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Photoinduced Tandem Reactions of Isoquinoline-1,3,4-trione with Alkynes To Build Aza-polycycles

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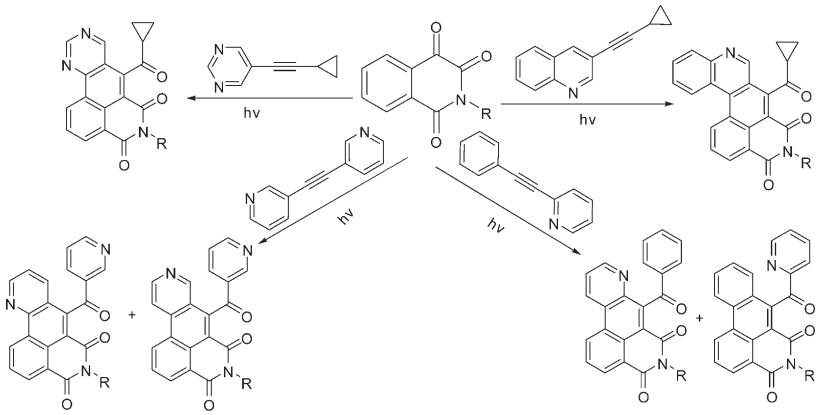

Photoinduced tandem reactions of isoquinoline-1,3,4-triones (**3**) with azaaryl substituted acetylenes (**4a**−**4o**) are described as an efficient method to build novel aza-polycycles. Most of the reactions proceeded *via* the tandem reaction sequence of photoinduced [2 + 2] cycloaddition (the Paterno−Büchi reaction)-oxetene electrocyclic ring opening-hexatriene to phenanthrene type electrocyclization-oxidative dehydrogenation. Using these photo tandem reactions of isoquinolinetrione with acetylenes substituted by different azaaryl rings including pyridine, pyrimidine, pyrazine, and quinoline, we were able to obtain diverse aza-polycyclic frameworks with isoquinolinedione fused with naphthalene, quinoline or isoquinoline, quinazoline, quinoxaline, and phenanthridine, respectively, with yields up to 85%. Regioselectivity of the [2 + 2] photocycloadditions and the electrocyclization reactions in the reaction sequence that leads to the formation of different aza-polycyclic ring systems is discussed. Changing the other substitution group on the azaaryl substituted acetylenes from benzene to pyridine or cyclopropane resulted in acetylenes with different photoreactivities with isoquinolinetrione and improved regioselectivity to form single aza-polycyclic products.

Introduction

Photoinduced organic reactions have played important roles in building diverse organic frameworks that are otherwise difficult to make.[1] Photocycloaddition along with subsequent cascade reactions has provided an expeditious way to construct various structures[1,2] including polycyclic compounds such as alkaloids,[1,3] polycyclic terpenoid,[4] and polycyclic heterocycles.[1,5] Synthesis of aza-polycyclic aromatic

(1) For reviews, see: (a) Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052. (b) Griesbeck, A. G.; Hoffmann, N.; Warzecha, K.. *Acc. Chem. Res.* **2007**, *40*, 128. (c) Winkler, J. D.; Bowen, C. M.; Liotta, F. *Chem. Rev.* **1995**, *95* (6), 2003. (d) Hoffmann, N. *Pure Appl. Chem.* **2007**, *79*, 1949.

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(3) For recent examples, see: (a) Winkler, J. D.; Axten, J. M. *J. Am. Chem. Soc.* **1998**, *120*, 6425. (b) White, J. D.; Ihle, D. C. *Org. Lett.* **2006**, *8*, 1081.

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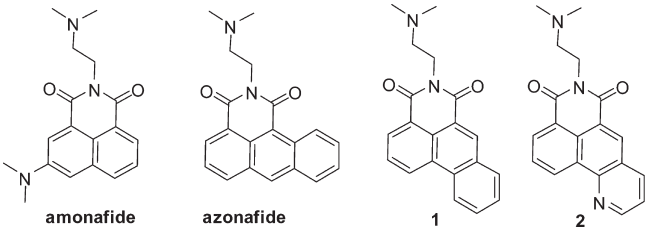
compounds with diversified structure is of current research interest[6] because aza-polycycles and their ring-substituted derivatives are important heterocycles with pharmocological and biological activities.[7] Aza-polycycles with isoquinoline-fused ring systems have been reported to have DNA binding and cleavage abilities.[8] Aza-polycyclic analogues of amonafide and azonafide, such as 5,6-dihydro-4*H*-dibenz[*de*,*g*]-isoquinoline-4,6-dione (**1**) or 5,6-dihydro-4*H*-quinolino-[7,6,5-*de*]isoquinoline-4,6-dione (**2**) derivatives (Scheme 1), have been found to have antitumor activities.[9,10] It is therefore interesting to develop convenient methods to build aza-polycycles with isoquinolinedione-fused moieties. Photoinduced cascade reactions that could lead to the formation of isoquinolinedione-fused polycyclic compounds from readily available materials such as carbonyl compounds and acetylenes could serve well for this purpose.

The Paterno−Büchi reaction is the photoinduced [2 + 2] cycloaddition between an nπ* excited carbonyl compound and alkenes or alkynes.[11] Paterno−Büchi reactions of carbonyl compounds and alkenes have been widely investigated both in synthetic and mechanistic aspects,[12] and the regioselectivity and stereoselectivity of these reactions have been of much current research interest.[13] However, photocycloadditions of carbonyl compounds with alkynes have not been explored extensively so far[14] compared with alkenes. It is known that Paterno−Büchi reactions of carbonyl compounds with alkynes usually give quinone methides as the result of rearrangements of the labile oxetenes formed by the [2 + 2] cycloaddition.[15] In our previous work on photoinduced electron transfer reactions between *o*-diones and diverse electron donors,[16,17] we found that Paterno−Büchi reactions between *o*-diones and acetylenes followed by subsequent spontaneous thermal and photochemical transformations of the oxetene primary product may result in the formation of complex polycyclic heterocycles.[17] For example, the photoreactions between *N*-acetylisatin and terminal acetylenes were found to give novel final products such as dispiro[oxindole[3,2′]furan[3′,3″]oxindole]s as a result of the tandem reactions with quinone methide formation as the initial step.[17a,b] The versatile roles played by quinone methides as intermediates in the photo tandem reactions indicated that it is important to choose the right combination of carbonyl compounds and acetylenes to induce desired tandem reactions *via* quinone methide intermediates.

SCHEME 1. Bioactive Isoquinolinedione-Fused Polycyclic Compounds



Isoquinoline-1,3,4-trione and its derivatives have been known as redox mediators of photosystems I and also have been used as herbicides.[18] Recently it was reported that isoquinoline-1,3,4-trione derivatives are potent caspase-3 inhibiotors[19] and can attenuate β-amyloid-induced apoptosis of neuronal cells.[20] As an important *o*-dione species, isoquinolinetrione has been used as building block in the

(5) For recent examples, see: (a) Feldman, K. S.; Hester, D. K.; Iyer, M. R.; Munson, P. J.; Silva Lopez, C.; Nieto Faza, O. *J. Org. Chem.* **2009**, *74*, 4958. (b) Winkler, J. D.; Axten, J.; Hammach, A. H.; Kwak, Y.-S.; Lengweiler, U.; Lucero, M. J.; Houk, K. N. *Tetrahedron* **1998**, *54*, 7045. (c) Tzvetkov, N. T.; Neumann, B.; Stammler, H. G.; Mattay, J. *Eur. J. Org. Chem.* **2006,** *2,* 351.

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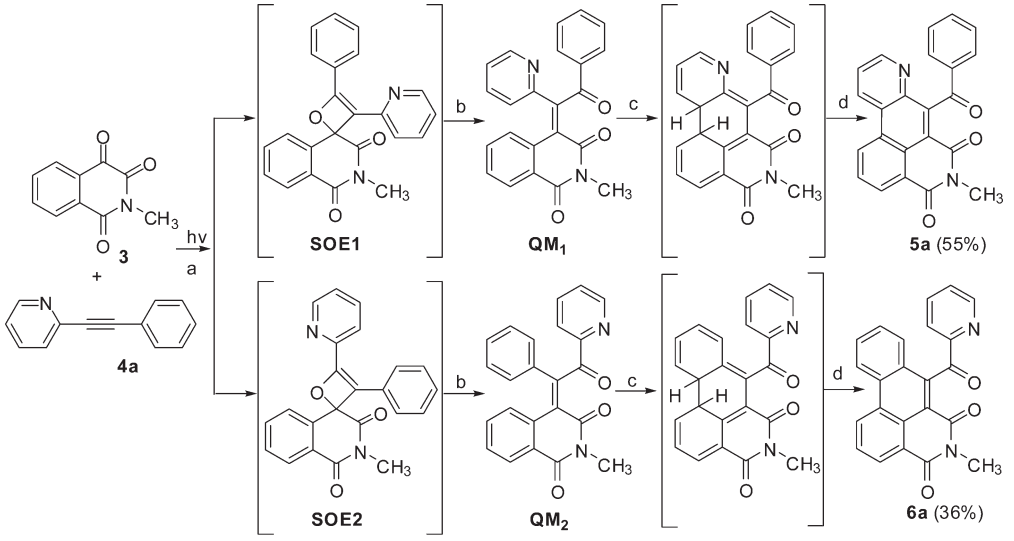
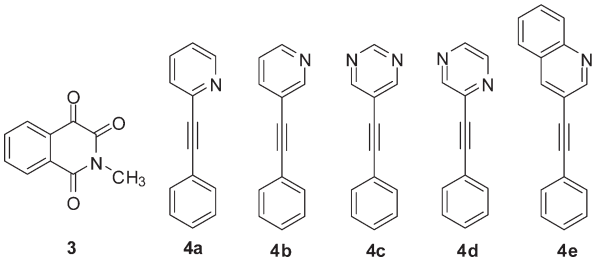
SCHEME 2. Proposed Pathway for the Photoinduced Tandem Reaction between Isoquinolinetrione and 2-(Phenylethynyl)pyridine



synthesis of benzo[*c*]phenanthridine alkaloids.[21] The C4 carbonyl group in isoquinoline-1,3,4- trione provides an ideal photoreactive site for photoinduced reactions that may result in diverse isoquinoline-related heterocycles. However, its photoreaction has rarely been studied. In our preliminary study on photoreactions between isoquinolinetrione and diphenylacetylenes,[17c] we observed an photoinduced sequential reaction that provided an efficient one-pot method to prepare dibenz[*de*,*g*]-(2*H*)-isoquinoline-4,6-dione derivatives. To explore further on the applications of similar sequential reactions to form different azaaryl-fused isoquinolinedione derivative, we synthesized a series of azaaryl substituted acetylenes and investigated their photoreactions with 1,3,4-isoquinolinetrione **3**. The reactions proceeded *via* a sequential photocycloaddition-oxetene rearrangement-cyclization-dehydrogenation sequence and resulted in the formation of novel isoquinoline-fused aza-polycyclic derivatives.

Results and Discussion

Photoreactions of Isoquinolinetrione (3) with 1-Phenyl-2-azaarylethynes 4a−4e.



A series of 2-azaaryl substituted phenylacetylene (**4a**−**4e**) in which the azaaryl is pyridine, pyrimidine, pyrazine, or quinoline were prepared, and their photoreactions with *N*-methyl 1,3,4-isoquinolinetrione **3** were investigated. Formation of various isoquinoline-fused aza-polycyclic compounds was observed in the photoreactions of these different acetylenes with isoquinolinetriones. Solvent for the photoreactions was optimized, and reactions in acetonitrile gave the highest conversion rate of 1,3,4-isoquinolinetrione **3** compared with reactions in benzene, acetone, and dichloromethane. For acetylenes with two different substitution groups, their photoinduced tandem reactions with isoquinolinetrione are proposed to proceed *via* different quinone methide intermediates whose structure determines the framework of the polycycles in the final products. For example, photolysis of *N*-methyl-1,3,4-isoquinolinetrione **3** and 2-(phenylethynyl)-pyridine **4a** in acetonitrile resulted in the formation of a quinoline fused isoquinolinedione **5a** (55%) and a naphthelene fused isoquinolinedione **6a** (36%). The regioselectivity of the initial photocycloaddition step plays a decisive role in the ratio of naphthalene-fused isoquinolinedione derivative to other isoquinolinedione-fused aza-polycycles in the final products. To get accurate information on the regioselectivity involved in the photoreactions, the reaction mixtures were analyzed by HPLC to give the relative ratio of different products.

The photoinduced tandem reaction was proposed to proceed *via* the pathway shown in Scheme 2. Photoinduced [2 + 2] cycloaddition (Paterno−Büchi reaction) between the acetylene **4a** and isoquinolinetrione **3** led to formation of the unstable spirooxetene (SOE) intermediates. Triplet state of isoquinolinetrione ^{3}**3*** was confirmed to be the reactive excited state since the presense of quencher such as styrene or quinoline quenched the reaction effectively as we described before.[17c] The Paterno−Büchi reaction between the excited **3** and **4a** proceeded *via* the two oxetene intermediates **SOE1** and **SOE2** with regioselectivity. Rearrangement of **SOE1** gave the quinone methide **QM1**, while **SOE2** gave **QM2** correspondingly. Although quinone methides were the final products for most Paterno−Büchi reactions between quinone and alkynes,[17a,22d] **QM1** and **QM2** formed here were further involved in a spontaneous electrocyclization and subsequent oxidative dehydrogenation reaction,

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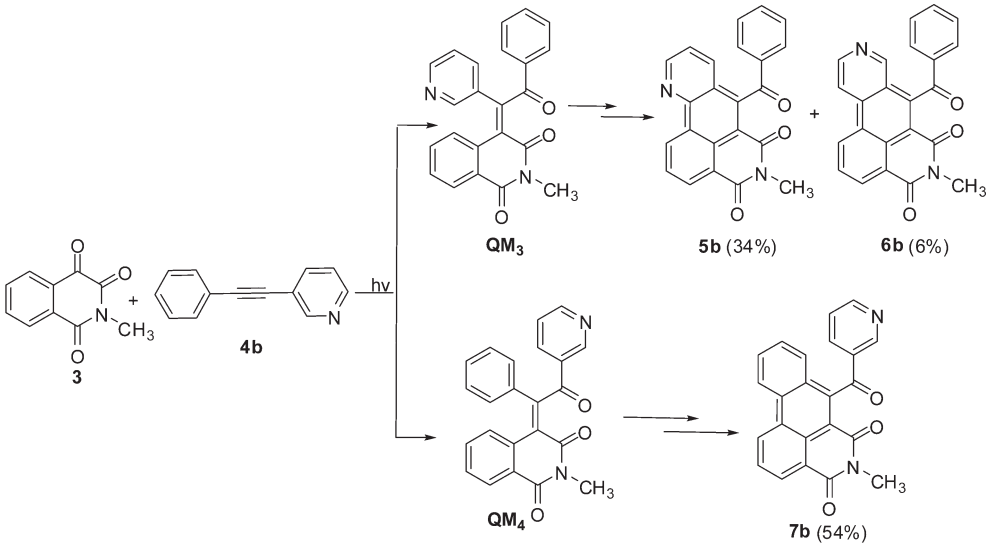
SCHEME 3. Quinone Methide Intermediates and Aza-polycyclic Products Formed in the Photoreaction between isoquinolinetrione 3 and 3-(Phenylethynyl)pyridine 4b



and the reaction ended with the formation of the aza polycyclic products **5a** and **6a**.

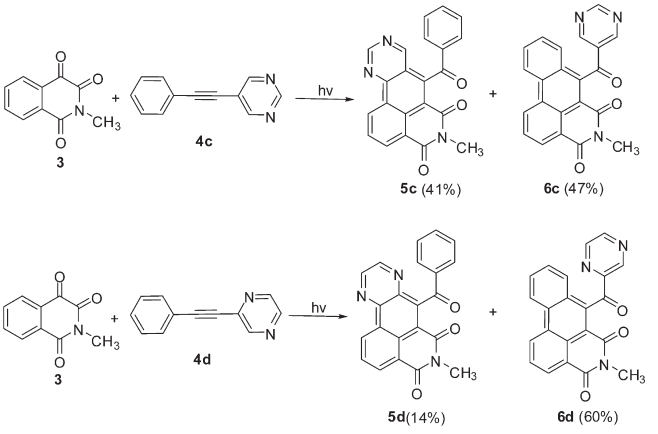
The transformation of the quinone methides **QM1** and **QM2** to **5a** and **6a** is similar to the stilbene−phenanthrene phototransformation.[22] It is noteworthy that the tandem reaction could happen even if the reaction was performed under Ar atmosphere. Since alkenes such as cyclohexene has been found to act as an oxidant for a similar dehydrogenation reaction,[23] we questioned whether the C=C bond in the quinone methide intermediates **QM1** and **QM2** could be the oxidant for the dehydrogenation step. However, the absence of hydrogenated quinone methides in the final products as the corresponding reduced species was against this possibility. Therefore, we believe that a trace amount of oxygen in the reaction mixture should have played an essential role in the oxidation leading to the final aza-polycyclic compounds. The favorable geometry in **QM1** and **QM2** made the following transformation to **5a** and **6a** spontaneous under the reaction conditions with trace amount of O_2 as oxidant.

The regioselectivity of the initial photocycloaddition step could be attributed to the relative stability of the corresponding diradical intermediates **DR1** and **DR2** (Figure 1 in Supporting Information). **SOE1** was formed by radical recombination of the diradical intermediate **DR1** with one radical adjacent to the 2-pyridinyl group, while **SOE2** was formed from **DR2** with one radical adjacent to the phenyl group. A DFT calculation on the triplet 1,4-diradicals **DR1** and **DR2** at the UB3LYP/6-31G level showed no distinct difference on their energy level. It is in accord with the poor regioselectivity of the initial photocycloaddition reaction as shown in Scheme 2 that finally leads to the similar yields of **5a** and **6a** (55% and 36% respectively) in the final products.

Photolysis of *N*-methyl-1,3,4-isoquinolinetrione **3** and 3-(phenylethynyl)pyridine **4b** resulted in a quinoline fused isoquinolinedione **5b** (34%), an isoquinoline fused isoquinolinedione **6b** (6%), and a naphthelene fused isoquinolinedione **7b** (54%) (Scheme 3). While **5b** and **6b** were formed through the same quinone methide intermediate $\mathbf{QM_3}$, **7b** was from the other quinone methide isomer $\mathbf{QM_4}$. The relative ratio of the product in the reaction mixture showed that the two quinone methide intermediates $\mathbf{QM_3}$ and $\mathbf{QM_4}$ were also formed with little regioselectivity. However, the cyclization of the intermediate $\mathbf{QM_3}$ is highly regioselective, with the α-C of the N atom on the pyridine ring being the predominant site of electrocyclization and dehydrogentation to give **5b** as the major product, while cyclization at the alternative site (C4 in the pyridine ring) contributes only slightly to give **6b** as a minor product. It therefore indicates that the electron-negative N atom made its adjacent position more labile for electrocyclization.

Other than phenyl pyridinyl acetylenes, 3-(phenylethynyl) pyrimidine **4c** and 2-(phenylethynyl) pyrazine **4d** were also used in the photoreactions with isoquinolinetrione **3**. Final products isolated from the reaction mixture and their corresponding quinone methide precursors are shown in scheme 4. The photoreaction between **3** and **4c** proceeded smoothly and within 48 h of irradiation all of the starting material **3** could be converted to give two major products **5c** and **6c** (41% and 47%, respectively). Again the similar yields of the quinazoline fused isoquinolinedione **5c** and the naphthalene

SCHEME 4. Photoinduced Cascade Reactions between Isoquinolinetrione 3 with 4c and with 4d



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SCHEME 5. Regioselective Photocycloaddition and Regiospecific Electrocyclization Involved in the Photo Tandem Reaction Sequence of 3 with 4e

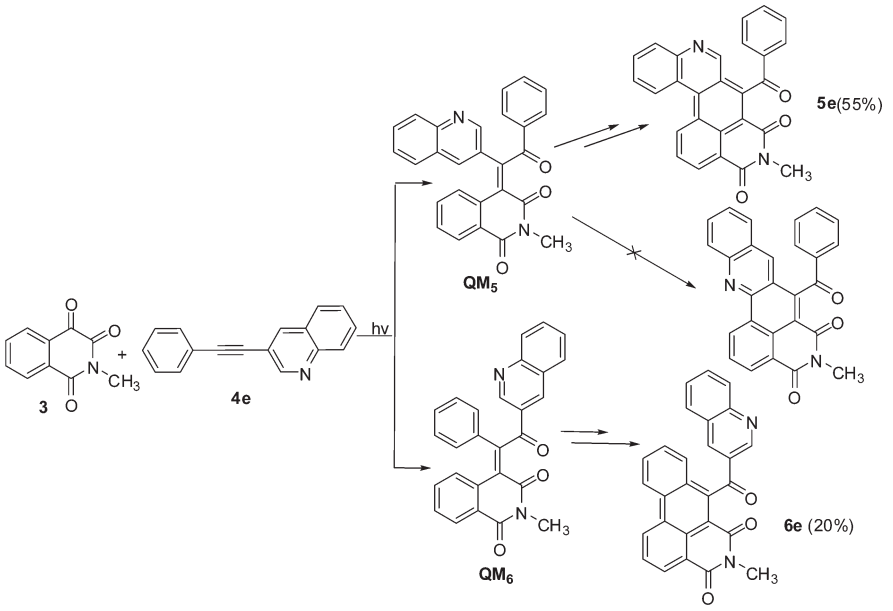


TABLE 1. Results of the Photoreactions of *N*-Methyl-1,3,4-isoquinolinetrione 3 with Pyridinyl Aza-arynyl Acetylenes

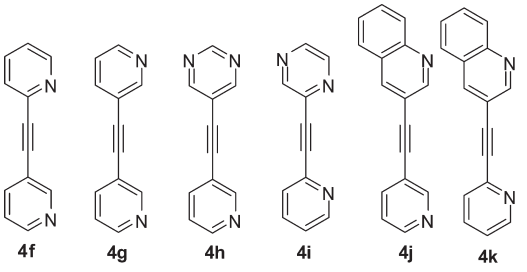
entry	alkyne	irradiation time (h)	conversion (%)	products and yield[a]
1	**4f**	48	72	**5f** (13%), **6f** (61%), **7f** (23%)
2	**4g**	48	100	**5g** (30%), **6g** (64%)
3	**4h**	48	100	**5h** (33%), **6h** (18%), **7h** (30%), **8h** (9%)
4	**4i**	48	45	**5i** (88%), **6i** (8%)
5	**4j**	60	30	**5j** (80%)
6	**4k**	60	28	**5k** (85%)

[a]isolated yield based on consumed isoquinolinetrione **3**

fused isoquinolinedione **6c** indicated poor regioselectivity in the photocycloaddition step. On the other side, when 2-(phenylethynyl) pyrazine **4d** was irradiated together with isoquinolinetrione **3**, the quinoxaline fused isoquinolinedione **5d** was formed in a yield of 14% while its isomer **6d** accounted for 60% of the products. This indicates that the initial photocyclization is more regioselective. It is also noteworthy that the pyrazine substitution on the acetylene seemed to be an unfavorable factor on the reactivity since only 85% of **3** was consumed after 48 h of irradiation.

As a representative example of photoreaction between isoquinolinetrione with quinoline substituted acetylene, the reaction between **3** with 3-(phenylethynyl)quinoline **4e** was also investigated. The absorption wavelength of **4e** is longer than that of **4a**−**4d**, and the partial overlap of its absorption spectrum with that of isoquinolinetrione resulted in competitive absorption with **3**. Therefore, slower reaction of **4e** with **3** was observed compared with **4a**−**4d**. Upon 60 h of irradiation at 400 nm, a maximum of 70% conversion of **3** could be achieved, and prolonged irradiation did not increase the conversion significantly. Based on the converted isoquinolinetrione, the yields of **5e** and **6e** were 55% and 20%, respectively, indicating a moderate regioselectivity of the initial photocycloaddition reaction. It is noteworthy that only two isomers were detected in the final products instead of three possible isomers as shown in Scheme 5. Only the phenanthridine fused isoquinolinedione **5e** formed from the intermediate $\mathbf{QM_5}$, and no acridine fused product was isolated. The C4 position in the quinoline ring is preferred for further cyclization, leading to a highly regioselective cyclization of the quinone methide $\mathbf{QM_5}$.

Photoreactions of Isoquinolinetrione with Pyridinyl Aza-arynyl Acetylenes.



To further explore whether the regioselectivity of the photoinduced tandem reaction is controllable through proper combinations of different substitution groups at the two ends of the acetylene, we synthesized acetylenes with pyridine at one end and another aza-aryl group at the other (**4f**−**4k**) and investigated their photoreactions with isoquinolinetrione **3**. We observed that pyridine substituted at C2 and C3 contributed differently to the regioselectivity as well as the reactivity of the acetylenes in their photoreactions with isoquinolinetrione. The 1,2-di(pyridin-2-yl)ethyne with two 2-pyridinyl substituents showed very low reactivity with isoquinolinetrione **3**. When one of the 2-pyridinyl groups was replaced by the 3-pyridinyl group as in **4f**, it could convert 72% isoquinolinetrione **3** into the tetracyclic products after 48 h of irradiation (Table 1). The regioselectivity in the photocycloaddition and electrocyclization steps in the tandem reaction of **3** with **4f** is shown in Scheme 6. The amount of the products **6f** and **7f** with the original 3-pyridinyl ring cyclized with the isoquinolinedione was almost 6 times more than that of **5f**, which derived from

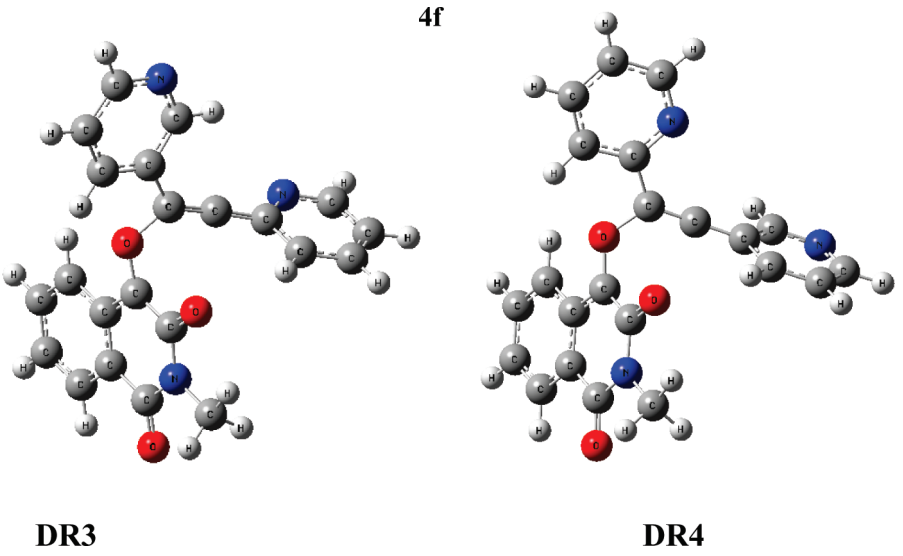
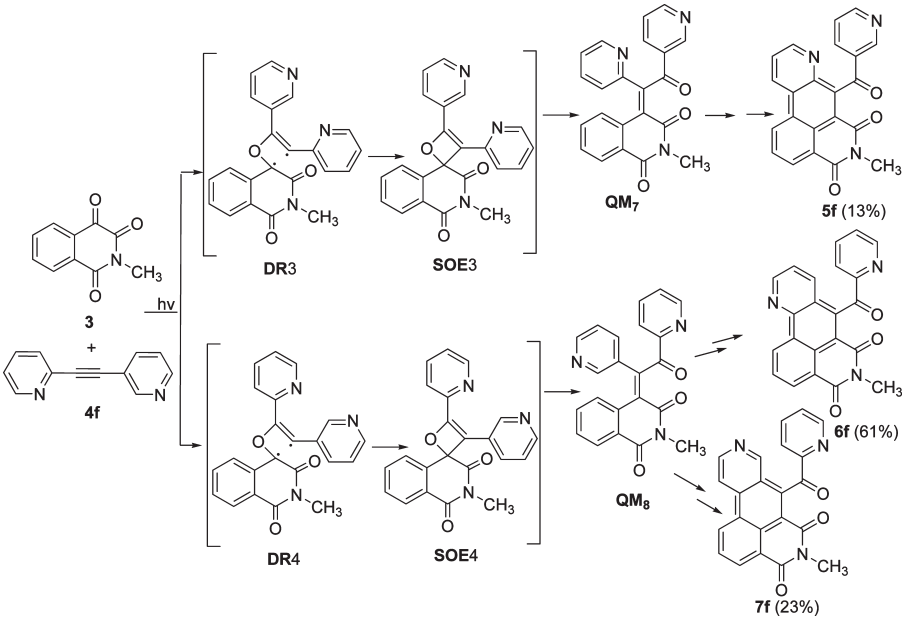


FIGURE 1. Structures of diradical intermediates **DR3** and **DR4**.

SCHEME 6. Regioselectivity in the Photocycloaddition and Electrocyclization Steps in the Reaction Sequence of 3 with 4f



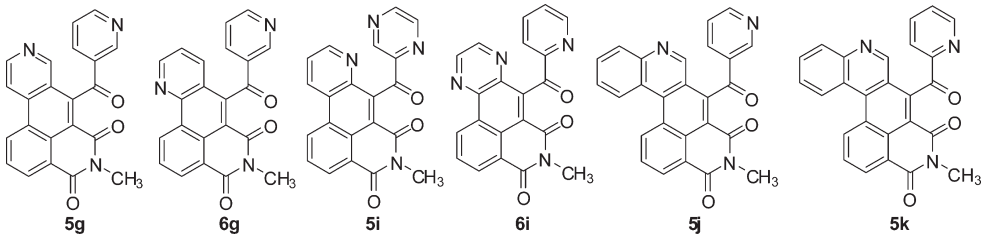
the cyclization of the original 2-pyridinyl ring with the isoquinolinedione.

We envision that this regioselectivity results from the relative stability of the 1,4-diradical intermediate in the Paterno–Buchi-type reaction[24] and suggests a greater thermodynamic stability of the 1,4-diradical intermetidates **DR4** than the corresponding regioisomeric diradicals **DR3** (Scheme 6). We carried out a DFT calculation on the structures of the triplet 1,4-diradicals **DR3** and **DR4** at the UB3LYP/6-31G level, and it turns out that the α-pyridinyl vinyl radical center has a linear structure (pyridinyl to C=C bond angle: 173° in **DR3** and 174° in **DR4**) as shown in Figure 1, with the spin bearing carbon atom having an sp hybridization so that the pyridinyl π system is orthogonal with the vinyl C=C π orbital but is parallel with the singly occupied p-orbital at the sp-hybridized carbon atom, resulting in unpaired electron delocalization to the pyridinyl. The DFT calculation on the relative energy showed that the diradical **DR4** was 2.0 kcal·mol^{-1} lower than **DR3**, which could have contributed to the regioselectivity of the photocycloaddition as shown in Scheme 6.

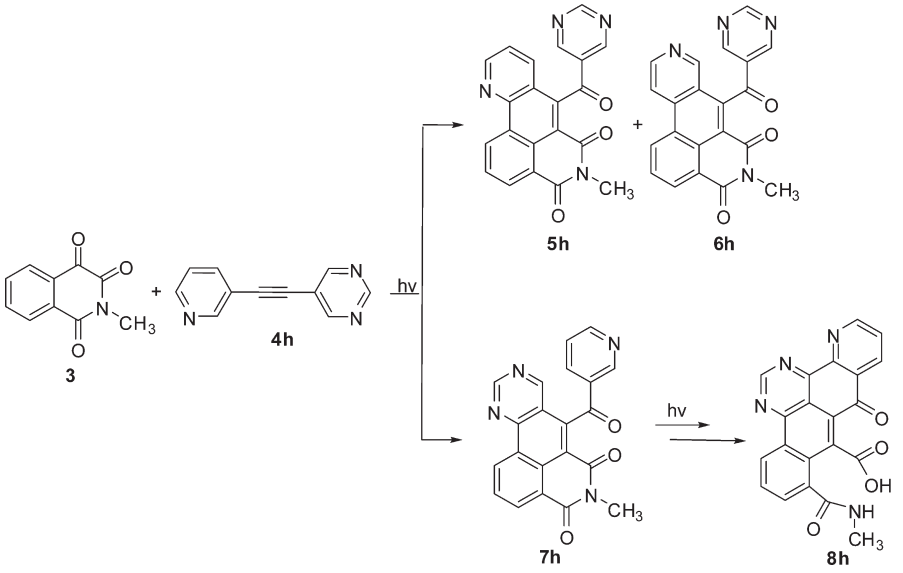
The regioselectivity in the electrocyclization of the 3-pyridinyl with the isoquinolinedione in the quinone methide intermediate showed an obvious preference on the α-position of pyridine N over the other available site. The relative ratio of **5b**/**6b** in Scheme 3 and **6f**/**7f** in Scheme 6 consistently showed the tendency. Therefore it is not surprising that reaction of **3** with the symmetrically substituted acetylene

(24) (a) Freilich, S. C.; Peters, K. S. *J. Am. Chem. Soc.* **1981**, *103* (20), 6255. (b) Schepp, N. P.; Johnston, L. J. *J. Am. Chem. Soc.* **1996**, *118* (12), 2872. (c) Peters, K. S. *Adv. Electron. Trans. Chem.* **1994**, *4*, 27. (d) Eckert, G.; Goez, M. *J. Am. Chem. Soc.* **1994**, *116* (26), 11999. (e) Friedrich, L. E.; Bower, J. D. *J. Am. Chem. Soc.* **1973**, *95* (20), 6869.

SCHEME 7. Chemical Structure of Products from the Photoreactions of 3 with 4g, 4i, 4j, and 4k, Respectively



SCHEME 8. Primary and Secondary Products Formed in the Photoreaction between 3 and 4h



4g gave **5g** and **6g** (Scheme 7) with a ratio of 1:2 (Table 1). Moreover, it is interesting that we found an overconjugated product **8h** in the reaction between **3** and **4h** (Scheme 8). The product **8h** was formed from the primary product **7h** through further electrocyclization of the 3-pyridinyl with the quinazoline-fused isoquinolinedione. The primary product **7h** was also isolated from the reaction mixture, and its structure has been confirmed by X-ray single crystallagraphic analysis (Supporting Information). Transformation from **7h** to **8h** was observed by irradiating the solution containing **7h** with >400 nm light. The highly conjugated product **8h** showed poor solubility but strong fluorescent emission around 430 nm even in diluted solutions (Supporting Information). The isoquinoline-fused isoquinolinedione **6h**, whose structure has also been confirmed by X-ray single crystallagraphic analysis (Supporting Information), could not undergo further electrocyclization to form overconjugated systems like **8h** under similar reaction conditions.

Products of the photoreactions between isoquinolinetrione **3** and **4i**, **4j**, and **4k**, respectively, are shown in Scheme 7. High regioselectivity was found in the reaction of isoquinolinetrione **3** with the quinoline pyridine substituted acetylene**s 4j** and **4k**. The yields of different products as well as the conversion rate of the isoquinolinetrione **3** are listed in Table 1. Compared with other acetylenes, lower reactivity was observed in the acetylenes **4i**, **4j**, and **4k** with isoquinolinetrione **3**. Less than 50% **3** could be converted into aza-polycyles even after prolonged photo irradiation. The relatively low reactivity of **4i** might be attributed to the less stabilizing effect of 2-pyridinyl or 2-pyrazinyl group on the diradical intermediates. The competitive absorption of **4j** and **4k** might be one reason for the low conversion rate of isoquinolinetrione **3** in its photoreactions with these acetylenes. On the other side, the scattered distribution of the precipitated final product in the reaction mixture might also lead to the low conversion of the reactants because light to excite the isoquinolinetrione for photoreaction was blocked or scattered. However, it is worth mentioning that it was very convenient to get the pure product **5j** or **5k** from the reaction mixture of **3** with **4j** or **4k** because the sole product just precipitated out along with the photoirradiation. Pure **5j** or **5k** could be isolated simply by collecting the precipitate.

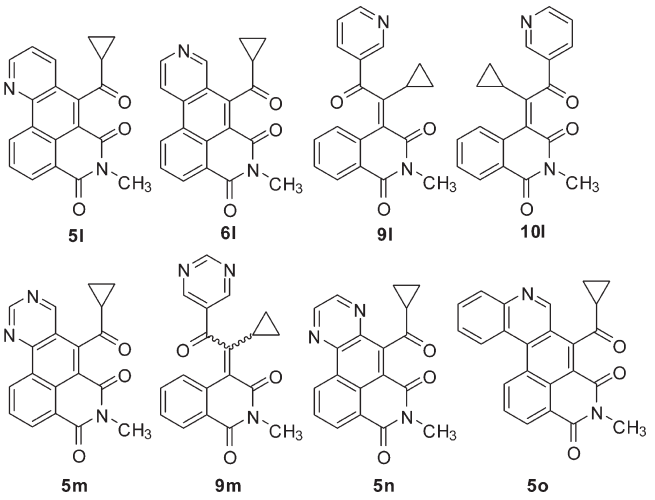
Photoreactions of Isoquinolinetrione with Alkyl Arynyl Acetylenes. The photoinduced tandem reaction was then extended to acetylenes with only one aryl substitution group since it might lead to quinone methides products which may serve as evidence for our proposed mechanism for these photo cascade reactions. It turned out that terminal acetylenes with only one aryl substituent had very poor reactivity with isoquinolinetrione. No aza-polycyclic compounds could be obtained in the photoreactions of isoquinolinetrione with 2-pyridinyl acetylene or 3-pyridinyl acetylene. Electron withdrawing group such as ester group linked to the acetylene also made the alkyne unreactive toward **3**. However, acetylenes with an azazryl substituent on one end and an alkyl group on the other end showed reasonable reactivity in the photoreactions with isoquinolinetriones **3** (Table 2).

TABLE 2. Results of the Photoreactions of Isoquinolinetrione 3 with Alkyl Arynyl Acetylenes

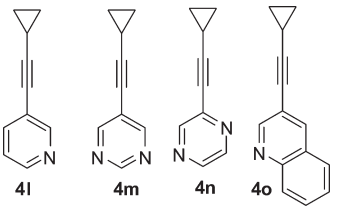
entry	alkyne	atmosphere	irradiation Time (h)	conversion (%)	products and yield[a]
1	**4l**	Ar	12	71	**5l** (38%), **6l** (31%), **9l** (10%), **10l** (8%)[b]
		O_2	12	80	**5l** (41%), **6l** (31%),**9l** (9%), **10l** (7%)[b]
2	**4m**	Ar	12	90	**5m** (62%), **9m** (21%)[b]
		O_2	12	93	**5m** (69%), **9m** (18%)[b]
3	**4n**	Ar	48	nr[c]	
		O_2	12	46	**5n** (59%)
4	**4o**	Ar	12	45	**5o** (69%)
		O_2	12	57	**5o** (88%)

[a]Yield based on consumed isoquinolinetrione. [b]Exact ratio quantified by HPLC. [c]No reaction.

SCHEME 9. Products Isolated from the Photo Tandem Reactions between 3 and Acetylenes 4l−4o



Therefore several aza-aryl cyclopropyl acetylenes **4l−4o** were synthesized from ethynylcyclopropane and the corresponding azaaryl bromides (see Experimental Section for detail). The photoreactions of these azaaryl cyclopropyl acetylenes with isoquinolinetrione **3** were then investigated.



Reaction between **3** and **4l** gave four compounds in the final products. Except for the polycyclic products **5l** and **6l**, two quinone methide products **9l** and **10l** were also isolated from the reaction mixture as expected (Scheme 9). The cyclopropyl group linked to the C=C bond in the quinone methide moiety made it impossible for further electrocyclization. The presence of **9l** and **10l** in the final product serves as solid evidence for the proposed sequences of the photoinitiated cascade reaction *via* quinone methide intermediates as shown in Scheme 2. Similar reaction pattern was found between **3** and **4 m,** leading to the products including quinozaline-fused isoquinolinedione derivative **5m** and quinone methide products **9m** as a mixture of its (*E*)-/(*Z*)- conformers.

It is noteworthy that the photoreactions between **3** and alkyl arynyl acetylenes proceeded under O_2 atmosphere showed similar or higher conversion of **3** to the aza-polycyclic products than the ones proceeded under Ar atmosphere (Table 2). Among all the aza-aryl substituted acetylenes, 2-(cyclopropylethynyl)pyrazine 4n showed the most obvious dependence on the amount of O_2 in the reaction mixture. Reaction between **3** and **4n** could hardly happen under Ar atmosphere even after 48 h irradiation, while under O_2 atmosphere a conversion of 46% could be achieved with the formation of quinoxaline-fused isoquinolinedione derivative **5n**. The reaction between 3-(cyclopropylethynyl) quinoline **4o** and **3** was also facilitated under O_2 atmosphere. A conversion of 57% could be achieved under O_2 atmosphere after 12 h of irradiation, whereas the one under Ar was 45%. And the yield of the phenanthridine-fused isoquinolinedione derivative **5o** based on converted **3** was obviously higher under O_2 atmosphere (88%) than under Ar atmosphere (69%). It further confirmed our assumption that the dehydrogenation step in the tandem reaction was facilitated by trace amount of O_2 remained in the reaction mixture.

Conclusions

In summary, we have developed the photoinduced tandem reactions of isoquinoline-1,3,4-trione with various azaaryl substituted acetylenes to provide a convenient one-pot synthesis of a diversity of aryl and azaaryl fused isoquinolinedione derivatives. Initiated by the photoinduced [2 + 2] cycloaddition between the carbonyl group on isoquinolinetrione and the acetylene, most of the reactions proceeded *via* the sequential photocycloaddition-oxetene rearrangement-electrocyclization-dehydrogenation sequence. Regioselectivity in the [2 + 2] cycloaddition and in the electrocyclization reaction determines the framework of the final aza-polycyclic products. Since both the photocyclization and the electrocyclization reactions are found to be regioselective by adjusting the combination of substitution groups on the alkynes, it is possible to use these tandem photoreactions to build specific aryl or azaaryl fused isoquinolinediones as novel aza-polycycles with potential applications. Detailed biological studies on the application of these compounds for photoinduced DNA cleavage and as microRNA inhibitors are underway in our group.

Experimental Section

Synthesis of Substituted Acetylenes. Acetylenes **4a−4e** were prepared from phenylacetylene and corresponding bromo-substituted heterocycles according to reported procedure,[20] and **4f** and **4g** were prepared by the Sonagashira coupling of 3-ethynylpyridine with 2-bromopyridine and 3-bromopyridine respectively according to a reported method. For acetylenes including **4h−4o**, which have not been reported before, detailed

information on their synthesis and characterization was given below.

5-(Pyridin-3-ylethynyl)pyrimidine (4h). A solution of 5-bromo pyrimidine (1.4 g, 9 mmol) and Et_3N (9 mL) in THF (20 mL) was purged with nitrogen for 10 min at room temperature. 3-Ethynylpyridine (1.1 g, 10.8 mmol) was added to the solution at room temperature under an nitrogen atmosphere, followed by addition of $Pd(PPh_3)_4$ (1.08 g, 0.76 mmol). The mixture was stirred under an nitrogen atmosphere at 50 °C for 8 h. The reaction mixture was cooled to room temperature and then concentrated under vacuum. The residue was diluted with diethyl ether (50 mL), and filtered through a filter paper to get rid of the catalyst. The filtrate was washed with water (20 mL × 3) and the ether layer was separated, dried over anhydrous sodium sulfate, and concentrated. The crude product was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 2:1) as a brown solid (1.3 g, 80%), mp 76−78 °C; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.12(s, 1H), 8.83(s, 2H), 8.75(s, 1H), 8.57(d, 1H, J = 5.1), 7.79(d, 1H, J = 7.8), 7.27(dd, 1H, J = 5.4, 7.5); ^{13}C NMR (75 MHz; $CDCl_3$) δ 85.6, 92.8, 119.2, 123.2, 128.5, 132.0, 138.7, 149.7, 152.4, 157.2, 158.8; MS m/z (% base) 182(1), 181(M^+, 100), 127(25), 100(1), 86(2), 84(6), 49(8). Anal. Calcd for $C_{11}H_7N_3$: C, 72.92; H, 3.89; N, 23.19. Found: C, 72.87; H, 3.80; N, 23.29.

2-(Pyridin-2-ylethynyl)pyrazine (4i). Similar to the procedure to make **4h** as discribed above, **4i** was prepared from 2-chloropyrazine (1.0 g, 9 mmol) and 2-ethynylpyridine (1.1 g,10.8 mmol) and purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give a yellow solid (1.4 g, 87%), mp 42−44 °C; ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.83(d, 1H, J = 1.5), 8.65(qd, 1H, J = 0.9, 5.1), 8.59(dd, 1H, J = 1.8, 2.7), 8.52(t, 1H, J = 2.7), 7.72(dt, 1H, J = 2.1, 7.8), 7.62(td, 1H, J = 1.2, 8.1) 7.31(m, 1H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 84.8, 91.5, 123.8, 127.9, 136.3, 139.5, 141.9, 143.4, 144.5, 148.1, 150.3; MS m/z (% base) 182(1.5), 181(M^+, 100), 180(2), 129(37), 128(12), 101(2), 84(3), 44(7). Anal. Calcd for $C_{11}H_7N_3$: C, 72.92; H, 3.89; N, 23.19. Found: C, 72.91; H, 3.89; N, 23.20.

3-(Pyridin-3-ylethynyl)quinoline (4j). Similar to the procedure to make **4h** as discribed above, **4j** was prepared from 3-ethynylpyridine(1.1 g, 10.8 mmol) and 3-bromo quinoline (1.8 g, 9 mmol) and purified by flash column chromatography on silica gel (mobile phase petroleum ether/ethyl acetate 1:1) as a white solid (1.6 g, 80%), mp 88−90 °C; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.0 (d, 1H, J = 2.1), 8.83(d, 1H, J = 1.8), 8.59(dd, 1H, J = 1.2, 4.8), 8.33(d, 1H, J = 1.8), 8.10(d, 1H, J = 8.4), 7.87(td,1H, J = 1.8, 8.1), 7.86(d, 1H, J = 7.8), 7.78(dt, 1H, J = 1.8, 7.2), 7.57(t, 1H, 6.9), 7.30(dd, 1H, 4.8, 8.4); ^{13}C NMR (75 MHz; $CDCl_3$) δ 89.3, 90.0, 116.8, 120.0, 123.3, 127.3, 127.6, 127.8, 129.6, 130.6, 138.7, 138.8, 147.2, 149.2, 152.0, 152.5; MS m/z (% base) 231(1), 230(M^+, 100), 229(8). Anal. Calcd for $C_{16}H_{10}N_2$: C, 83.46; H, 4.38; N, 12.17. Found: C, 83.44; H, 4.37; N, 12.18.

3-(Pyridin-2-ylethynyl)quinoline (4k). Similar to the procedure to make **4h** as discribed above, **4k** was prepared from 2-ethynylpyridine (1.1 g, 10.8 mmol) and 3-bromo quinoline (1.8 g, 9 mmol) and purified by flash column chromatography on silica gel (mobile phase petroleum ether/ethyl acetate 2:1) as a pale yellow crystal(1.5 g, 75%), mp 91−93 °C; ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.98(d, 1H, J = 2.1), 8.57(d, 1H, J = 3.9), 8.28(d, 1H, J = 2.1), 8.03d, 1H, J = 8.1), 7.70(d, 1H, 8.1), 7.63(m, 2H), 7.50(m, 2H), 7.17(dd, 1H, J = 2.8, 7.5); ^{13}C NMR (75 MHz; $CDCl_3$) δ 86.2, 91.6, 116.4, 123.2, 127.3, 127.7, 128.5, 129.4, 130.4, 132.1, 136.2, 139.1, 142.8, 147.0, 150.2, 152.0; MS m/z (% base) 231(1), 230(M^+, 100), 229(45), 128(2). Anal. Calcd for $C_{16}H_{10}N_2$: C, 83.46; H, 4.38; N, 12.17. Found: C, 83.46; H, 4.35; N, 12.20.

3-(Cyclopropylethynyl)pyridine (4l). A solution of $Pd(PPh_3)_4$-(1.08 g, 0.76 mmol) and Et_3N (9 mL) in THF (20 mL) was purged with nitrogen for 10 min at room temperature. 3-Bromopyridine (1.4 g, 9 mmol) was then added at room temperature under an nitrogen atmosphere followed by addition of cyclopropyl acetylene (1.18 g, 18 mmol) and CuI (30 mg). The mixture was stirred under an nitrogen atmosphere at 40 °C overnight. The reaction mixture was cooled to room temperature and then concentrated under vacuum. The residue diluted with diethyl ether (50 mL) and filtered through a filter paper. The mixture was washed with water (20 mL × 3). The ether layer was separated, dried over anhydrous sodium sulfate, and concentrated to give the crude product. The product was then purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1) to give pale yellow liquid (1.2 g, 70%); ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.60(d, 1H, J = 2.1), 8.47(dd, 1H, J = 1.8, 4.8), 7.66(td, 1H, J = 1.8, 7.8), 7.20(dd, 1H, J = 4.8, 7.8), 1.47(m, 1H), 0.91(m, 2H), 0.84(m, 2H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 0.2, 8.7, 72.5, 97.1, 121.1, 122.8, 138.4, 147.8, 152.3; MS m/z (% base) 143(M^+, 100), 142(62), 141(6), 117(6), 116(5), 115(27), 86(11), 84(18), 49(46), 44(22). Anal. Calcd for $C_{10}H_9N$: C, 83.88; H, 6.34; N, 9.78. Found: C, 83.81; H, 6.34; N, 9.80.

5-(Cyclopropylethynyl)pyrimidine (4m). Similar to the procedure to make **4l** as discribed above, **4m** was prepared from cyclopropyl acetylene (1.18 g, 18 mmol) and 5-bromo pyrimidine (1.4 g, 9 mmol). The purified **4m** after flash column chromatographyappeared as yellow oil (1 g, 77%); ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.04(s, 1H), 8.66(s, 2H), 1.46(m, 1H), 0.91(m, 4H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 0.24,8.9, 69.1, 101.1, 120.5, 156.0, 158.7; MS m/z (% base) 144(M^+, 100), 143(27), 117(9), 116(9), 90(60), 89(72), 62(17). Anal. Calcd for $C_9H_8N_2$: C, 74.98; H, 5.59; N, 19.43. Found: C, 74.92; H, 5.60; N, 19.42.

2-(Cyclopropylethynyl)pyrazine (4n). Similar to the procedure to make **4l** as discribed above, **4n** was prepared from cyclopropyl acetylene (1.18 g, 18 mmol) and 2-chloro pyrazine (1 g, 9 mmol). Further purification by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1) gave **4n** as pale yellow oil (0.8 g, 61%); ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.51(d, 1H, J = 1.5), 8.40(d, 1H, J = 2.4), 8.34(d, 1H, J = 2.7), 1.44(m, 1H), 0.86(m, 4H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 0.2, 9.0, 72.98, 98.8, 140.7, 142.2, 144.1, 147.6; MS m/z (% base) 144(M^+, 100), 143(25), 118(33), 91(22), 86(6), 84(10), 64(8), 49(13). Anal. Calcd for $C_9H_8N_2$: C, 74.98; H, 5.59; N, 19.43. Found: C, 74.99; H, 5.52; N, 19.40.

3-(Cyclopropylethynyl)quinoline (4o). Similar to the procedure to make **4l** as discribed above, **4o** was prepared from cyclopropyl acetylene (1.18 g, 18 mmol) and 3-bromo quninoline (1.8 g, 9 mmol) was obtained overnight, the crude product was purified by using column chromatography on silica gel to give **4o** as a dark yellow oil (1.1 g, 63%); ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.84(d, 1H, J = 1.8), 8.11(s, 1H), 8.04(d, 1H, J = 8.4), 7.65(m, 2H), 7.50(t, 1H, J = 7.5), 1.50(m, 1H), 0.89(m, 4H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 0.4, 8.9, 73.2, 97.2, 118.2, 127.1, 127.4, 127.3, 129.3, 129.6, 138.0, 146.5, 152.5; MS m/z (% base) 194(1), 193(M^+, 100), 192(62), 191(17), 167(3), 165(7). Anal. Calcd for $C_{14}H_{11}N$: C, 87.01; H, 5.74; N, 7.25. Found: C, 87.09; H, 5.72; N, 7.25.

General Procedures for the Preparative Photolysis of Isoquinolinetrione with Acetylenes. The light source was a medium-pressure mercury lamp (500 W) in a cooling water jacket that was further surrounded by a layer of filter solution (1 cm thick, 20% aqueous sodium nitrite) to cut off light of wavelength shorter than 400 nm. The solution of isoquinolinetrione and an excess amount of acetylenes in anhydrous acetonitrile was purged with dry argon for 10 min and then irradiated under continuous argon purging. The reaction course was monitored by TLC. At the end of the reaction, the solvent was removed under reduced pressure, and the residue was separated by flash chromatography on a silica gel column.

Photolysis of 3 with 4a. A solution of **3** (378 mg, 2 mmol) and **4a** (716 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a complete conversion of isoquinolinetrione. Workup as described above

gave the products **5a** and **6a** as a mixture. The ratio of the two products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with chloroform as eluents afforded pure analytic samples of **5a** and **6a**.

7-Benzoyl-5-methyl-4*H*-isoquinolino[5,4-*fg*]quinoline-4,6(5*H*)-dione (5a). Yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.05(dd, 1H, J = 8.7, 1.8), 9.00(m, 2H), 8.78(dd, 1H, J = 7.5, 0.9), 8.04(t, 1H, J = 7.8), 7.88(dd, 2H, J = 8.1), 7.74(q, 1H, J = 4.5), 7.55(tt, 1H, J = 7.2, 2.1), 7.43(t, 2H, J = 7.5), 3.48(s, 1H); ^{13}C NMR (75 MHz; d_6-DMSO) δ 27.3, 121.4, 123.6, 125.3, 125.8, 128.0, 128.8, 129.0, 129.1, 129.8, 130.8, 132.6, 133.3, 137.7, 144.8, 145.7, 151.9, 163.3, 163.8, 195.8; MS m/z (% base) 367(3), 366(M+, 45), 337(100), 323(10), 289(10), 253(11), 105(2), 77(9). Anal. Calcd for $C_{23}H_{14}N_2O_3$: C, 75.41; H, 3.82; N, 7.65. Found: C, 75.19; H, 4.03; N, 7.75.

5-Methyl-7-picolinoyl-5,6-dihydro-4*H*-dibenz[*de*,*g*]isoquinoline-4,6-dione (6a). White powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.02(d, 1H, J = 7.5), 8.7(d, 1H, J = 7.8), 8.67(d, 1H, J = 7.5), 8.52(d, 1H, J = 7.8), 8.42(d, 1H, J = 4.8), 8.01(td, 1H, J = 7.5, 1.8), 7.94(t, 1H, J = 7.8), 7.84(td, 1H, J = 7.2, 1.2), 7.77(d, 1H, J = 8.1), 7.60(m, 1H), 7.45(m, 1H), 3.43(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.1, 122.1, 123.1, 123.3, 125.9, 127.2, 127.8, 128.2, 128.4, 128.5, 129.2, 130.3, 130.4, 132.0, 137.3, 146.8, 149.3, 154.3, 164.2, 164.3, 198.1; MS m/z (% base), 366(M$^+$, 1), 337(49), 288(100). Anal. Calcd for $C_{23}H_{14}N_2O_3$: C, 75.41; H, 3.82; N, 7.65. Found: C, 75.27; H, 4.21; N, 7.69.

Photolysis of 3 with 4b. A solution of **3** (378 mg, 2 mmol) and **4b** (716 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a complete conversion of isoquinolinetrione. Workup as described above gave the products **5b**, **6b**, and **7b** as a mixture. The ratio of the three products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with chloroform/methanol as eluents afforded pure analytic samples of **6b** and **7b**. Crude **5b** was further purified by flash column chromatagraph with petroleum ether/ethyl acetate as eluents.

7-Benzoyl-5-methyl-4*H*-isoquinolino[4,5-*gh*]quinoline-4,6(5*H*)-dione (5b). Pale yellow crystal; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.58(dd, 1H, J = 8.1, 0.9), 9.12(dd, 1H, J = 4.2, 1.8), 8.73(dd, 1H, J = 7.2, 1.2), 8.09(dd, 1H, J = 8.4, 1.8), 7.99(t, 1H, J = 8.1), 7.85(d, 2H, J = 7.2), 7.5(m, 2H), 7.41(t, 2H, J = 7.8), 3.42(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.1, 118.2, 122.5, 123.2, 123.9, 127.0, 128.4, 128.6, 128.9, 130.1, 130.5, 131.9, 133.7, 135.7, 136.7, 144.2, 147.1, 152.3, 163.2, 163.8, 196.3; MS m/z (% base) 367(4), 366(M$^+$, 18), 337(12), 289(100), 105(15), 77(9). Anal. Calcd for $C_{23}H_{14}N_2O_3$: C, 75.41; H, 3.82; N, 7.65. Found: C, 75.49; H, 3.87; N, 7.64.

7-Benzoyl-5-methyl-4*H*-Benzo[*de*]pyrido[4,3-*g*]isoquinoline-4,6(5*H*)-dione (6b). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.17(s, 1H), 9.05(dd, 1H, J = 8.4, 1.2), 8.95(d, 1H, J = 6), 8.84(dd, 1H, J = 7.5, 1.2), 8.54(d, 1H, J = 5.4), 8.06(t, 1H, J = 8.1), 7.87(d, 2H, J = 7.2), 7.61(tt, 1H, J = 7.5, 1.2), 7.46(t, 2H, J = 7.8), 3.46(s, 3H); MS m/z (ESI, % base) 389(M + Na$^+$, 20%), 755(2M + Na$^+$, 100%). Anal. Calcd for $C_{23}H_{14}N_2O_3$: C,75.41; H, 3.82; N, 7.65. Found: C, 75.12; H, 4.00; N, 6.91.

5-methyl-7-nicotinoyl-5,6-dihydro-4*H*-dibenz[*de*,*g*]isoquinoline-4,6(5*H*)-dione (7b). White powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.05(d, 1H, J = 8.1), 8.78(m,4H), 8.42(d,1H, J = 7.8), 8.01(t, 1H, J = 7.8), 7.91(t, 1H, J = 7.5), 7.78(d, 1H, J = 8.4), 7.67(t, 1H, J = 7.5), 7.52(m, 1H), 3.45(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.3, 118.4, 123.5, 123.6, 124.2, 125.8, 128.5, 128.6, 128.8, 128.9, 129.5, 130.9, 131.0, 132.4, 133.1, 135.9, 144.0, 150.2, 153.6, 163.9, 164.1, 196.1; MS m/z (% base) 367(10), 366(M$^+$, 48), 337(14), 289(10), 288(100), 106(11), 78(20). Anal. Calcd for $C_{23}H_{14}N_2O_3$: C, 75.41; H, 3.82; N, 7.65. Found: C, 75.27; H, 3.91; N, 7.78.

Photolysis of 3 with 4c. A solution of **3** (378 mg, 2 mmol) and **4c** (720 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a complete conversion of isoquinolinetrione. Workup as described above gave the products **5c** and **6c** as a mixture. The ratio of the two products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with chloroform as eluent afforded pure analytic samples of **5c** and **6c**.

7-Benzoyl-5-methyl-4*H*-isoquinolino[4,5-*gh*]quinazoline-4,6(5*H*)-dione (5c). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.64(dd, 1H, J = 8.4, 0.9), 9.62(s, 1H), 9.28(s, 1H), 8.92(dd, 1H, J = 7.5, 1.5), 8.13(t, 1H, J = 7.8), 7.86(d, 2H, J = 7.2), 7.63(t, 1H, J = 7.5), 7.48(t, 2H, J = 7.5), 3.48(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.5, 121.4, 123.3, 128.9, 129.0, 129.4, 129.2, 131.1, 134.3, 134.5, 136.7, 143.1, 151.5, 158.0, 159.0, 162.9, 163.6, 195.2; MS m/z (% base), 367(M$^+$, 100), 338(13), 290(35), 105(51), 77(28). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.81; H, 3.72; N, 11.03.

5-Methyl-7-(pyrimidine-5-carbonyl)-5,6-dihydro-4*H*-dibenz[*de*,*g*]-isoquinoline-4,6(5*H*)-dione (6c). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.36(s, 1H), 9.10(s, 2H), 9.05(d, 1H, J = 7.8), 8.84(d, 1H, J = 8.4), 8.73(d, 1H, J = 7.2), 8.0(t, 1H, J = 7.8), 7.93(t, 1H, J = 7.2), 7.7(m, 2H), 3.45(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.4, 118.6, 123.4, 123.8, 125.5, 128.0, 128.3, 128.7, 128.9, 129.2, 129.6, 130.5, 131.0, 131.3, 132.4, 142.5, 156.9, 161.4, 164.0, 194.6; MS m/z (% base), 367(M$^+$, 79), 338(5), 288(100). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.93; H, 3.58; N, 11.31.

Photolysis of 3 with 4d. A solution of **3** (378 mg, 2 mmol) and **4d** (720 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a 85% conversion of isoquinolinetrione. Workup as described above gave the products **5d** and **6d** as a mixture. The ratio of the three products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with chloroform/methanol as eluents afforded pure analytic samples of **5d** and **6d**.

7-Benzoyl-5-methyl-4*H*-isoquinolino[5,4-*fg*]quinoxaline-4,6(5*H*)-dione (5d). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.57(dd, 1H, J = 8.1, 1.2), 9.08(d, 1H, J = 1.8), 8.96(d, 1H, J = 1.8), 8.86(dd, 1H, J = 7.5, 1.2), 8.11(t, 1H, J = 8.4), 7.86(d, 2H, J = 8.4), 7.58(tt, 1H, J = 7.5, 1.8), 7.44(t, 2H, J = 7.8), 3.49(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.5, 121.8, 123.2, 127.5, 128.8, 129.0, 129.2, 130.1, 130.6, 132.8, 133.6, 137.2, 141.2 142.9, 145.2, 146.2 146.5, 163.1, 163.8, 195.8; MS m/z (% base), 368(6), 367(M$^+$, 100), 338(25), 290(40), 254(39), 105(10), 77(17). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.66; H, 3.76; N, 11.12.

5-Methyl-7-(pyrazine-2-carbonyl)-5,6-dihydro-4*H*-dibenz[*de*,*g*]-isoquinoline-4,6(5*H*)-dione (6d). White powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.69(s, 1H), 9.03(d, 1H, J = 8.1), 8.81(d, 1H, J = 8.1), 8.75(d, 1H, J = 2.7), 8.70(d, 1H, J = 7.5), 8.38(s, 1H), 7.97(t, 1H, J = 8.1), 7.89(t, 1H, 7.2), 7.78(d, 1H, J = 7.8), 7.66(t, 1H, J = 7.5), 3.43(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.3, 118.7, 123.3, 123.6, 125.8, 128.3, 129.0, 129.5, 130.7, 130.8, 132.2, 143.8, 144.2, 145.1, 147.9, 148.9, 164.3, 164.4, 197.2; MS m/z (% base), 367(M$^+$, 2), 339(0.9), 288(100). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.73; H, 3.84; N, 11.21.

Photolysis of 3 with 4e. A solution of **3** (378 mg, 2 mmol) and **4e** (916 mg, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a 70% conversion of isoquinolinetrione. Workup as described above gave the products **5e** and **6e** as a mixture. Flash column chromatagraph with chloroform/methanol as eluents afforded pure analytic samples of **5e** (55%) and **6e** (20%).

7-Benzoyl-5-methyl-4*H*-isoquinolino[4,5-*jk*]phenanthridine-4,6(5*H*)-dione (5e). Yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.47(d, 1H, J = 8.4), 9.21(s, 1H), 9.00(d, 1H, J = 8.1), 8.91(dd, 1H, J = 7.2, 1.2), 8.38(d, 1H, J = 7.8), 8.11(t, 1H, J = 7.5), 7.97(t, 1H, J = 7.2), 7.87(m, 2H), 7.58(tt, 1H, J = 6, 1.5), 7.44(t, 1H, J = 7.5), 3.49(s, 3H); MS m/z (% base), 416(M$^+$, 100), 387(30), 339(34), 105(18), 77(21). Anal. Calcd for $C_{27}H_{16}N_2O_3$: C, 77.87; H, 3.87; N, 6.73. Found: C, 77.71; H, 3.98; N, 6.72.

5-Methyl-7-(quinoline-3-carbonyl)-5,6-dihydro-4*H*-dibenz[*de*,*g*]-isoquinoline-4,6(5*H*)-dione (6e). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.41(s, 1H), 9.05(d, 1H, J = 8.4), 8.83(d, 1H, J = 8.4), 8.71(d, 1H, J = 7.5), 8.54(s, 1H), 8.17(d, 1H, J = 8.4), 7.97(t, 1H, J = 8.4), 7.79−7.92(m, 4H), 7.64(t, 1H, J = 7.1), 7.56(t, 1H, J = 7.2), 3.41(s, 3H); MS m/z (% base), 416(M^+, 100), 387(32), 288(95), 128(10). Anal. Calcd for $C_{27}H_{16}N_2O_3$: C, 77.87; H, 3.87; N, 6.73. Found: C, 77.81; H, 3.88; N, 6.66.

Photolysis of 3 with 4f. A solution of **3** (378 mg, 2 mmol) and **4f** (720 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a 72% conversion of isoquinolinetrione. Workup as described above gave the products **5f**, **6f** ,and **7f** as a mixture. The ratio of the three products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with chloroform as eluents afforded pure analytic sample **6f** and the mixture of **7f** and **5f**. Then flash column chromatagraph with ethyl ether/petroleum ether afforded a few pure analytic samples **5f** and **7f**.

5-Methyl-7-nicotinoyl-4*H*-isoquinolino[5,4-*fg*]quinoline-4,6(5*H*)-dione (5f). White powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.07(dd, 1H, J = 1.8, 8.4), 8.99(dt, 1H, J = 0.9, 4.8), 8.98(s, 1H), 8.77(m, 3H), 8.42(td, 1H, J = 2.1, 8.1), 8.06(dd, 1H, J = 7.5, 8.4), 7.77(q, 1H, J = 4.5), 7.49(m, 1H), 3.47(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.4, 121.5, 123.7, 124.0, 124.7, 125.8, 128.0, 128.5, 129.0, 129.1, 131.2, 131.5, 133.1, 135.8, 144.5, 146.1, 150.5, 151.7, 153.2, 163.5, 163.8, 195.5; MS m/z (% base), 368(4), 367(M^+, 48), 338(29), 324(20), 310(100), 289(30), 282(32), 254(30), 78(10). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.78; H, 3.61; N, 11.47,

5-Methyl-7-picolinoyl-4*H*-isoquinolino[4,5-*gh*]quinoline-4,6(5*H*)-dione (6f). white powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.65(dd, 1H, J = 8.4, 0.6), 9.16(dd, 1H, J = 4.5, 1.8), 8.76(dd, 1H, J = 7.5, 1.2), 8.51(d, 1H, J = 7.5), 8.4(d, 1H, J = 3.9), 8.09(dd, 1H, J = 8.1, 1.2), 8.02(t, 2H, J = 7.8), 7.59(q, 1H, J = 4.5), 7.46(m, 1H), 3.43(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.3, 118.9, 122.4, 122.7, 123.3, 124.5, 127.6, 128.5, 130.4, 130.9, 132.1, 136.0, 136.3, 137.6, 145.8, 147.4, 149.4, 152.2, 154.2, 164.0, 164.3, 197.3; MS m/z (% base), 367(M^+, 3), 339(83), 338(50), 310(5), 290(9), 289(100), 78(8). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.65; H, 3.65; N, 11.56.

5-Methyl-7-picolinoyl-4*H*-benzo[*de*]pyrido[4,3-*g*]isoquinoline-4,6(5*H*)-dione (7f). White powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.13(s, 1H), 9.05(dd, 1H, J = 0.9, 8.1), 8.94(d, 1H, J = 6), 8.84(dd, 1H, J = 1.2, 7.5), 8.58(d, 1H, J = 5.1), 8.56(dt, 1H, J = 1.2, 7.8), 8.41(d, 1H, J = 4.8), 8.04(m, 2H), 7.49(m, 1H), 3.45(s, 3H); MS m/z (% base), 367(M^+, 48), 338(30), 310(100), 289(30), 78(10). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.81; H, 3.57; N, 11.39.

Photolysis of 3 with 4g. A solution of **3** (378 mg, 2 mmol) and **4g** (720 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a complete conversion of isoquinolinetrione. Workup as described above gave the products **5g** and **6g** as a mixture. The ratio of the three products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with chloroform/methanol as eluents afforded pure analytic samples of **5g** and **6g**.

5-Methyl-7-nicotinoyl-4*H*-benzo[*de*]pyrido[4,3-*g*]isoquinoline-4,6(5*H*)-dione (5g). Pale yellow crystal; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.08(s, 1H), 9.0(d, 1H, J = 8.1), 8.94(d, 1H, J = 5.1), 8.78(d, 3H, J = 7.2), 8.50(d, 1H, J = 5.7), 8.33(dt, 1H, J = 8.1, 1.8), 8.03(t, 1H, J = 7.8), 7.47(dd, 1H, J = 7.8, 5.1), 3.40(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.4, 116.5, 119.6, 123.6, 124.0, 124.4, 127.2, 127.7, 129.1, 129.3, 132.7, 132.9, 135.8, 136.6, 142.9, 148.8, 150.3, 151.5, 154.1, 163.3, 163.5, 194.8; MS m/z (% base), 368(7), 367(M^+, 100), 338(22), 289(95), 106(18), 78(20). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.74; H, 3.84; N, 11.37.

5-Methyl-7-nicotinoyl-4*H*-isoquinolino[4,5-*gh*]quinoline-4,6(5*H*)-dione (6g). Colorless crystal; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.65(dd, 1H, J = 8.1, 1.2), 9.18(dd, 1H, J = 4.2, 1.5), 8.81(m, 3H),8.23(d, 1H, J = 4.2), 8.08(m, 2H), 7.59(q, 1H, J = 4.2), 7.47(dd, 1H, J = 8.1, 4.8), 3.44(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.4, 119.0, 122.9, 123.7, 123.8, 124.3, 127.2, 129.1, 130.6, 131.0, 132.4, 132.7, 135.5, 135.9, 142.8, 147.6, 150.2, 152.8, 154.0, 163.7, 164.0, 195.3; MS m/z (% base), 368(4), 367(M^+, 52), 338(10), 289(100), 106(4), 78(10). Anal. Calcd for $C_{22}H_{13}N_3O_3$: C, 71.93; H, 3.54; N, 11.44. Found: C, 71.66; H, 3.71; N, 11.21.

Photolysis of 3 with 4h. A solution of **3** (378 mg, 2 mmol) and **4h** (724 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a complete conversion of isoquinolinetrione. Workup as described above gave the products **5h**, **6h**, **7h**, and **8h** as a mixture. The ratio of the four products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with chloroform/methanol as eluents afforded pure analytic samples of **5 h**, **6h**, **7h**, and **8h**.

5-Methyl-7-(pyrimidine-5-carbonyl)-4*H*-isoquinolino[4,5-*gh*]-quinoline-4,6(5*H*)-dione (5h). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.69(dd, 1H, J = 8.1, 1.2), 9.37(s, 1H), 9.22(dd, 1H, J = 4.5, 1.8), 9.09(s, 2H), 8.83(dd, 1H, J = 7.5, 1.2), 8.10(m, 2H), 7.65(q, 1H, J = 4.2), 3.46(s, 3H); ^{13}C NMR (75 MHz; d_6-DMSO) δ 27.3, 119.7, 123.3, 123.5, 124.6, 127.3, 129.5, 130.1, 130.2, 130.3, 131.7, 135.8, 140.9, 147.1, 153.4, 157.4, 161.8, 163.9, 194.2; MS m/z (% base), 368(M^+, 100), 289(80), 176(3), 107(4), 79(3). Anal. Calcd for $C_{21}H_{12}N_4O_3$: C, 68.48; H, 3.28; N, 15.21. Found: C, 68.37; H, 3.49; N, 15.21,

5-Methyl-7-(pyrimidine-5-carbonyl)-4*H*-benzo[*de*]pyrido[4,3-*g*]-isoquinoline-4,6(5*H*)-dione (6h). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.35(s, 1H), 9.11(s, 1H), 9.09(s, 2H), 9.03(d, 1H, J = 7.5), 8.97(d, 1H, J = 6), 8.79(dd, 1H, J = 7.5, 0.9), 8.55(d, 1H, J = 6.3), 8.07(t, 1H, J = 8.1), 3.42(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.5, 116.7, 119.6, 123.8, 127.1, 127.9, 129.2, 129.6, 130.3, 133.2, 136.8, 149.0, 151.1, 156.9, 161.8, 163.4, 193.3; MS m/z (% base), 368(M^+, 100), 339(10), 289(47), 176(3), 107(4), 79(3). Anal. Calcd for $C_{21}H_{12}N_4O_3$: C, 68.47; H, 3.26; N, 15.21. Found: C, 68.70; H, 3.51; N, 15.14.

5-Methyl-7-nicotinoyl-4*H*-isoquinolino[4,5-*gh*]quinazoline-4,6(5*H*)-dione (7h). Pale yellow crystal; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.57(s, 1H), 9.54(dd, 1H, J = 8.1, 1.2), 9.21(s, 1H), 8.80(m, 3H), 8.32(dt, 1H, J = 8.1, 1.2), 8.07(t, 1H, J = 8.4), 7.49(m, 1H), 3.4(s, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 27.5, 120.1, 121.0, 123.2, 124.4, 128.8, 129.1, 129.8, 131.1, 132.5, 134.4, 135.8, 141.3, 150.2, 151.5, 154.4, 158.3, 158.7, 163.0, 163.4, 193.9; MS m/z (% base), 368(M^+, 100), 339(20), 290(57), 178(11), 106(10), 78(15). Anal. Calcd for $C_{21}H_{12}N_4O_3$: C, 68.47; H, 3.26; N, 15.21. Found: C, 68.45; H, 3.46; N, 14.91.

10-(Methylcarbamoyl)-8-oxo-8*H*-benzo[*e*]pyrido[3,2-*j*]perimidine-9-carboxylic Acid (8h). Pale yellow powder; ^{1}H NMR (300 MHz; d_6-DMSO) δ 12.99(s, 1H), 9.30(d, 1H, J = 8.1), 8.87(s, 1H), 8.72(d, 1H, J = 7.5), 8.69(dd, 1H, J = 1.5, 4.5), 8.58(d, 1H, J = 3.3), 8.12(m, 2H), 7.48(dd, 1H, J = 5.1, 8.1), 3.23(s, 3H); MS m/z (% base), 384(M^+, 0.9), 356(2.5), 341(3.3), 327(97), 306(100), 106(2.7), 78(14). Anal. Calcd for $C_{21}H_{12}N_4O_4$: C, 65.62; H, 3.15; N, 14.58. Found: C, 65.45; H, 3.40; N, 14.62.

Photolysis of 3 with 4i. A solution of **3** (378 mg, 2 mmol) and **4i** (724 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h to reach a 45% conversion of isoquinolinetrione. Workup as described above gave the products **5i** and **6i** as a mixture. The ratio of the three products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with petroleum ether/ethyl acetate as eluents afforded pure analytic samples of **5i** and **6i**.

5-Methyl-7-(pyrazine-2-carbonyl)-4*H*-isoquinolino[5,4-*fg*]-quinoline-4,6(5*H*)-dione (5i). White powder; ^{1}H NMR (300 MHz;

$CDCl_3$) δ 9.70(s, 1H), 9.03(d, 1H, J = 8.4), 8.94(m, 2H), 8.74(m, 2H), 8.36(s, 1H), 8.02 (t, 1H, J = 7.5), 7.72(m, 1H), 3.46(s, 3H); MS m/z (% base), 368(M^+, 28), 340(10), 289(100). Anal. Calcd for $C_{21}H_{12}N_4O_3$: C, 68.47; H, 3.26; N, 15.21. Found: C, 68.50; H, 3.31; N, 15.24.

5-Methyl-7-picolinoyl-4*H*-isoquinolino[5,4-*fg*]quinoxaline-4,6(5*H*)-dione (6i). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.55(dd, 1H, J = 8.1, 1.2), 9.06(d, 1H, J = 2.1), 8.91(d, 1H, J = 1.8), 8.83(dd, 1H, J = 7.5, 1.5), 8.56(d, 1H, J = 7.5), 8.43(d, 1H, J = 4.2), 8.08(m, 2H), 7.50(m, 1H), 3.47(s, 3H); MS m/z (% base), 368(M^+, 21), 340(100), 325(8), 290(30), 177(4), 78(3). Anal. Calcd for $C_{21}H_{12}N_4O_3$: C, 68.47; H, 3.26; N, 15.21. Found: C, 68.40; H, 3.41; N, 15.24.

Photolysis of 3 with 4j. A solution of **3** (378 mg, 2 mmol) and **4j** (924 mg, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 60 h to reach a 30% conversion of isoquinolinetrione. The yellow solid precipitated from the solution was filtrated and rinsed with acetonitrile to give the pure product **5j** (80%).

5-Methyl-7-nicotinoyl-4*H*-isoquinolino[4,5-*jk*]phenanthridine-4,6(5*H*)-dione (5j). Yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.48(d, 1H, J = 8.4), 9.18(s, 1H), 9.01(d, 1H, J = 8.4), 8.92(d, 1H, J = 7.5), 8.81(bs, 2H), 8.48(d, 1H, J = 8.1), 8.37(d, 1H, J = 7.2), 8.14(t, 1H J = 7.8), 7.98(t, 1H, J = 7.2), 7.89(t, 1H, J = 6.9), 7.57(t, 1H, J = 4.8), 3.49(s, 3H); MS m/z (% base), 417(M^+, 100), 388(31), 339(40), 78(10). Anal. Calcd for $C_{26}H_{15}N_3O_3$: C, 74.81; H, 3.62; N, 10.07. Found: C, 74.77; H, 3.70; N, 10.12,

Photolysis of 3 with 4k. A solution of **3** (378 mg, 2 mmol) and **4k** (924 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 60 h to reach a 28% conversion of isoquinolinetrione. Dark yellow solid precipitated from the reaction solution was filtrated and rinsed with acetonitrile to give the pure product **5k**(85%).

5-Methyl-7-picolinoyl-4*H*-isoquinolino[4,5-*jk*]phenanthridine-4,6(5*H*)-dione (5k). Dark yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.45(d, 1H, J = 8.4), 9.17(s, 1H), 9.01(d, 1H, J = 7.8), 8.88(dd, 1H, J = 7.5, 0.9), 8.57(d, 1H, J = 7.8), 8.38−8.44(m, 2H), 8.02−8.11(m, 2H), 7.96(t, 1H, J = 6.9), 7.88(t, 1H, J = 7.2),7.46−7.50(m, 1H), 3.47(s, 3H); MS m/z (% base), 417(M^+, 90), 388(100), 339(25), 78(4). Anal. Calcd for $C_{26}H_{15}N_3O_3$: C, 74.81; H, 3.62; N, 10.07. Found: C, 74.90; H, 3.60; N, 10.11,

Photolysis of 3 with 4l. A solution of **3** (378 mg, 2 mmol) and **4l** (572 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 48 h. Workup as described above gave the products **5l**, **6l** and **9l**, **10l** as a mixture. The ratio of the four products was determined by HPLC with acetonitrile and water gradient eluting. Flash column chromatagraph with chloroform as eluents afforded pure analytic samples of **5l**, **6l** and **9l**, **10l**.

7-(Cyclopropanecarbonyl)-5-methyl-4*H*-isoquinolino[4,5-*gh*]-quinoline-4,6(5*H*)-dione (5l). White powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.58(dd, 1H, J = 8.4, 1.5), 9.17(dd, 1H, J = 4.5, 1.8), 8.75(dd, 1H, J = 4.5, 1.2), 8.24(dd, 1H, J = 8.4, 1.5), 7.99(t, 1H, J = 7.5), 7.68(q, 1H, J = 4.2), 3.57(s, 3H), 2.34(m, 1H), 1.83(m, 1H), 1.16−1.42(m, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 12.2, 14.1, 23.9, 27.4, 116.8, 122.7, 122.8, 123.4,127.3, 128.5, 130.1, 130.7, 132.1, 135.9, 147.1, 147.7, 152.4, 163.8, 164.1, 206.5; MS m/z (% base), 330(M^+, 20), 302(100), 289(86), 246(18), 247(20), 218(7). Anal. Calcd for $C_{20}H_{14}N_2O_3$: C, 72.72; H, 4.27; N, 8.48. Found: C, 72.68; H, 4.25; N, 8.51.

7-(Cyclopropanecarbonyl)-5-methyl-4*H*-benzo[*de*]pyrido[4,3-*g*]-isoquinoline-4,6(5*H*)-dione (6l). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.33(s, 1H), 8.98(m, 2H), 8.80(d, 1H, J = 6.3), 8.51(d, 1H, J = 5.4), 8.01(t, 1H, J = 7.5), 3.57(s, 3H), 2.39(m, 1H), 1.90(m, 1H), 1.52(m, 1H), 1.20−1.40(m, 2H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 12.7, 14.7, 24.2, 27.5, 116.3, 117.5, 123.1, 123.5, 127.3, 127.4, 128.7, 128.9, 132.6, 136.7, 147.2, 148.5, 151.9, 163.4, 163.7, 206.1; MS m/z (% base), 330(M^+, 24), 302(89), 289(100), 272(8), 246(16), 218(9). Anal. Calcd for $C_{20}H_{14}N_2O_3$: C, 72.72; H, 4.27; N, 8.48. Found: C, 72.70; H, 4.28; N, 8.44.

(*E*)-4-(1-Cyclopropyl-2-oxo-2-(pyridin-3-yl)ethylidene)-2-methyl-isoquinoline-1,3(2*H*,4*H*)-dione (9l). Yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.0(d, 1H, J = 2.1), 8.78(dd, 1H, J = 5.4, 1.8), 8.34(dd, 1H, J = 7.8, 1.2), 8.24−8.29(m, 2H), 7.72(td, 1H, J = 7.5, 1.5), 7.57(td, 1H, J = 7.8, 0.9), 7.47(qd, 1H, J = 5.4, 0.9), 3.19(s, 3H), 2.28(m, 1H), 1.30(m, 1H), 1.16(m, 1H), 1.0(m, 1H), 0.73(m, 1H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 9.9, 10.2, 15.6, 27.3, 124.0, 125.2, 126.3, 127.6, 129.1, 129.7, 131.6, 132.0, 133.0, 135.3, 149.7, 153.5, 156.8, 164.1, 164.6, 192.8; MS m/z (% base), 332(M^+, 33), 304(100), 275(7), 169(11), 106(77), 78(54). Anal. Calcd for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.43. Found: C, 72.30; H, 4.81; N, 8.41.

(*Z*)-4-(1-Cyclopropyl-2-oxo-2-(pyridin-3-yl)ethylidene)-2-methyl-isoquinoline-1,3(2*H*,4*H*)-dione (10l). Yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.89(d, 1H, J = 2.1), 8.65(dd, 1H, J = 4.5, 1.5), 8.06(m, 1H), 8.23(td, 1H, J = 1.8, 8.1), 8.14(dd, 1H, J = 1.2, 7.8), 7.81(dt, 1H, J = 1.5, 7.2), 7.63(dt, 1H, J = 1.2, 7.5), 7.98(dt, 1H, J = 8.1, 1.8), 7.25(m, 4H), 3.46(s, 3H), 3.07(m, 1H), 0.43−1.28(m, 4H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 8.5, 9.4, 14.0, 27.5, 123.9, 125.1, 125.7, 126.7, 128.9, 129.2, 130.6, 132.8, 132.9, 136.0, 150.5, 154.4, 155.0, 164.4, 166.0, 195.0; MS m/z (% base), 332(M^+, 24), 304(100), 275(7), 169(7), 106(52), 78(34). Anal. Calcd for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.43. Found: C, 72.29; H, 4.88; N, 8.38.

Photolysis of 3 with 4m. A solution of **3** (378 mg, 2 mmol) and **4m** (576 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 24 h to reach a 96% conversion of isoquinolinetrione. Workup as described above gave the products **5m** and **9m**. Flash column chromatagraph with chloroform/methanol as eluents afforded pure analytic samples of **5m** and **9m**.

7-(Cyclopropanecarbonyl)-5-methyl-4*H*-isoquinolino[4,5-*gh*]-quinazoline-4,6(5*H*)-dione (5m). White powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.60(s, 1H), 9.54(dd, 1H, J = 8.1, 1.2), 9.38(s, 1H), 8.84(dd, 1H, J = 7.8, 1.5), 8.05(t, 1H, J = 7.5), 3.56(s, 3H), 2.37(m, 1H), 1.89(m, 1H), 1.22−1.46(m, 3H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 12.6, 14.8, 24.3, 27.6, 118.0, 120.1, 123.2, 128.8, 129.1, 129.3, 131.0, 134.2, 145.6, 151.7, 158.1, 159.1, 163.3, 163.7, 205.1; MS m/z (% base), 331(M^+, 5), 303(100), 290(35), 276(16), 273(7), 178(15). Anal. Calcd for $C_{19}H_{13}N_3O_3$: C, 68.88; H, 3.95; N, 12.68. Found: C, 68.86; H, 3.97; N, 12.70.

(*E*)-4-(1-Cyclopropyl-2-oxo-2-(pyrimidin-5-yl)ethylidene)-2-methylisoquinoline-1,3(2*H*,4*H*)-dione (9m). Yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.36(s, 1H), 9.16(s, 2H), 8.34(dd, 1H, J = 8.1, 1.2), 8.26(d, 1H, J = 8.1), 7.73(td, 1H, J = 7.5, 1.5), 7.59(td, 1H, J = 8.1, 1.2), 3.20(s, 3H), 2.28(m, 1H), 1.35(m, 1H), 1.16(m, 1H), 1.10(m, 1H), 0.71(m, 1H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 10.0, 10.2, 15.3, 27.4, 125.5, 126.2, 127.6, 129.2, 129.5, 129.8, 131.6, 133.2, 155.5, 156.5, 161.2, 163.9, 164.6, 190.9; MS m/z (% base), 333(M^+, 7), 305(100), 169(15), 107(40). Anal. Calcd for $C_{19}H_{15}N_3O_3$: C, 68.46; H, 4.54; N, 12.61. Found: C, 68.47; H, 4.50; N, 12.69.

Photolysis of 3 with 4n. A solution of **3** (378 mg, 2 mmol) and **4n** (576 m g, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength >400 nm for 12 h in oxygen atmosphere. Workup as described above gave the product **5n**. Flash column chromatagraph with chloroform/methanol as eluents afforded pure analytic samples of **5n** (21%).

7-(Cyclopropanecarbonyl)-5-methyl-4*H*-isoquinolino[5,4-*fg*]-quinoxaline-4,6(5*H*)-dione (5n). White powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.48(dd, 1H, J = 7.8, 1.2), 9.07(s, 2H), 8.78(dd, 1H, J = 7.5, 1.2), 8.03(t, 1H, J = 7.8), 3.58(s, 3H), 2.35(m, 1H), 1.80(m, 1H), 1.54(m, 1H), 1.13−1.26(m, 2H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 11.4, 13.4, 23.7, 27.4, 119.9, 122.9, 127.2, 128.8, 129.6, 130.3, 132.5, 140.0, 142.8, 146.0, 146.1, 147.2, 163.1,

163.7, 205.2; MS *m*/*z* (% base), 331(M^+, 1), 304(2), 303(100), 290(65), 288(6), 273(4), 177(2). Anal. Calcd for $C_{19}H_{13}N_3O_3$: C, 68.88; H, 3.95; N, 12.68. Found: C, 68.81; H, 3.99; N, 12.69.

Photolysis of 3 with 4o. A solution of **3** (378 mg, 2 mmol) and **4o** (772 mg, 4 mmol) in acetonitrile (100 mL) was irradiated with light of wavelength > 400 nm for 48 h. Workup as described above gave the product **5o**. Flash column chromatagraph with chloroform/methanol as eluents afforded pure analytic samples of **5o**.

7-(Cyclopropanecarbonyl)-5-methyl-4*H*-isoquinolino[4,5-*jk*]-phenanthridine-4,6(5*H*)-dione (5o). Pale yellow powder; ^{1}H NMR (300 MHz; $CDCl_3$) δ 9.37(d, 1H, J = 8.4), 9.36(s, 1H), 8.90(d, 1H, J = 8.1), 8.83(dd, 1H, J = 1.2, 7.5), 8.35(dd, 1H, J = 1.2, 8.1), 8.03(t, 1H, J = 8.1), 7.93(dt, 1H, J = 1.5, 7.2), 7.83(dt, 1H, J = 1.5, 7.2), 3.59(s, 3H), 2.43(m, 1H), 1.92(m, 1H), 1.55(m, 1H), 1.24−1.38(m, 2H); ^{13}C NMR (75 MHz; $CDCl_3$) δ 12.8, 14.9, 24.6, 27.5, 117.5, 121.1, 123.2, 123.3, 127.5, 127.9,128.2, 128.3, 128.7, 130.6, 130.9, 132.4, 134.2, 135.3, 146.6, 147.3, 150.0, 163.4, 163.9, 206.4; MS *m*/*z* (% base), 381(1), 380(M^+, 35), 352(100), 339(54), 337(4), 322(3), 296(6), 44(2). Anal. Calcd for $C_{24}H_{16}N_2O_3$: C, 75.78; H, 4.24; N, 7.36. Found: C, 75.78; H, 4.23; N, 7.40.

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Supporting Information Available: General experimental information; structure and DFT calculation on the diradical intermediates **DR1** and **DR2**; ORTEP drawing of compound **6h** and **7h**; CIF files of **6h** and **7h**; UV absorption and fluorescent emission of representative aza-polycyclic products; copies of ^{1}H and ^{13}C NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.