OL | Organic Letters

Cite This: Org. Lett. XXXX, XXX, XXX–XXX

Letter

pubs.acs.org/OrgLett

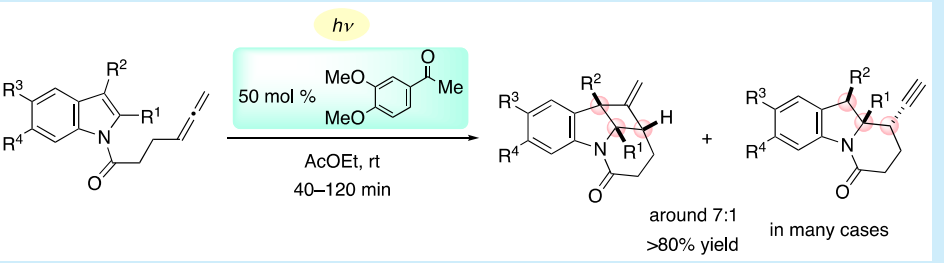
Stereoselective Construction of Methylenecyclobutane-Fused Indolines through Photosensitized [2+2] Cycloaddition of Allene-Tethered Indole Derivatives

Noriyoshi Arai*,† and Takeshi Ohkuma*,†,‡

†Division of Applied Chemistry, Faculty of Engineering, Hokkaido University, Sapporo, Hokkaido 060-8628, Japan

‡Frontier Chemistry Center, Faculty of Engineering, Hokkaido University, Sapporo, Hokkaido 060-8628, Japan

Supporting Information



ABSTRACT: Irradiation of 1-(hexa-4,5-dienoyl)indole derivatives in the presence of an aromatic ketone by a high-pressure mercury lamp through Pyrex glass gave the corresponding cyclized products stereoselectively in high yields. The major part of the products was an all-*cis*-fused methylenecyclobutane-type compound produced through [2+2] cycloaddition, accompanied by small amounts of alkynes via 1,5-hydrogen transfer of a biradical intermediate. Among a range of aromatic ketones, 3′,4′-dimethoxyacetophenone was found to sensitize the substrate quite effectively.

Cyclobutanes are versatile synthetic building blocks that offer a balance between the inherent rigidity of a small-ring compound and a greater stability toward ring-opening reactions compared with cyclopropanes.[1] Recently, cyclobutanes have also attracted attention in drug discovery due to the growing demand for lipophilic conformationally restricted analogues of known scaffolds rather than bulky aromatic compounds.[2−6] The photochemical [2+2] cycloaddition reaction is one of the most popular and facile methods of constructing four-membered cyclic compounds represented by cyclobutanes.[7,8]

Indoline-fused cyclic compounds form an important core of bioactive natural products, and they are also typical structural motifs in several useful pharmaceuticals.[9] Novel fused cyclic indoline frameworks are of interest in bioactive screening for new pharmaceutical candidates.[10] To meet the demand for such frameworks, new methods of synthesizing diverse indoline derivatives are needed. To date, a number of synthetic methods have been reported for this important class of compounds, whereas there has been much less exploration of cyclobutane-fused indolines.[11,12] The [2+2] photocycloaddition using 1-acylindoles as components is an exception. It has been extensively examined to access the cyclobutane-fused compounds.[13−17]

The [2+2] photocycloaddition between 1-acylindoles and substituted ethenes is known to proceed under the sensitization of acetophenone with Pyrex-filtered irradiation (>300 nm) to yield cyclobutane-fused indolines, though reactions with 1-aroylindoles can be performed without the sensitizer.[13] However, the reactions required large excesses of alkenes to obtain acceptable yields of the products in many cases, and the regioselectivity, namely, head-to-head or head-to-tail selectivity, depended on the electronic properties of the alkenes employed.[14,15] To overcome this problem, intramolecular cycloadditions were investigated by tethering the alkene to the acyl substituent of the indoles. This strategy gave the [2+2] adducts regio- and stereoselectively, while the resulting cyclobutane ring did not have any functional groups that were useful for further molecular transformation.[18]

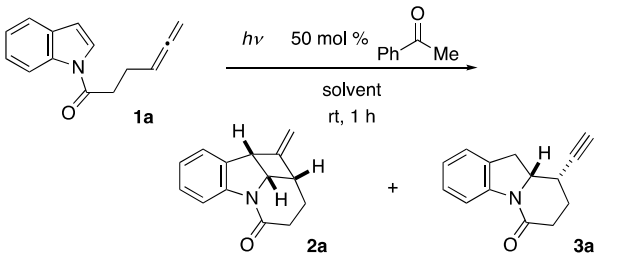
In the course of our investigation of the photochemistry of five-membered heteroaromatic compounds,[19] we envisaged that reactions between 1-acylindoles and allenes would give methylenecyclobutane-fused indolines that are readily functionalized by transforming the methylene moiety. To the best of our knowledge, such photochemical transformation has never been reported in the literature.[20] After extensive screening of photosensitizers, we found that 3′,4′-dimethoxyacetophenone sensitizes the intramolecular [2+2] cycloaddition between indoles and allenes quite effectively. We report herein the photocyclization of 1-(hexa-4,5-dienoyl)-indole derivatives with this particular sensitizer, which yielded tetracyclic cyclobutane-fused indoline derivatives in a highly stereoselective manner.

Received: January 24, 2019

DOI: 10.1021/acs.orglett.9b00309
Org. Lett. XXXX, XXX, XXX–XXX

We first attempted a reaction of 1-(hexa-4,5-dienoyl)indole (**1a**)[21] sensitized by acetophenone in a range of solvents under irradiation by a high-pressure mercury lamp through Pyrex glass (Table 1). The solvents were thoroughly degassed by freeze−thaw cycles before use. The reaction was conducted at room temperature and discontinued in 1 h irrespective of the conversion of **1a**. The reaction proceeded well in aromatic or medium polar solvents, giving methylenecyclobutane-type product **2a** in moderate yield, unexpectedly accompanied by terminal alkyne **3a** (entries 1−3). The reaction pathway forming **3a** is discussed in detail in the following section. When isolated **2a** was irradiated under the reaction conditions, it was recovered unchanged almost quantitatively. The reactions in a halogenated solvent (entry 4) and highly polar solvents (entries 5 and 6) gave inferior results. We chose ethyl acetate as the best solvent because it gave the highest yield of **2a** and the cleanest reaction, although benzene was the most frequently employed solvent in the previous studies.

Table 1. Solvent Screen[a]

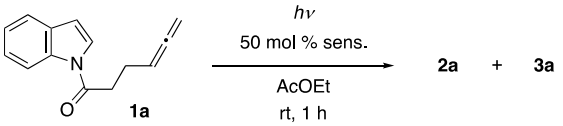


entry	solvent	conversion (%)[b]	**2a** (%)[b]	**3a** (%)[b]
1	benzene	84	54	10
2	AcOEt	90	62	10
3	MTBE	80	50	10
4	CH_2Cl_2	57	28	5
5	MeCN	74	42	5
6	MeOH	53	32	5

[a]All reactions were carried out in a Pyrex test tube by external irradiation with a high-pressure Hg lamp at a concentration of 10 mM. [b]Determined by the ^{1}H NMR integral ratio using 1,1,2,2-tetrachloroethane as an internal standard.

Next, we screened photosensitizers (Table 2). Acetophenone nicely sensitized the reaction, as shown in the previous table, whereas the reaction was substantially slowed in the absence of the sensitizer, resulting in a much lower yield of the photoadducts with unidentified messy byproducts (entries 1 and 2). Benzophenone and xanthone, which like acetophenone are typical triplet sensitizers, gave inferior yields, though the starting material **1a** was completely consumed in 1 h (entries 3 and 4, respectively). This difference between acetophenone and benzophenone (or xanthone) is difficult to explain. Though generation of different triplet states by each sensitizer or participation of electron-transfer sensitization might be possible, details should be elucidated via further investigation. These results prompted us to carry out the reaction by using a range of substituted acetophenones, to gain information about the electronic effect on the reaction. Neither the electron-withdrawing nor the electron-donating groups improve the yield of **2a**, but the reaction with 4′-methoxyacetophenone reduced the amounts of byproducts (entries 5−7). We then conducted a reaction with di- or trialkoxy-substituted acetophenones (entries 8−10). This revealed that 3′,4′-dimethoxyacetophenone (**4**) was the sensitizer of choice for this reaction, affording the cyclized products **2a** and **3a** in a 92% combined yield (entry 9). The 2′,6′-isomer was not as effective as **4** (entry 11). Though the 2′,4′-isomer was equally effective (entry 12), for budgetary reasons we chose the 3′,4′-isomer for further investigations. The amounts of the sensitizer were reduced to 30 mol %, with little sacrifice of the product yield (Table S1). The triplet energy (E_T) of **1a** is not known, but those of 1-benzoylindole and 1-methylindole are reported as 68 and 69.3 kcal/mol, respectively, in the literature.[15f,22] While ketones that have an E_T of nearly 70 kcal/mol sensitized **1a** well, 2-acetonaphthone that has a much smaller E_T (59 kcal/mol) did not give the product (**2a** or **3a**) at all (entry 13). The small conversion might be attributed to side reaction(s) via slight absorption by **1a** itself. These results are consistent with the triplet sensitization mechanism described below.

Table 2. Screen of Photosensitizers[a]



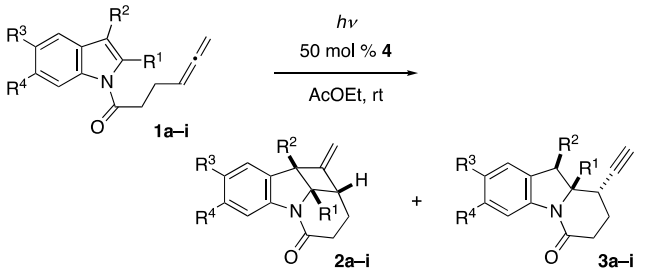
entry	sensitizer[b]	E_T (kcal/mol)	conversion (%)[c]	**2a** (%)[c]	**3a** (%)[c]
1	AP	73.6[d]	90	62	10
2	none		37	12	trace
3	benzophenone	68.5[d]	100	41[e]	trace
4	xanthone	74.2[d]	100	30[e]	trace
5	4′-Cl-AP	71.7[f]	91	61	10
6	4′-F-AP	72.8[g]	71	46	7
7	4′-MeO-AP	70.1[f]	86	58	9
8	3′,4′-(OCH_2O)-AP	65.8[h]	88	64	10
9	3′,4′-$(MeO)_2$-AP	67.3[f]	100	80	12
10	3′,4′,5′-$(MeO)_3$-AP		98	18	9
11	2′,6′-$(MeO)_2$-AP		60	35	6
12	2′,4′-$(MeO)_2$-AP		100	78	12
13	2-acetonaphthone	59.3[d]	11	0	0

[a]All reactions were carried out in a Pyrex test tube by external irradiation with a high-pressure Hg lamp at a concentration of 10 mM. [b]AP, acetophenone. [c]Determined by the ^{1}H NMR integral ratio using 1,1,2,2-tetrachloroethane as an internal standard. [d]From ref 23. [e]1,3,5-Trimethoxybenzene was used as an internal standard. [f]From ref 24. [g]From ref 25. [h]From ref 26.

With the optimized conditions in hand, we explored the reaction using a variety of indole derivatives (Table 3). The reactions listed in Table 3 were carried out in a photochemical reaction vessel for internal irradiation. The reactions were discontinued as soon as possible after consumption of the starting materials. The result of the reaction with **1a** was comparable to that with external irradiation, with **2a** and **3a** being isolated with an only slight loss (entry 1). The substituents at the benzene ring of indole had a strong influence on the reaction. The reactions of **1b** (5-Me), **1c** (5-F), and **1d** (6-Cl) gave comparable yields of the cyclized products (entries 2−4, respectively), while a somewhat lower yield was obtained in the case of 5-Br-substituted **1e** (entry 5). It should be noted that ring junctures were created with perfect diastereoselectivity, suggesting the high potential of this reaction for the stereoselective synthesis of indolines with fused rings. In entry 5, small amounts of debrominated products (namely, **2a** and **3a**) were detected but could not be isolated. Introduction of the 5-MeO or 5-CO_2Me group

DOI: 10.1021/acs.orglett.9b00309
Org. Lett. XXXX, XXX, XXX−XXX

Table 3. Substrate Screen[a]



entry	substrate	R^1	R^2	R^3	R^4	time (min)	2 (%)[b]	3 (%)[b]
1	**1a**	H	H	H	H	40	71	11
2	**1b**	H	H	Me	H	40	69	13
3	**1c**	H	H	F	H	40	72	14
4	**1d**	H	H	H	Cl	40	69	14
5	**1e**	H	H	Br	H	60	58	15[c]
6	**1f**	H	H	MeO	H	120	26	5
7	**1g**	H	H	CO_2Me	H	120	46	*d*
8	**1h**	H	Me	H	H	40	71	13
9	**1i**	Ph	H	H	H	180	14	2

[a]All reactions were carried out in a Pyrex reaction vessel for photochemical reaction by internal irradiation with a high-pressure Hg lamp at a concentration of 10 mM. [b]Yields of the isolated product. [c]In this case, separation of the products was too difficult and, as a result, pure **3e** was not obtained. The yield was calculated by a proportional distribution based on the integrals of ^{1}H NMR of the mixture. [d]This product had an estimated yield of <5%, but it could not be separated from the unidentified byproducts.

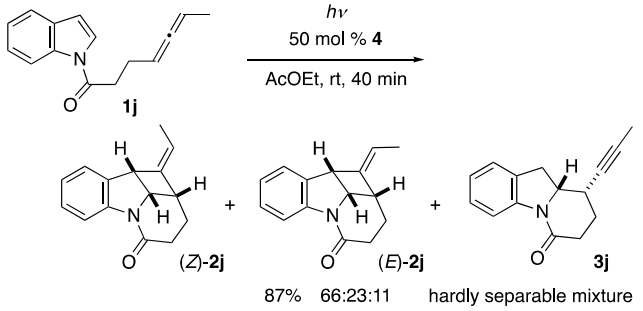
reduced the reaction rate, giving the products in moderate yields (entry 6 or 7, respectively). These results turned out to be caused by undesirable side reactions, such as deacylation and acyl migration of the indole substrates (photo-Fries rearrangement),[27] which are common pathways in the photochemical reaction of 1-acylated indoles. Irradiation of 3-Me-substituted substrate **1h** afforded the [2+2] adduct with a quaternary carbon **2h** accompanied by stereoselective formation of alkyne **3h** (entry 8). The reaction with **1i** became complex, giving the cycloadducts only in low yields (entry 9). A deacylated compound, 2-phenylindole, was the main product (22%) in this reaction.[27]

This reaction worked well when the allene terminus was substituted with a methyl group. When the internal allenyl acylindole **1j** was irradiated under the typical conditions, the cycloaddition products (*Z*)-**2j**, (*E*)-**2j**, and **3j** were obtained in 87% combined yield in a 66:23:11 ratio (Scheme 1). Unfortunately, the separation was quite difficult, but **3j** was separated from a geometrical mixture of **2j** by repeated thin-layer chromatography.

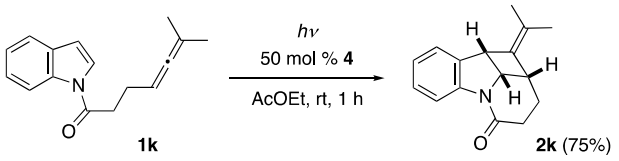
Irradiation of a substrate with two terminal methyl groups **1k** gave the [2+2] adduct **2k** as a sole product in high yield (Scheme 2). This result strongly suggested that the alkyne **3** mentioned above was produced through internal transposition of hydrogen at the allene terminal to position 3 of indole.

To elucidate the mechanism underlying the formation of alkyne **3**, a substrate that was dideuterated at the allene terminal was prepared (**1a**-d_2) and then irradiated under the typical conditions (Scheme 3). The reaction gave [2+2] adduct **2a**-d_2 and alkyne **3a**-d_2 in which a deuterium was introduced at position 3 of indole from the same side as the alkynyl moiety. This result clearly shows that the hydrogen on

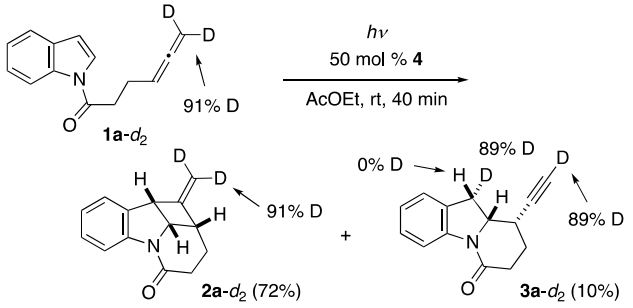
Scheme 1. Reaction of a Substrate with Disubstituted Allene



Scheme 2. Reaction of a Substrate with Trisubstituted Allene



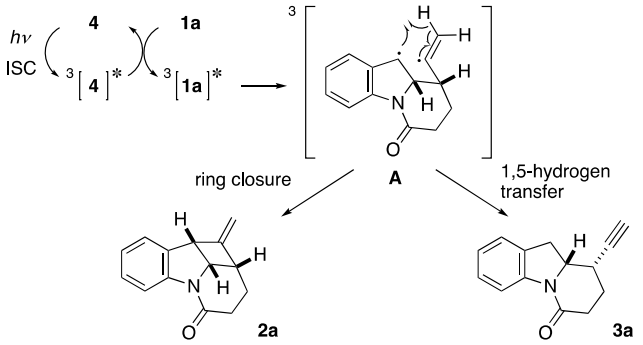
Scheme 3. Reaction of a Dideuterated Substrate



the down side of position 3 comes from the terminus of the allene moiety.

Though the detailed mechanism is not clear at this stage, we presume that the reaction pathway is as shown in Scheme 4

Scheme 4. Plausible Reaction Pathway



based on the results presented above and information from the literature.[15] Triplet **1a**, which is generated by sensitizations with the triplet **4**, makes an internal carbon−carbon bond between position 2 of indole and the allene moiety to form the tricyclic biradical intermediate **A**. The mechanism underlying this type of radical bond formation has been well established in the photoreaction between indoles and alkenes.[15f] When the intermediate **A** undergoes ring closure accompanied by

DOI: 10.1021/acs.orglett.9b00309
Org. Lett. XXXX, XXX, XXX−XXX

intersystem crossing (ISC), the [2+2] adduct **2a** is produced. On the other hand, alkyne **3a** is formed via the competitive 1,5-hydrogen transposition. The formation of **2a** and **3a** through direct excitation of **1a** seems less likely, because the photoabsorption of **1a** in the range of Pyrex-filtered ultraviolet is much less effective than that of **4**.

In conclusion, we have developed an unprecedented [2+2] photochemical cycloaddition reaction of 1-(hexa-4,5-dienoyl)-indole derivatives. 3′,4′-Dimethylacetophenone acts as a quite effective photosensitizer in this reaction. With appropriate substrates, the reaction proceeds cleanly in <1 h to afford synthetically valuable methylenecyclobutane-fused indolines and alkynyl compounds in high yield. The perfect diastereoselection in this reaction is noteworthy. A plausible reaction pathway is proposed on the basis of some mechanistic experiments.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b00309.

Table S1, experimental procedures, and spectral data (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: n-arai@eng.hokudai.ac.jp.
*E-mail: ohkuma@eng.hokudai.ac.jp.

ORCID

Noriyoshi Arai: 0000-0003-0964-223X

Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) Reviews on cyclobutanes: (a) Namyslo, J. C.; Kaufmann, D. E. *Chem. Rev.* **2003**, *103*, 1485−1537. (b) Lee-Ruff, E.; Mladenova, G. *Chem. Rev.* **2003**, *103*, 1449−1483.

(2) Reviews: (a) Goldberg, F. W.; Kettle, J. G.; Kogej, T.; Perry, M. W. D.; Tomkinson, N. P. *Drug Discovery Today* **2015**, *20*, 11−17. (b) Marson, C. M. *Chem. Soc. Rev.* **2011**, *40*, 5514−5533. (c) Grygorenko, O. O.; Radchenko, D. S.; Volochnyuk, D. M.; Tolmachev, A. A.; Komarov, I. V. *Chem. Rev.* **2011**, *111*, 5506−5568.

(3) (a) Levterov, V. V.; Michurin, O.; Borysko, P. O.; Zozulya, S.; Sadkova, I. V.; Tolmachev, A. A.; Mykhailiuk, P. K. *J. Org. Chem.* **2018**, *83*, 14350−14361. (b) Druzhenko, T.; Skalenko, Y.; Samoilenko, M.; Denisenko, A.; Zozulya, S.; Borysko, P. O.; Sokolenko, M. I.; Tarasov, A.; Mykhailiuk, P. K. *J. Org. Chem.* **2018**, *83*, 1394−1401.

(4) Vasiuta, R. I.; Gorichko, M. V. *Tetrahedron Lett.* **2014**, *55*, 466−468.

(5) Radchenko, D. S.; Michurin, O. M.; Grygorenko, O. O.; Scheinpflug, K.; Dathe, M.; Komarov, I. V. *Tetrahedron* **2013**, *69*, 505−511.

(6) (a) Lovering, F. *MedChemComm* **2013**, *4*, 515−519. (b) Lovering, F.; Bikker, J.; Humblet, C. *J. Med. Chem.* **2009**, *52*, 6752−6756.

(7) Reviews: (a) Poplata, S.; Tröster, A.; Zou, Y.-Q.; Bach, T. *Chem. Rev.* **2016**, *116*, 9748−9815. (b) Bach, T.; Hehn, J. P. *Angew. Chem., Int. Ed.* **2011**, *50*, 1000−1045. (c) Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052−1103. (d) Hehn, J. P.; Müller, C.; Bach, T. In *Handbook of Synthetic Photochemistry*; Albini, A., Fagnoni, M., Eds.; Wiley-VCH: Weinheim, Germany, 2010; pp 171−215. (e) Hoffmann, N. In *Handbook of Synthetic Photochemistry*; Albini, A., Fagnoni, M., Eds.; Wiley-VCH: Weinheim, Germany, 2010; pp 137−169. (f) Fleming, S. A.; Bradford, C. L.; Gao, J. J. In *Organic Photochemistry*; Ramamurthy, V., Schanze, K. S., Eds.; Marcel Dekker: New York, 1997; pp 187−243. (g) Crimmins, M. T.; Reinhold, T. L. *Org. React.* **1993**, *44*, 297−588.

(8) Recent examples: (a) Hörmann, F. M.; Chung, T. S.; Rodriguez, E.; Jakob, M.; Bach, T. *Angew. Chem., Int. Ed.* **2018**, *57*, 827−831. (b) Fort, D. A.; Woltering, T. J.; Alker, A. M.; Bach, T. *J. Org. Chem.* **2014**, *79*, 7152−7161. (c) Brimioulle, R.; Bach, T. *Science* **2013**, *342*, 840−843. (d) White, J. D.; Li, Y.; Kim, J.; Terinek, M. *J. Org. Chem.* **2015**, *80*, 11806−11817. (e) Hurtley, A. E.; Lu, Z.; Yoon, T. P. *Angew. Chem., Int. Ed.* **2014**, *53*, 8991−8994. (f) Burckle, A. J.; Vasilev, V. H.; Burns, N. Z. *Angew. Chem., Int. Ed.* **2016**, *55*, 11476−11479. (g) Fort, D. A.; Woltering, T. J.; Nettekoven, M.; Knust, H.; Bach, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 10169−10172. (h) Navarro, R.; Reisman, S. E. *Org. Lett.* **2012**, *14*, 4354−4357.

(9) (a) Dunlop, J.; Marquis, K. L.; Lim, H. K.; Leung, L.; Kao, J.; Cheesman, C.; Rosenzweig-Lipson, S. *CNS Drug Rev.* **2006**, *12*, 167−177. (b) Hibino, S.; Choshi, T. *Nat. Prod. Rep.* **2001**, *18*, 66−87. (c) Lounasmaa, M.; Tolvanen, A. *Nat. Prod. Rep.* **2000**, *17*, 175−191.

(10) (a) Blanco-Ania, D.; Gawade, S. A.; Zwinkels, L. J. L.; Maartense, L.; Bolster, M. G.; Benningshof, J. C. J.; Rutjes, F. P. J. T. *Org. Process Res. Dev.* **2016**, *20*, 409−413. (b) Mo, Y.; Zhao, J.; Chen, W.; Wang, Q. *Res. Chem. Intermed.* **2015**, *41*, 5869−6877. (c) Martin, V. I.; Goodell, J. R.; Ingham, O. J.; Porco, J. A., Jr.; Beeler, A. B. *J. Org. Chem.* **2014**, *79*, 3838−3846. (d) Podoll, J. D.; Liu, Y.; Chang, L.; Walls, S.; Wang, W.; Wang, X. *Proc. Natl. Acad. Sci. U. S. A.* **2013**, *110*, 15573−15578.

(11) (a) Wang, Y.; Xie, F.; Lin, B.; Cheng, M.; Liu, Y. *Chem. - Eur. J.* **2018**, *24*, 14302−14315. (b) Zi, W.; Zuo, Z.; Ma, D. *Acc. Chem. Res.* **2015**, *48*, 702−711. (c) Zhang, D.; Song, H.; Qin, Y. *Acc. Chem. Res.* **2011**, *44*, 447−457. (d) Liu, D.; Zhao, G.; Xiang, L. *Eur. J. Org. Chem.* **2010**, *2010*, 3975−3984.

(12) Formation of cyclobut[*b*]indolines: (a) Ogawa, N.; Yamaoka, Y.; Takikawa, H.; Tsubaki, K.; Takasu, K. *J. Org. Chem.* **2018**, *83*, 7994−8002. (b) Nandi, R. K.; Guillot, R.; Kouklovsky, C.; Vincent, G. *Org. Lett.* **2016**, *18*, 1716−1719. (c) Miyoshi, T.; Aoki, Y.; Uno, Y.; Araki, M.; Kamatani, T.; Fujii, D.; Fujita, Y.; Takeda, N.; Ueda, M.; Kitagawa, H.; Emoto, N.; Mukai, T.; Tanaka, M.; Miyata, O. *J. Org. Chem.* **2013**, *78*, 11433−11443. (d) Walter, H.; Sauter, H.; Schneider, J. *Helv. Chim. Acta* **1993**, *76*, 11433−11443.

(13) Julian, D. R.; Foster, R. *J. Chem. Soc., Chem. Commun.* **1973**, 311−312.

(14) (a) Ikeda, M.; Ohno, K.; Mohri, S.-i.; Takahashi, M.; Tamura, Y. *J. Chem. Soc., Perkin Trans. 1* **1984**, *1*, 405−412. (b) Ikeda, M.; Ohno, K.; Takahashi, M.; Uno, T.; Tamura, Y.; Kido, M. *J. Chem. Soc., Perkin Trans. 1* **1982**, *1*, 741−748. (c) Ikeda, M.; Ohno, K.; Uno, T.; Tamura, Y. *Tetrahedron Lett.* **1980**, *21*, 3403−3406. (d) Ikeda, M.; Uno, T.; Homma, K.-i.; Ohno, K.; Tamura, Y. *Synth. Commun.* **1980**, *10*, 437−449.

(15) (a) Weedon, A. C.; Zhang, B. *Synthesis* **1992**, *1992*, 95−100. (b) Hastings, D. J.; Weedon, A. C. *J. Org. Chem.* **1991**, *56*, 6326−6331. (c) Hastings, D. J.; Weedon, A. C. *Tetrahedron Lett.* **1991**, *32*, 4107−4110. (d) Oldroyd, D. L.; Weedon, A. C. *J. Photochem. Photobiol., A* **1991**, *57*, 207−216. (e) Hastings, D. J.; Weedon, A. C. *Can. J. Chem.* **1991**, *69*, 1171−1181. (f) Disanayaka, B. W.; Weedon, A. C. *Can. J. Chem.* **1990**, *68*, 1685−1692.

(16) Winkler, J. D.; Scott, R. D.; Williard, P. G. *J. Am. Chem. Soc.* **1990**, *112*, 8971−8975.

(17) Martin, V. I.; Goodell, J. R.; Ingham, O. J.; Porco, J. A., Jr.; Beeler, A. B. *J. Org. Chem.* **2014**, *79*, 3838−3846.

(18) (a) Oldroyd, D. L.; Weedon, A. C. *J. Org. Chem.* **1994**, *59*, 1333−1343. (b) Oldroyd, D. L.; Weedon, A. C. *J. Chem. Soc., Chem. Commun.* **1992**, 1491−1492.

(19) (a) Arai, N.; Mizota, M.; Ohkuma, T. *Org. Lett.* **2015**, *17*, 86−89. (b) Arai, N.; Mizota, M.; Ohkuma, T. *Heterocycles* **2015**, *90*, 607−616. (c) Arai, N.; Tanaka, K.; Ohkuma, T. *Org. Lett.* **2012**, *14*, 1488−1491. (d) Arai, N.; Tanaka, K.; Ohkuma, T. *Tetrahedron Lett.* **2010**, *51*, 1273−1275.

DOI: 10.1021/acs.orglett.9b00309
Org. Lett. XXXX, XXX, XXX−XXX

(20) Au(I)-catalyzed [2+2] cycloadditions between indoles and allenes have been reported: (a) Huang, W.; Zhang, Y.-C.; Jin, R.; Chen, B.-L.; Chen, Z. *Organometallics* **2018**, *37*, 3196−3209. (b) Niemeyer, Z. L.; Pindi, S.; Khrakovsky, D. A.; Kuzniewski, C. N.; Hong, C. M.; Joyce, L. A.; Sigman, M. S.; Toste, F. D. *J. Am. Chem. Soc.* **2017**, *139*, 12943−12946. (c) Ocello, R.; De Nisi, A.; Jia, M.; Yang, Q.-Q.; Monari, M.; Giacinto, P.; Bottoni, A.; Miscione, G. P.; Bandini, M. *Chem. - Eur. J.* **2015**, *21*, 18445−18453. (d) Jia, M.; Monari, M.; Yang, Q.-Q.; Bandini, M. *Chem. Commun.* **2015**, *51*, 2320−2323. (e) Mei, L.-Y.; Wei, Y.; Tang, X.-Y.; Shi, M. *J. Am. Chem. Soc.* **2015**, *137*, 8131−8137. (f) Faustino, H.; Bernal, P.; Castedo, L.; López, F.; Mascareñas, J. L. *Adv. Synth. Catal.* **2012**, *354*, 1658−1664. (g) Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 16804−16805.

(21) The series of indole derivatives used in this study could be conveniently prepared by Tokuyama's condensation method: Umehara, A.; Ueda, H.; Tokuyama, H. *J. Org. Chem.* **2016**, *81*, 11444−11453.

(22) Wilkinson, F.; Garner, A. *Photochem. Photobiol.* **1978**, *27*, 659−670.

(23) Herkstroeter, W. G.; Lamola, A. A.; Hammond, G. S. *J. Am. Chem. Soc.* **1964**, *86*, 4537−4540.

(24) Lathioor, E. C.; Leigh, W. J. *Photochem. Photobiol.* **2006**, *82*, 291−300.

(25) Lin, Z.-P.; Aue, W. A. *Spectrochim. Acta, Part A* **2000**, *56*, 111−117.

(26) Yang, N. C.; McClure, D. S.; Murov, S. L.; Houser, J. J.; Dusenbery, R. *J. Am. Chem. Soc.* **1967**, *89*, 5466−5468.

(27) Deacylation and acyl migration are known as main pathways in the photochemical [2+2] cycloaddition of 1-acylindoles: (a) Carruthers, W.; Evans, N. *J. Chem. Soc., Perkin Trans. 1* **1974**, *1*, 1523−1525. (b) Somei, M.; Natsume, M. *Tetrahedron Lett.* **1973**, *14*, 2451−2454. See also refs 15d and 15e.

DOI: 10.1021/acs.orglett.9b00309
Org. Lett. XXXX, XXX, XXX−XXX