Activation of anthraquinone's electrophilicity by light
for a dynamic C-O bond

Vasily N. Bykov,[a,b] Stepan A. Ukhanev,[a] Igor A. Ushakov,[a] Anna V. Vologzhanina,[c]
Evgenii A. Antsiferov,[b] Lyubov S. Klimenko,[d] Andrey G. Lvov[a,b]*

[a] A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 1 Favorsky St., Irkutsk, 664033, Russia, e-mail: lvov-andre@yandex.ru

[b] Irkutsk National Research Technical University, 83 Lermontov St., Irkutsk, 664074, Russia

[c] A. N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Science, 28 Vavilova St., Moscow, 119991, Russia

[d] Yugra State University, 16 Chekhov St., Khanty-Mansiysk, 628012, Russia
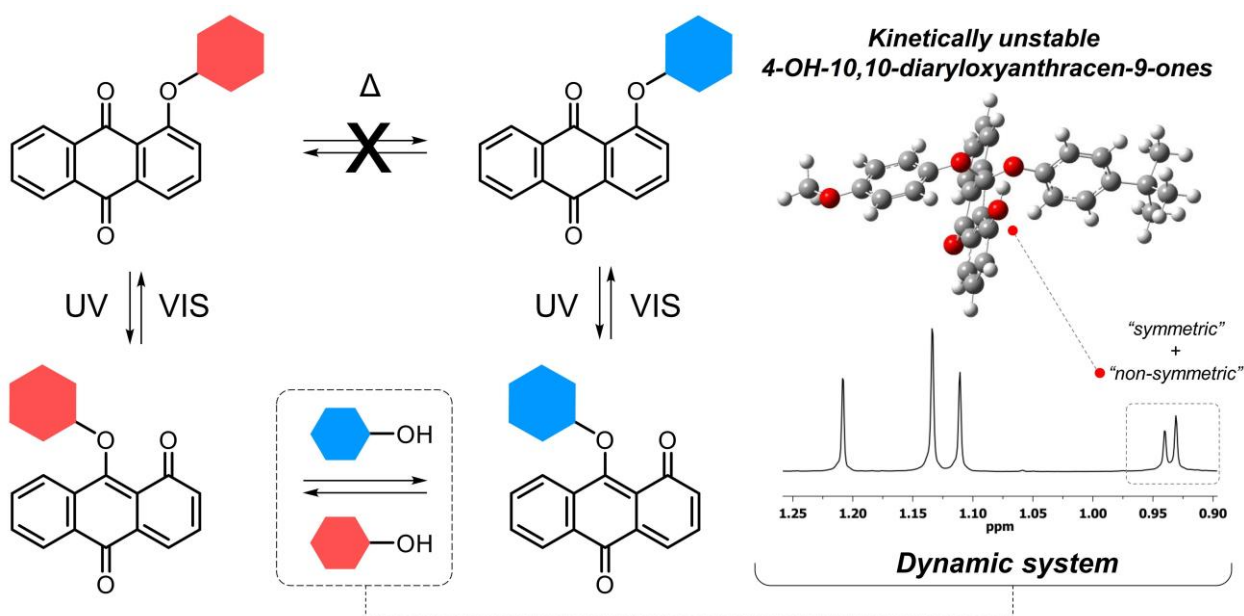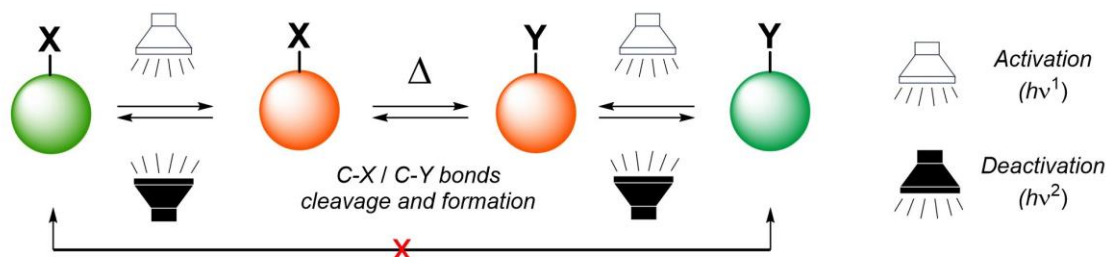
Abstract

Coupling of photoswitching with dynamic covalent chemistry enables the control of the formation and cleavage of covalent bonds by light irradiation. *Peri*-aryloxyanthraquinones feature an exclusive ability to switch electrophilicity by interconversion between *para-* and *ana*-quinone isomers, which was used for the first time for implementation of a dynamic C-O bond. Photogenerated *ana*-isomers undergo a concerted *oxa*-Michael addition of phenols to give hitherto unknown 4-hydroxy-10,10-diaryloxyanthracen-9-ones. These species were found to be in equilibrium with the corresponding *ana*-quinones, thus forming a dynamic covalent system of a new type. Withdrawal of the colored *ana*-quinones from the equilibria by visible-light irradiation resulted in two *para*-quinones with "locked" aryloxy groups.

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Photoswitching is a reversible interconversion of an organic molecule between two or more isomeric states under light irradiation.[1] A rational incorporation of a photoswitchable unit into a chemical system / material allows one to implement precise spatiotemporal control of various properties or trigger chemical processes in a selected volume.[2–4] In the past decade, this concept was probed in the emerging field of dynamic covalent (DC) chemistry[5] that manipulates the formation and cleavage of high-energy bonds aiming at the development of degradable, recyclable and healable materials[6–8] as well as drug delivery platforms.[9] In this way, reversible light-induced isomerization of a switchable molecule allows temporal chemical activation of certain functional groups that makes it possible to establish a dynamic covalent system enabling exchange of fragments to occur (Scheme 1A). Returning the switch to its initial state by light with a different wavelength leads to termination of the exchange and formation of a system with a new constitution. Various families of photochromic compounds have been exploited to implement photocontrollable DC systems (Scheme 1B). The activation of chemical activity for triggering a dynamic system could be achieved by changing the electronic properties (photocyclization of diarylethenes) or by spatial reconfiguration leading to enabling/disabling of intramolecular hydrogen bonding (*E*-/*Z*-isomerization of azobenzenes and acylhydrazones). Scheme 1C shows selected examples of switches for light-controllable DC bonds. Reversible switching of **DAE-1** enables a significant acceleration of imine exchange for two carboxaldehyde groups, which was used for the creation of a self-healing amino-functionalized polysiloxane (Scheme 1C).[10] Photocyclization of **DAE-2** leads to unmasking of the carbonyl group which participates in the reversible condensation with amines and hydrazides.[11] The unique spectral profile of this reaction gave an opportunity for bidirectional manipulation of the DC system by selective illumination of C=O or C=N species. **DAE-3** was successfully used in the controllable formation of C-O, C-N, and C-S bonds and was applied for the release of bioactive molecules, modification of surfaces, and creation of polymers exhibiting degradability/recyclability.[12] Light-induced switching of **AH**[13] and **AB**[14] enabled the control of (trans)esterification of boronate esters due to a high impact of the molecule's geometry on the possibility of the formation of intramolecular hydrogen bonds.

The application of the majority of known types of photoswitches in DC chemistry requires a special design and decoration of the photoactive core by certain functional groups. For example, common diarylethenes and azobenzenes themselves do not possess an *innate* ability to participate in DC systems (e.g., compare the parent diarylethene structure with **DAE-1,2,3** at Figure 1). Among diarylethenes, only a subgroup of α-cyano-derivatives undergoes the C=C bond cleavage and formation in the presence of strong bases.[15] In addition, some potentially photoactive[16] acylhydrazones could undergo exchange of building blocks under certain conditions.[17] In our work we show that *peri*-aryloxyanthraquinones (PAQs) are a unique family of photoswitches possessing
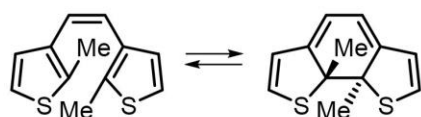
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an intrinsic ability to form systems with a dynamic C-O bond. Light-induced migration of an aryl group in PAQs led to the more electrophilic *ana*-isomer (1,10-anthraquinone), which undergoes a hitherto unknown *oxa*-Michael addition of phenols to give 4-Hydroxy-10,10-DiaryloxyAnthracen-9-ones (**HDA**, Scheme 1D). The **HDA** species are in equilibrium with *ana*-quinones and phenols, providing dynamic C-O bond.

Figure 1. Manipulating covalent bonds *via* photoswitching: a concept (A). Known photoswitches for DC systems (B). Selected examples of light-controllable DC bonds (C). Reversible photochemical arylotropy of PAQs and phenol addition to the photogenerated *ana*-isomer (D).

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Since the discovery by Gerasimenko in 1971,[18] PAQs were studied in a few research projects for the development of light-controllable electrodes,[19,20] multi-addressable switches,[21] and luminescent materials,[22] but their potential has not been fully realized to date.[23] To implement PAQs in DC chemistry, we used anthraquinone *para*-**2**, comprising an aryloxy group at position 1 and an additional amide substituent at position 2 (Figure 2A). The molecular structure of *para*-**2** obtained by X-ray crystallography disclosed an almost orthogonal arrangement of the 4-(*tert*-butyl)phenoxy substituent relative to the anthraquinone's plane (dihedral angle 88.7°), facilitating the migration of the aryl group. As a typical member of PAQs family,[23] *para*-**2** displays positive photochromism under UV light (λ^{ex} = 365 nm) irradiation (Figure 2B). During this process, the slightly yellow *para*-**2** (λ^{max} = 370 nm, ε = 12500 $M^{-1}cm^{-1}$) isomerizes into the red *ana*-**2** (λ^{max} = 545 nm, ε = 6500 $M^{-1}cm^{-1}$). The reaction occurs *via* spirocyclic biradical **SPI**, as was proved by Wirz et al.[24] Irradiation by green light (λ^{ex} = 512 nm) restore the initial spectra due to quantitative conversion of *ana*-**2** back to *para*-**2**. The quantum yield of the direct and back photoreactions was 0.32 and 0.014, respectively. The switching between *para*-**2** and *ana*-**2** could be performed at least 5 times in dry dichloromethane in the presence of air without notable fatigue. The isomerization led to the notable changes in the ^{1}H NMR spectra. The aromaticity loss and formation of a system of conjugated double bonds led to a notable shift of NH and H^3 protons, while the singlet of *tert*-butyl group changes only slightly (Figure 2B). The photostationary state conversion was found to occur by 80%, and irradiation by green light led to the restoration of the initial spectra.

The initial isomers of PAQs are stable 9,10-anthraquinones (the sample of *para*-**2** was stored under ambient conditions for a few decades without any degradation). In turn, the photogenerated isomers of PAQs are chemically active 1,10-anthraquinones (*ana*-quinones). Such compounds, as Boldt has demonstrated in the 1970s,[25,26] have a pronounced reactivity and undergo addition of nucleophilic species at position 9. To reveal the difference between the properties of the *para*-**2** / *ana*-**2** couple, we performed cyclic voltammetry and DFT calculations. *Para*-**2** has a reversible reduction wave at -1.3 V *vs.* Fc$^+$/Fc (Figure 2C). Exposure to light led to the appearance of a new reversible peak at -0.8 V corresponding to the *ana*-isomer, which is a better electron acceptor.[22] The isomerization led to decrease in the LUMO level and an increase in HOMO, as well as a change in their topology (Figure 2D). The electronic density of HOMO and LUMO of *ana*-**2** are located mainly on the 1,5-naphthaquinone part, in contrast to the *para*-isomer. The shape of electron density on LUMO ensures the nucleophile attack at position 9 (Figure S23). These results clearly demonstrate that PAQs give an opportunity to trigger the electrophilicity of a quinone by light in a reversible manner.
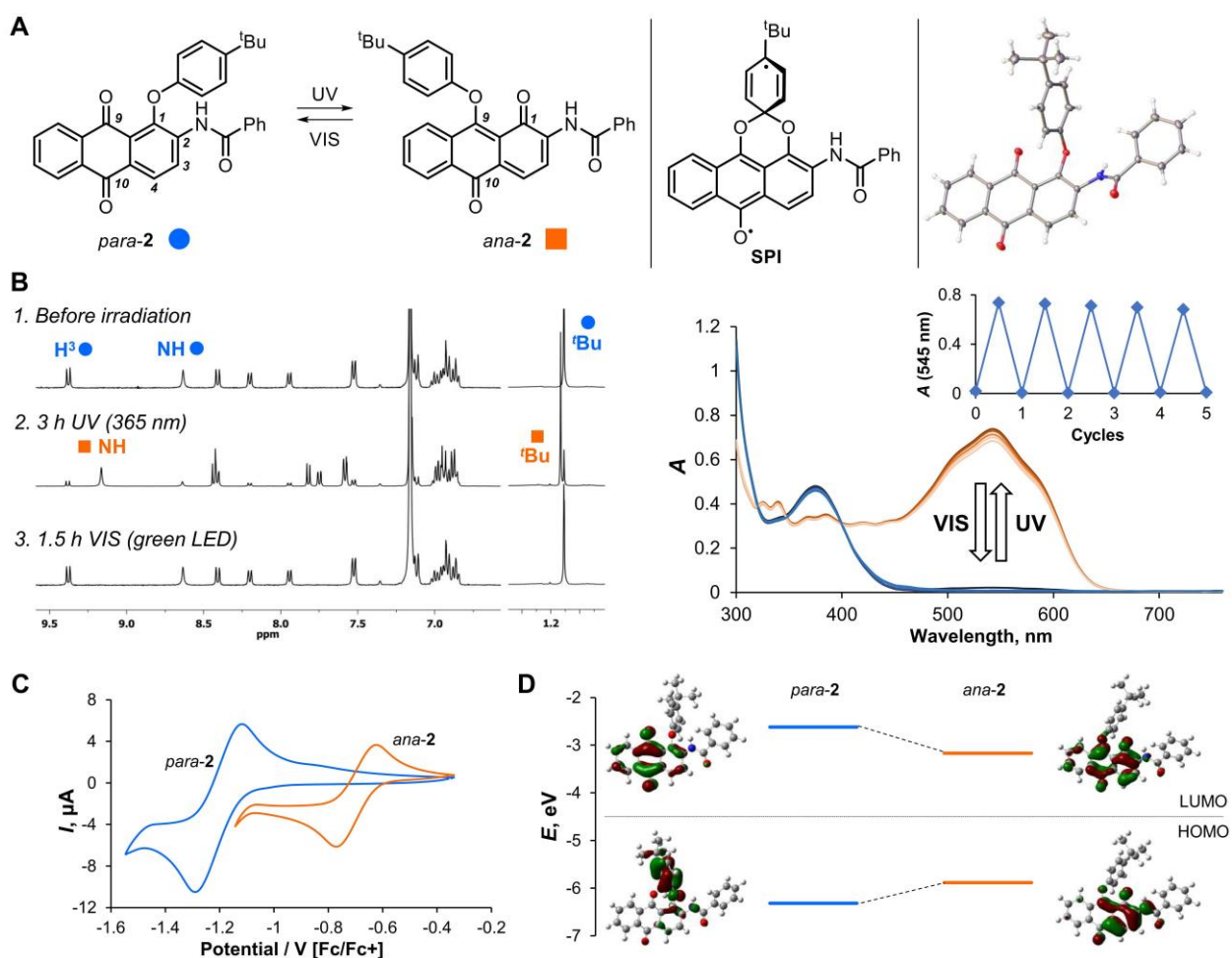
Figure 2. Photoswitching of *para*-**2**, the structure of biradical intermediate and molecular structure of *para*-**2** according to X-ray crystallography (A). ^{1}H NMR (solvent = benzene) and absorbance (solvent = dichloromethane) spectra after UV (365 nm) and green light irradiation (B). Cyclic voltammetry in the reduction region performed on *para*-**2** (blue line) and *ana*-**2** (orange line); acetonitrile / 0.1 M Bu$_4$NPF$_6$ (scan rate 0.1 V/s^{-1}) (C). Calculated HOMO and LUMO of *para*-**2** (blue line) and *ana*-**2** (orange line) (D).

To implement dynamic chemistry based on PAQs, we used the known[25,27,28] reactivity the *ana*-quinones towards nucleophiles. We assumed that the addition of 4-(*tert*-butyl)phenol (**TBP**) to *ana*-**2** would lead to the **HDA** adduct **3** with two equal aryloxy groups (Figure 3A). In contrast to the reactions of photogenerated *ana*-quinones with amines and alcohols,[27,29] this reaction should not lead to irreversible loss of switchable properties because back elimination would lead exclusively to *ana*-**2**. Indeed, irradiation of *para*-**2** in the presence of 1 equiv. **TBP** gave a mixture of *ana*-**2** and adduct **3** according to NMR spectroscopy (Figure 3B). The diaryloxy intermediate **3** featured a peak of two ^{t}Bu groups at 0.94 ppm as well as a resonance of hydroxy and amide groups at 8.70 and 8.56 ppm, respectively (the assignment was proved by HSQC NMR technique, Figure S2). Irradiation by green light led to complete disappearance of both

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photoproducts and restoration of the initial spectrum. According to DFT calculations (Table S11), **3** absorbs exclusively in the UV region. This means that **3** exists in thermal equilibrium with *ana-***2** and **TBP**, and withdrawal of the colored *ana*-quinone from the system by visible-light irradiation led to the disappearance of **3**. Addition of **TBP** to a pre-irradiated solution of *para-***2** led to the immediate formation of **3**, proving that it is a ground-state reaction (Figure S1).
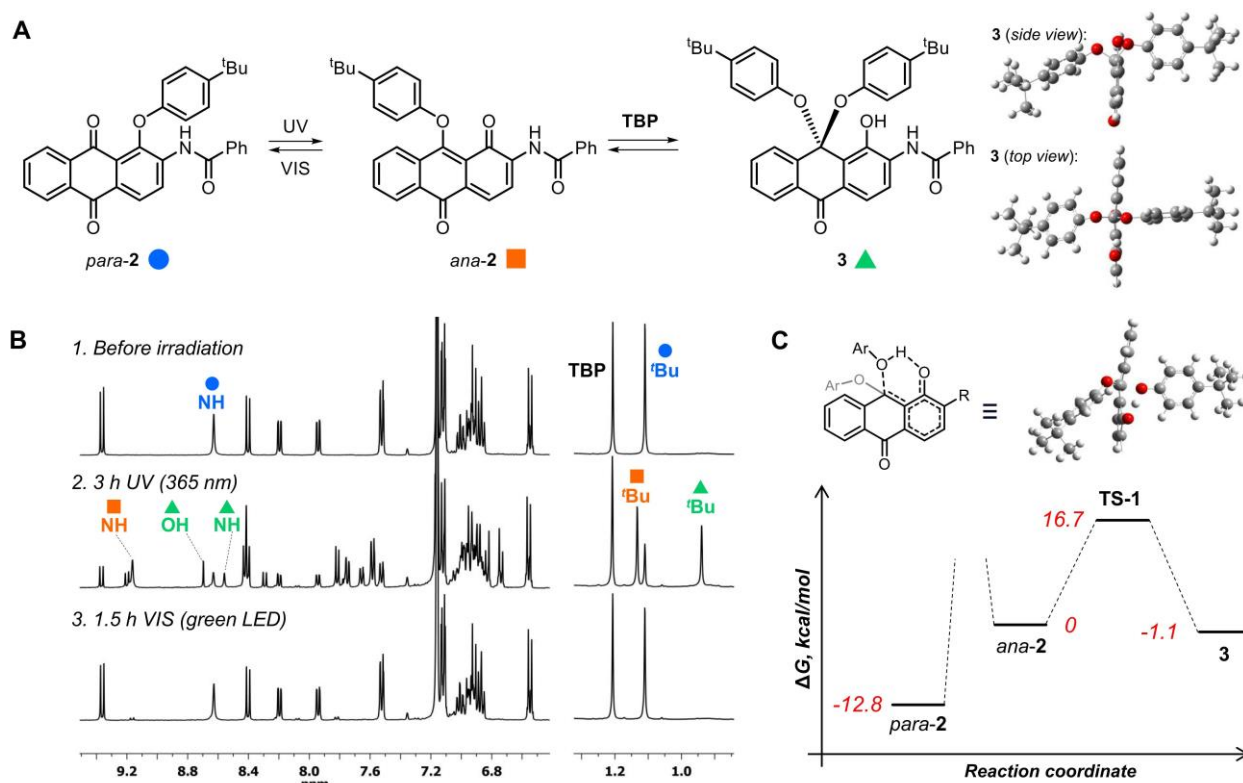

Figure 3. Reversible *oxa*-Michael addition of **TBP** to photogenerated *ana-***2** and the optimized structure of the 4-hydroxy-10,10-diaryloxyanthracen-9-one intermediate **3** (A). ^{1}H NMR spectra of a mixture of *para-***2** and **TBP** upon UV (365 nm) and green light irradiation (B). Energy profile of light-triggered addition of **TBP** to *para-***2**.

HDA species were not described previously, and we used density functional theory (DFT) calculations at PBE0/6-31G(d,p) level of theory to get preliminary data on their formation and structure. According to the calculations, **3** features two non-equivalent aryloxy groups with pseudo-equatorial and pseudo-axial orientations (Figure 3A), in accordance with the data for the related 9,9-dihydroanthracene[30] and anthrone[31] derivatives. Both aryloxy groups are directed away from the molecule and orthogonally to each other. Conformational analysis disclosed that the population of the major conformer is *ca.* 94% (Section VI.2 in SI). Obviously, **3** is formed by an *oxa*-Michael addition of **TBP** to the enone part of *ana-***2**. However, optimization of an initial zwitterionic intermediate of conjugated addition resulted directly in **3**. This allowed us to assume that the reaction occurs *via* a concerted mechanism, and we succeeded in localization of the six-centered transition state **TS-1** with an activation energy as low as 16.7 kcal/mol (Figure 3C).

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During nucleophilic addition of **TBP**, the existing aryloxy group leans to one side and becomes pseudo-axial, while the attacking group remains in a pseudo-equatorial position. The reaction is accompanied by restoration of phenol ring aromaticity that could favor the conjugated addition similarly to the recent example of thiol-Michael reaction.[32]

Finally, we probed the dynamic exchange of aryloxy groups in mixtures of the photogenerated *ana*-**2** with *para*-substituted (methoxy-, methyl-, chloro-, and nitro-) derivatives of phenol. In the initial state, *para*-**2** does not react with substituted phenols (Figures S8-11), but activation of electrophilicity paves a way to the exchange of aryloxy groups. Addition of 1 equiv. 4-methoxyphenol (**MOP**) to a pre-irradiated solution of *para*-**2** instantly led to the formation of the expected "non-symmetric" **HDA 4** with two different aryloxy groups and traces of *ana*-**7** bearing a methoxy-substituted aryloxy group and free **TBP** according to ^{1}H NMR spectroscopy (Figure 5B, spectrum c). The structure of **4** is proved by correlating the peaks of tBu, OMe, OH and NH groups as well as mass-spectrometry (Section IV in SI). After 1 h, the composition of the mixture changes significantly (spectrum d). We identified the emergence of two "symmetric" **HDA** species, **7** and **3**. After 24 h in the dark, the system contained three **HDA** species **4**, **6**, and **3** as well as two *ana*-quinones (*ana*-**2** and *ana*-**5**) in a ratio of *ca.* 1.00 : 1.4 : 0.2 : 0.5 : 0.7. Irradiation with green light completely shifted the thermal equilibrium from the **HDA**s to the *ana*-quinones due to the irreversible conversion of the latter species to the *para*-isomers. After the completion of back isomerization, the ratio between *para*-**2** and *para*-**5** was close to 1:1 (spectrum f). Utilization of a larger excess of **MOP** made it possible to increase the conversion from *para*-**2** to *para*-**5** up to 67% (Figure S3). In comparison with **TBP** addition (Figure 5C), the *oxa*-Michael reaction of **MOP** with *ana*-**2** is more exergonic and features a smaller energy barrier (15.2 *vs.* 16.7 kcal/mol). Rapid equilibrium[33] between conformers **4′** and **4″** of "non-symmetric" **HDA** enables connection between *ana*-**2** and *ana*-**5** in the dynamic system. Experiments with 4-methyl- and 4-chloro-substituted results gave the relevant results, and light-caused exchange of aryloxy group with *para*-**2** was observed (Figures S4, S5). The reaction of *ana*-**2** with 4-nitrophenol also led to the formation of the corresponding **HDA** intermediate. However, visible light irradiation led only to the traces of the exchange product (Figure S6). Thus, nucleophilicity of a phenol has a significant impact on the efficiency of aryloxy exchange.
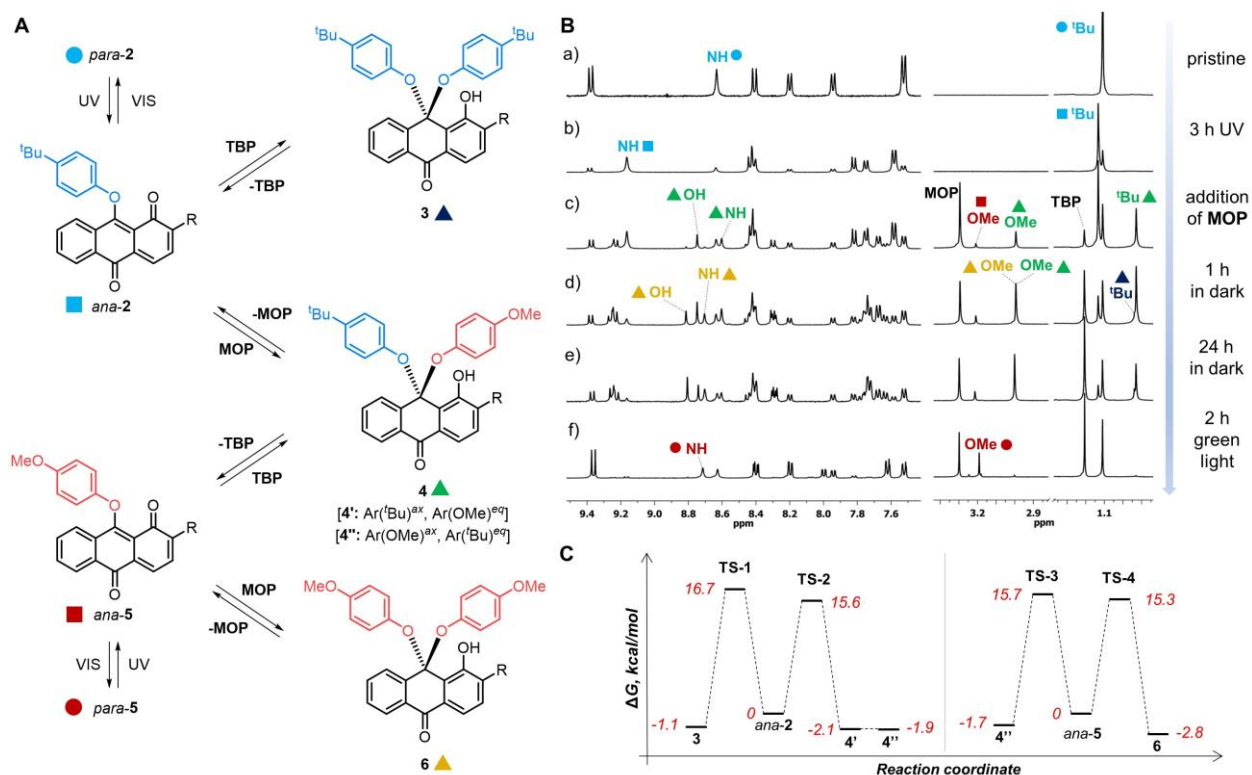
Figure 5. The dynamic multicomponent system launched by addition of 4-methoxyphenol (**MOP**) to *ana*-**2** (A) and ^{1}H NMR spectra of this process (B). The energy profile of the reactions of *ana*-quinones with phenols (C).

In conclusion, we presented *peri*-aryloxyanthraquinones (PAQs) as a unique class of photoswitches with an innate yet controllable ability to form dynamic covalent (DC) systems. The light-induced isomerization of PAQs from *para*- to *ana*-quinone increases the electrophilicity and enables the *oxa*-Michael addition of phenols towards 4-hydroxy-10,10-diaryloxyanthracen-9-ones. Their equilibrium with the corresponding *ana*-quinones open a way for exchange of different aryloxy groups. Deactivation of the DC system is performed by visible light irradiation, thus fixing the result of aryloxy group's exchange. Our findings could be used for the controllable conjugation of photoswitchable PAQs[23] with phenol-containing molecules and materials.

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