JOC Article

Synthesis of Indazoles by the [3+2] Cycloaddition of Diazo Compounds with Arynes and Subsequent Acyl Migration

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The [3+2] cycloaddition of a variety of diazo compounds with *o*-(trimethylsilyl)aryl triflates in the presence of CsF or TBAF at room temperature provides a very direct, efficient approach to a wide range of potentially biologically and pharmaceutically interesting substituted indazoles in good to excellent yields under mild reaction conditions. Simple diazomethane derivatives afford *N*-unsubstituted indazoles or 1-arylated indazoles, depending upon the stoichiometry of the reagents and the reaction conditions, while dicarbonyl-containing diazo compounds undergo carbonyl migration to afford 1-acyl or 1-alkoxycarbonyl indazoles selectively.

Introduction

The indazole moiety is a frequently found subunit in pharmaceuticals with important biological[1] and powerful pharmacological activities, including anti-inflammatory,[2] anti-tumor,[3] anti-HIV,[4] anti-cancer,[5] and anti-platelet activities,[6] plus serotonin 5-HT_3 receptor antagonist activity.[7] A variety of methods for the preparation of indazoles have been reported due to the importance of indazoles in the pharmaceutical industry.[8,9] However, the development of efficient and general methodologies for the synthesis of a wide variety of indazoles and derivatives has met with limited success and significant limitations remain. For example, the need for harsh reaction conditions and high temperatures often limits the scope and applications. Potentially hazardous and explosive intermediates[9d] sometimes limit applications in large-scale processes. In addition, most of the present procedures involve several steps and lack overall efficiency. Considering the limitations of these previous procedures and the importance of such indazole derivatives, a simple, efficient, and general method to synthesize indazoles and their derivatives would be quite attractive.

Recently, we have had considerable success using arynes prepared in situ from *o*-(trimethylsilyl)aryl triflates under mild reaction conditions in a variety of synthetic processes.[10]

(1) For a review, see: Brase, S.; Gil, C.; Knepper, K. *Bioorg. Med. Chem.* **2002**, *10*, 2415.

(2) (a) Runti, C.; Baiocchi, L. *Int. J. Tissue React.* **1985**, *7*, 175. (b) Bistochi, G. A.; De Meo, G.; Pedini, M.; Ricci, A.; Brouilhet, H.; Bucherie, S.; Rabaud, M.; Jacquignon, P. *Farmaco, Ed. Sci.* **1981**, *36*, 315. (c) Picciola, G.; Ravenna, F.; Carenini, G.; Gentili, P.; Riva, M. *Farmaco, Ed. Sci.* **1981**, *36*, 1037.

(3) Keppler, B. K.; Hartmann, M. *Met.-Based Drugs* **1994**, *1*, 145.

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(8) For earlier examples, see: (a) Elguero, J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: New York, 1984; Vol. 5, p 167. (b) Kovach, E. G.; Barnes, D. E. *J. Am. Chem. Soc.* **1954**, *76*, 1176.

(9) For recent examples, see: (a) Song, J. J.; Yee, N. K. *Org. Lett.* **2000**, *2*, 519. (b) Song, J. J.; Yee, N. K. *Tetrahedron Lett.* **2001**, *41*, 2937. (c) Frontana-Uribe, B. A.; Moinet, C. *Tetrahedron* **1998**, *54*, 3197. (d) Stadlbauer, W. *Sci. Synth.* **2002**, *12*, 227. (e) Akazome, M.; Kondo, T.; Watanabe, Y. *J. Org. Chem.* **1994**, *59*, 3375. (f) Caron, S.; Vazquez, E. *Synthesis* **1999**, 588. (g) Fernandez, P. A.; Bellamy, T.; Kling, M.; Madge, D. J.; Selwood, D. L. *Heterocycles* **2001**, *55*, 1813. (h) Yoshida, T.; Matsuura, N.; Yamamoto, K.; Doi, M.; Shimada, K.; Morie, T.; Kato, S. *Heterocycles* **1996**, *43*, 2701. (i) Jukin, K.; Hsu, M. C.; Fernando, D.; Leanna, M. R. *J. Org. Chem.* **2006**, *71*, 8166.

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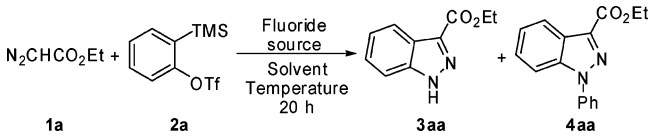
TABLE 1. Optimization of the Reaction Conditions[a]

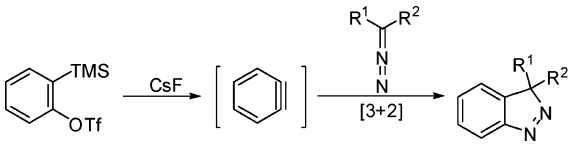


1a 2a 3aa 4aa

entry	1a (equiv)	2a (equiv)	fluoride (equiv)	solvent	temp (°C)	yield[b] of 3aa (%)	yield[b] of 4aa (%)
1	1.0	1.2	CsF (2.0)	MeCN	rt	30	36
2	**1.0**	**2.4**	**CsF (4.0)**	**MeCN**	**rt**	**0**	**97**
3	1.2	1.0	CsF (2.0)	MeCN	rt	38	28
4	1.2	1.0	CsF (2.0)	MeCN	80	10	43
5	1.5	1.0	CsF (2.0)	MeCN	rt	55	17
6	1.2	1.0	TBAF (1.2)	THF	rt	36	30
7	1.2	1.0	TBAF (1.2)	THF	−78 to rt	78	8
8	**1.5**	**1.0**	**TBAF (1.2)**	**THF**	**−78 to rt**	**85**	**<5**

[a] All reactions were carried out on approximately a 0.3 mmol scale at a 0.08 M concentration. [b] Isolated yields.

Continuing our interests in this chemistry, we decided to study aryne cycloaddition chemistry. We envisioned the synthesis of indazoles by the [3+2] cycloaddition reaction of diazo compounds with arynes as a very attractive strategy, since arynes are quite reactive, yet they can be generated under very mild reaction conditions with many functional groups readily tolerated. Although the reaction of benzyne and diazo compounds was reported a long time ago,[11] that process employed explosive *o*-benzenediazonium carboxylate as the benzyne precursor, and only one example with ethyl diazoacetate was reported with no yield indicated. Herein, we wish to report in full our results on the synthesis of indazoles and derivatives by the [3+2] cycloaddition reaction of diazo compounds and arynes under mild reaction conditions (eq 1), a process that affords excellent yields of indazoles.[12] This process exhibits several very attractive features, namely mild reaction conditions, good functional group tolerance, direct preparation of several different substituted indazole ring systems, excellent yields, and good scale-up possibilities.



(1)

Results and Discussion

Reaction Optimization of Ethyl Diazoacetate with Benzyne. We first allowed ethyl diazoacetate (**1a**) to react with 1.2 equiv of the parent benzyne generated in situ by reaction of commercially available *o*-(trimethylsilyl)phenyl triflate (**2a**) with excess CsF in acetonitrile at room temperature for 20 h. We were pleased to find that such reaction conditions afforded the desired indazole product, albeit as a 1:1.2 mixture of ethyl indazole-3-carboxylate (**3aa**) and ethyl *N*-phenylindazole-3-carboxylate (**4aa**) in a combined 66% yield (Table 1, entry 1). Obviously, the reaction did not stop at the [3+2] cycloadduct **3aa**, but in fact underwent further arylation to form **4aa**, a process not unexpected in view of our previous work on the *N*-arylation of amines by arynes.[10f]

We then surveyed a series of reaction conditions in the hope of optimizing the formation of each of these products (Table 1). We quickly found that either **3aa** or **4aa** could be prepared almost exclusively by simply varying the stoichiometry and reaction conditions. Thus, running the reaction with 2.4 equiv of the benzyne precursor **2a** selectively afforded the *N*-arylated indazole **4aa** in an excellent 97% isolated yield (Table 1, entry 2) without contamination of the simple cycloaddition product **3aa**. In our initial attempts (Table 1, entries 3−6) to obtain **3aa** as a single major product, we were unable to suppress the formation of **4aa**. With use of 1.2 equiv of **1a** at room temperature, only a 38% yield of **3aa** was obtained, alongside a 28% yield of **4aa** (Table 1, entry 3). The ratio of these products was even worse when the reaction was carried out at 80 °C (Table 1, entry 4). Somewhat better results were obtained with 1.5 equiv of **1a** (Table 1, entry 5). In the hope of more rapidly generating the benzyne and therefore the initial cycloadduct, thus leaving less benzyne for *N*-arylation, we examined analogous reactions using the more soluble fluoride reagent tetra-*n*-butylammonium fluoride (TBAF) in THF. Using 1.2 equiv of **1a** and TBAF at room temperature only gave a disappointing 36% yield of **3aa** plus a 30% yield of **4aa** (Table 1, entry 6). However, starting the same reaction at −78 °C and allowing it to slowly warm on its own to room temperature gave a much improved 78% yield of **3aa** and only an 8% yield of **4aa** (Table 1, entry 7). Finally, by employing 1.5 equiv of **1a** and 1.2 equiv of TBAF in THF at the low temperature afforded an 85% yield of **3aa** and less than a 5% yield of **4aa** (Table 1, entry 8).

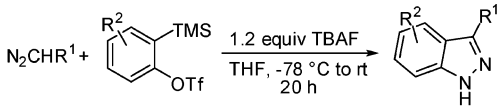
Reaction Scope of the Cycloaddition of Monosubstituted Diazomethane Derivatives with Arynes. With efficient, high yielding, selective procedures for the preparation of both N−H and N−Ar indazoles now available, we next explored the scope and limitations of the 1*H*-indaozle synthesis using a range of substrates (Table 2).

The reaction of ethyl diazoacetate (**1a**) with a variety of benzyne precursors was first explored (Table 2, entries 1−6). All *o*-silylaryl triflates examined (**2a**−**f**) reacted with **1a** to afford the desired 1*H*-indazoles in moderate to good yields. The

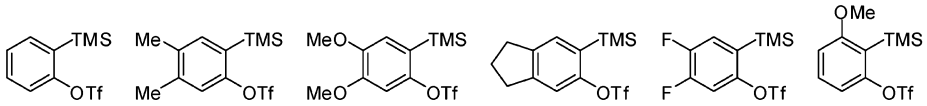
(11) (a) Huisgen, R.; Knorr, R. *Naturwissenschaften* **1961**, *48*, 716. (b) Reid, W.; Schön, M. *Ann. Chem.* **1965**, *869*, 141. (c) García-Abbad, E.; García-López, M. T.; García-Muñoz, G.; Stud, M. *J. Heterocycl. Chem.* ***1976***, *13*, *1241*. (d) Baum, G.; Bernard, R.; Shechter, H. *J. Am. Chem. Soc.* **1967**, *89*, 5307. (e) Baum, G.; Shechter, H. *J. Org. Chem.* **1976**, *41*, 2120. (f) Yamazaki, T.; Shechter, H. *Tetrahedron Lett.* **1972**, *13*, 4533. (g) Yamazaki, T.; Shechter, H. *Tetrahedron Lett.* **1973**, *14*, 1417. (h) Yamazaki, T.; Baum, G.; Shechter, H. *Tetrahedron Lett.* **1974**, *15*, 4421.

(12) During our preparation of the manuscript, Yamamoto published a communication on similar work, see: Jin, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3323.

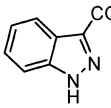
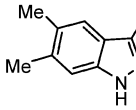
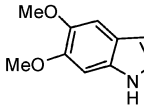
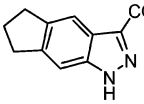
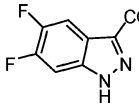
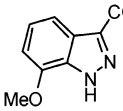
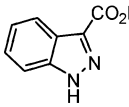
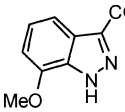
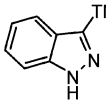
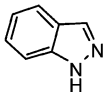
TABLE 2. Formation of 1*H*-Indazoles by Cycloaddition with Monosubstituted Diazomethane Derivatives[a]



1 2 3



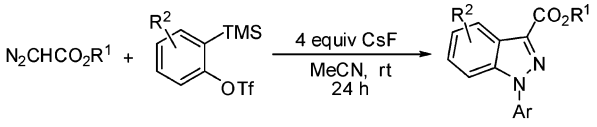
2a 2b 2c 2d 2e 2f

entry	diazo compound[b]	R^1	benzyne precursor	product **3**	yield[c] (%)
1	**1a**	CO_2Et	**2a**	 **3aa**	85
2	**1a**	CO_2Et	**2b**	 **3ab**	87
3	**1a**	CO_2Et	**2c**	 **3ac**	84
4	**1a**	CO_2Et	**2d**	 **3ad**	80
5	**1a**	CO_2Et	**2e**	 **3ae**	45
6	**1a**	CO_2Et	**2f**	 **3af**	58
7	**1b**	CO_2Me	**2a**	 **3ba**	76
8	**1b**	CO_2Me	**2f**	 **3bf**	65
9	**1c**	TMS	**2a**	 **3ca**	0
10	**1c**	TMS	**2a**	 **3ca'**	43[d]

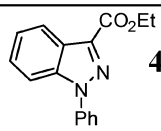
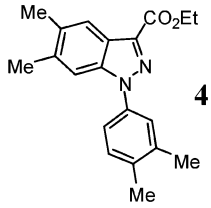
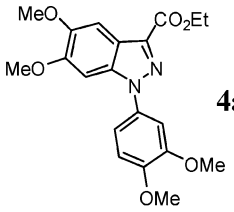
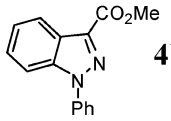
[a] All reactions were carried out on approximately a 0.3 mmol scale (based on benzyne precursor) at a 0.08 M concentration. [b] 1.5 equiv was used. [c] Isolated yields based on benzyne precursor. [d] Reaction was carried out in 10:1 THF/MeOH.

only problematic substrate was the electron-poor difluoro analogue **2e**, which, under the specified reaction conditions, only afforded the indazole product **3ae** in a 45% isolated yield (Table 2, entry 5) with contamination by several other unidentifiable

TABLE 3. Formation of *N*-Aryl 1*H*-Indazoles by Cycloaddition with Monosubstituted Diazomethane Derivatives[a]



1 2 4

entry	diazo compound	R^1	benzyne precursor[b]	product **4**	yield[c] (%)
1	**1a**	Et	**2a**	 **4aa**	97
2	**1a**	Et	**2b**	 **4ab**	88
3	**1a**	Et	**2c**	 **4ac**	94
4	**1b**	Me	**2a**	 **4ba**	92

[a] All reactions were carried out on approximately a 0.3 mmol scale (based on diazo compound) at a 0.08 M concentration. [b] 2.4 equiv was used. [c] Isolated yields based on the diazo compound.

side products. Noteworthy is the fact that the unsymmetrical benzyne precursor **2f** reacted with complete regioselectivity to afford exclusively product **3af** in a 58% yield (Table 2, entry 6). This regioselectivity presumably arises from nucleophilic attack of the diazo compound selectively at the position meta to the methoxy group of the aryne intermediate due to more favorable steric and electronic effects. Analogous regioselectivity has been observed in our previous chemistry with this aryne.[10]

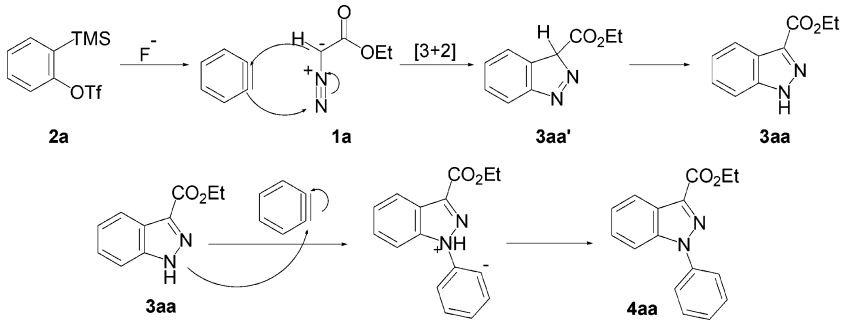
We have examined analogous chemistry using two other monosubstituted diazomethane derivatives with different benzyne precursors under our optimized conditions to produce 1*H*-indazoles (Table 2, entries 7−10). Like the ethyl ester **1a**, the methyl ester **1b** reacted to furnish the desired product in comparable yields (Table 2, entries 7 and 8). However, the commercially available TMS-substituted diazomethane **1c** afforded none of the desired cycloadduct under our optimized conditions (Table 2, entry 9). Running the reaction in the presence of MeOH afforded the parent indazole with loss of the TMS group in a 43% yield (Table 2, entry 10). The same result has been reported by Yamamoto and co-workers.[12]

We have also performed a few reactions directed toward the selective formation of the *N*-arylated indazoles **4** under the optimized reaction conditions reported in Table 1, entry 2. Thus, using an excess of the *o*-silylaryl triflate (2.4 equiv) in the presence of CsF (4.0 equiv) gave the corresponding *N*-arylated indazoles in excellent yields (Table 3). A variety of benzyne precursors can be employed in this process, leading to fairly complex structures.

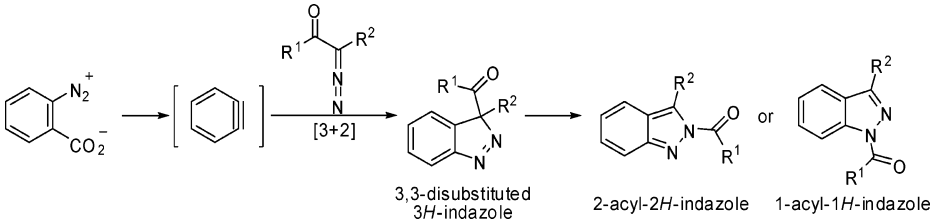
Mechanism. As to the mechanism of this cycloaddition chemistry, we propose that the initial reaction involves a [3+2] cycloaddition between the diazoacetate derivative and the aryne to generate compound **3aa′** (Scheme 1). This intermediate then undergoes a 1,3-hydrogen shift, or two 1,5-hydrogen shifts, under the reaction conditions to yield the observed indazole product **3aa**. If an excess of the aryne is employed, indazole **3aa** reacts further with the excess aryne to afford the *N*-arylated indazole **4aa**.

Reaction Scope of the Cycloaddition of Disubstituted Diazo Compounds with Arynes and the Observation of Acyl Migration. We next examined the cycloaddition of disubstituted diazo substrates that do not have hydrogen on the diazo carbon. Since the anticipated products cannot undergo a hydrogen shift, one might expect the formation of nonaromatized 3,3-disubstituted 3*H*-indazoles as the final products. However, substrates bearing acyl groups on the diazo carbon are known to undergo an initial [3+2] cycloaddition with benzyne generated from diazotized anthranilic acid to afford such 3,3-disubstituted 3*H*-indazole intermediates, followed by an acyl migration to provide 2-acyl-2*H*-indazoles or 1-acyl-1*H*-indazoles (Scheme 2), depending upon the substrates.[11h]

SCHEME 1. Proposed Mechanism for the Formation of 1*H*-Indazoles and *N*-Aryl 1*H*-Indazoles



SCHEME 2. Literature Examples of Cycloaddition and Acyl Migration



With such possibilities in mind, we surveyed the scope of the cycloaddition of several different diazo compounds with arynes (Table 4). To our surprise, our results are different in some cases from those reported previously in the literature.[11h]

We first allowed a couple of diazo compounds having two carbonyl groups attached to the diazo carbon[13] to react with the benzyne precursor **2a** under our standard reaction conditions (Table 4, entries 1−4). Thus, diethyl diazomalonate (**1d**) reacted with **2a** to give a single product in an 85% yield (Table 4, entry 1). However, spectroscopic data clearly indicated a product that does not resemble a simple [3+2] cycloadduct, since the two ethyl groups are clearly differentiated in both the ^{1}H NMR and ^{13}C NMR spectra. Further ^{13}C NMR spectroscopic analysis revealed that the peaks for the carbonyl carbons have shifted significantly upfield, including one carbon (ca. 150 ppm) significantly beyond the normal range for esters. Such data were clearly indicative of an isomerization. X-ray analysis revealed an unambiguous acyl migration to form the corresponding 1-acyl-1*H*-indazole **6da**.[14] The structure **6da** is consistent with the spectroscopic data we have obtained. This result confirmed that acyl migration may occur and is indeed predominant in this case. The driving force for such a migration may include restoration of the aromaticity.

Similar observations have been made in the reaction of diazo compounds **1e**, **1f**, and **1g**. In each of these cases, the product of acyl migration was the exclusive product. Interestingly, ketone carbonyls clearly migrate in preference to esters and amides (Table 4, entries 3 and 4). Despite this subsequent migration process, all products have been isolated cleanly in good to excellent yields.

We next performed the reaction of **1g** with a range of benzyne precursors (Table 4, entries 4−7). The reaction seems to be quite general, providing the acyl migration products **6** in good to excellent yields, except when the electron-poor benzyne precursor **2e** was employed (Table 4, entry 7). This aryne afforded a complex reaction mixture.

Although the aforementioned diazo compounds reacted quite successfully with benzynes in this process, in sharp contrast, diazo compounds with two carbonyl groups present in a ring (**1h**, **1i**, and **1j**) do not even undergo cycloaddition (Table 2, entries 8−10). Thus, these diazo compounds were simply recovered unreacted after the reaction with no product being formed. This is quite surprising, since **1h** has been reported in the literature[11f] to react with benzyne generated from diazotized anthranilic acid, followed by an acyl migration to provide indazolo[2,3-*b*]isoquinoline-7,12-dione **6ha**. Of course, the difference in the nature of the benzyne precursors and the methods used to generate the benzynes may play an important role in the reactivity, but such a dramatic difference in behavior was quite unexpected.

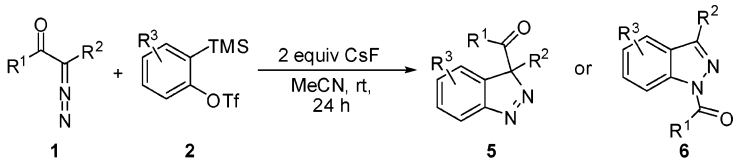
We have also investigated cycloadditions employing a variety of disubstituted diazo compounds with one or no carbonyl groups attached to the diazo carbon.[15] Along these lines, ethyl diazophenylacetate (**1k**) was first examined. The reaction between **1k** and **2a** afforded two products (Table 4, entry 11). While the major product (ca. 72% yield) was the indazole **5ka** where no acyl migration had taken place, we did observe a minor product (ca. 25% yield) corresponding to the migration product **6ka**. These two products could be clearly differentiated by their ^{13}C NMR spectra; the quaternary carbon at ∼100 ppm and the ester carbonyl at ∼170 ppm clearly suggest that the major product has structure **5ka**. Similarly, the reaction between **1k** and **2f**, and the reactions between **1*l*** and **2a** and **2f** all proceeded smoothly to give the products **5kf**, **5*l*a**, and **5*l*f** respectively as the predominant products (Table 4, entries 13−15). In contrast, the reaction of **1k** and **2b** furnished solely the migration product **6kb** (Table 4, entry 12). It was surprising that the product formed was so dependent upon the structure of the starting material. We envisioned that this dependency may be partially attributed to a reluctance of the ester group to migrate, thus complicating the situation. To test

(13) These types of diazo compounds have been prepared by diazo transfer from 4-(acetoamido)benzenesulfonyl azide, see: Davies, J. R.; Kane, P. D.; Moody, C. J. *Tetrahedron* **2004**, *60*, 3967.

(14) See the Supporting Information for the X-ray structure.

(15) Compounds **1k**, **1*l***, and **1n** have also been prepared by diazo transfer, but under different conditions. For preparation of compounds **1k** and **1*l***, see: Bachmann, S.; Fielenbach, D.; Jørgensen, K. A. *Org. Biomol. Chem.* **2004**, *2*, 3044. For preparation of compound **1n**, see: Lee, J. C.; Yuk, J. Y *Synth. Commun.* **1995**, *25*, 1511.

TABLE 4. Cycloaddition with Disubstituted Diazomethane Derivatives and Subsequent Acyl Migration[a]



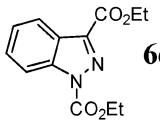
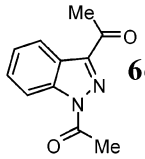
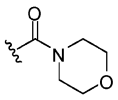
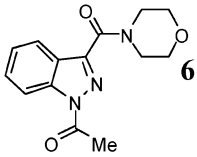
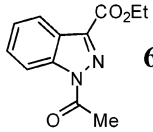
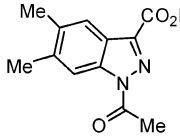
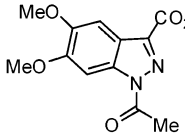
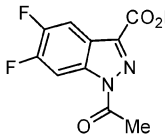
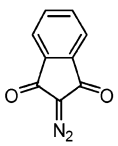
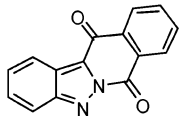
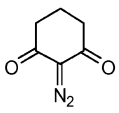
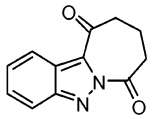
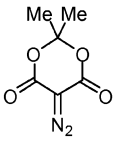
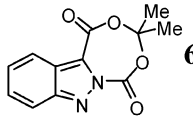
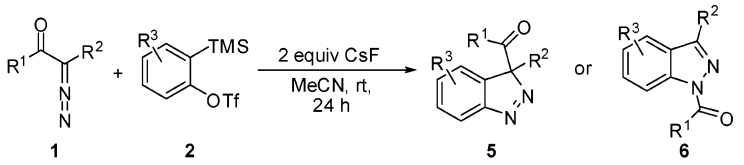
entry	diazo compound	R^1	R^2	benzyne precursor[b]	product	yield[c] (%)
1	**1d**	OEt	CO_2Et	**2a**	 **6da**	85
2	**1e**	Me	C(O)Me	**2a**	 **6ea**	97
3	**1f**	Me		**2a**	 **6fa**	83
4	**1g**	Me	CO_2Et	**2a**	 **6ga**	90
5	**1g**	Me	CO_2Et	**2b**	 **6gb**	85
6	**1g**	Me	CO_2Et	**2c**	 **6gc**	92
7	**1g**	Me	CO_2Et	**2e**	 **6ge**	complex mixture
8	**1h**			**2a**	 **6ha**	0
9	**1i**			**2a**	 **6ia**	0
10	**1j**			**2a**	 **6ja**	0

Table 4. (Continued)



entry	diazo compound	R^1	R^2	benzyne precursor[b]	product	yield[c] (%)
11	**1k**	OEt	Ph	**2a**	**5ka**	72
					6ka	25
12	**1k**	OEt	Ph	**2b**	**6kb**	55
13	**1k**	OEt	Ph	**2f**	**5kf**	44
14	**1l**	OEt	Bn	**2a**	**5la**	84
15	**1l**	OEt	Bn	**2f**	**5lf**	56
16	**1m**	Ph	Ph	**2a**	**6ma**	92
17	**1n**	OEt	$P(O)(OEt)_2$	**2a**	**4aa**	45[d]
18	**1o**			**2a**	**5oa**	87

[a] All reactions were carried out on approximately 0.3 mmol scale (based on the diazo compound) in 0.1 M concentration. [b] 1.1−1.2 equiv was used. [c] Isolated yields based on the diazo compound. [d] A 55% yield was obtained when 2.4 equiv of the benzyne precursor was used.

this hypothesis, compound **1m**[16] with a ketone moiety was studied. As expected, this compound reacted smoothly with the parent benzyne precursor **2a** to give exclusively the acyl migration product **6ma** in an excellent yield (Table 4, entry 16). This result further supports the conclusion that ketone carbonyls are more prone to migration than ester carbonyls.

The reactions of a couple other diazo compounds are also noteworthy. Triethyl diazophosphonoacetate (**1n**) reacted smoothly with benzyne precursor **2a**, but instead of obtaining either **5** or

(16) Compounds **1m** and **1o** were prepared according to a literature procedure, see: Javed, M. I.; Brewer, M. *Org. Lett.* **2007**, *9*, 1789.

6, we obtained the *N*-arylated indazole **4aa** in a 45% yield (Table 4, entry 17). Obviously, this cycloaddition reaction is accompanied with a loss of the phosphonate group, as well as further arylation by the benzyne. Although we are not sure at what stage the phosphonate group is lost, we have been able to increase the yield by adding more benzyne precursor **1a** to the reaction to be consistent with the apparent stoichiometry. Thus, running the same reaction with 2.4 equiv of **1a** resulted in an improved yield of 55%. We also studied the cycloaddition of diphenyldiazomethane **1o**,[16] which does not have any carbonyl groups on the diazo carbon. This compound reacted uneventfully to furnish the desired, unrearranged product in an 87% yield (Table 4, entry 18).

Conclusions

In summary, an efficient route to a variety of indazoles and their derivatives has been developed. It involves the reaction of a variety of diazo compounds with *o*-silylaryl triflates in the presence of CsF or TBAF to afford the corresponding [3+2] cycloadducts in good to excellent yields. Diazo compounds bearing a hydrogen undergo tautomerization to the corresponding 1*H*-indazoles. Use of an excess of the aryne precursor affords excellent yields of *N*-aryl-1*H*-indazoles. Diazo compounds with carbonyl groups attached to the diazo carbon undergo acyl migration to form the corresponding 1-acyl indazoles. This methodology provides a useful new route to indazoles, which should find application in the construction of molecules with interesting biological properties and pharmaceutical potential.

Experimental Section

General Procedure for Synthesis of the indazoles from Monosubstituted Diazo Compounds. To a solution of the *o*-silylaryl triflate (0.3 mmol) and the diazo compound (0.45 mmol) in THF (4 mL) at −78 °C was slowly added TBAF (0.36 mmol) with stirring. The reaction mixture was allowed to gradually warm up to room temperature and then stirred for an additional 10 h. The resultant solution was diluted with brine (20 mL) and extracted with diethyl ether (20 mL). The combined organic layers were dried over Na_2SO_4 or $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired 1*H*-indazole product.

Ethyl 1*H*-indazole-3-carboxylate (3aa): white solid; mp 132−134 °C (lit.[17] mp 130 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.88 (br s, 1 H), 8.21 (d, J = 7.8 Hz, 1 H), 7.83 (d, J = 8.4 Hz, 1 H), 7.47 (m, 1 H), 7.33 (m, 1 H), 4.57 (q, J = 7.2 Hz, 2 H), 1.47 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 141.5, 136.3, 127.2, 123.2, 122.3, 121.7, 111.5, 61.1, 14.4; HRMS (EI) calcd for $C_{10}H_{10}N_2O_2$ 190.0742, found 190.0748.

General Procedure for Synthesis of the *N*-Aryl Indazoles from Monosubstituted Diazo Compounds. To a solution of the *o*-silylaryl triflate (0.72 mmol) and the diazo compound (0.3 mmol) in MeCN (4 mL) was added CsF (1.2 mmol) in one portion. The reaction mixture was stirred at room temperature for 24 h. The resultant solution was diluted with brine (20 mL) and extracted with ethyl acetate (20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired product.

Ethyl 1-phenyl-1*H*-indazole-3-carboxylate (4aa): white solid; mp 112−113 °C (lit.[18] mp 112−114 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, J = 8.0, 0.8 Hz, 1 H), 7.66−7.73 (m, 3 H), 7.32−7.54 (m, 5 H), 4.54 (q, J = 7.2 Hz, 2 H), 1.48 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 140.4, 139.4, 137.2, 129.7, 128.2, 127.8, 124.6, 124.1, 123.8, 122.7, 111.1, 61.4, 14.7; IR ($CDCl_3$) 3058, 3045, 2978, 2934, 2897, 1725, 1593, 1478 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{14}N_2O_2$ 266.1055, found 266.1060.

General Procedure for Synthesis of the Indazoles from Disubstituted Diazo Compounds. To a solution of the *o*-silylaryl triflate (0.35 mmol) and the diazo compound (0.3 mmol) in MeCN (4 mL) was added CsF (0.6 mmol) in one portion. The reaction mixture was stirred at room temperature for 24 h. The resultant solution was diluted with brine (20 mL) and extracted with ethyl acetate (20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired product.

Ethyl 3-phenyl-3*H*-indazole-3-carboxylate (5ka): white solid; mp 58−59 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15−8.18 (m, 1 H), 7.86−7.89 (m, 1 H), 7.59−7.63 (m, 2 H), 7.35−7.38 (m, 3 H), 7.48−7.51 (m, 2 H), 4.20−4.27 (m, 2 H), 1.23 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 157.5, 137.7, 132.9, 130.4, 130.0, 128.9, 128.8, 127.3, 124.8, 122.1, 101.1, 62.7, 13.8; IR ($CDCl_3$) 3016, 2926, 2856, 1734, 1641 cm^{-1}; LRMS (EI) 210-(21), 180(38), 165(100), 152(51), 139(28), 115(27), 89(41), 82-(46); HRMS (EI) calcd for $C_{16}H_{14}N_2O_2$ 266.1055, found 266.1060.

Ethyl 3-phenyl-1*H*-indazole-1-carboxylate (6ka): white solid; mp 76−79 °C (some impurities present); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, J = 8.5 Hz, 1 H), 7.80−7.95 (m, 3 H), 7.38−7.58 (m, 5 H), 4.61 (q, J = 7.0 Hz, 2 H), 1.53 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.9, 150.6, 141.2, 131.6, 129.4, 129.1, 128.8 ,128.3, 124.3, 124.2, 121.4, 114.8, 64.3, 14.5; LRMS (EI) 266(100), 194(47), 165(16); HRMS (EI) calcd for $C_{16}H_{14}N_2O_2$ 266.1055, found 266.1060.

Acknowledgment. We are grateful to the National Institutes of Health and Kansas University Center of Excellence in Chemical Methodologies and Library Development (P50 GM069663) for their generous financial support. We also thank Dr. Arkady Ellern for the X-ray analysis of compound **6da**.

Supporting Information Available: Characterization of the final products, including full ^{1}H and ^{13}C NMR spectra, and the X-ray structure of compound **6da**, including a CIF file and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Dalla Croce, P. *Synthesis* **1984**, 982.