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GENERATION AND REACTIONS OF HETEROAROMATIC ARYNES USING HYPERVALENT IODINE COMPOUNDS

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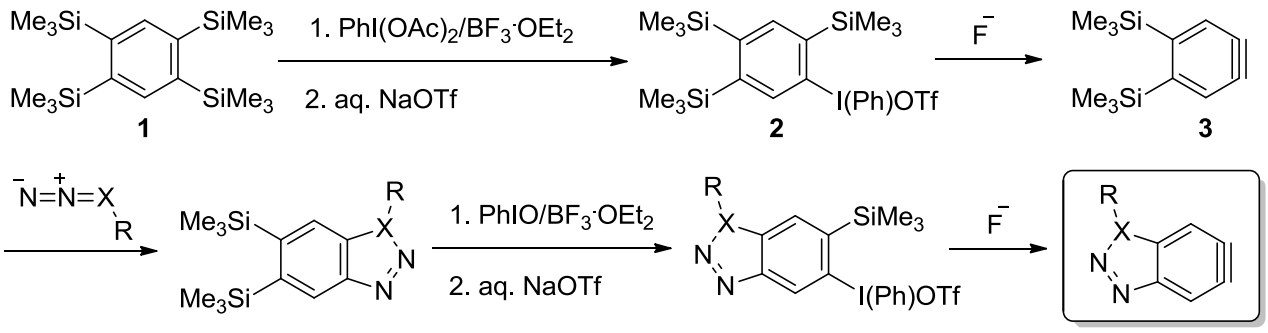
Abstract – The heterocyclic aryne precursors, (phenyl)[1-phenyl-6-(trimethylsilyl)benzotriazol-5-yl]iodonium triflate and [3-ethoxycarbonyl-6-(trimethylsilyl)indazol-5-yl](phenyl)iodonium triflate, were prepared from the cycloadducts of 4,5-bis(trimethylsilyl)benzyne generated from (phenyl)[2,4,5-tris(trimethylsilyl)phenyl]iodonium triflate. These precursors provide the corresponding arynes, 1-phenyl-5,6-didehydrobenzotriazole and 3-ethoxycarbonyl-5,6-didehydroindazole, to give the corresponding polycyclic heteroaromatic compounds in good to high yields.

Heterocyclic aromatic compounds are important compounds which attract much attention as functional materials as well as materials of pharmaceutical and agricultural chemicals. Arynes are suitable reactive intermediates to construct annulated aromatic compounds using cycloaddition reactions.[1] In recent years, the applications of arynes to the synthesis of polycyclic aromatic compounds and the total synthesis of natural products were reviewd.[2] The significance of the aryne strategy is still noted in organic chemistry. However, arynes bearing a heterocyclic skeleton were little reviewed until now, in spite of having recognized the importance in chemistry. Very recently, it was reviewed about the use of heterocyclic arynes in organic synthesis, stating that mild conditions are required for the generation of heterocyclic arynes.[3] We have so far studied on hypervalent iodine benzyne precursors which can generate benzynes under mild conditions.[4] Very recently, we developed an efficient synthesis of (phenyl)[2,4,5-tris(trimethylsilyl)phenyl]iodonium triflate (**2**) from 1,2,4,5-tetrakis(trimethylsilyl)benzene (**1**) using (diacetoxyiodo)benzene [$PhI(OAc)_2$], and found that this iodonium triflate **2** was utilized as an synthetic equivalent of 1,4-benzdiyne.[5]

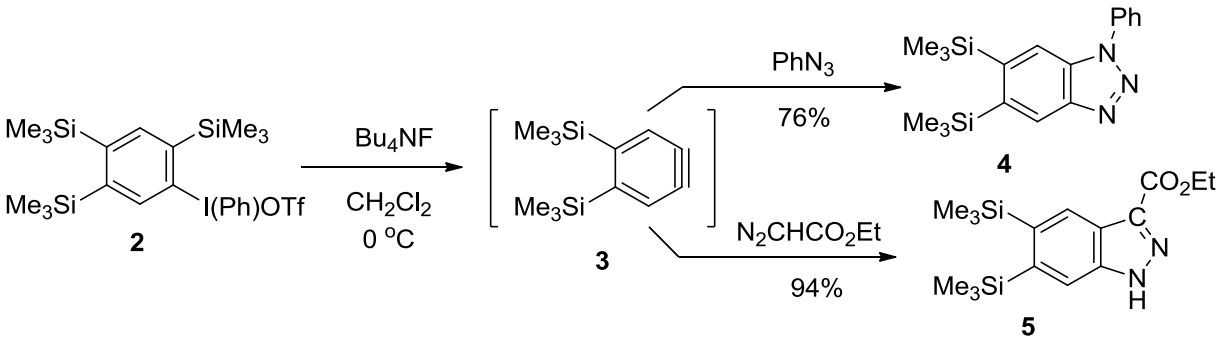
Dedicated with respect to Prof. Dr. Isao Kuwajima on the occasion of his 77th birthday

Thus, as shown in Scheme 1, we expected that the 1,4-benzdiyne strategy was applicable to synthesis of heterocyclic aryne precursors using cycloaddition reactions of aryne **3** with phenylazide or ethyl diazoacetate. In order to confirm the aryne strategy described in Scheme 1, we conducted the synthesis of iodonium triflates having heterocyclic skeletons and the generation of the corresponding heterocyclic arynes. Here we want to report the synthesis and reactions of aryne precursors bearing triazole and indazole skeletons.



Scheme 1

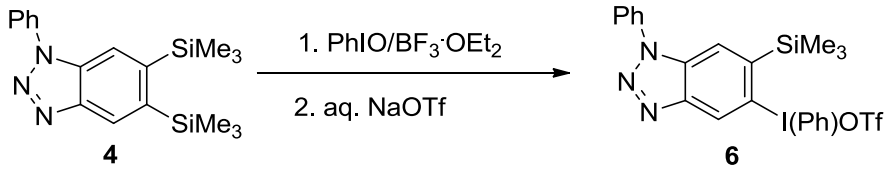
At first, we examined the cycloaddition reaction of 4,5-bis(trimethylsilyl)benzyne (**3**) with phenylazide or ethyl diazoacetate using 2,4,5-tris(trimethylsilyl)phenyliodonium triflate **2**, as shown in Scheme 2. The preparation of iodonium triflate **2** was conducted according to our method reported recently.[5] When iodonium triflate **2** was treated with a THF solution of Bu_4NF in the presence of phenylazide in CH_2Cl_2 at 0 °C, the cycloadduct **4** was obtained in 76% yield. Similarly, the reaction of iodonium triflate **2** with Bu_4NF in the presence of ethyl diazoacetate gave the cycloadduct **5** in 94% yield. These results indicate that 4,5-bis(trimethylsilyl)benzyne (**3**) was generated under mild conditions and efficiently trapped with phenylazide or ethyl diazoacetate. The cycloaddition proceeded without any damage of two trimethylsilyl groups. Then, the disilyl cycloadducts thus obtained were converted to the corresponding aryne precursors.



Scheme 2

The conversion of 1-phenyl-5,6-bis(trimethylsilyl)benzotriazole (**4**) to a didehydrobenzotriazole precursor was conducted using a hypervalent iodine reagent. The results are given in Table 1. The reaction was performed as follows. First, iodosylbenzene was treated with $BF_3{\cdot}OEt_2$ in CH_2Cl_2 to activate it and then reacted with bis(trimethylsilyl)benzotriazole **4**. Although the reaction mixture was treated with aqueous NaOTf to convert to the triflate salt, no desired product was obtained (Entry 1). Next, the similar reaction was conducted in 1,2-dichloroethane at 40 °C. The desired iodonium triflate **6** was obtained in 8% yield (Entry 2), but elevation of the reaction temperature did not improve the result (Entries 3 and 4). When the solvent was replaced by acetonitrile, the yield of iodonium triflate **6** increased (Entry 5) to 51%. However, the reaction with $PhI(OAc)_2$ instead of PhIO resulted in lowering the yield (Entry 6).

Table 1. Synthesis of a Didehydrobenzotriazole Precursor

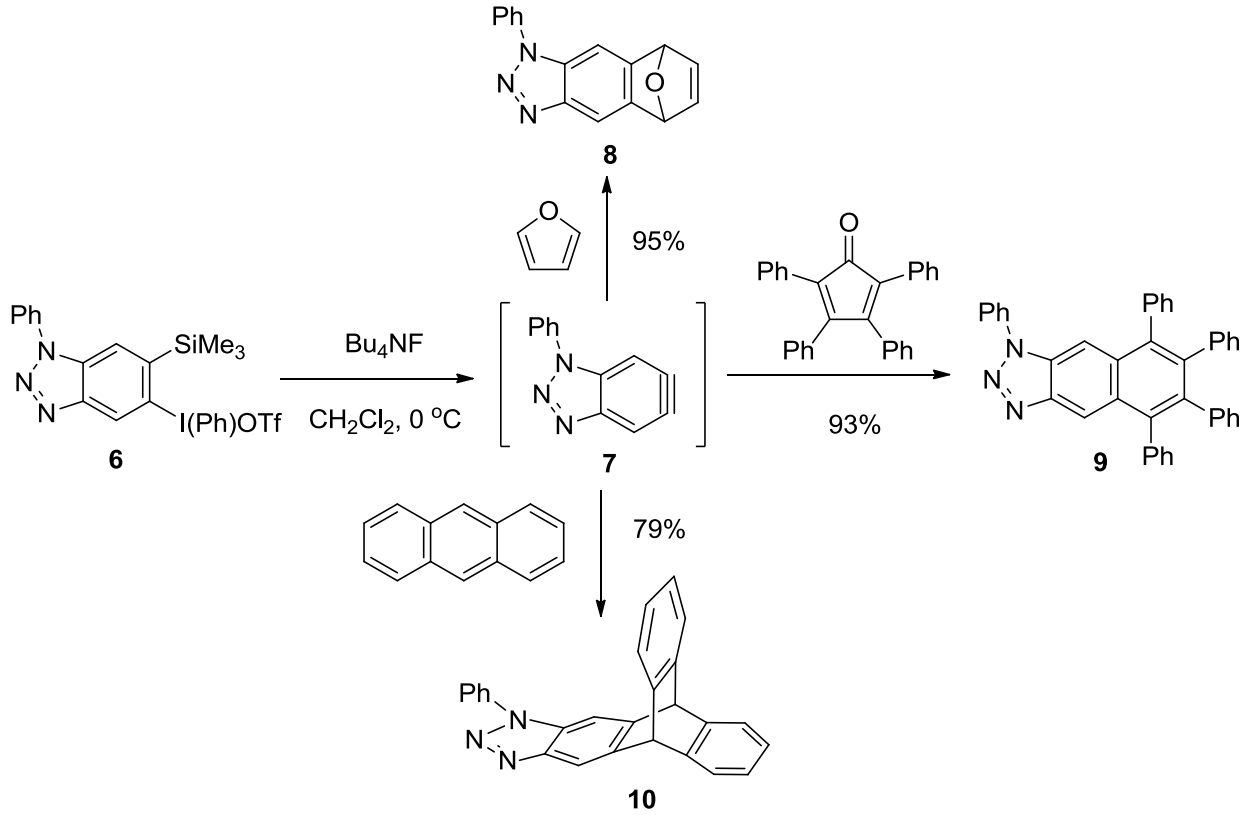


4 **6**

Entry	Substrate (mmol)	PhIO (mmol)	$BF_3{\cdot}OEt_2$ (mmol)	Solvent (mL)	Time (h)	Temp (°C)	Yield (%)[a]
1	0.5	0.6	3.0	DCM (4)	2	0	0
2	0.2	0.24	1.2	DCE (2)	5	40	8
3	0.2	0.24	1.2	DCE (2)	5	60	4
4	0.2	0.24	1.2	DCE (2)	5	80	6
5	2.0	2.4	12	MeCN (20)	4	40	51
6	0.5	0.6[b]	1.2	MeCN (2)	4	40	15

[a] Isolated yield. [b] $PhI(OAc)_2$ was used instead of PhIO.

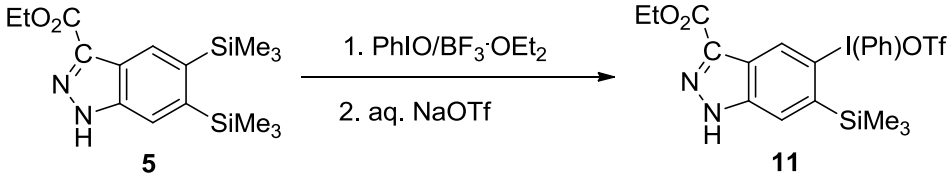
Generation of an aryne from iodonium triflate **6** was conducted by the reaction of **6** with Bu_4NF. When iodonium trifalte **6** was treated with 1.2 equivalents of Bu_4NF in the presence of furan (5 equivalents) in CH_2Cl_2 at 0 °C, the cycloadduct **8** with furan was obtained in 95% isolated yield. In the case of tetraphenylcyclopentadienone as a trapping agent, the reaction of **6** with Bu_4NF gave the cycloadduct **9** in 93% isolated yield, which was derived from the cycloaddition of aryne **7** with teteraphenylcyclopentadienone followed by decarbonylation. In addition, the reaction of **6** with Bu_4NF in the presence of anthracene gave the cycloadduct **10** derived from the cycloaddition of **7** with anthracene, in 79% yield.



Scheme 3

In analogy with the synthesis of didehydrobenzotriazole precursor **6**, the reaction of disilyl-substituted indazole **5** was conducted using PhIO activated with $BF_3{\cdot}OEt_2$ in MeCN and followed by treating with aqueous NaOTf. The desired iodonium triflate **11** was obtained in 91% yield (Table 2, Entry 1). Moreover, the reaction with $PhI(OAc)_2$ activated with $BF_3{\cdot}OEt_2$ also gave the iodonium triflate **11** in 72% yield (Entry 2).

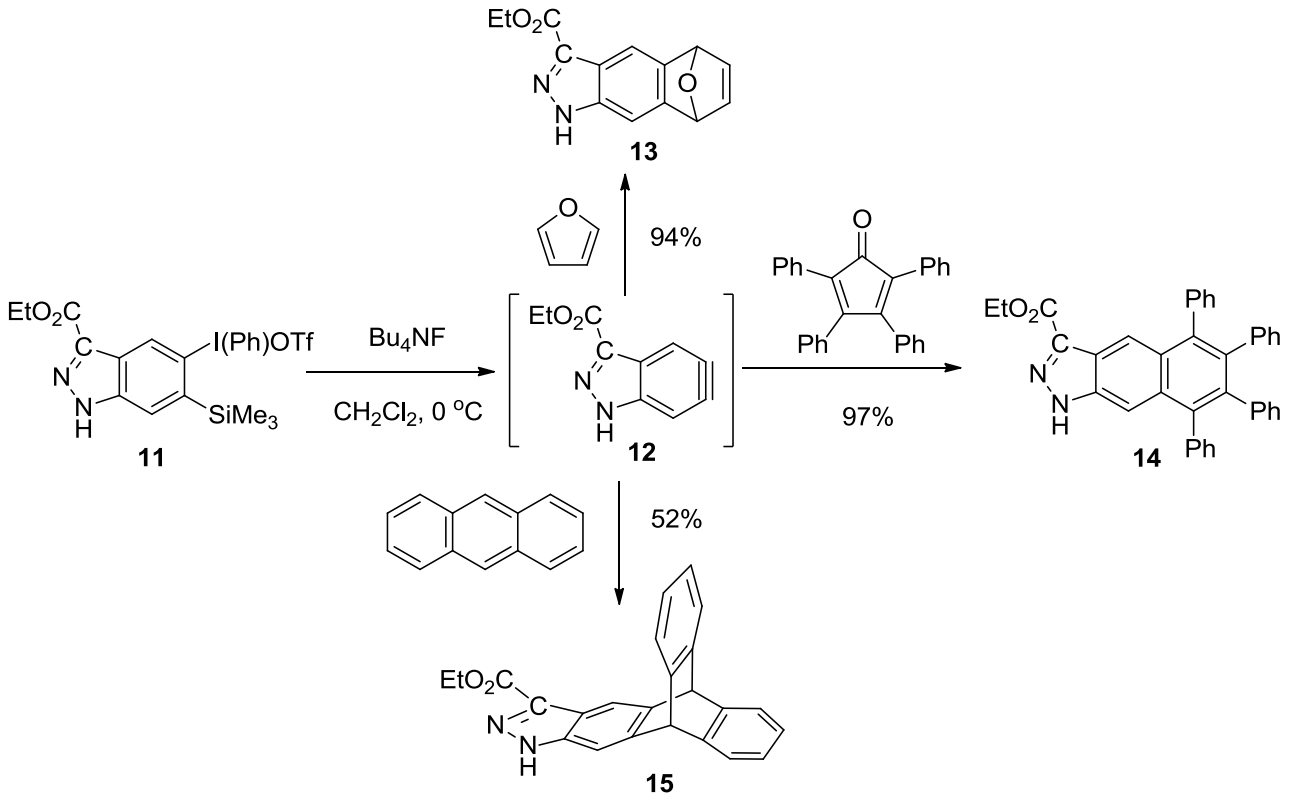
Table 2. Synthesis of a Didehydroindazole Precursor



Entry	**5** (mmol)	PhIO (mmol)	$BF_3{\cdot}OEt_2$ (mmol)	Solvent (mL)	Time (h)	Temp (°C)	Yield (%)[a]
1	1	1.2	6	MeCN (10)	1	40	91
2	0.5	0.6[b]	1.2	CH_2Cl_2 (5)	0.5	rt	72

[a] Isolated yield. [b] $PhI(OAc)_2$ was used instead of PhIO.

When the iodonium triflate **11** was treated with Bu_4NF in the presence of furan in CH_2Cl_2 at 0 °C, the cycloadduct **13** with furan was obtained in 94% isolated yield. This reaction indicates that 3-ethoxycarbonyl-5,6-didehydroindazole (**12**) is generated almost quantitatively under the present reaction conditions. The trapping reaction with tetraphenylcyclopentadienone gave the cycloadduct **14** with **12** in 97% isolated yield. In the case of anthracene as a trapping reagent, tripticene derivative **15** was obtained in 52% isolated yield.



Scheme 4

In summary, we have demonstrated that two new heterocyclic arynes, 1-phenyl-5,6-didehydrobenzotriazole (**7**) and 3-ethoxycarbonyl-5,6-didehydroindazole (**12**), can be generated efficiently from the corresponding iodonium triflates **6** and **11**. The cycloaddition of the heterocyclic arynes **7** and **12** with furan, tetraphenylcyclopentadienone, or anthracene provides the corresponding annulated heterocyclic compounds in good to high yields. These results suggest that the heterocyclic aryne strategy is useful to construct the polycyclic heteroaromatic compounds.

EXPERIMENTAL

All solvents and starting materials were used during the research work as received without further purification unless otherwise indicated. ^1H and ^{13}C NMR were recorded on a Agilent 400-MR NMR

spectrometer (TMS as an internal standard). Melting points were measured with a Yanaco micro melting point apparatus and are uncorrected. High resolution mass spectra were measured by the Analytical Center, Institute for Materials Chemistry and Engineering, Kyushu University. Column chromatographic separation was carried out using Silica Gel 60, spherical (Kanto Chemical Co.). Pre-coated plates (silica gel 60 F_{254}, MERCK) were used for TLC examination.

Preparation of 1-Phenyl-5,6-bis(trimethylsilyl)benzotriazole (4)

To a solution of (phenyl)[tris(trimethylsilyl)phenyl]iodonium triflate (**2**) (1 mmol) and phenylazide (5 mmol) in CH_2Cl_2 (5 mL) was added a THF solution of Bu_4NF (1 mmol) at 0 °C and stirred for 20 min at this temperature. The reaction mixture was poured into water and extracted with CH_2Cl_2 (10 mL × 3). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The product was separated by column chromatography on silica gel (hexane/AcOEt) to give 1-phenyl-5,6-bis(trimethylsilyl)benzotriazole (**4**) (0.258 g, 76%) as white crystals. Mp 116-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.44 (s, 9H), 0.46 (s, 9H), 7.52 (t, *J* = 8 Hz, 1H), 7.64 (t, *J* = 8 Hz, 2H), 7.79 (d, *J* = 8 Hz, 2H), 8.10 (s, 1H), 8.51 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 2.0, 2.1, 117.2, 122.6, 127.5, 128.5, 129.9, 131.7, 137.0, 141.4, 146.2, 146.5. HRMS (EI) calcd for $C_{18}H_{25}N_3Si_2$ (M^+): 339.1587; found: 339.1589.

Preparation of 3-Ethoxycarbonyl-5,6-bis(trimethylsilyl)indazole (5)

The similar reaction of **2** (2 mmol) and ethyl diazoacetate (10 mmol) in CH_2Cl_2 (10 mL) was carried out using a THF solution of Bu_4NF (2 mmol). Workup of the reaction mixture gave 3-ethoxycarbonyl-5,6-bis(trimethylsilyl)indazole (**5**) (0.628 g, 94%) as white crystals. Mp 198-200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.456 (s, 9H), 0.459 (s, 9H), 1.53 (t, *J* = 7 Hz, 2H), 4.58 (q, *J* = 7 Hz, 3H), 8.30 (d, *J* = 7 Hz, 1H), 8.60 (s, 1H), 12.9 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 2.1, 2.2, 14.4, 61.0, 119.8, 121.4, 129.0, 136.0, 139.0, 141.4, 144.3, 163.4. HRMS (EI) calcd for $C_{16}H_{26}N_2O_2Si_2$ (M^+): 334.1533; found: 334.1533.

Preparation of (Phenyl)[1-phenyl-6-(trimethylsilyl)benzotriazol-5-yl]iodonium Triflate (6)

To a mixture of benzotriazole **4** (2 mmol) and PhIO (2.4 mmol) in MeCN (20 mL) was added $BF_3{\cdot}OEt_2$ (12 mmol) and the mixture was stirred at 40 °C for 4 h. The reaction mixture was poured into an aqueous solution of NaOTf (20 mmol) and stirred vigorously. The product was extracted with CH_2Cl_2 (20 mL × 3). The combined organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting solid was filtered and washed with hexane to give (phenyl)[1-phenyl-6-(trimethylsilyl)benzotriazol-5-yl]iodonium triflate (**6**) (0.315 g, 51%) as yellow crystals. Mp 91-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.50 (s, 9H), 7.46-7.89 (m, 10H), 8.04 (s, 1H), 9.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.3, 114.6, 114.7, 120.1, 123.2, 129.7, 130.2, 132.1, 132.3,

133.0, 133.2, 133.7, 135.8, 145.2, 147.9. HRMS (FAB) calcd for $C_{21}H_{21}IN_3Si$ (M^+–OTf): 470.0544; found 470.0549.

Trapping Reactions of a 5,6-Didehydrobenzotriazole (7)

To a solution of iodonium triflate **6** (0.2 mmol) and a dienophile (1 mmol) in CH_2Cl_2 (1 mL) was slowly added a THF solution of Bu_4NF (0.24 mmol). The mixture was stirred at 0 °C for 20 min. The reaction mixture was poured into water and extracted with CH_2Cl_2 (10 mL × 3). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The product was separated by column chromatography on silica gel (hexane/AcOEt).

5,9-Epoxy-5,9-dihydro-1-phenyl-1*H*-naphtho[2,3-*d*]triazole (8)

The product was obtained as white crystals, mp 119-121 °C; yield 0.050 g (95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 (s, 1H), 5.85 (s, 1H), 7.00 (d, *J* = 3 Hz, 1H), 7.07 (d, *J* = 3 Hz, 1H), 7.52-7.54 (m, 2H), 7.61 (t, *J* = 8 Hz, 2H), 7.72 (d, *J* = 8 Hz, 2H), 7.84 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.8, 81.9, 103.0, 111.3, 123.2, 128.9, 129.8, 131.4, 136.8, 141.6, 142.9, 144.7, 145.0, 149.2. HRMS (EI) calcd for $C_{16}H_{11}N_3O$ (M^+): 261.0902; found: 261.0907.

1,5,6,7,8-Pentaphenyl-1*H*-naphtho[2,3-*d*]triazole (9)

The product was obtained as yellow crystals, mp 232-233 °C; yield 0.102 g (93%). The spectra were in accord with the reported ones.[5b]

5,10[1',2']-Benzeno-1-phenyl-1*H*-anthra[2,3-*d*]triazole (10)

The product was obtained as yellow crystals, mp 197-199 °C; yield 0.059 g (79%). The spectra were in accord with the reported ones.[5b]

Preparation of [3-Ethoxycarbonyl-6-(trimethylsilyl)indazol-5-yl](phenyl)iodonium Triflate (11)

To a mixture of indazole **5** (1 mmol) and PhIO (1.2 mmol) in MeCN (10 mL) was added BF_3·OEt_2 (6 mmol) and the mixture was stirred at 40 °C for 1 h. The reaction mixture was poured into an aqueous solution of NaOTf (10 mmol) and stirred vigorously. The product was extracted with CH_2Cl_2 (10 mL × 3). The combined organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting solid was filtered and washed with hexane to give [3-ethoxycarbonyl-6-(trimethylsilyl)indazol-5-yl](phenyl)iodonium triflate (**11**) (0.559 g, 91%) as white crystals. Mp 218-220 °C; ^{1}H NMR (400 MHz, CD_3CN) δ 0.43 (s, 9H), 1.42 (t, *J* = 7 Hz, 3H), 4.47 (q, *J* = 7 Hz, 2H), 7.50 (t, *J* = 8 Hz, 2H), 7.64 (t, *J* = 8 Hz, 1H), 7.79 (d, *J* = 8 Hz, 2H), 8.10 (s, 1H), 9.12 (s, 1H), 12.4 (s, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 0.6, 14.9, 62.6, 114.4, 115.1, 123.6, 126.2, 133.6, 133.7, 134.1, 136.1, 138.3, 143.0, 143.9, 162.9. HRMS (FAB) calcd for $C_{19}H_{22}IN_2O_2Si$ (M^+–OTf): 465.0495; found: 465.0495.

Trapping Reactions of a Didehydroindazole (12)

To a solution of iodonium triflate **11** (0.2 mmol) and a dienophile (1 mmol) in CH_2Cl_2 (1 mL) was slowly added a THF solution of Bu_4NF (0.24 mmol). The mixture was stirred at 0 °C for 20 min. The reaction mixture was poured into water and extracted with CH_2Cl_2 (10 mL × 3). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The product was separated by column chromatography on silica gel (hexane/AcOEt). In the trapping reaction with anthracene, iodonium triflate **11** (0.1 mmol) was used.

Ethyl 5,8-Epoxy-5,8-dihydro-1*H*-benzo[*f*]indazole-3-carboxylate (13)

The product was obtained as white crystals, mp 173-174 °C; yield 0.048 g (94%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (t, J = 7 Hz, 3H), 4.54 (q, J = 7 Hz, 2H), 5.77 (s, 1H), 5.80 (s, 1H), 6.97-7.04 (m, 2H), 7.58 (s, 1H), 7.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 61.1, 81.88, 81.91, 104.4, 112.5, 120.2, 140.5, 141.6, 142.6, 143.0, 147.8, 163.0 (one carbon overlapped). HRMS (EI) calcd for $C_{14}H_{12}N_2O_3$ (M^+): 256.0848; found: 256.0850.

Ethyl 5,6,7,8-Tetraphenyl-1*H*-benzo[*f*]indazole-3-carboxylate (14)

The product was obtained as white crystals, mp 330-332 °C; yield 0.106 g (97%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J = 7 Hz, 3H), 4.39 (q, J = 7 Hz, 2H), 6.88 (m, 10H), 7.24-7.28 (m, 10H), 7.76 (s, 1H), 8.57 (s, 1H), 10.4 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 61.1, 106.0, 120.7, 122.2, 125.36, 125.41, 126.6, 127.6, 127.7, 129.7, 131.1, 131.3, 131.3, 131.4, 132.3, 137.1, 137.5, 137.7, 139.3, 139.5, 139.6, 139.8, 140.4, 162,6 (5 carbons overlapped). HRMS (FAB) calcd for $C_{38}H_{28}N_2O_2$ (M^+): 544.2151; found: 544.2149.

Ethyl 5,10[1',2']-Benzeno-1*H*-naphtho[2,3-*f*]indazole-3-carboxylate (15)

The product was obtained as yellow crystals, mp 195-197 °C; yield 0.038 g (52%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (t, J = 7 Hz, 3H), 4.51 (q, J = 7 Hz, 2H), 5.47 (s, 1H), 5.53 (s, 1H), 7.00-7.02 (m, 4H), 7.38-7.43 (m, 4H), 7.58 (s, 1H), 8.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 53.8, 54.2, 61.0, 105.9, 115.8, 120.3, 123.7, 123.7, 125.5, 125.7, 136.2, 139.8, 140.7, 144.2, 144.8, 144.9, 162.9. HRMS (EI) calcd for $C_{24}H_{18}N_2O_2$ (M^+): 366.1368; found: 366.1366.

REFERENCES

1. (a) M. Winkler, H. H. Wenk, and W. Sander, 'Reactive Intermediate Chemistry', ed. by R. A. Moss, M. S. Platz, and M. J. Jones, John Wiley & Sons: Hoboken, 2004, pp. 741-794; (b) H. H. Wenk, M. Winkler, and W. Sander, *Angew. Chem. Int. Ed.*, 2003, **42**, 502; (c) H. Pellissier and M. Santelli, *Tetrahedron*, 2003, **59**, 701; (d) H. Hart, 'The Chemistry of Triple-bonded Functional Groups, Supplement C2' ed. by S. Patai, John Wiley and Sons: Chichester, 1994, Chapt. 18, pp. 1017-1134; (e) S. V. Kessar, 'Comprehensive Organic Synthesis', ed. by B. M. Trost and I. Fleming, Pergamon

Press: New York, 1991, Vol. 4, pp. 483-515; (f) T. L. Gilchrist, 'The Chemistry of Triple-bonded Functional Groups, Supplement C', ed. by S. Patai and Z. Rappoport, John Wiley and Sons: Chichester, 1983, Chapt. 11, pp. 383-419; (g) R. W. Hoffmann, 'Chemistry of Acetylenes', ed. by H. G. Viehe, Dekker: New York, 1969, pp. 1063-1148; (h) R. W. Hoffmann, 'Dehydrobenzene and Cycloalkynes', Academic Press: New York, 1967; (i) T. Kitamura, *Aus. J. Chem*., 2010, **63**, 987.

2. (a) C. M. Gampe and E. M. Carreira, *Angew. Chem. Int. Ed*., 2012, **51**, 3766; (b) A. Bhunia, S. R. Yetra, and A. T. Biju, *Chem. Soc. Rev*., 2012, **41**, 3140; (c) P. M. Tadross and B. M. Stoltz, *Chem. Rev*., 2012, **112**, 3550; (d) H. Yoshida and K. Takaki, *Synlett,* 2012, **23**, 1725; (e) D. Pérez, D. Peña, and E. Guitián, *Eur. J. Org. Chem*., 2013, 5981.
3. A. E. Goetz and N. K. Garg, *J. Org. Chem*., 2014, **79**, 846.
4. (a) T. Kitamura, M. Todaka, and Y. Fujiwara, *Org. Synth*., 2002, **78**, 104; (b) T. Kitamura, M. Yamane, K. Inoue, M. Todaka, N. Fukatsu, Z. Meng, and Y. Fujiwara, *J. Am. Chem. Soc.*, 1999, **121**, 11674; (c) T. Kitamura and M. Yamane, *J. Chem. Soc., Chem. Commun*., 1995, 983.
5. (a) T. Kitamura, K. Gondo, and T. Katagiri, *J. Org. Chem.*, 2013, **78**, 3421; (b) K. Gondo and T. Kitamura, *Adv. Synth. Catal*., 2014, **356**, 2017.