transport between the arene rings. Biphenyl is known to have a dihedral angle of 30–40° in solution, thus maximizing conjugation while minimizing steric interactions between *ortho* hydrogens.[3] Biaryls capable of controllable modulation in their geometries and degree of conjugation could therefore ultimately become useful when applied to sensing, optical switching, molecular logic devices, or molecular electronic technologies. A few studies have been reported describing reversible biaryl dihedral angle restriction as a strategy for molecular switching of the degree of extended conjugation but, to the author's knowledge, none have employed pH as the stimulus.[1a,1d,4]

Biaryl lactones have been shown to be capable of unidirectional aryl–aryl bond rotation via sequential addition of chemical stimuli.[5] The lactone unit is the key feature in these systems: it can be cleaved, modified, and reformed under specific reaction conditions. These studies have not, however, explored the fundamental nature of how simple biaryl lactone cleavage and reformation could rapidly and reversibly affect through-ring conjugation and intramolecular charge transfer (ICT). To this end, we have synthesized two new 4,4′-disubstituted donor–acceptor 6*H*-benzo[*c*]chromen-6-one switches (**1** and **2**) and have determined that the lactone unit can be instantaneously cleaved and reformed following addition of basic and acidic stimuli, respectively, leading to rapid modulation of molecular geometry. The extent of ICT is directly correlated to the planar geometry of the lactonized state and the non-planar geometry of the ring-opened state and is readily probed with UV–vis and fluorescence spectroscopy. Many elegant pH-driven switches of molecular conformation, configuration, and complexation have been reported.[6] However, most synthetic molecules capable of pH-induced ICT modulation operate by functional group protonation and deprotonation and not by changes in molecular geometries.[7] Biaryl lactones **1** and **2** are pH-driven switches of both molecular geometry and ICT.

Biaryl lactone **1**[8] was prepared via aromatic nitration and esterification of **3** to afford **4** (Scheme 1). This was followed by microwave-mediated Suzuki coupling[9] with boronic acid **6**. Lactonization of **7** with boron tribromide[10] achieved **1** while serendipitously leaving the *p*-methoxy unit unchanged. Biaryl lactone **2** was synthesized by reducing the nitro unit on **4** with $SnCl_2$ to the aniline and subsequent iodination. The iodoarene then underwent selective Pd-catalyzed cyanation[11] exclusively at the iodo-substituted carbon to afford **5**. Microwave-mediated Suzuki coupling of **5** with **6** was unsuccessful, resulting in hydration of the cyano unit. However, Suzuki coupling under more standard conditions and lactonization with boron tribromide[10] resulted in lactone **2**, also leaving the *p*-methoxy unit unchanged.

Lactones **1** and **2** were studied to determine the ideal conditions for rapid pH-driven switching in the same reaction pot (Scheme 2).

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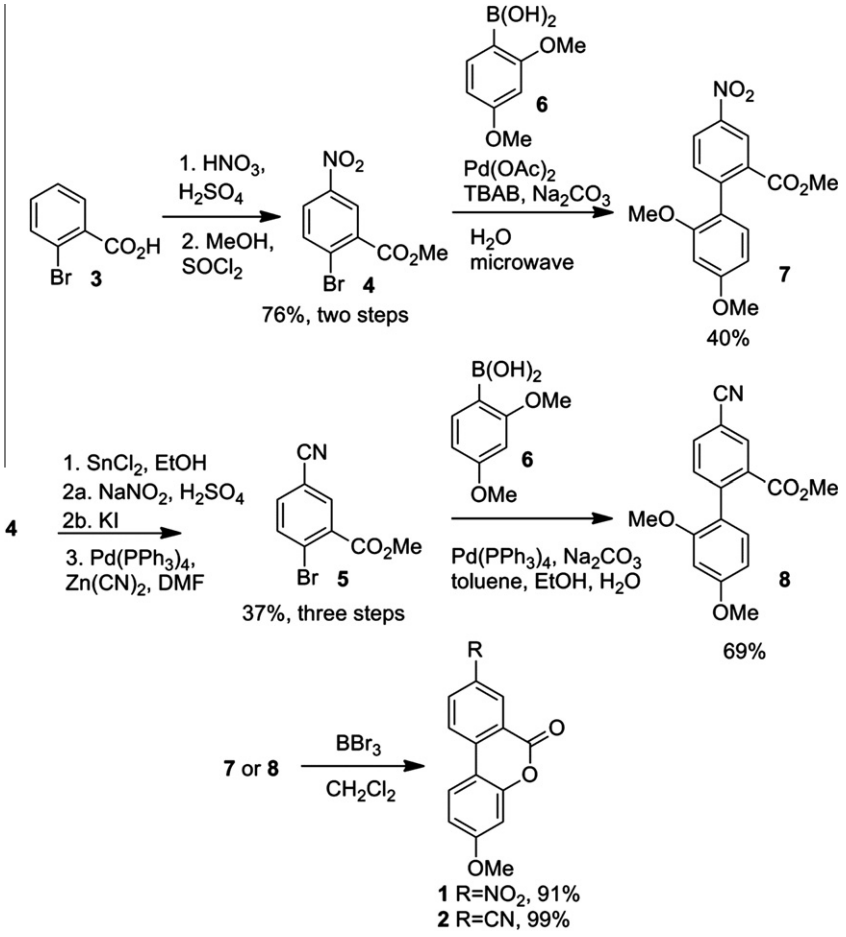
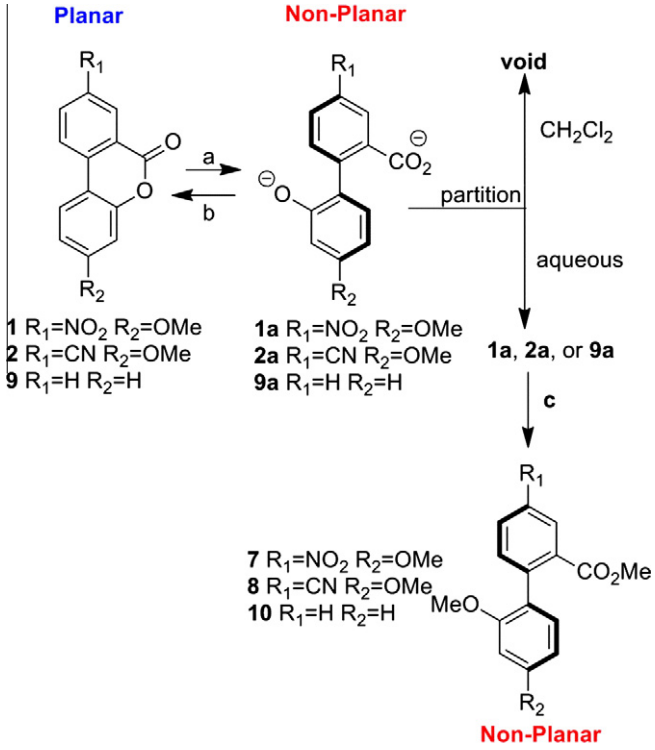


Scheme 1. Syntheses of biaryl lactone switches **1** and **2**.

Cleavage of the lactone unit in other 6*H*-benzo[*c*]chromen-6-one derivatives in base and formation of the lactone in acid is known but it has not been reported to occur in the same pot.[12] We anticipated some difficulty due to the expected differences in solubility of the two states. Initial attempts to switch **1** or **2** under multiple biphasic conditions were unsuccessful. However, either lactone dissolved in 1:2 CH_3OH–THF resulted in instantaneous ring-cleavage upon addition of 5% aq NaOH as the stimulus, readily observable by a visible color change (yellow to red for **1** to **1a** and colorless to yellow for **2** to **2a**). Similarly, the use of tetrabutylammonium hydroxide (TBA-OH) as the stimulus also resulted in instantaneous ring-opening of **1** or **2** dissolved in CH_3CN. Rapid lactonization of **1a** or **2a** back to **1** or **2** was achieved upon addition of a second stimulus, aqueous HCl or trifluoroacetic acid (TFA), as easily observed by a return to the original solution color. The switching process could also be readily monitored with ^{1}H NMR spectroscopy by observing the relative upfield shifts of the protons resonating in the aromatic region as **1** and **2** was converted into **1a** and **2a**.[13] Product analysis after one switching cycle revealed that **1** and **2** were the only species present, each recovered in a near-quantitative yield. Unsubstituted biaryl lactone **9** was also prepared from 9-fluorenone[14] to directly compare with donor–acceptor lactones **1** and **2**. All three compounds (**1**, **2**, and **9**) were observed to rapidly and efficiently cycle between their open and closed states upon each consecutive addition of acid or base.

To further characterize the pH-driven switching processes, **1**, **2**, or **9** was dissolved in 1:2 CH_3OH–THF, 5% aq NaOH was added, and immediately partitioned into CH_2Cl_2 and water (Scheme 2). The CH_2Cl_2 layer was evaporated to reveal that the amount of **1**, **2**, or **9** remaining in the reaction was negligible (less than 1% of the initial mass). Acidification of the aqueous-soluble **1a**, **2a**, and **9a** to achieve the protonated forms for characterization without complete lactonization back to **1**, **2**, or **9** proved to be difficult, as was also indicated in other studies of analogous compounds.[5a,12a] Therefore, to unambiguously identify the aqueous-soluble ring-opened state (**1a**, **2a**, and **9a**), the alkaline aqueous layer was reacted with dimethylsulfate and tetrabutylammonium bromide (TBAB). Analysis revealed that **1**, **2**, and **9** had been completely converted into **7**, **8**, and **10**, supporting the presence of the ring-opened states (**1a**, **2a**, or **9a**) in the alkaline media.

The biaryl lactones were examined by UV–vis spectroscopy[15] to determine the effect that pH-driven switching would have on conjugation through the biaryl unit (Fig. 1). Donor–acceptor **1** and **2** dissolved in CH_3CN both exhibited intense ICT bands at 356 nm (ε = 172185 M^{-1} cm^{-1}) and 317 nm (ε = 36686 M^{-1} cm^{-1}), respectively. A significant attenuation of the ICT band and a corresponding bathochromic shift was immediately observed upon addition of TBA-OH to afford non-planar **1a** and **2a**. The observed red-shift of the dianionic ring-opened states (**1a** and **2a**) was determined to be due to the *ortho*-phenoxide generated upon lactone cleavage being a stronger electron donor than the *para*-methoxy group present in the ring-closed state (**1** and **2**). This was supported by examination of the ring-opened analogs **7** and **8**, both containing methoxy units in place of phenoxides, and noting the hypsochromic shift relative to **1a** and **2a**. However, the large decrease in the charge transfer band intensity of ring-opened states (**1a** and **2a**) and their methylated analogs (**7** and **8**) compared to the ring-closed states (**1** and **2**) is direct evidence of the attenuation of conjugation between the



Scheme 2. pH-Driven switching studies. Reagents: (a) CH_3CN and TBA-OH or 1:2 CH_3OH–THF and aq NaOH; (b) aq HCl or TFA; (c) Me_2SO_4, TBAB, CH_2Cl_2.

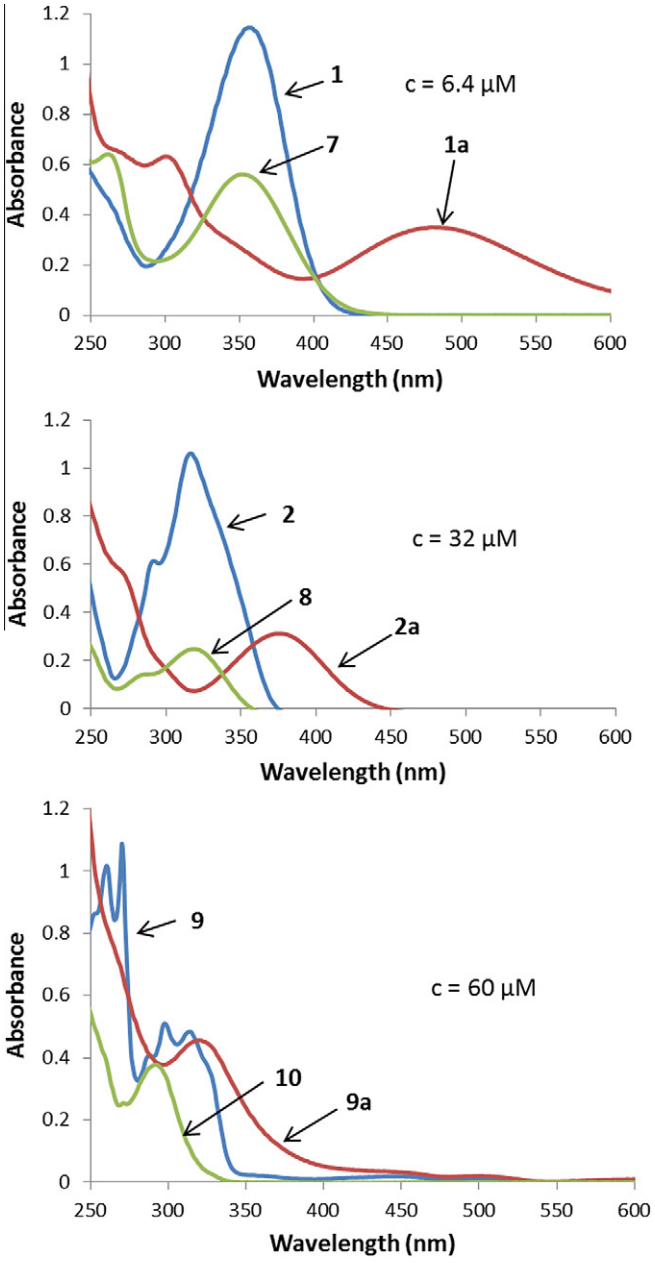


Figure 1. Electronic absorption spectra of **1**, **2**, and **9**, their corresponding ring-opened products **1a**, **2a**, and **9a**, and the methyl-trapped ring-opened species **7**, **8**, and **10**, at the noted concentrations in CH_3CN. Spectra of **1a**, **2a**, and **9a** were taken upon addition of TBA-OH to **1**, **2**, and **9**, at the noted concentrations in CH_3CN.

two rings in the ring-opened state. Additionally, unsubstituted **9** exhibited comparatively small changes in its spectra upon pH-driven ring-opening to **9a**, illustrating the significance of the donor and acceptor units. Compounds **1** and **2** are therefore capable of rapid and reversible pH-driven ICT modulation which directly corresponds to changes in their molecular geometries.

The switching process was also examined at various pH values (Fig. 2).[15] To analyze ring-opening, aq. NaOH at varying pH was added to samples of **1** or **2** dissolved in 1:2 CH_3OH–THF. Each reaction mixture was extracted with CH_2Cl_2 and analyzed by UV–vis to determine the relative amount of **1** or **2** remaining after addition of base at differing pH. For both **1** and **2** very little ring-opening occurred when the pH is < 12. However, addition of aq. NaOH with pH >12 resulted in all of **1** or **2** ring-opening to **1a** or **2a**. To analyze ring-closing, 5% aq NaOH was added in excess to **1** or **2** dissolved in 1:2 CH_3OH–THF. The aqueous layer was separated, divided, and each aliquot acidified with aq HCl to a specific pH. Each sample was extracted with CH_2Cl_2 and analyzed by UV–vis to determine the relative amount of **1** or **2** afforded by ring-closing in acid at differing pH. It was found that, for both **1** and **2**, very little conversion occurred when the pH of the acid is >5. However, addition of aq HCl with pH values <5 resulted in all of **1a** or **2a** ring-closing back to **1** or **2**.

Some compounds containing the 6*H*-benzo[*c*]chromen-6-one unit have been reported to be brightly fluorescent.[16] The luminescence of planar lactone switches **1** and **2** was therefore examined and directly compared to the ring-opened states **1a** and **2a**. Solutions of lactone **1** and **2** exhibit faint green[17] and bright blue luminescence, respectively, when irradiated with a UV lamp (Fig. 3). However, the luminescence is immediately attenuated upon addition of TBA-OH to **1** or **2** generating **1a** or **2a**. The luminescence could be rapidly regenerated upon addition of TFA. The compounds were further analyzed using fluorescence spectroscopy.[18] The cyano-containing **2** emits at 420 nm (λ_{ex} = 316 nm) and nitro-containing **1** emits at 515 nm (λ_{ex} = 370 nm). After addition of TBA-OH, neither compound exhibited fluorescence at the previous excitation wavelength. The luminescence properties of **1** and **2** can therefore be rapidly modulated via pH-driven switching. Analog **9** without donor or acceptor units did not visibly luminesce.

In conclusion, donor–acceptor biaryl lactone switches **1** and **2** have been synthesized and are reversibly, rapidly, and efficiently switched upon changes in pH resulting in a geometry modulation. The increased degree of through-ring conjugation in the ring closed state leads to enhanced ICT and luminescence. The decreased degree of through-ring conjugation in the ring-opened state leads to attenuated ICT and a lack of luminescence. The 6*H*-benzo[*c*]chromen-6-one moiety has been shown to be an attractive molecular switch prototype and further studies are planned to explore the effect of functional groups, tethering units,

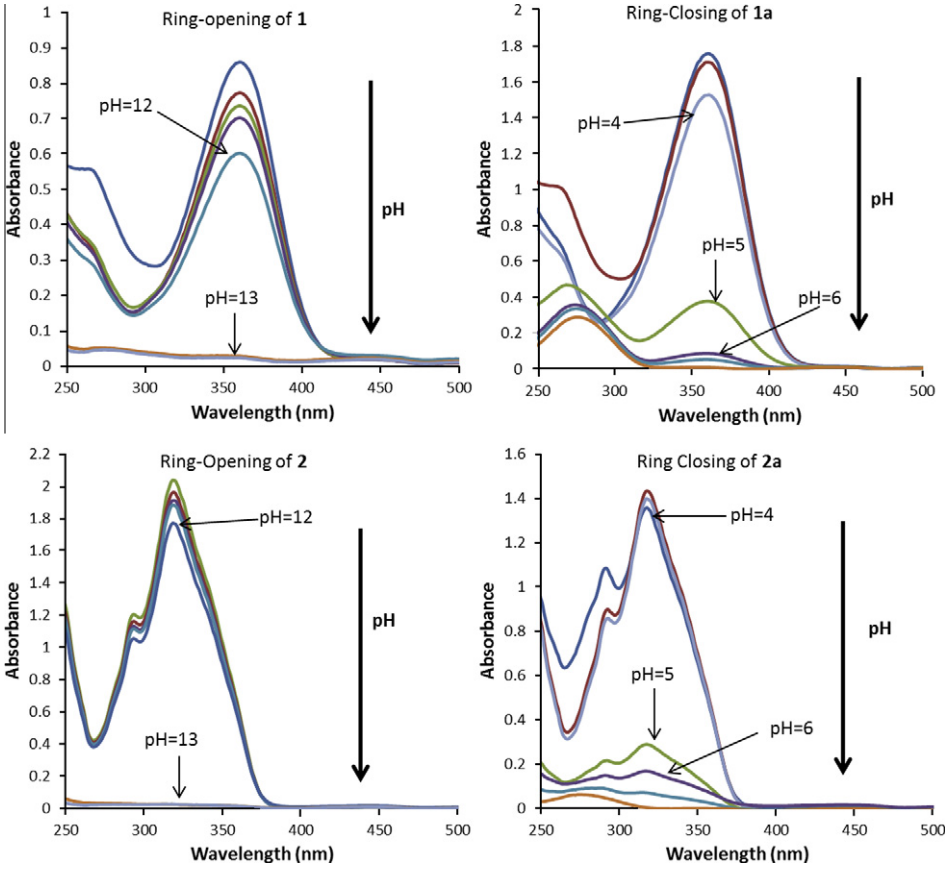


Figure 2. UV–Vis spectra of CH_2Cl_2 indicating the relative amounts of **1** or **2** present extractions after treatment at various pH.

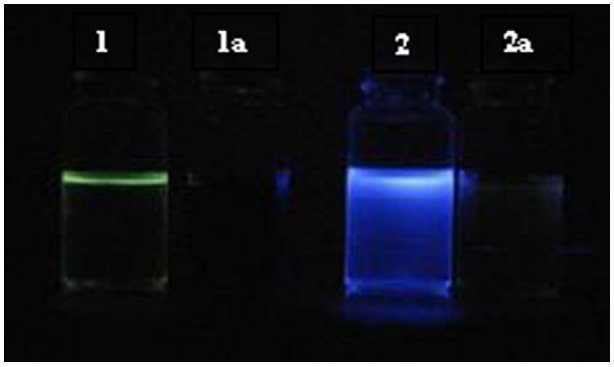


Figure 3. Photograph of, from left to right, samples of **1**, **1a**, **2**, and **2a** dissolved in CH_3CN irradiated under a UV lamp. Compounds **1a** and **2a** were generated via addition of TBA-OH to **1** and **2**, respectively.

and conjugation length on switching capabilities, ICT, and fluorescence.

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Supplementary data

Supplementary data (Details of spectroscopic studies, experimental procedures, and characterization data for all new compounds) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.09.016.

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