OL | Organic Letters

pubs.acs.org/OrgLett Letter

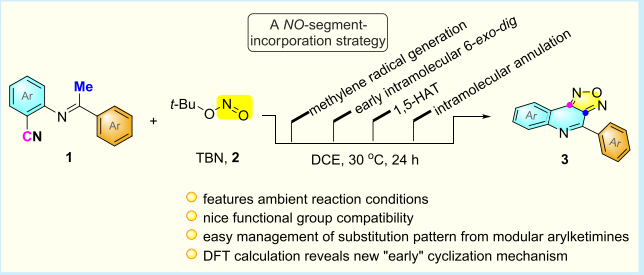
Assembly of Furazan-Fused Quinolines via an Expeditious Metal-Free [2+2+1] Radical Tandem Cyclization Process

Guobo Deng, Ronglin Zhong, Jianxin Song, Pui Ying Choy, and Fuk Yee Kwong*

Cite This: *Org. Lett.* 2021, 23, 6520–6524 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: A [2+2+1]-NO-segment-incorporating heteroannulative cascade is described. This versatile method, particularly using modular cyanoarylated ketimine substrates, allows efficient access to structurally diversified quinolines embedded with an oxadiazole core. This metal-free protocol proceeds smoothly at 30 °C, offers easy manipulation of substituents on the quinoline moiety, and tolerates a spectrum of functional groups. Density functional theory calculation revealed that the cyano moiety is crucial to facilitate the early cyclization step in this heteroannulation process and is different from the previously established late cyclization mechanistic interpretation.

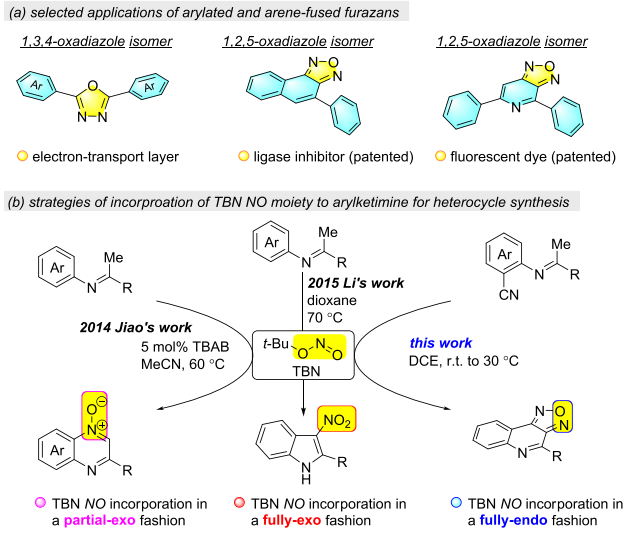


The heterocycle constitutes as an important structural motif in many natural products, pharmaceutically useful intermediates, and functional materials.[1−3] Indeed, the strategy to enable specific heteroatom incorporation plays a crucial role in synthetic organic chemistry as the resulting compound would alternatively give an appealing property when compared to that of its structurally similar all-carbon entity. Furazan, particularly the 1,2,5-oxadiazole, is a non-natural origin heterocycle among four existing isomers.[4−6] In fact, furazan exhibits versatile properties with respect to material and pharmaceutical applications (Scheme 1a).[7,8] For instance, the 1,3,4-isomer serves as an electron-transport layer[9−11] and the 1,2,5-oxadiazole isomer can be applied as a ligase inhibitor[12] and a fluorescent dye.[13,14]

With regard to the significance of these unique furazan scaffolds, unremitting investigations have been conducted with respect to new synthetic protocol development. Traditional methods of preparing arylated/arene-fused furazans are the dehydration of prefunctionalized 1,2-dioximes and using simple furazans as primitive substrates,[15−17] as well as lengthy, multistep, and in particular sequential reactions using anilines or *o*-halonitroarene compounds as early starting materials.[18−20]

In fact, there has been no general and direct approach to reaching these arylated/arene-fused furazans with fascinating structural complexity using highly attractive modular substrates. In 2014, Jiao[21] reported the reaction between modular arylated ketimines[22] and TBN (*tert*-butyl nitrite)[23,24] for accessing quinoxaline *N*-oxides (Scheme 1b). The NO segment of TBN was incorporated in a partially *exo* fashion. In 2015, Li showed the synthesis of 3-nitroindoles using TBN.[25] Via this strategy, the NO moiety was installed in a fully *exo* manner. As a continuation of our interest in investigating fused arenes,[26−29] we are intrigued about whether the furazan can be feasibly assembled from TBN via a fully *endo*-selective NO incorporation pathway (Scheme 1b).

Scheme 1. Selected Applications of Arylated and Arene-Fused Furazans and Recent Synthetic Strategies of Incorporation of TBN NO into Arylketimines

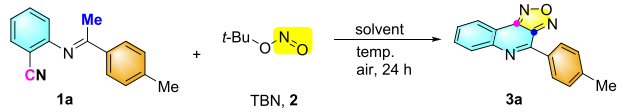


Received: July 12, 2021
Published: August 9, 2021

https://doi.org/10.1021/acs.orglett.1c02326
Org. Lett. 2021, 23, 6520–6524

We started to embark on the prototypical investigations by employing arylketimine **1a** and TBN (**2**) as model substrates (Table 1). An evaluation of the reaction temperature revealed

Table 1. Optimization of Reaction Conditions[a]



entry	solvent	temp (°C)	yield (%)[b]
1	MeCN	70	27
2	MeCN	50	51
3	MeCN	30	56
4	MeCN	25	52
5[b]	MeCN	30	36
6[c]	MeCN	30	60
7[c]	DCM	30	43
8[c]	dioxane	30	30
9[c]	toluene	30	39
10[c]	DMA	30	30
11[c]	DCE	30	71
12[c]	$MeNO_2$	30	64
13[d]	DCE	30	69
14[e]	DCE	30	65

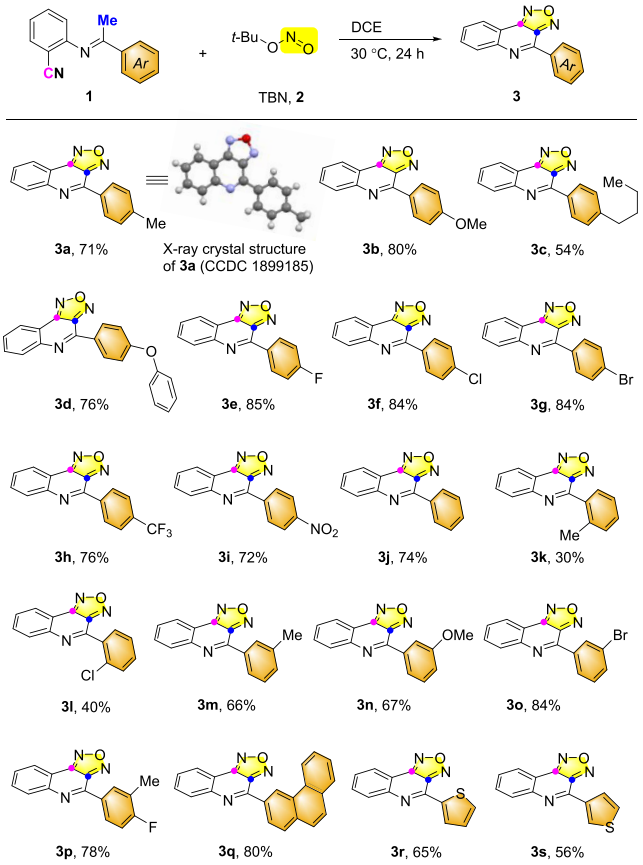
[a]**1a** (0.2 mmol) and **2** (0.8 mmol) were stirred in the indicated solvent (2 mL) at the indicated temperature for 24 h under a benchtop air atmosphere. Isolated yields are reported. [b]Under a nitrogen atmosphere. [c]Under an oxygen atmosphere. [d]With 0.6 mmol of **2**. [e]With 1.0 mmol of **2**.

that the range of 25−30 °C was the best (entries 1−4). A higher reaction temperature resulted in a lower product yield due to the possible decomposition of the starting materials (entry 1). Among the commonly used solvents that were screened, DCE was found to be the solvent of choice (entries 6−12). Desired product **3a** was obtained in 71% isolated yield under DCE solvent (entry 11). Alternating the stoichiometry of the starting materials did not provide a beneficial outcome (entries 13 and 14).

With the optimized reaction conditions in hand, we next investigated the scope of this tandem cyclization process with regard to the substituents attached to arylketimines (Scheme 2). In general, good product yields were afforded among various substituents at the arene ring tested. The structure of product **3a** was confirmed by X-ray crystallographic analysis (see the Supporting Information for details). No significant electronic effect was observed for the arene ring attached to the arylketimines (*p*-OMe vs *p*-CF_3; product **3b** vs **3h**). Halo groups, such as -F, -Cl, and -Br, were found to be compatible during the course of the reaction (products **3e**−**3g**, **3o**, and **3p**). It is notable that the intact -Br groups in products **3g** and **3o** are particularly useful as the resulting compounds can be further functionalized using established cross-coupling technology. Nevertheless, the steric influence was prominent. Products **3k** and **3l** with *ortho* substituents resulted in lower yields. π-Extended furazan could be assembled in good yield (product **3q**). Heterocyclic substituents, for instance, 2-thienyl and 3-thienyl groups, were compatible under these reaction conditions (products **3r** and **3s**).

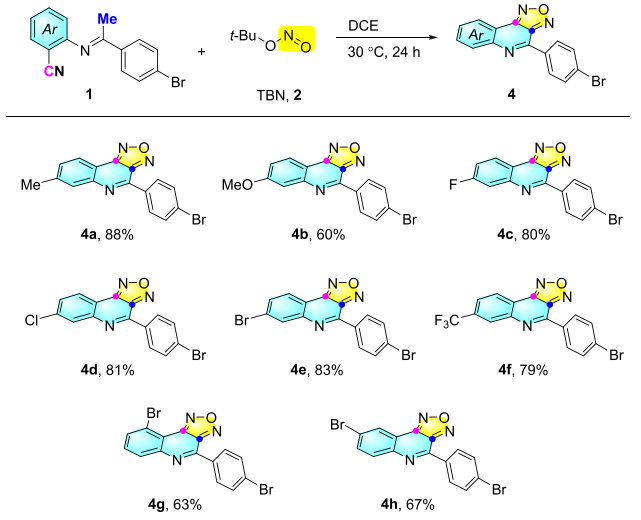
The reaction scope was further evaluated by testing various substituents at the benzonitrile moiety of **1** (Scheme 3). Functional groups such as -OMe, -F, -Cl, and -Br were well-

Scheme 2. Substrate Scope of Arylketiminebenzonitrile 1[a]



[a]**1** (0.2 mmol) and **2** (0.8 mmol) were stirred in DCE (2 mL) at 30 °C for 24 h under an oxygen atmosphere. Isolated yields are reported.

Scheme 3. Scope of the Arylnitrile Ring of Arylketimine 1[a]



[a]**1** (0.2 mmol) and **2** (0.8 mmol) were stirred in DCE (2 mL) at 30 °C for 24 h under an oxygen atmosphere. Isolated yields are reported.

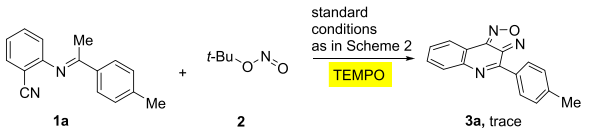
tolerated (products **4b**−**4e**, respectively). The highly electron-withdrawing -CF_3 group located at the *para* position of the nitrile moiety did not affect the annulation process (product **4f**). Slightly lower yields were attained when the bromo substituent is at the *ortho* or *meta* position to the nitrile moiety (products **4g** and **4h**). In addition, we attempted to use butyl

https://doi.org/10.1021/acs.orglett.1c02326
Org. Lett. 2021, 23, 6520−6524

methyl ketone instead of **1**, yet no corresponding product was observed from GC-MS analysis.

To shed light on the possible mechanism of this cascade cyclization process, a radical trapping experiment was carried out (Scheme 4). The reaction was inhibited by the radical scavenger tetramethylpiperidin-1-oxyl (TEMPO). Essentially no desired product was detected by GC/GC-MS analysis.

Scheme 4. Radical Trapping Experiment[a]



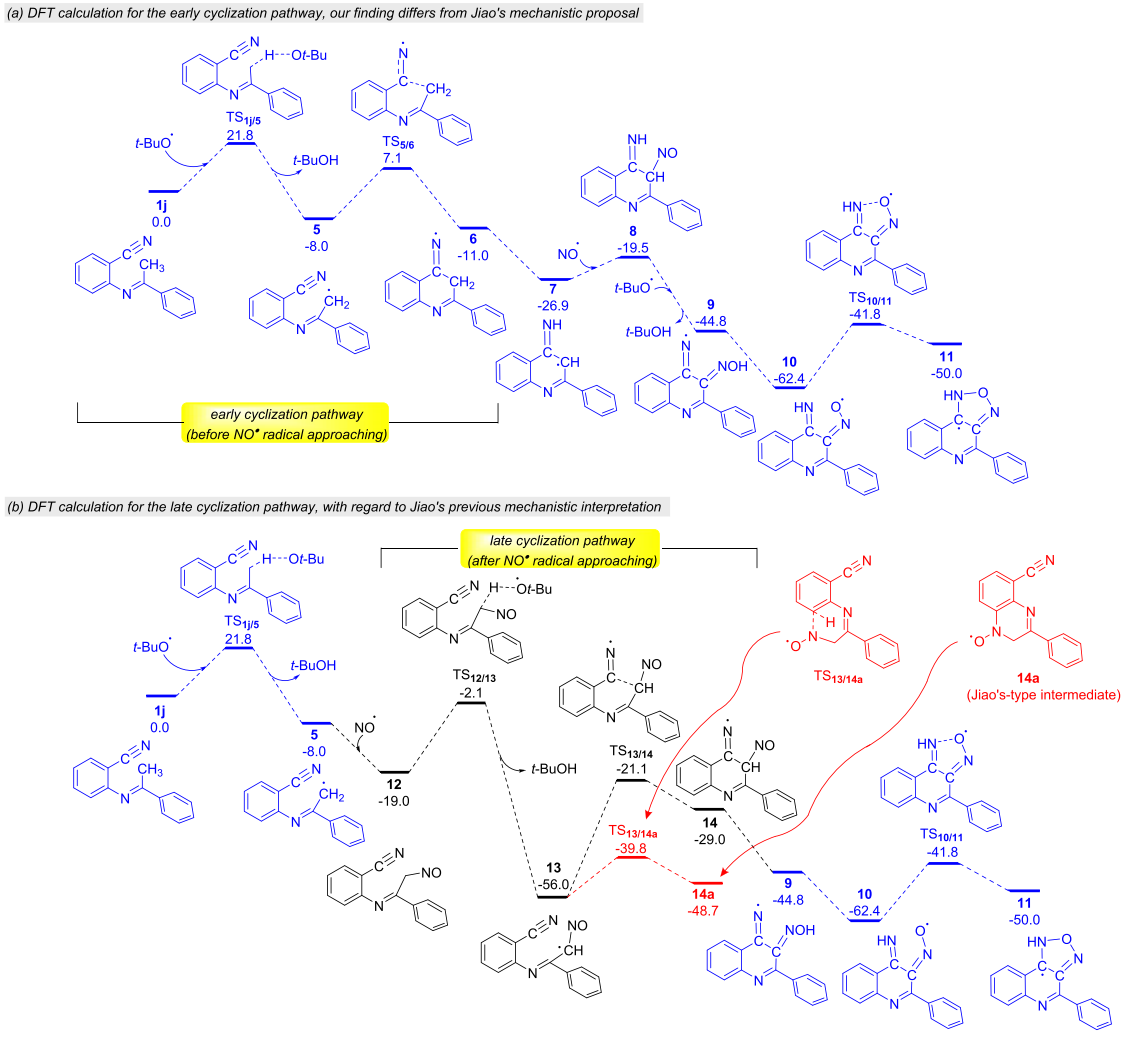
[a]Reaction conditions were the same as in Scheme 2, with TEMPO (0.8 mmol) added.

To investigate the reaction mechanism, DFT calculations were performed (Scheme 5).[30] α-H atom abstraction of **1j** by *in situ*-generated *t*-BuO$^\bullet$ leads to intermediate **5** (Scheme 5a). The cyano group of **5** is crucial for facilitating generation of the six-membered ring from the methylene radical, in which it is energetically favorable for the delivery of intermediate **6**. Thus, the early cyclization pathway before the impending NO$^\bullet$ radical is conceivable. In contrast, another opportunity for cyclization is the late annulation pathway after NO$^\bullet$ radical approaching (Scheme 5b, black part), as opposed to the suggestion by Jiao and co-workers.[21] The NO segment-incorporated intermediate **12** is believed to attain a thermodynamically stable radical intermediate **13**.

This intermediate allows the formation of Jiao's product **14a** under an energetically more favorable pathway (Scheme 5b, red part; $TS_{13/14}$ vs $TS_{13/14a}$). Nevertheless, it is found to be less probable to go over $TS_{13/14}$ (barrier of 34.9 kcal/mol) for the delivery of the ultimate furazan species **11**. In fact, we also did not observe any **14a** or its derivatives during the course of our study. These results on the contrary indicated that in the presence of the cyano group, the early cyclization pathway is more plausible than the late annulation route for attaining the entirely new framework, the arene-fused furazans.

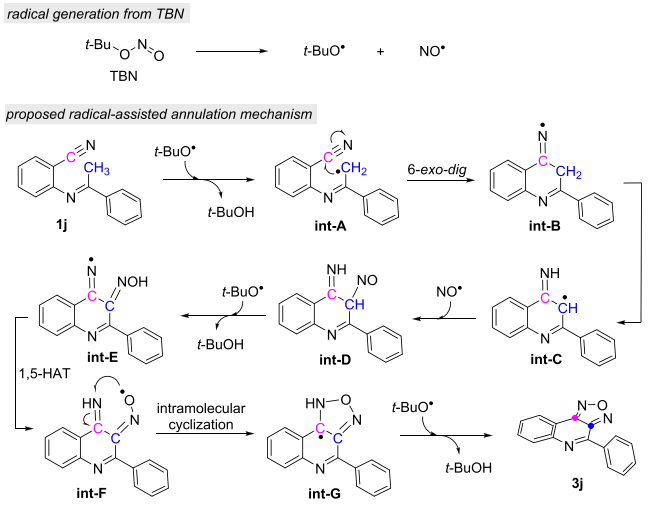
A proposed mechanism is illustrated with the support of a radical trapping experiment and DFT calculation (Scheme 6). *t*-BuO$^\bullet$ and NO$^\bullet$ radicals are generated *in situ* from TBN.[31] *t*-BuO$^\bullet$ carries out α-H atom abstraction of **1j** to give methylene radical **int-A**.[32] The 6-*exo*-*dig* cyclization is proposed for producing the six-membered ring species **int-B**.[33] The NO$^\bullet$ radical then reacts with methylidyne radical **int-C** and delivers NO segment-incorporated intermediate **int-D**. The putative

Scheme 5. DFT Energy Profile of Possible Reaction Mechanisms (with respect to Jiao's work)



https://doi.org/10.1021/acs.orglett.1c02326
Org. Lett. 2021, 23, 6520−6524

Scheme 6. A Proposed Mechanism



int-E undergoes 1,5-HAT to afford species **int-F**, and subsequent intramolecular cyclization generates **int-G**. Finally, the resulting furazan product **3j** is attained via the H atom abstraction process.

In conclusion, we have succeeded in showing a facile [2+2+1]-NO segment-incorporating heteroannulative cascade process. This transition metal-free protocol proceeds smoothly under ambient reaction conditions and realizes easy manipulation of a conceivable substituent pattern on fused arene/arylated furazans. Thus, this new modular method exhibits good product framework diversity and complexity and decent product yields and allows good functional group compatibility, particularly the -Br and -Cl groups where they are often found to be impermissible in existing metal-catalyzed aromatic ring-forming processes. It is worth noting that DFT calculation reveals a new possible early cyclization pathway, which is contrary to the precedented literature mechanistic interpretation. This complementary theoretical result indicates the rich potential of introducing other unsaturated moieties at the *ortho* position of modular arylketamine for the assembly of new structural frameworks.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c02326.

Experimental procedures and spectroscopic data for all compounds (PDF)

Accession Codes

CCDC 1899185 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Fuk Yee Kwong − *State Key Laboratory of Synthetic Chemistry and Department of Chemistry, The Chinese University of Hong Kong, New Territories, Hong Kong SAR, P. R. China;* orcid.org/0000-0001-9105-1740; Email: fykwong@cuhk.edu.hk

Authors

Guobo Deng − *State Key Laboratory of Synthetic Chemistry and Department of Chemistry, The Chinese University of Hong Kong, New Territories, Hong Kong SAR, P. R. China; Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research, Ministry of Education, Hunan Normal University, Changsha, Hunan 410081, P. R. China;* orcid.org/0000-0002-5470-5706

Ronglin Zhong − *State Key Laboratory of Synthetic Chemistry and Department of Chemistry, The Chinese University of Hong Kong, New Territories, Hong Kong SAR, P. R. China;* orcid.org/0000-0002-8896-1767

Jianxin Song − *Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research, Ministry of Education, Hunan Normal University, Changsha, Hunan 410081, P. R. China;* orcid.org/0000-0002-1756-5898

Pui Ying Choy − *State Key Laboratory of Synthetic Chemistry and Department of Chemistry, The Chinese University of Hong Kong, New Territories, Hong Kong SAR, P. R. China;* orcid.org/0000-0003-2765-0110

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c02326

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the Research Grants Council of Hong Kong (GRF, 14307418-18P), the National Natural Science Foundation of China (21602057), and the CUHK Direct Fund (4053445) for financial support. The authors also thank the Open Research Fund Project of Key Laboratory of Hunan Province (2018TP1017) and the Hong Kong Scholars program (XJ2017009 and XJ2020-072) for financial support. The authors are thankful for financial support from the Innovation and Technology Commission (HKSAR) to the State Key Laboratory of Synthetic Chemistry.

■ REFERENCES

(1) Alvarez-Builla, J.; Vaquero, J. J.; Barluenga, J. *Modern Heterocyclic Chemistry*; Wiley-VCH Verlag Gmbh & Co. KGaA: Weinheim, Germany, 2011.

(2) Joule, J. A.; Mills, K. *Heterocyclic Chemistry*; Wiley-Blackwell: Hoboken, NJ, 2010.

(3) Eicher, T.; Hauptmann, S.; Speicher, A. *The Chemistry of Heterocycles: Structures, Reactions, Synthesis, and Applications*; Wiley-VCH Verlag Gmbh & Co. KGaA: Weinheim, Germany, 2012.

(4) For pioneering studies, see: (a) Olofson, R. A.; Michelman, J. S. Furazans and Furazanium Salts. *J. Am. Chem. Soc.* **1964**, *86*, 1863. (b) Olofson, R. A.; Michelman, J. S. Furazan. *J. Org. Chem.* **1965**, *30*, 1854.

(5) For recent book chapters, see: (a) Nikonov, G. N.; Bobrov, S. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier: Amsterdam, 2008; Vol. 5, Chapter 5.05, pp 315−395. (b) Chiacchio, U.; Romeo, G. In *Modern Heterocyclic Chemistry*, 1st ed.; Alvarez-Builla, J., Vaquero, J. J., Barluenga, J., Eds..; Wiley-VCH Verlag Gmbh & Co. KGaA: Weinheim, Germany, 2011; Chapter 13, pp 1047−1252.

(6) For a recent review, see: Sheremetev, A. B. The chemistry of furazans fused to six- and seven-membered heterocycles with one heteroatom. *Russ. Chem. Rev.* **1999**, *68*, 137.

(7) For the most recent review describing the applications of furazan in material sciences, see: (a) Fershtat, L. L.; Makhova, N. N. 1,2,5-Oxadiazole-Based High-Energy-Density Materials: Synthesis and Performance. *ChemPlusChem* **2020**, *85*, 13. For previous examples, see: (b) He, G. S.; Tan, L.-S.; Zheng, Q.; Prasad, P. N. Multiphoton Absorbing Materials: Molecular Designs, Characterizations, and Applications. *Chem. Rev.* **2008**, *108*, 1245.
(8) For the most recent review describing the applications of furazan in pharmaceutical sciences, see: Mancini, R. S.; Barden, C. J.; Weaver, D. F.; Reed, M. A. Furazans in Medicinal Chemistry. *J. Med. Chem.* **2021**, *64*, 1786.
(9) Rehmann, N.; Ulbricht, C.; Köhnen, A.; Zacharias, P.; Gather, M. C.; Hertel, D.; Holder, E.; Meerholz, K.; Schubert, U. S. Advanced Device Architecture for Highly Efficient Organic Light-Emitting Diodes with an Orange-Emitting Crosslinkable Iridium(III) Complex. *Adv. Mater.* **2008**, *20*, 129.
(10) Chan, L.-H.; Lee, R.-H.; Hsieh, C.-F.; Yeh, H.-C.; Chen, C.-T. Optimization of High-Performance Blue Organic Light-Emitting Diodes Containing Tetraphenylsilane Molecular Glass Materials. *J. Am. Chem. Soc.* **2002**, *124*, 6469.
(11) Lee, Y.-Z.; Chen, X.; Chen, S.-A.; Wei, P.-K.; Fann, W.-S. Soluble Electroluminescent Poly(phenylene vinylene)s with Balanced Electron- and Hole Injections. *J. Am. Chem. Soc.* **2001**, *123*, 2296.
(12) Ramesh, U.; Look, G.; Huang, J.; Singh, R.; Mattis, R. B. Ubiquitin ligase inhibitors. U.S. Patent 0282818A1, 2005.
(13) Kadowaki, M.; Kida, N.; Shiga, Y.; Lu, G. H. Benzothiadiazole derivative and use of said compound. Japanese Patent 2011231245A, 2011.
(14) Mataka, S.; Takahashi, K.; Imura, T.; Tashiro, M. Reduction of 4,7-diphenyl-1,2,5-thia(oxa)diazolo[3,4-*c*]pyridines affording 2,5-diphenyl-3,4-diaminopyridines and ring closure of the diamines to fluorescent azaheterocycles. *J. Heterocycl. Chem.* **1982**, *19*, 1481.
(15) Willer, R. L.; Moore, D. W. Synthesis and chemistry of some furazano- and furoxano[3,4-*b*]piperazines. *J. Org. Chem.* **1985**, *50*, 5123.
(16) Sheremetev, A. B. Chemistry of furazans fused to five-membered rings. *J. Heterocycl. Chem.* **1995**, *32*, 371.
(17) Sheremetev, A. B.; Andrianov, V. G.; Mantseva, E. V.; Shatunova, E. V.; Aleksandrova, N. S.; Yudin, I. L.; Dmitriev, D. E.; Averkiev, B. B.; Antipin, M. Y. Synthesis of secondary and tertiary aminofurazans. *Russ. Chem. Bull.* **2004**, *53*, 596.
(18) Lipilin, D. L.; Smirnov, O. Y.; Churakov, A. M.; Strelenko, Y. A.; Ioffe, S. L.; Tartakovsky, V. A. A New Cyclization Involving the Diazonium and ortho-(*tert*-Butyl)-NNO-azoxy Groups − Synthesis of 1,2,3,4-Benzotetrazine 1-Oxides. *Eur. J. Org. Chem.* **2002**, *2002*, 3435.
(19) Takakis, I. M.; Hadjimihalakis, P. M. Preparation of benzofuroxans and benzofurazans of 2,3,4,5-tetrahydrobenzo[*b*][1,4]dioxocin and related compounds. *J. Heterocycl. Chem.* **1990**, *27*, 177.
(20) Takakis, I. M.; Hadjimihalakis, P. M. Unexpected chlorination products as a result of self-diazotization of three amino-dinitro-2,3,4,5-tetrahydrobenzo[*b*][1,4]dioxocin Derivatives. *J. Heterocycl. Chem.* **1991**, *28*, 1657.
(21) Chen, F.; Huang, X.; Li, X.; Shen, T.; Zou, M.; Jiao, N. Dehydrogenative N-Incorporation: A Direct Approach to Quinoxaline N-Oxides under Mild Conditions. *Angew. Chem., Int. Ed.* **2014**, *53*, 10495.
(22) For a recent example showing the application of *in situ*-generated aryl ketimines for tandem reaction, see: Wu, J.; Zhou, Y.; Wu, T.; Zhou, Y.; Chiang, C.-W.; Lei, A. From Ketones, Amines, and Carbon Monoxide to 4-Quinolones: Palladium-Catalyzed Oxidative Carbonylation. *Org. Lett.* **2017**, *19*, 6432.
(23) For the most recent review describing TBN as a multitasking reagent, see: Dahiya, A.; Sahoo, A. K.; Alam, T.; Patel, B. K. *tert*-Butyl Nitrite (TBN), a Multitasking Reagent in Organic Synthesis. *Chem. - Asian J.* **2019**, *14*, 4454.
(24) For the most recent review concerning the TBN as a versatile reagent in organic synthesis, see: Li, P.; Jia, X. *tert*-Butyl Nitrite (TBN) as a Versatile Reagent in Organic Synthesis. *Synthesis* **2018**, *50*, 711.
(25) Deng, G.-B.; Zhang, J.-L.; Liu, Y.-Y.; Liu, B.; Yang, X.-H.; Li, J.-H. Metal-free nitrative cyclization of *N*-aryl imines with *tert*-butyl nitrite: dehydrogenative access to 3-nitroindoles. *Chem. Commun.* **2015**, *51*, 1886.
(26) Zhao, Q.; Fu, W. C.; Kwong, F. Y. Palladium-Catalyzed Regioselective Aromatic Extension of Internal Alkynes through a Norbornene-Controlled Reaction Sequence. *Angew. Chem., Int. Ed.* **2018**, *57*, 3381.
(27) Li, M.; Kwong, F. Y. Cobalt-Catalyzed Tandem C−H Activation/C−C Cleavage/C−H Cyclization of Aromatic Amides with Alkylidenecyclopropanes. *Angew. Chem., Int. Ed.* **2018**, *57*, 6512.
(28) Fu, W. C.; Kwong, F. Y. A denitrogenative palladium-catalyzed cascade for regioselective synthesis of fluorenes. *Chem. Sci.* **2020**, *11*, 1411.
(29) He, X.; Li, R.; Choy, P. Y.; Liu, T.; Wang, J.; Yuen, O. Y.; Leung, M. P.; Shang, Y.; Kwong, F. Y. DMAP-Catalyzed Annulation Approach for Modular Assembly of Furan-Fused Chromenes. *Org. Lett.* **2020**, *22*, 9444.
(30) DFT calculation: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, rev. D.01; Gaussian, Inc.: Wallingford, CT, 2013.
(31) For recent selected references describing the radical intermediate generation from TBN, see: (a) Liu, Y.; Zhang, J.-L.; Song, R.-J.; Qian, P.-C.; Li, J.-H. Cascade Nitration/Cyclization of 1,7-Enynes with *t*BuONO and H_2O: One-Pot Self-Assembly of Pyrrolo[4,3,2-de]quinolinones. *Angew. Chem., Int. Ed.* **2014**, *53*, 9017. (b) Shen, T.; Yuan, Y.; Jiao, N. Metal-free nitro-carbocyclization of activated alkenes: a direct approach to synthesize oxindoles by cascade C−N and C−C bond formation. *Chem. Commun.* **2014**, *50*, 554. (c) Yang, X.-H.; Song, R.-J.; Li, J.-H. Metal-Free [4 + 2] Annulation of Arylalkynes with *tert*-Butyl Nitrite through C(sp^2)-H Oxidation to Assemble Benzo[*e*][1,2]oxazin-4-ones. *Adv. Synth. Catal.* **2015**, *357*, 3849. (d) Chen, R.; Zhao, Y.; Fang, S.; Long, W.; Sun, H.; Wan, X. Coupling Reaction of Cu-Based Carbene and Nitroso Radical: A Tandem Reaction To Construct Isoxazolines. *Org. Lett.* **2017**, *19*, 5896.
(32) For a literature example showing the methylene radical generation assisted by TBN radical derivatives, see: Shu, Z.; Ye, Y.; Deng, Y.; Zhang, Y.; Wang, J. Palladium(II)-Catalyzed Direct Conversion of Methyl Arenes into Aromatic Nitriles. *Angew. Chem., Int. Ed.* **2013**, *52*, 10573.
(33) For a literature example showing the possible *6-exo-dig* cyclization using TBN derivatives, see: Yang, J.; Liu, Y.-Y.; Song, R.-J.; Peng, Z.-H.; Li, J.-H. Copper-Mediated 1,2-Difunctionalization of Styrenes with Sodium Arylsulfinates and *tert*-Butyl Nitrite: Facile Access to α-Sulfonylethanone Oximes. *Adv. Synth. Catal.* **2016**, *358*, 2286.

https://doi.org/10.1021/acs.orglett.1c02326
Org. Lett. 2021, 23, 6520−6524