CL-190150 Received: February 25, 2019 | Accepted: March 26, 2019 | Web Released: June 22, 2019

# Preparation of Tetrazole-fused π-Conjugated Molecules and Their Fluorescence Behavior

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New tetrazole-fused π-conjugated molecules were prepared from dibromobenzonitriles by repeated regioselective Sonogashira-Hagihara cross-coupling with acetylenes and intramolecular nucleophilic cyclizations. The conjugated tetracyclic compounds exhibited fluorescence with lifetimes of nanosecond order. From TD-DFT calculations, excited state wavefunctions of compounds indicated that the $\text{HOMO}-1 \rightarrow \text{LUMO}$ and $\text{HOMO} \rightarrow \text{LUMO}+1$ mainly became the first excited state ($S_0 \rightarrow S_1$) to contribute significantly to light emission.

**Keywords:** Tetrazole | π-Conjugated molecule | Fluorescence

Tetrazole is composed of four consecutive nitrogens and one carbon[1] and frequently used as one of the useful heterocycles in the field of medicine (Figure 1, A), because the acidity of tetrazole is similar to carboxylic acid but its lipophilicity is more pronounced, so that the introduction of tetrazole could improve the characteristics of potential pharmaceutical agents.[2,3] Tetrazoles display the chemical property of decomposition with release of nitrogen gas by heat, impact, or UV irradiation. For example, while 5-aminotetrazole is utilized as an explosive for airbags of cars (Figure 1, B),[4] tetrazole derivatives have been extensively studied in the field of molecular probes by UV irradiation, the so-called photoclick reaction (Figure 1, C).[5] Conjugated molecules containing tetrazole and linked with unsaturated bonds such as acetylenes have been also reported as organic electronics molecules as shown in Figure 1, D.[6]

On the other hand, hetero π-conjugated molecules **2**, which are the modification of π-conjugated molecules **1** by incorporating several heteroatoms, are widely used in the field of organic electronics due to physical properties such as fluorescence and specific redox responses.[7] However, as far as we know, compounds **3**, where electron-deficient tetrazole is incorporated directly into a π-conjugated skeleton, has rarely been reported so far and its physical properties should be interesting (Scheme 1).[8] Thus, we herein report the synthesis of tetrazole-fused π-conjugated compounds by using regioselective Sonogashira-Hagihara cross-coupling followed by intramolecular nucleophilic cyclization and their optical properties including photoluminescence spectra.

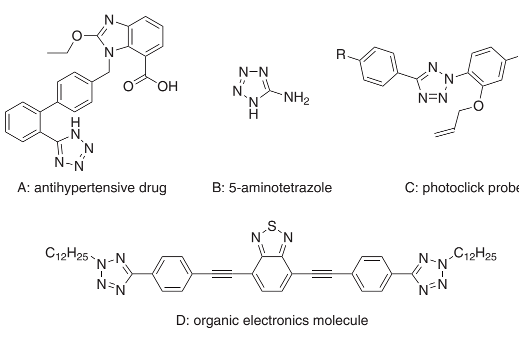
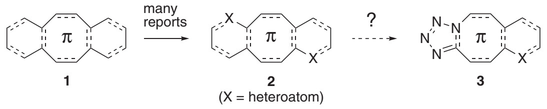


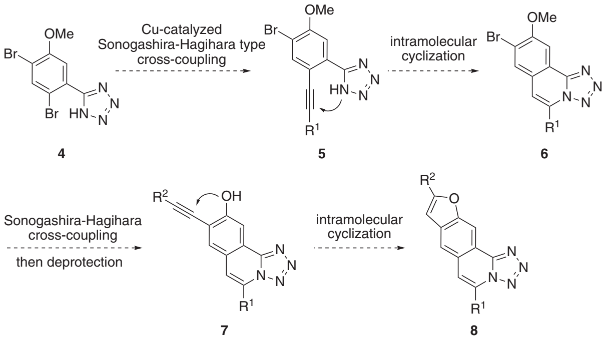
**Figure 1.** Tetrazoles Contained in Useful Compounds.

We aimed at preparing D-π-A-type molecules[9] and planned to make a tetrazole-fused π-conjugated compound where the isoquinoline ring became the central π skeleton and π-electron deficient tetrazole ring[10] and also π-electron rich furan ring[11,12] were fused to isoquinoline ring. The target molecules **8** were prepared from dibromoaryltetrazole **4** via regioselective Sonogashira-Hagihara cross-coupling to acetylenes **5** and intramolecular nucleophilic cyclizations to **7**, as shown in Scheme 2.

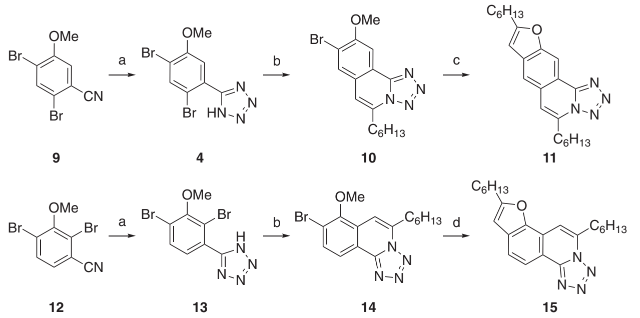
In greater detail, dibromoaryltetrazole **4** was derived from dibromobenzonitrile **9**[13] and $Bu_3SnN_3$ in good yield even in the presence of the other functional groups (Scheme 3). Subsequently, the copper-catalyzed regioselective Sonogashira-Hagihara cross-coupling with 1-octyne, followed by spontaneous intramolecular cyclization, proceeded to afford the corresponding tetrazole-fused tricyclic product **10** as a single isomer.[10f] Finally, the second Sonogashira-Hagihara cross-coupling reaction took place at the remaining bromo group of **10**, followed by demethylation and cyclization in the presence of $BBr_3$, to give desired tetracyclic product **11** in a good yield. Tetrazole **13**,



**Scheme 1.** Incorporation of Tetrazole in π-Conjugated Compounds.



**Scheme 2.** Synthetic Plan of Tetrazole- and Furan-fused π-Conjugated Compounds.



**Scheme 3.** Syntheses of Tetrazole- and Furan-fused π-Conjugated Compounds **11** and **15**. Reagents and conditions: (a) $Bu_3SnN_3$ (3 equiv), xylene, 150 °C, 12 h; (b) 1-octyne (4 equiv), CuI (20 mol %), $K_2CO_3$ (4 equiv), DMSO, 100 °C, 24 h; (c) 1-octyne (4 equiv), $Pd(PPh_3)_2Cl_2$ (1 mol %), $PPh_3$ (2 mol %), CuI (2 mol %), $Et_3N$, 80 °C, 15 h, then $BBr_3$ (3 equiv), $CH_2Cl_2$, −78 °C to rt, 12 h; (d) 1-octyne (4 equiv), $Pd(PPh_3)_2Cl_2$ (1 mol %), $PPh_3$ (2 mol %), CuI (2 mol %), $Et_3N$, 80 °C, 15 h.

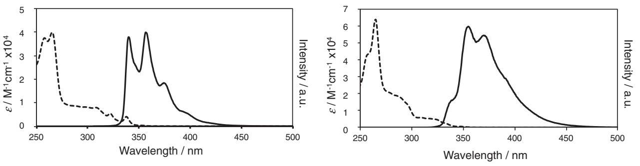


**Figure 2.** UV-Vis Absorption (Dashed Line) and PL Spectra (Solid Line) of Compound **11** (Left: 3.51 × $10^{-5}$ M) and **15** (Right: 2.11 × $10^{-5}$ M) in Dichloromethane ($\lambda_{ex}$ = 280 nm).

prepared from benzonitrile **12**[13] by an analogous treatment with $Bu_3SnN_3$, regioselectively reacted with 1-octyne at the sterically more hindered bromo group to afford tricyclic compound **14**. During Sonogashira-Hagihara cross-coupling reaction with **14** and 1-octyne, the similar demethylation and intramolecular cyclization simultaneously progressed to afford the corresponding tetracyclic molecule **15**. These compounds were characterized by $^1H$ and $^{13}C$ NMR spectroscopy, IR, and ESI mass spectroscopy.[14]

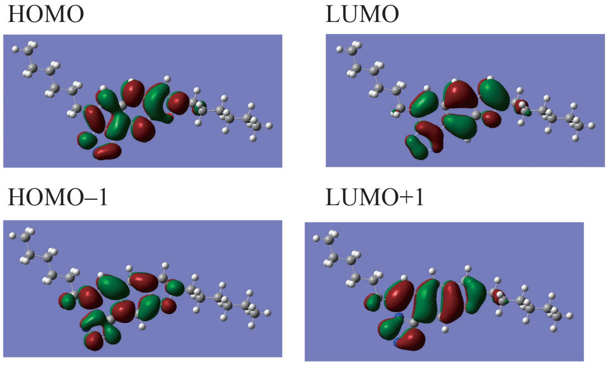
Figure 2 shows the photoluminescence (PL) spectra of compounds **11** and **15** in dichloromethane. The fluorescence bands at high energy of compounds **11** and **15** appeared at 340.0 and 354.2 nm, respectively. Fluorescence quantum yields ($\Phi_f$) were $\Phi_f = 0.26$ and 0.18 for **11** and **15**, respectively, with an absolute PL quantum yield measurement system (see Experimental Section for details). To study the origin of the PL emissions, the fluorescence lifetimes for compounds **11** and **15** were also measured in dichloromethane. It was revealed that these compounds have each PL component, which decays as a single luminescent component with lifetimes of nanosecond order (**11**: 5.1 ns, **15**: 7.2 ns, and $\lambda_{ex} = 280$ nm).

Intriguingly, each radiative rate constant (**11**: 5.10 × $10^7$ $s^{-1}$, **15**: 2.50 × $10^7$ $s^{-1}$) and oscillator strength (**11**: 1.45 × $10^8$ $s^{-1}$, **15**: 1.14 × $10^8$ $s^{-1}$) was calculated from the above fluorescence quantum yields and fluorescence lifetimes, and the number of compound **11** was larger than that of compound **15**.

To elucidate the origin of the observed fluorescence, TD-DFT calculations were performed for **11** and **15** at the CAM-B3LYP/6-31G* level using Gaussian09.[15] The highest occupied molecular orbitals (HOMOs) and lowest unoccupied molecular orbitals (LUMOs) of **11** and **15** are representatively shown in Figure 3 with the excited wavefunctions (The calculated HOMO–LUMO levels, **11**: HOMO −6.07 eV, LUMO −1.47 eV, **15**: HOMO −6.10 eV, LUMO −1.36 eV).

(a) Compound **11**

$$\Psi_1 = 0.57\phi_{\mathrm{HOMO-1\to LUMO}} - 0.35\phi_{\mathrm{HOMO\to LUMO+1}}$$
$$\Psi_2 = 0.62\phi_{\mathrm{HOMO\to LUMO}} + 0.29\phi_{\mathrm{HOMO-1\to LUMO+1}}$$



(b) Compound **15**

$$\Psi_1 = 0.47\phi_{\mathrm{HOMO-1\to LUMO}} - 0.42\phi_{\mathrm{HOMO\to LUMO+1}} - 0.20\phi_{\mathrm{HOMO\to LUMO}} - 0.18\phi_{\mathrm{HOMO-1\to LUMO+1}}$$
$$\Psi_2 = 0.54\phi_{\mathrm{HOMO\to LUMO}} + 0.34\phi_{\mathrm{HOMO-1\to LUMO+1}} + 0.19\phi_{\mathrm{HOMO-1\to LUMO}} - 0.18\phi_{\mathrm{HOMO\to LUMO+1}}$$

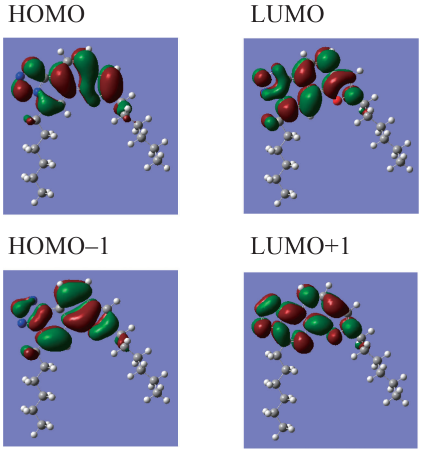


**Figure 3.** Grand State Wavefunctions of Compound **11** (a) and **15** (b) and Their Contributed MOs.

The HOMO and LUMO are localized mainly on the central isoquinoline moiety of **11** and **15**, while in the HOMOs, the lone pairs on the oxygen or nitrogen atoms play a pivotal role in π-system expansion; in the LUMOs, the antibonding orbitals of the central isoquinoline ring serve to promote the expansion of the π-system. Excited state wavefunctions of **11** and **15** indicated that the HOMO−1 → LUMO and HOMO → LUMO+1 mainly contributed to the first excited state ($S_0 \to S_1$) that greatly provides the light emission and the HOMO → LUMO became the second excited state ($S_0 \to S_2$). Since compound **15** exhibits a similarity in the calculated results, it means that the luminescence of the skeleton shown in Figure 3 will be enhanced by the transition dipole moment along a long axis localized on π-electronic systems (Figure 3). The simulated absorption spectrum, comprising a linear combination of oscillator strengths obtained via TD-DFT calculations, shows good agreement with the excitation profiles (see Supporting Information, Table S1). Additionally, TD-DFT calculations also showed that the transition moment of compound **11** differs from that of compound **15** at the first excited state (see Supporting Information). This means that positions of heteroarenes like tetrazole and furan rings changed total transition moment of the molecules to effect radiative rate constants and oscillator strengths.

In summary, we synthesized new structures, hetero-π-conjugated compounds fused with tetrazole and furan rings, by using repeated regioselective Sonogashira-Hagihara cross-coupling of acetylenes and dibromoaryltetrazoles and intramolecular nucleophilic cyclizations. Each tetracycle has PL component, which decays through one relaxation pathway with lifetimes of nanosecond order, respectively. TD-DFT calculations shows that the HOMOs and LUMOs are located mainly in the central isoquinoline parts of each molecule. Thus, the tetrazole-fused polycyclic compounds had delocalized and rigid π-conjugated systems with fluorescence independent of the positions of heterocycles. Further investigations on the optical properties of the new structures and their application to organic materials are underway.

This work was supported in part by JSPS KAKENHI Grant Numbers 26410112, 17H06347, and 17K05855, the PRESTO Program on Molecular Technology and FRONTIER (A.I.) from the Japan Science Technology Agency (JST) Grant Numbers JPMJPR14KC and JPMJPR17P2, Tonen General Sekiyu Research Foundation, The Asahi Glass Foundation, Foundation for Interaction in Science & Technology, The Iwatani Naoji Foundation, Tokuyama Science Foundation, and Research Foundation for Electrotechnology of Chubu. We are also grateful to Prof. Dr. Shohei Saito (Kyoto University) for TD-DFT calculations and helpful discussions.

Supporting Information is available on https://doi.org/10.1246/cl.190150.

## References and Notes

1 Reviews: a) R. R. Gupta, M. Kumar, V. Gupta, *Heterocyclic Chemistry II, Five-Membered Heterocycles*, Springer-Verlag Berlin and Heidelberg GmbH & Co. KG, Berlin, **1999**, pp. 513–525. b) V. A. Ostrovskii, G. I. Koldobskii, R. E. Trifonov, *Comprehensive Heterocyclic Chemistry III*, Elsevier, **2008**, Vol. 6, pp. 257–423. doi:10.1016/B978-008044992-0.00517-4. c) A. Sarvary, A. Maleki, *Mol. Diversity* **2015**, *19*, 189. d) V. A. Ostrovskii, E. A. Popova, R. E. Trifonov, in *Advances in Hetrocyclic Chemistry*, ed. by E. Scrive, C. Ramsden, Academic Press, San Diego, **2017**, Vol. 123, pp. 1–62. doi:10.1016/bs.aihch.2016.12.003.

2 Reviews: a) R. J. Herr, *Bioorg. Med. Chem.* **2002**, *10*, 3379. b) C.-X. Wei, M. Bian, G.-H. Gong, *Molecules* **2015**, *20*, 5528.

3 a) D. J. Carini, J. V. Duncia, P. E. Aldrich, A. T. Chiu, A. L. Johnson, M. E. Pierce, W. A. Price, J. B. Santella, III, G. J. Wells, R. R. Wexler, P. C. Wong, S.-E. Yoo, P. B. M. W. M. Timmermans, *J. Med. Chem.* **1991**, *34*, 2525. b) K. Kubo, Y. Kohara, E. Imamiya, Y. Sugiura, Y. Inada, Y. Furukawa, K. Nishikawa, T. Naka, *J. Med. Chem.* **1993**, *36*, 2182. c) K. Kubo, Y. Kohara, Y. Yoshimura, Y. Inada, Y. Shibouta, Y. Furukawa, T. Kato, K. Nishikawa, T. Naka, *J. Med. Chem.* **1993**, *36*, 2343.

4 a) S. V. Levchik, O. A. Ivashkevich, A. I. Balabanovich, A. I. Lesnikovich, P. N. Gaponik, L. Costa, *Thermochim. Acta* **1992**, *207*, 115. b) G. Wu, H. Yuzawa, T. Matsuzawa, M. Arai, M. Tamura, *J. Jpn. Explos. Soc.* **1994**, *55*, 66.

5 a) W. Song, Y. Wang, J. Qu, M. M. Madden, Q. Lin, *Angew. Chem., Int. Ed.* **2008**, *47*, 2832. b) W. Song, Y. Wang, J. Qu, Q. Lin, *J. Am. Chem. Soc.* **2008**, *130*, 9654. c) Z. Yu, L. Y. Ho, Q. Lin, *J. Am. Chem. Soc.* **2011**, *133*, 11912. d) P. An, Z. Yu, Q. Lin, *Chem. Commun.* **2013**, *49*, 9920.

6 J. L. Westrup, L. W. Oenning, M. M. da Sliva Paula, R. da Costa Duarte, F. S. Rodembusch, T. E. A. Frizon, L. da Silva, A. G. Dal-Bó, *Dyes Pigm.* **2016**, *126*, 209.

7 Reviews: a) S. Yamaguchi, C. Xu, T. Okamoto, *Pure Appl. Chem.* **2006**, *78*, 721. b) S. Yamaguchi, A. Wakamiya, *Pure Appl. Chem.* **2006**, *78*, 1413. c) T. Baumgartner, R. Réau, *Chem. Rev.* **2006**, *106*, 4681. d) A. Loudet, K. Burgess, *Chem. Rev.* **2007**, *107*, 4891. e) A. Fukazawa, S. Yamaguchi, *Chem.—Asian J.* **2009**, *4*, 1386. f) Y. Matano, H. Imahori, *Org. Biomol. Chem.* **2009**, *7*, 1258. g) K. Takimiya, S. Shinamura, I. Osaka, E. Miyazaki, *Adv. Mater.* **2011**, *23*, 4347. h) M. E. Cinar, T. Ozturk, *Chem. Rev.* **2015**, *115*, 3036.

8 Though some tetrazole-fuse π-conjugated compounds have been already reported, their physical properties have not been investigated: a) P. A. S. Smith, J. M. Clegg, J. H. Hall, *J. Org. Chem.* **1958**, *23*, 524. b) G. Hajos, A. Messmer, A. Neszmelyi, L. Parkanyi, *J. Org. Chem.* **1984**, *49*, 3199. c) M. A. M. Taha, S. M. El-Badry, *Monatsh. Chem.* **2008**, *139*, 1261. d) R. S. Upadhayaya, P. D. Shinde, A. Y. Sayyed, S. A. Kadam, A. N. Bawane, A. Poddar, O. Plashkevych, A. Földesi, J. Chattopadhyaya, *Org. Biomol. Chem.* **2010**, *8*, 5661. e) M. Rahimizadeh, M. Bakavoli, Z. Gordi, S. M. Seyedi, *J. Iran. Chem. Soc.* **2011**, *8*, 1135. f) P. Borah, P. S. Naidu, P. J. Bhuyan, *Tetrahedron Lett.* **2012**, *53*, 5034. g) S. N. Sirakanyan, A. Geronikaki, D. Spinelli, A. A. Hovakimyan, A. S. Noravyan, *Tetrahedron* **2013**, *69*, 10637.

9 Reviews: a) N. Robertson, *Angew. Chem., Int. Ed.* **2006**, *45*, 2338. b) B. Albinsson, M. P. Eng, K. Pettersson, M. U. Winters, *Phys. Chem. Chem. Phys.* **2007**, *9*, 5847. c) J.-M. Ji, H. Zhou, H. K. Kim, *J. Mater. Chem. A* **2018**, *6*, 14518. d) G. Zhang, J. Zhao, P. C. Y. Chow, K. Jiang, J. Zhang, Z. Zhu, J. Zhang, F. Huang, H. Yan, *Chem. Rev.* **2018**, *118*, 3447.

10 a) M. Kai, A. Noda, H. Noda, S. Goto, *Chem. Pharm. Bull.* **1988**, *36*, 3604. b) S. Donnelly, J. Grimshaw, J. Trocha-Grimshaw, *J. Chem. Soc., Chem. Commun.* **1994**, 2171. c) L. W. Deady, S. M. Devine, *J. Heterocycl. Chem.* **2004**, *41*, 549. d) J. M. Keith, *J. Org. Chem.* **2006**, *71*, 9540. e) C.-W. Tsai, S.-C. Yang, Y.-M. Liu, M.-J. Wu, *Tetrahedron* **2009**, *65*, 8367. f) L. Shi, R. Wang, H. Yang, Y. Jiang, H. Fu, *RSC Adv.* **2013**, *3*, 6278.

11 Reviews: a) U. H. F. Bunz, *Angew. Chem., Int. Ed.* **2010**, *49*, 5037. b) O. Gidron, M. Bendikov, *Angew. Chem., Int. Ed.* **2014**, *53*, 2546. c) H. Tsuji, E. Nakamura, *Acc. Chem. Res.*

**2017**, *50*, 396.

12 Z. Zhao, H. Nie, C. Ge, Y. Cai, Y. Xiong, J. Qi, W. Wu, R. T. K. Kwok, X. Gao, A. Qin, J. W. Y. Lam, B. Z. Tang, *Adv. Sci.* **2017**, *4*, 1700005.

13 For the preparation of dibromobenzonitriles **9** and **12**, see the Supporting Information.

14 For data of characterization, see the Supporting Information.

15 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, D. J. Fox, *Gaussian 09, Revision D.01 and E.01*, Gaussian, Inc., Wallingford, CT, **2013**.