FACILE AND EFFICIENT SYNTHESIS OF INDAZOLE DERIVATIVES BY 1,3-CYCLOADDITION OF ARYNES WITH DIAZO COMPOUNDS AND AZOMETHINE IMIDES

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Dedicated to Dr. Alfred Bader on the occasion of his 85th birthday in recognition of his outstanding contributions to the science of chemistry.

N-Unsubstituted indazoles **3** and 1-arylindazoles **4** are readily available in good to high yields through [3+2] cycloaddition of 2-(trimethylsilyl)aryl triflates **1** and diazo compounds in the presence of KF or CsF under mild reaction conditions. Furthermore, we found that azomethine imides also underwent cycloaddition reaction with 2-(trimethylsilyl)phenyl triflates (**1a**) in the presence of KF to afford indazolone derivatives **6** in moderate yields.
Keywords: [3+2] Cycloaddition; 1,3-Dipolar cycloaddition; Arynes; Diazo compounds; Azomethine imides; Indazoles.

1*H*-Indazoles are an important class of heterocycles that display a wide range of pharmacological activities, including antifertility, antiarthritic, anti-inflammatory, and contraceptive activity, as well as antagonistic activity to the 5-HT_3 receptor[1]. Owing to their potential usefulness, considerable effort has been devoted to the development of efficient methods for the construction of indazole skeletons (Scheme 1)[2]. The common preparation routes are diazotization of the corresponding 2-alkylanilines[2a] and nitrosation of the *N*-acetyl derivatives of 2-alkylanilines (Jacobson modification)[2b–2d]. Another attractive route is the condensation of 2-substituted benzaldehydes with hydrazine[2e,2f]. However, the reaction conditions of these methods are fairly harsh, usually strong acids or high temperatures are needed. An interesting method is the 1,3-dipolar cycloaddition of benzyne (generated from diazotized anthranilic acid) with diazoalkanes[3] and azomethine imines[4]. For example, α-diazoketones react with benzyne to give 3-acyl-3*H*-indazoles, which further isomerize to 2-acyl-2*H*-indazoles

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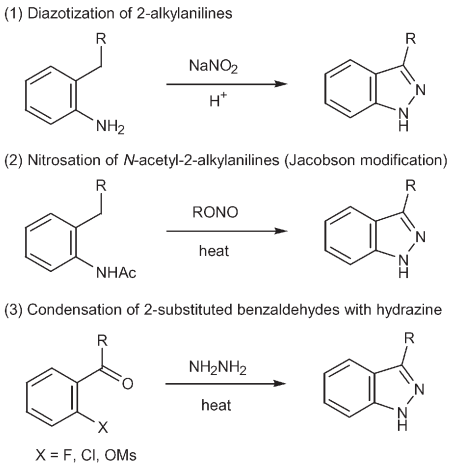
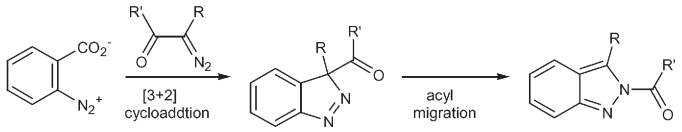
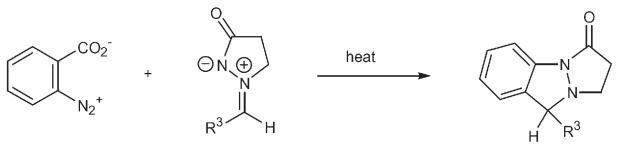


SCHEME 1
General methods for the synthesis of 1*H*-indazoles

(Eq. (*1*))[3c–3e]. In addition, azomethine imines also reported to undergo cycloaddition reaction with benzyne precursor, benzene-1-diazonium-2-carboxylate, to afford indazolone derivatives (Eq. (*2*))[4b]. However, these cycloaddition approaches often employed explosive and hazardous benzyne precursors, and necessarily have not wide scope. Therefore, the development of an efficient and general synthetic method to indazole derivatives is much desirable.



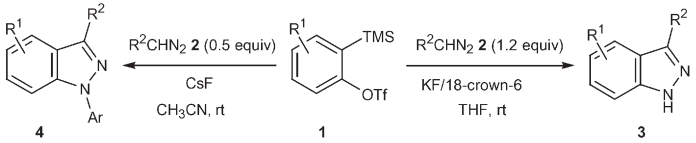
(*1*)



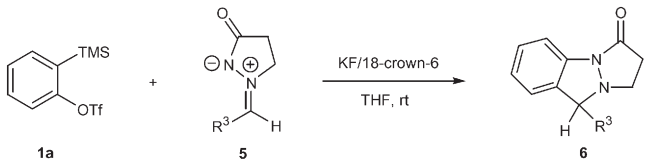
(*2*)

It is well known that benzyne is generated in situ from 2-(trimethylsilyl)phenyl triflate (**1a**) under very mild reaction conditions[5]. Accordingly, a variety of synthetic methods using **1a** (via a benzyne intermediate) have been investigated, including cycloadditions[6], and nucleophilic addition re-

actions[7]. Recently, we have developed catalytic, general synthetic protocols for useful nitrogen-containing heterocycles, such as tetrazoles and 1,2,3-triazoles, through the [3+2] cycloadditions of alkynes, nitriles, and isonitriles with trimethylsilyl azide[8]. In continuation of our interest in the development of efficient methods for the synthesis of useful heterocycles, and in benzyne chemistry[6c–6f], we investigated the cycloaddition of benzyne with diazo compounds and azomethine imides. The [3+2] cycloaddition of arynes, generated from silylaryl triflates **1**, and various diazomethane derivatives **2** proceeded smoothly under very mild conditions, depending merely on the conditions, to give *N*-unsubstituted 1*H*-indazoles **3** or 1-aryl indazoles **4** in good to high yields (Eq. (*3*))[9a]. Furthermore, the cycloaddition of 2-(trimethylsilyl)phenyl triflate (**1a**) with azomethine imides **5** under similar reaction conditions afforded the tricyclic indazolone derivatives **6** in moderate yields (Eq. (*4*)). Herein, we report a detailed investigation of these cycloaddition synthetic methods.



(*3*)



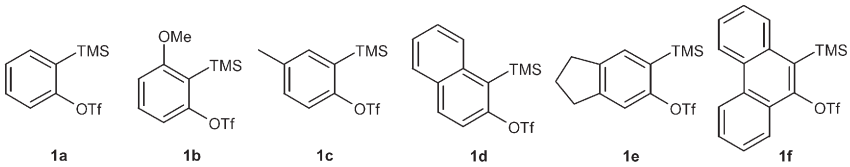
(*4*)

RESULTS AND DISCUSSION

Synthesis of N-Unsubstituted 1H-Indazoles from 2-(Trimethylsilyl)aryl Triflates and Diazomethanes

Initially, in the cycloaddition of commercially available 2-(trimethylsilyl)-phenyl triflate (**1a**) and ethyl diazoacetate (**2a**), we focused on screening the fluoride sources for the formation of *N*-unsubstituted 1*H*-indazole **3a**. Treatment of **1a** with **2a** (1.2 equiv.) in the presence of KF (3.0 equiv.) and 18-crown-6 (3.5 equiv.) in THF at room temperature for 24 h afforded 3-(ethoxycarbonyl)-1*H*-indazole (**3a**)[10a] in 80% yield (Table I, entry 1). Although CsF or Bu_4NF could be used instead of KF to generate benzyne in

situ from **1a**, the yield of **3a** decreased to 63 and 54%, respectively (Table I, entries 2 and 3).



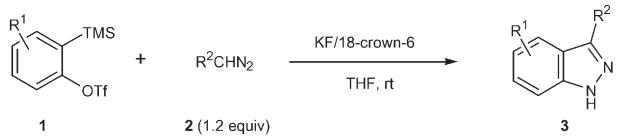
1a **1b** **1c** **1d** **1e** **1f**

With the optimized reaction conditions in hand, this cycloaddition reaction was extended to various diazo compounds **2** and the substituted aryne precursors **1b**–**1f** to explore the regioselectivity of the reaction and to test whether the methodology is general for the synthesis of functionalized 1*H*-indazoles or not[10b]. When the reaction of **1a** with **2b** was carried out under the standard reaction conditions, the corresponding indazole **3b** was obtained in a high yield (Table I, entry 4). Diazo(trimethylsilyl)methane (**2c**) underwent the cycloaddition reaction in the presence of CsF in a mixture of CH_3CN and MeOH to give the 50% yield of 3-unsubstituted indazole **3c** with loss of the TMS group (Table I, entry 5), while no desired product was obtained in the absence of MeOH. The reaction was also applied to diazo(phenyl)methane (**2d**), affording 3-phenyl-1*H*-indazole **3d** in 90% yield (entry 6). It is noteworthy that 3-methoxy-2-(trimethylsilyl)phenyl triflate (**1b**) reacts smoothly with **2a** to afford the corresponding indazole **3e** as a single product in 83% yield without formation of the regioisomer (entry 7). However, in the case of benzyne precursors **1c** and **1d**, the reaction gave a ca. 1:1 mixture of regioisomers (entries 8 and 9). The regioselective formation of **3e** can be explained by the electronic effect of the 3-OMe group on the nucleophilic attack of benzyne, and a favorable steric effect[7e]. The benzyne precursors **1e** and **1f** efficiently underwent the cycloaddition reaction, giving the indane **3h** and phenanthrene derivatives **3i** in 90 and 70% yields, respectively (entries 10 and 11).

Synthesis of 1-aryl-1H-Indazoles from 2-(Trimethylsilyl)aryl Triflates and Diazomethanes

1-Aryl-1*H*-indazoles are frequently found in important pharmaceuticals with biological activities[1]. Recently, some useful methodologies for synthesis of 1-aryindazoles have been developed including the Pd-catalyzed cyclization of arylhydrazones of 2-halobenzaldehydes[11] and Cu-catalyzed

TABLE I
Synthesis of *N*-unsubstituted 1*H*-indazoles **3**[a]



1 **2** (1.2 equiv) **3**

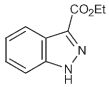
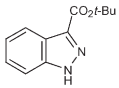
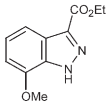
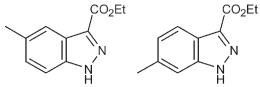
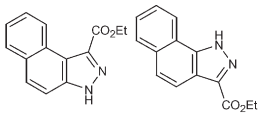
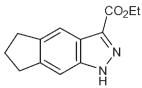
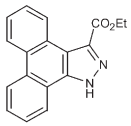
Entry	**1**	**2**	R^2	Product	**3**	Yield, %[b]
1	**1a**	**2a**	CO_2Et		**3a**	80
2[c]	**1a**	**2a**	CO_2Et		**3a**	63
3[d]	**1a**	**2a**	CO_2Et		**3a**	54
4	**1a**	**2b**	CO_2t-Bu		**3b**	89
5[e]	**1a**	**2c**	TMS		**3c**	50
6	**1a**	**2d**	Ph		**3d**	90
7	**1b**	**2a**	CO_2Et		**3e**	83
8[f]	**1c**	**2a**	CO_2Et		**3f** **3f′**	82 (1:1)
9	**1d**	**2a**	CO_2Et		**3g** **3g′**	70 (1:1)
10	**1e**	**2a**	CO_2Et		**3h**	90

TABLE I
(*Continued*)

Entry	1	2	R^2	Product	3	Yield, %[b]
11	**1f**	**2a**	CO_2Et		**3i**	70

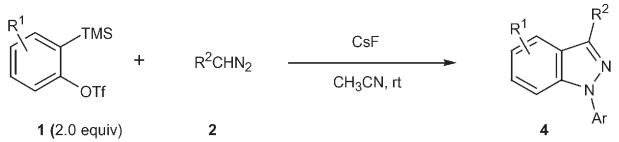
[a] The reaction of **1** (0.5 mmol) and **2** (0.6 mmol) was carried out in the presence of KF (3 equiv.) and 18-crown-6 (3.5 equiv.) in 0.25 M THF at r.t. for 24 h unless otherwise noted. [b] Yields of the isolated product. [c] The reaction was carried out in the presence of CsF (2.0 equiv.) in CH_3CN. [d] The reaction was carried out in the presence of Bu_4NF (2.0 equiv.) in CH_3CN. [e] The reaction was carried out in the presence of CsF (3.0 equiv.) in CH_3CN/MeOH (10:1, 0.25 M). [f] The ratio of regioisomers was determined by ^1H NMR spectroscopy.

N-arylation of indazoles[12]. However, these reactions usually required high temperatures and are limited to the formation of 3-unsubstituted indazoles. More recently, Liu and Larock reported a simple *N*-arylation of various amines with 2-silylphenyl triflates under very mild conditions[7d,7e]. We assume that a combination of our new method (Table I) and the protocol of Liu and Larock would provide a simple, efficient and one-pot procedure for *N*-arylated 1*H*-indazoles (Table II).

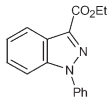
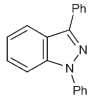
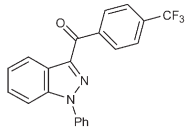
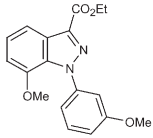
As expected, 1-phenyl-1*H*-indazole (**4a**) was readily obtained in 62% yield without formation of *N*-unsubstituted indazole when **1a** (2.0 equiv.) was treated with **2a** in the presence of an excess KF/18-crown-6 at room temperature (Table II, entry 1). However, when CsF was used instead of KF/18-crown-6 to generate benzyne, the yield increased to 79% and the reaction was complete in a much shorter time (24 h) (entry 2). Under the optimal reaction conditions, diazo(phenyl)methane (**2d**) also reacted well with **1a** to afford 1,3-diphenylindazole **4b** in 56% yield (entry 3). Similiarly, the reaction of benzoyl(diazo)methane (**2e**) with **1a** afforded the corresponding 1-arylindazole **4c** in a high yield (entry 4). The analogous reaction with the unsymmetrical silylaryl triflate **1b** afforded the *meta*-isomer **4d** in 68% yield with excellent regioselectivity (entry 5). This result clearly indicates that the nucleophile reacts at the *meta* position to a methoxy group rather than *ortho* position.

Mechanism: A proposed reaction mechanism for the formation of *N*-unsubstituted indazoles **3** and *N*-phenylindazoles **4** is shown in Scheme 2.

TABLE II
Synthesis of 1-phenyl-1*H*-indazoles **4**[a]

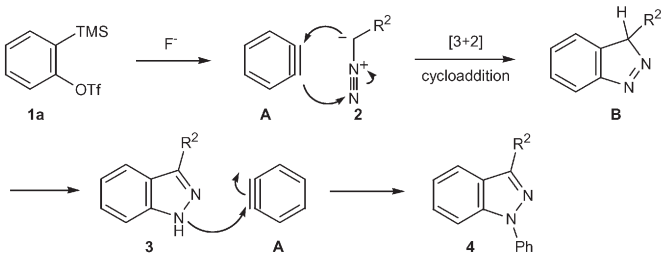


1 (2.0 equiv) **2** **4**

Entry	**1**	**2**	R^2	Product	**4**	Yield, %[b]
1[c]	**1a**	**2a**	CO_2Et		**4a**	62
2	**1a**	**2a**	CO_2Et			79
3	**1a**	**2d**	Ph		**4b**	54
4	**1a**	**2e**	4-$CF_3C_6H_4CO$		**4c**	89
5	**1b**	**2a**	CO_2Et		**4d**	50

[a] The reaction of **1** (0.5 mmol) and **2** (0.25 mmol) was carried out in the presence of CsF (6.0 equiv.) in CH_3CN (2 ml) at r.t. for 24 h unless otherwise stated. [b] Yield of the isolated product. [c] The reaction was carried out in the presence of KF (6.0 equiv.) and 18-crown-6 (7.0 equiv.) in THF for 48 h.

The highly active benzyne intermediate **A** is formed in situ from 2-(trimethylsilyl)phenyl triflate (**1a**) in the presence of a fluoride source. The [3+2] cycloaddition of benzyne **A** with 1,3-dipoles such as diazomethanes **2** affords the intermediate **B** which undergoes a 1,3-hydrogen shift to give the corresponding *N*-unsubstituted indazoles **3**. In the presence of an excess of benzyne **A**, the further hydroamination of **3** to benzyne would occur to form the *N*-phenylindazoles **4**.

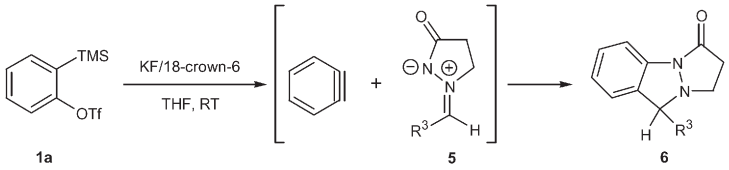


SCHEME 2
A proposed mechanism for the formation of *N*-unsubstituted indazoles **3** and *N*-phenylindazoles **4**

*Synthesis of Tricyclic Indazolone Derivatives **6** from 2-(Trimethylsilyl)aryl Triflates and Azomethine Imides*

Azomethine imides such as 3-oxopyrazolidin-1-ium-2-ides **5** are readily available from the reaction of pyrazolidin-3-one with an aldehyde. They are stable, easy-to-handle compounds[13]. 1,3-Dipolar cycloaddition of these dipoles with benzyne is often conducted at elevated temperatures and explosive benzyne precursors such as benzene-1-diazonium-2-carboxylates are used[4]. Inspired by the successful synthesis of various indazoles, we further investigated the [3+2] cycloaddition of 2-(trimethylsilyl)phenyl triflate (**1a**) with azomethine imide derivatives **5**. In an initial investigation, we examined the reaction of silylphenyl triflate **1a** with azomethine imine **5a** by using several fluoride sources. In the presence of KF combined with 18-crown-6 or CsF at room temperature, cycloadduct **6a** was obtained in 40 or 38% yield, respectively (Table III, entries 1 and 2). In contrast, Bu_4NF failed to give any desired product **6a**, and **1a** was decomposed under the reaction conditions (entry 3). Next, we have determined the scope of the KF/18-crown-6 promoted cycloaddition of **1a** with a range of imides of dipoles **5b**–**5g**. The reaction of the azomethine imides bearing electron-withdrawing (**5b**, **5c)** and electron-donating (**5d**, **5e**) phenyl groups at the imide group gave cycloadducts **6b**–**6e** in good yields regardless of *para*- or *ortho*-substituents on benzene rings (entries 4 to 7). Compound **5f** with disubstituted phenyl in the molecule also reacted with **1a** smoothly, affording the indazolone derivative **6f** in 58% yield (entry 8). The styryl-substituted azomethine imide **5g** was also a suitable dipole for the formation of the cycloaddition product **6g** (entry 9). Unfortunately, the reaction of **1a** with alkyl-substituted imides **5** (R^3 = Et, *t*-Bu) failed to give any de-

Table III
Synthesis of tricyclic indazolone derivatives **6**[a]



1a **5** **6**

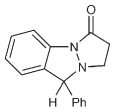
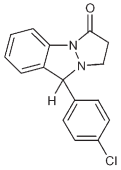
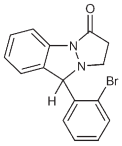
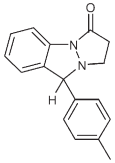
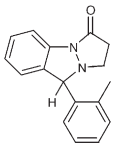
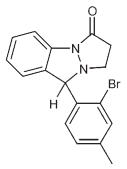
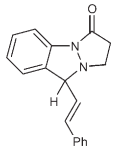
Entry	**5**	R^3	Product	**6**	Yield, %[b]
1	**5a**	Ph		**6a**	40
2[c]	**5a**	Ph			38
3[d]	**5a**	Ph			0
4	**5b**	4-ClC_6H_4		**6b**	43
5	**5c**	2-BrC_6H_4		**6c**	63
6	**5d**	4-MeC_6H_4		**6d**	50
7	**5e**	2-MeC_6H_4		**6e**	46

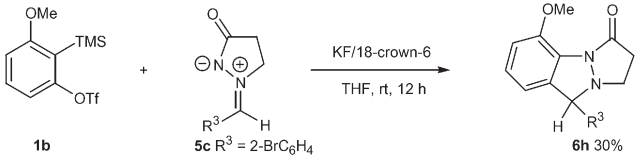
Table III
(*Continued*)

Entry	**5**	R^3	Product	**6**	Yield, %[b]
8	**5f**	2-Br-4-MeC_6H_3		**6f**	58
9	**5g**	(*E*)-styryl		**6g**	45

[a] The reaction of **1a** (0.2 mmol) and **5** (0.24 mmol) was carried out in the presence of KF (3 equiv.) and 18-crown-6 (3.5 equiv.) in 1 M THF at r.t. for 12 h unless otherwise stated. [b] Yield of the isolated product. [c] The reaction was carried out in the presence of CsF (3.0 equiv.) in CH_3CN. [d] The reaction was carried out in the presence of Bu_4NF (3.0 equiv.) in THF.

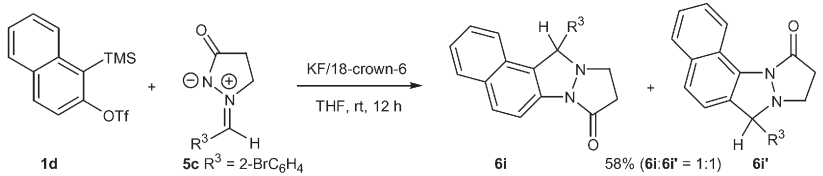
sired products and both **1a** and imides were decomposed under the reaction conditions.

Next, we examined the reaction of the substituted benzyne precursors, **1b**, **1d**, and **1e**, with azomethine imide **5c** under the standard reaction conditions. The reaction of 3-methoxy-2-(trimethylsilyl)phenyl triflate (**1b**) with **5c** gave the corresponding indazolone product **6h** in 30% yield as a single regioisomer in which the methoxy group was away from the hindered 2-bromophenyl substituent (Eq. (*5*)). Treatment of 1-(trimethylsilyl)naphthyl-2-triflate (**1d**) with azomethine imide **5c** afforded a nearly

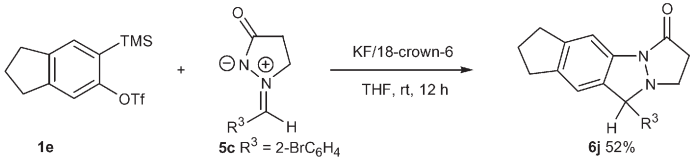


(*5*)

1:1 mixture of two regioisomers (Eq. (*6*)). The structures of regioisomers **6h** and **6i′** were determined unambiguously by NOE experiment as well as HMBC and DEPT analysis (Fig. 1). A similar reaction with the symmetrical silylaryl triflate **1e** produced the corresponding diazaindacenone derivative **6j** in 52% yield (Eq. (*7*)).



(*6*)



(*7*)

An efficient, facile, and general method for the synthesis of *N*-unsubstituted indazoles and 1-arylindazoles via the 1,3-dipolar cycloaddition of arynes with diazomethanes has been developed. By changing the reaction conditions, the controlled synthesis of either of the two products is possible. Furthermore, we have succeeded in the development of synthesis of tricyclic indazolone derivatives through the cycloaddition of 2-silylphenyl triflate with azomethine imides under very mild reaction conditions. Further studies on the application of the present method to the synthesis of biologically active compounds are in progress.

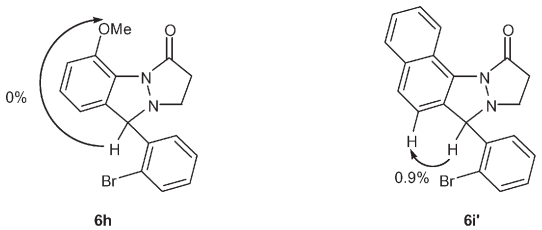


FIG. 1
NOE experiment of compounds **6h** and **6i′**

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on JEOL JMTC-270/54/SS (JASTEC, 300 and 500 MHz) spectrometers. ^{1}H NMR spectra are reported as follows: chemical shift in ppm (δ) relative to $CDCl_3$ at 7.26 ppm, integration, multiplicities (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broadened), and coupling constants (*J*) in Hz. ^{13}C NMR spectra reported in ppm (δ) relative to the central line of triplet for $CDCl_3$ at 77 ppm. IR spectra were recorded on a Shimadzu FTIR-8200A spectrometer; absorptions are reported in cm^{-1}. High-resolution mass spectra were obtained on a Bruker APEXIII spectrometer. Melting points were measured by MRK (No. 8026). Column chromatography was carried out employing Silica gel 60 N (spherical, neutral, 40–100 mm, Kanto Chemical Co.). Analytical thin-layer chromatography (TLC) was performed on precoated plate with 0.2 mm Kieselgel 60 F_{254} (Merck). Anhydrous acetonitrile (Wako), Tetrahydrofuran (Kanto), KF, CsF (Wako), 18-crown-6 (TCI), ethyl diazoacetate (**2a**), *tert*-butyl diazoacetate (**2b**), diazo(trimethylsilyl)methane (**2c**) (2.0 M solution in diethyl ether), 2-(trimethylsilyl)phenyl triflate (**1a**) (Aldrich), pyrazolidin-3-one hydrochloride (Across), were purchased and used as received. Aryne precursors **1b**, **1c**, **1d**, **1f** [14], **1e** [15], diazo(phenyl)methane (**2d**)[16] and diazo[4-(trifluoromethyl)benzoyl]methane (**2e**)[17], and 3-oxopyrazolidin-1-ium-2-ides **5a**–**5g** [13] were prepared according to the literature procedure. The procedures and characterization of final products **3a**–**3i** and **4a**–**4d** are available from ref.[9a].

Typical Procedure for the Synthesis of Indazolone Derivatives **6**

2-(Trimethylsilyl)phenyl triflate (**1a**) (50 µl, 0.2 mmol) was added to a THF (1 ml) solution of 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide (**5a**) (41.8 mg, 0.24 mmol), KF (35 mg, 0.6 mmol), and 18-crown-6 (185 mg, 0.7 mmol) in a pressure vial. After stirring at room temperature for 12 h, the reaction mixture was filtered through a short pad of Florisil and eluted with ethyl acetate. The filtrate was concentrated, and the residue purified by chromatography on silica gel using a mixture of hexane/EtOAc (5:1 to 3:1) as eluent to afford **6a** as a white solid (20 mg, 40%).

2,3-Dihydro-5-phenyl-1*H*,5*H*-pyrazolo[1,2-*a*]indazol-1-one (**6a**)

White solid, m.p. 154–158 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 2.85–2.73 m, 1 H (-CH-C(O)); 3.17–3.01 m, 2 H (N-CH-, -CH-C(O)); 3.64–3.54 m, 1 H (N-CH-); 5.09 s, 1 H (-CH-Ph); 6.85–6.83 m, 1 H (aromatic); 7.04–7.00 m, 1 H (aromatic); 7.30–7.23 m, 1 H (aromatic); 7.42–7.37 m, 5 H (aromatic); 7.60 d, 1 H, *J* = 7.8 (aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): 36.61, 52.21, 74.42, 112.72, 123.73, 124.82, 128.37, 128.59, 128.68, 128.82, 133.67, 135.01, 138.28, 162.60. IR (neat): 1687, 1603, 1482, 1463, 761, 698. HRMS (ESI): calculated for $C_{16}H_{14}N_2O$ $(M + Na)^+$ 273.0998, found 273.0997.

5-(4-Chlorophenyl)-2,3-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*]indazol-1-one (**6b**)

White solid, m.p. 142–144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 2.86–2.77 m, 1 H (-CH-C(O)); 3.16–3.02 m, 2 H (N-CH-, -CH-C(O)); 3.64–3.57 m, 1 H (N-CH-); 5.09 s, 1 H (-CH-Ph-Cl); 6.82 d, 1 H, *J* = 7.8 (aromatic); 7.07–7.02 m, 1 H (aromatic); 7.34–7.26 m, 1 H (aromatic); 7.38 m, 4 H (aromatic); 7.61 d, 1 H, *J* = 7.8 (aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): 36.54, 52.21, 73.75, 112.79, 123.58, 124.87, 128.88, 129.02, 129.67, 133.62, 124.47, 134.53,

136.97, 162.55. IR (neat): 1688, 1605, 1478, 1403, 1089, 845, 747. HRMS (ESI): calculated for $C_{16}H_{13}ClN_2O$ $(M + Na)^+$ 307.0609, found 307.0608.

5-(2-Bromophenyl)-2,3-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*]indazol-1-one (**6c**)

Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): 2.84–2.77 m, 1 H (-CH-C(O)); 3.14–3.02 m, 1 H (-CH-C(O)); 3.32–3.22 m, 1 H (N-CH-); 3.66–3.60 m, 1 H (N-CH-); 5.78 s, 1 H (-CH-Ph-Br); 7.06–6.97 m, 2 H (aromatic); 7.35–7.20 m, 3 H (aromatic); 7.65–7.56 m, 3 H (aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): 36.58, 52.60, 72.27, 112.74, 123.98, 124.10, 124.77, 128.05, 128.78, 129.78, 130.34, 132.85, 133.84, 133.86, 138.12, 162.83. IR (neat): 1687, 1604, 1483, 1463, 1404, 1025, 744. HRMS (ESI): calculated for $C_{16}H_{13}BrN_2O$ $(M + Na)^+$ 351.0103, found 351.0103.

2,3-Dihydro-5-(4-methylphenyl)-1*H*,5*H*-pyrazolo[1,2-*a*]indazol-1-one (**6d**)

Yellowish solid, m.p. 155–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 2.82 s, 3 H (-CH_3); 2.86–2.76 m, 1 H (-CH-C(O)); 3.18–3.01 m, 2 H (N-CH-, -CH-C(O)); 3.63–3.53 m, 1 H (N-CH-); 5.08 s, 1 H (-CH-Ph-Me); 6.86 d, 1 H, J = 7.5 (aromatic); 7.04 dd, 1 H, J_1 = 7.5, J_2 = 7.5 (aromatic); 7.32–7.20 m, 5 H (aromatic); 7.62 d, 1 H, J = 7.5 (aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): 21.16, 36.62, 52.10, 74.20, 112.71, 123.73, 124.78, 128.31, 128.60, 129.51, 133.72, 135.21, 135.22, 138.44, 162.56. IR (neat): 1688, 1604, 1478, 1404, 842, 803. HRMS (ESI): calculated for $C_{17}H_{16}N_2O$ $(M + Na)^+$ 287.1155, found 287.1155.

2,3-Dihydro-5-(2-methylphenyl)-1*H*,5*H*-pyrazolo[1,2-*a*]indazol-1-one (**6e**)

White solid, m.p. 129–133 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.41 s, 3 H (-CH_3); 2.85–2.80 m, 1 H (-CH-C(O)); 3.19–3.06 m, 2 H (N-CH-, -CH-C(O)); 3.63–3.59 m, 1 H (N-CH-); 5.41 s, 1 H (-CH-Ph-Me); 6.84 d, 1 H, J = 7.5 (aromatic); 7.04 dd, 1 H, J_1 = 7.5, J_2 = 7.5 (aromatic); 7.31–7.24 m, 4 H (aromatic); 7.46 d, 1 H, J = 7.5 (aromatic); 7.65 d, 1 H, J = 7.5 (aromatic). ^{13}C NMR (125 MHz, $CDCl_3$): 19.55, 36.70, 52.56, 71.63, 112.76, 123.45, 124.76, 126.44, 128.22, 128.54, 129.09, 130.94, 133.90, 134.94, 136.01, 136.77, 162.67. IR (neat): 1683, 1603, 1483, 1412, 1065, 761. HRMS (ESI): calculated for $C_{17}H_{16}N_2O$ $(M + Na)^+$ 287.1155, found 287.1153.

5-(2-Bromo-4-methylphenyl)-2,3-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*]indazol-1-one (**6f**)

Yellowish solid, m.p. 116–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 2.34 s, 3 H (-CH_3); 2.84–2.75 m, 1 H (-CH-C(O)); 3.12–3.00 m, 1 H (-CH-C(O)); 3.30–3.21 m, 1 H (N-CH-); 3.63–3.57 m, 1 H (N-CH-); 5.73 s, 1 H (-CH-Ph-Me(Br)); 6.96 d, 1 H, J = 7.8 (aromatic); 7.04 dd, 1 H, J_1 = 6.9, J_2 = 6.9 (aromatic); 7.14 d, 1 H, J = 6.9 (aromatic); 7.29 dd, 1 H, J_3 = 7.5, J_4 = 7.5 (aromatic); 7.42 d, 1 H, J = 7.8 (aromatic); 7.46 m, 1 H (aromatic); 7.62 d, 1 H, J = 7.8 (aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): 20.74, 36.58, 52.50, 72.04, 112.74, 123.95, 123.98, 124.78, 128.71, 128.96, 130.05, 133.23, 133.90, 134.15, 134.96, 140.15, 162.83. IR (neat): 1686, 1601, 1480, 1408, 1067, 752. HRMS (ESI): calculated for $C_{17}H_{15}BrN_2O$ $(M + Na)^+$ 365.0260, found 365.0260.

2,3-Dihydro-5-(*E*)-styryl-1*H*,5*H*-pyrazolo[1,2-*a*]indazol-1-one (**6g**)

Yellow solid, m.p. 128–132 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.84–2.77 m, 1 H (-CH-C(O)); 3.15–3.06 m, 2 H (-CH-C(O), N-CH-); 3.77–3.70 m, 1 H (N-CH-); 4.74 s, 1 H, J_2 = 8.0 (-CH-styryl); 6.32 dd, 1 H, J_1 = 16.0, J_2 = 8.0 (-CH=); 6.73 d, 1 H, J_1 = 16.0 (=CHPh); 7.10 d, 2 H, J_3 = 4.5 (aromatic); 7.32–7.29 m, 2 H (aromatic); 7.36 dd, 2 H, *J* = 7.0, *J* = 7.0 (aromatic); 7.46 d, 2 H, *J* = 7.0 (aromatic); 7.60 d, 1 H, *J* = 7.0 (aromatic). ^{13}C NMR (125 MHz, $CDCl_3$): 36.53, 52.17, 73.19, 112.96, 123.50, 124.78, 125.83, 126.68, 128.29, 128.69, 128.85, 133.70, 133.87, 134.67, 135.86, 162.64. IR (neat): 1672, 1605, 1485, 1459, 1410, 1074, 750. HRMS (ESI): calculated for $C_{18}H_{16}N_2O$ $(M + Na)^+$ 299.1155, found 299.1154.

5-(2-Bromophenyl)-2,3-dihydro-9-methoxy-1*H*,5*H*-pyrazolo[1,2,*a*]indazol-1-one (**6h**)

White solid, m.p. 180–183 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.77–2.72 m, 1 H (-CH-C(O)); 2.92–2.85 m, 1 H (-CH-C(O)); 3.31–3.25 m, 1 H (N-CH-); 3.42–3.38 m, 1 H (N-CH-); 3.55 s, 3 H ($-OCH_3$); 5.88 s, 1 H (-CH-PhBr); 6.58- 6.56 m, 1 H (aromatic); 7.14–7.11 m, 2 H (aromatic); 7.28–7.20 m, 3 H (aromatic); 7.56–7.55 m, 1 H (aromatic). ^{13}C NMR (125 MHz, $CDCl_3$): 36.45, 51.90, 55.47, 69.64, 105.52, 107.71, 119.93, 124.53, 127.74, 129.48, 130.41, 130.79, 132.63, 135.88, 137.55, 155.44, 163.72. IR (neat): 2841, 1688, 1600, 1471, 1394, 1264, 1084, 765. HRMS (ESI): calculated for $C_{17}H_{15}BrN_2O_2$ $(M + Na)^+$ 381.0209, found 381.0209.

7-(2-Bromophenyl)-8,9-dihydro-7*H*-7a,10a-diazapentaleno[1,2-*a*]naphthalen-10-one (**6i′**)

Yellowish solid, m.p. 74–77 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.97–2.91 m, 1 H (-CH-C(O)); 3.25–3.17 m, 1 H (-CH-C(O)); 3.41–3.35 m, 1 H (N-CH-); 3.71–3.67 m, 1 H (N-CH-); 5.98 s, 1 H (-CH-PhBr); 7.02 d, 1 H, *J* = 8.5 (aromatic); 7.22 dd, 1 H, J_1 = 7.5, J_1 = 7.5 (aromatic); 7.31 dd, 1 H, J_1 = 7.5, J_1 = 7.5 (aromatic); 7.60–7.48 m, 4 H (aromatic); 7.66 d, 1 H, J_1 = 7.5 (aromatic); 7.79 d, 1 H, J_1 = 7.5 (aromatic); 8.98 d, 1 H, *J* = 8.5 (aromatic). ^{13}C NMR (125 MHz, $CDCl_3$): 36.76, 51.86, 73.07, 120.73, 121.73, 124.36, 126.42, 126.54, 126.67, 126.99, 127.92, 128.11, 129.85, 130.68, 130.73, 131.95, 132.89, 134.23, 138.31, 163.74. IR (neat): 3059, 2845, 1686, 1408, 1355, 1095, 1024, 808, 752. HRMS (ESI): calculated for $C_{20}H_{15}BrN_2O$ $(M + Na)^+$ 401.0260, found 401.0260.

10-(2-Bromophenyl)-8,9-dihydro-10*H*-6b,9a-diazapentaleno[2,1-*a*]naphthalen-7-one (**6i**)

Yellow solid, m.p. 71–75 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.88–2.82 m, 1 H (-CH-C(O)); 3.03–2.95 m, 1 H (-CH-C(O)); 3.46–3.40 m, 1 H (N-CH-); 3.58–3.51 m, 1 H (N-CH-); 6.38 s, 1 H (-CH-PhBr); 7.07 d, 2 H, *J* = 8.5 (aromatic); 7.21–7.19 m, 2 H (aromatic); 7.39–7.26 m, 2 H (aromatic); 7.71–7.68 m, 1 H (aromatic); 7.80 d, 1 H, *J* = 8.5 (aromatic); 7.90 d, 1 H, *J* = 8.5 (aromatic); 7.95 d, 1 H, *J*= 8.5 (aromatic). ^{13}C NMR (125 MHz, $CDCl_3$): 36.44, 51.90, 71.01, 112.59, 123.05, 124.37, 124.72, 125.32, 127.36, 128.33, 128.82, 129.00, 130.07, 130.51, 131.29, 131.74, 132.91, 132.93, 137.75, 163.73. IR (neat): 3056, 2850, 1692, 1519, 1472, 1407, 1067, 1025, 812, 738. HRMS (ESI): calculated for $C_{20}H_{15}BrN_2O$ $(M + Na)^+$ 401.0260, found 401.0261.

9-(2-Bromophenyl)-1,2,5,6,7,9-hexahydro-3a,9a-diazacyclopenta[*a*]-s-indacen-3-one (**6j**)

Yellow solid, m.p. 149–150 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.08–2.01 m, 2 H (Ar-C-CH_2-C-Ar); 2.90–2.72 m, 5 H (-CH-C(O), Ar-CH_2-C-CH_2-Ar)); 3.09–3.02 m, 1 H (-CH-C(O)); 3.26–3.20 m, 1 H (N-CH-); 3.61–3.57 m, 1 H (N-CH-); 5.70 s, 1 H (-CH-PhBr); 6.78 s, 1 H (aromatic); 7.22–7.18 m, 1 H (aromatic); 7.34–7.31 m, 1 H (aromatic); 7.50 s, 1 H (aromatic); 7.63–7.58 m, 2 H (aromatic). ^{13}C NMR (125 MHz, $CDCl_3$): 25.72, 32.42, 32.74, 36.52, 52.50, 72.24, 109.03, 119.70, 124.10, 128.04, 129.65, 130.36, 132.36, 132.45, 132.78, 138.48, 141.09, 145.24, 162.35. IR (neat): 1696, 1608, 1482, 1405, 1314, 1083, 762. HRMS (ESI): calculated for $C_{19}H_{17}BrN_2O$ $(M + Na)^+$ 391.0416, found 391.0416.

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