New Synthetic Applications of Aryllead Triacetates. *N*-Arylation of Azoles

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Treatment of a variety of azoles or their anions with *p*-tolyllead triacetate in the presence of copper(II) acetate afforded the corresponding *N*-aryl derivatives, normally in excellent yields. Room temperature arylation of an aminobenzimidazole derivative was chemoselectively directed to the amino group.

Introduction

The search for arylation methods is an attractive field for synthetic and mechanistic studies.[1] Recent research efforts have focused mainly on the use of organometallic compounds, among which arylpalladium species,[2] arylbismuth pentavalent derivatives,[3] and aryllead triacetates[4] are particularly important. Most of these studies have been directed toward *C*-arylation reactions, and *N*-arylation has remained relatively unexplored.

N-Arylazoles are significant compounds due to their biological activity. For example, some *N*-arylimidazoles are useful as phosphodiesterase III inhibitors.[5] A number of *N*-arylpyrroles and *N*-arylpyrazoles have antiinflammatory activity.[6] Both *N*-arylimidazoles and *N*-arylpyrazoles bearing suitable polyhydroxylic side chains lower blood LDL-cholesterol by inhibition of HMG-CoA reductase,[7] and 1-(polyfluorophenyl)imidazoles have potential application as inhibitors of other enzymes.[8] Some *N*-(*para*-substituted phenyl)pyrazoles and indoles related to the angiotensin II-1 antagonist L-158809[9] show *in vitro* binding and *in vivo* activity similar to that of the parent compound.[10] Some *N*-arylpyrazoles are also useful as antipsoriatic and antirheumatic agents.[11] *N*-Aryl-1,2,3-benzotriazoles like octrizole, a UV-screen, also have useful properties.[12] Furthermore, *N*-arylation has been used for the protection of the imidazole ring of histidine.[13]

In spite of this interest, the preparation of *N*-arylazoles is severely restricted because nitrogen heterocycles are not good substrates for the traditional arylation reagents. Thus, the Ullmann reaction[14] can only be performed using activated aryl halides, which requires harsh reaction conditions and very often gives low yields. Although recent developments like the use of microwave irradiation[15] and ultrasound-aided phase-transfer catalysis without solvent[16] have improved the results for certain substrates, the Ullmann and related reactions are still far from being a general solution to the problem of azole arylation. Several other arylating reagents have occasionally been reported to react with some azoles, including arynes,[17] diaryliodonium salts,[18] and organobismuth reagents,[3,19] and some examples of photochemical arylations are also known;[20] benzotriazole reacts with very activated aryl halides in the absence of catalysis.[21] The range of substrates employed in all these literature precedents is usually restricted to indole and its derivatives, and hence previous workers have often been forced to resort to indirect, multistep syntheses for the transformation of arylamines into *N*-arylazoles.[22] There is, therefore, a clear need for a general method that allows the efficient *N*-arylation of azoles and we give here our full report[23] of the use of aryllead triacetates for this purpose, using *p*-tolyllead triacetate[24b] as a model aryllead reagent.

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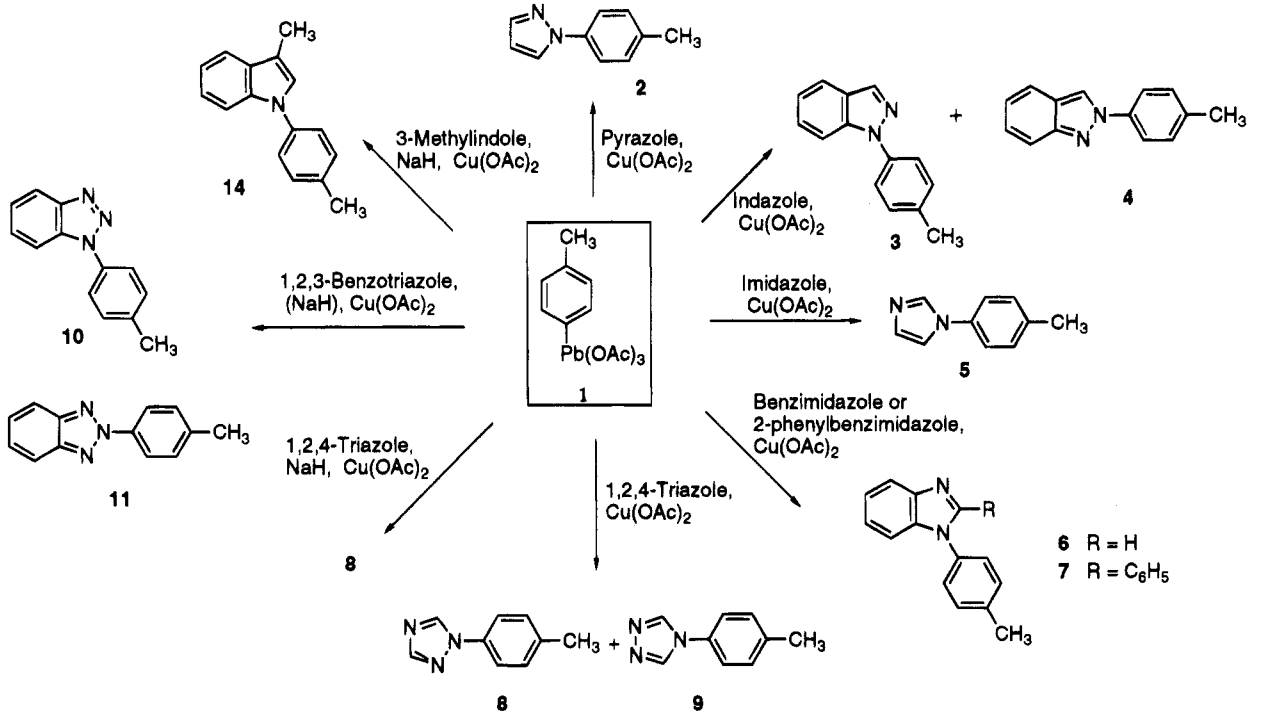
Table 1. Conditions and Yields of the *N*-Arylation Reactions of Azole and Azole Anions

entry	starting compound(s)	product(s)	yield/%[a]	conditions[b] time/h	temp/°C	solvent
1	pyrazole	**2**	86	4	90	CH_2Cl_2–DMF (2:1)
2	indazole	**3**	58	16	25	CH_2Cl_2
		4	29			
3	imidazole	**5**	82	6	90	CH_2Cl_2–DMF (2:1)
4	benzimidazole	**6**	98	4.5	90	CH_2Cl_2
5	benzimidazole-DPE	**6**	88	5.5	90	CH_2Cl_2
6	2-phenylbenzimidazole	**7**	75	4.5	90	CH_2Cl_2–DMF (10:1)
7	1,2,4-triazole	**8**	18	24	80	CH_2Cl_2–DMF (2:3)
		9	5			
8	1,2,4-triazole–NaH	**8**	81	24	85	CH_2Cl_2–DMF (6:1)
		9	0			
9	1,2,3-benzotriazole	**10**	23	38	140	CH_2Cl_2
		11	6			
10[c]	1,2,3-benzotriazole-NaH	**10**	14 (47)[d]	48	85	CH_2Cl_2
		11	2 (6)			
11[c]	3-methylindole–NaH	**14**	19 (24)[e]	16	50	CH_2Cl_2

[a] Yields are given for isolated, purified compounds. [b] 1.1 equiv of **1** was used in all cases, except for entry 8 (2.2 equiv). [c] The yields in parentheses are based on recovered starting material. [d] Together with 46% of tetrakis(*p*-tolyl)lead (**12**) and 8% of bis(1-benzotriazolyl)-methane (**13**). [e] Together with 50% of bis(*p*-tolyl) ether (**15**).

Scheme 1. Reactions between *p*-Tolyllead Triacetate 1 and Azole and Azole Anions



***N*-Arylation of Azoles by *p*-Tolyllead Triacetate.** Although aryllead triacetates[24] have been employed for the arylation of a variety of nucleophiles,[25-28] the only type of organic *N*-nucleophiles whose reactivity toward aryllead triacetates had been established prior to our work were arylamines.[29] As regards azoles, the only antecedent of their reactivity toward aryllead triacetates consisted on the failure of the attempted reaction between phenyllead triacetate and indole under the conditions previously employed for the arylation of aromatic amines.[29a-c]

As shown in Scheme 1 and Table 1, pyrazole, imidazole, and their benzo derivatives react cleanly with *p*-tolyllead

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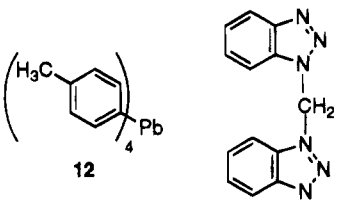
triacetate to give *N*-monoarylated derivatives in excellent yields. Typical reaction conditions involve reflux of a dichloromethane solution of the starting azole and a slight excess (1.1 equiv) of *p*-tolyllead triacetate, in the presence of a catalytic amount of copper(II) acetate, followed by workup with aqueous hydrogen sulfide to remove copper species. In the case of indazole (entry 2), the two expected arylation products **3** and **4** were isolated in a ratio **3**:**4** = 3:1, which is in agreement with the relative reactivities of both indazole tautomers, as determined in other reactions.[16,30] The arylations were only slightly sensitive to steric hindrance and electronic effects in the vicinity of the reacting nitrogen atom, as shown by comparison of the results obtained for benzimidazole (entry 4) and 2-phenylbenzimidazole (entry 6).

The results for 1,2,4-triazole (entry 7) and 1,2,3-benzotriazole (entry 9) were less satisfactory, probably due to the combined electron-withdrawing effects of two pyridine-like nitrogen atoms; the forcing conditions necessary for the arylation to take place led to complex mixtures, from which the desired arylation products **8**, **9** and **10**, **11** were isolated in only moderate yields (entries 7 and 9). Fortunately, the sodium derivative of 1,2,4-triazole, prepared by addition of a slight excess of sodium hydride to the starting material, reacted cleanly with **1**, yielding the 1-arylated derivative **8** as the only product in 81% yield. 1,2,3-Benzotriazole anion, however, is less reactive toward **1**, and their reaction could not be carried to completion. Also, due to the slow arylation, two more reaction products were isolated besides the desired *N*-arylated derivatives, namely tetrakis(*p*-tolyl)-lead **12**, presumably a decomposition product of **1**, and bis(1,2,3-benzotriazol-1-yl)methane **13**, probably formed in the reaction between the benzotriazole anion and the dichloromethane used as solvent. Identification of the two arylation products of 1,2,4-triazole (compounds **8** and **9**) was straightforward since the symmetry of **9** led to a single triazole resonance in its ^{1}H-NMR spectrum; a similar criterion, supported also by ^{13}C-NMR data, was applied to the distinction between **10** and **11**.

For the arylation of 3-methylindole, similar treatment of a solution of its anion with **1** led to the formation of an inseparable mixture of two reaction products, which were identified as the *N*-arylated indole **14** in moderate yield (19%, 24% based on recovered 3-methylindole) and bis(*p*-tolyl) ether (**15**), probably from oxidative decomposition of **1**. Previous attempts at arylation of indole with phenyllead triacetate had failed,[29a-c] but the reactivity of indoles toward organobismuth reagents was known. Indole itself yielded 3-phenylated derivatives as the main reaction products, while its anion gave 3,3-diphenyl derivatives[31] with two different organobismuth compounds. Similarly, 3-methylindole anions afforded the corresponding 3-arylated derivatives.[32] The latter substrate was *N*-phenylated in 21% yield under copper catalysis.[33]

As regards the mechanism of the azole arylation, it can be considered similar to the one proposed by Barton *et al.* for copper-catalyzed amine arylation by aryllead triacetates,[29b,c] since our arylations fulfill the following conditions: (a) No reaction takes place in the absence of copper species, and (b) the addition of large amounts of a radical trapping agent, namely 1,1-diphenylethylene (DPE) has little effect on the reaction (entry 5 of Table 1), thus excluding a free-radical mechanism.



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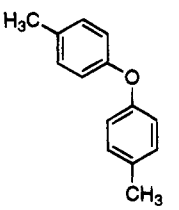

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Chemoselectivity Studies

The experimental conditions necessary for the arylation of azoles are harsher than those required for arylamines.[29a-c] Nevertheless, the question arose of whether treatment with *p*-tolyllead triacetate would allow chemoselective arylation of the amino group in aminoazole derivatives; 2-phenyl-1*H*-benzimidazol-6(5)-amine (**19**) was chosen as a model for these studies. This compound was prepared by reduction with stannous chloride in hydrochloric acid of the corresponding nitro derivative **18**, available by treatment of 2-phenylbenzimidazole (**16**)[34] with fuming nitric acid. The latter was a known reaction, although the very early date of the initial report prevented a full structural assignment, and 2-(4-nitrophenyl)benzimidazole was also considered as a possible structure for the nitration product of **16**.[35] Our spectral data confirm the structure **18**, since the expected signals for $C_{4(7)}$–H (7.78, d, J = 8.8 Hz), $C_{5(6)}$–H (8.15, dd, J = 8.8 and 2.2 Hz), and $C_{7(4)}$–H (8.24, d, J = 2.2 Hz) can be observed in its ^{1}H-NMR spectrum, and signals assignable to an aromatic AB system are absent. Alternatively, **18** could be prepared by oxidative cyclization of 2-(benzylideneamino)-4-nitroaniline (**17**) in refluxing nitrobenzene, thus providing independent confirmation of its structure. When the aminobenzimidazole **19** was treated with a slight excess of *p*-tolyllead triacetate at room temperature and in the presence of copper(II) acetate, arylation took place selectively on the amino group, yielding **20** as the only reaction product (Scheme 2). Therefore, aromatic amino groups can be chemoselectively arylated by **1** in the presence of a benzimidazole nitrogen atom.

Conclusion

The arylation of diazoles and triazoles or their anions by *p*-tolyllead triacetate compares very favorably with the Ullmann and related methods in that the conditions employed are much milder and the yields are usually excellent and reproducible. Furthermore, the wide range of aryllead triacetates now available[24] widens the scope of the arylation with respect to the Ullmann reaction, which works only with activated aryl halides. Other methods for azole arylation were previously known, but their use is restricted mainly to indole derivatives, where our method gives poor results. The arylation of aromatic

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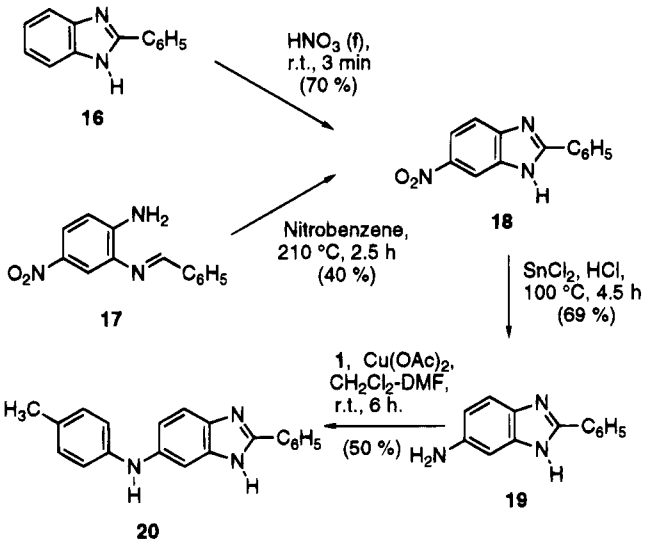
Scheme 2. Chemoselective Arylation of the Amino Group in 2-Phenyl-1*H*-benzimidazol-6(5)-amine by *p*-Tolyllead Triacetate



amino groups suffers no interference from azole nitrogen atoms, as shown by the transformation of 2-phenyl-1*H*-benzimidazol-6-amine (**19**) into 2-phenyl-6(5)-(*p*-tolylamino)-1*H*-benzimidazole (**20**).

Experimental Section

General. Melting points are uncorrected. IR spectra were recorded with all solid compounds compressed into KBr pellets and liquid compounds placed (neat or dissolved in the minimum amound of bromoform) between NaCl plates. NMR spectra were obtained at 250 or 300 MHz for ^{1}H and 75.4 or 62.9 MHz for ^{13}C with $CDCl_3$ and DMSO-d_6 as solvents. Mass spectra were obtained by ionization by electron impact at 70 eV; samples were introduced into the ionization chamber *via* gas chromatography. Combustion elemental analyses were determined by the Servicio de Microanálisis, Universidad Complutense. Reactions were monitored by thin layer chromatography, on aluminum plates coated with silica gel with fluorescent indicator. Solutions were dried with anhydrous Na_2SO_4 and evaporated under reduced pressure (water aspirator) in a rotary evaporator. Separations by flash chromatography were performed on silica gel (230–400 mesh). All reagents were of commercial quality and were used as received. *p*-Tolyllead triacetate was prepared according to reference 24b. The expression "petroleum ether" refers to the fraction boiling at 40–60 °C.

***N*-Arylation of Azoles. General Procedure.** A solution or suspension of the starting azole (0.37 to 0.84 mmol), *p*-tolyllead triacetate (1.1 equiv), and copper(II) acetate (10 mg) in CH_2Cl_2 (2–5 mL) was refluxed in a bath at the temperatures and for the times indicated in each case. CH_2Cl_2 slowly boiled off during heating, although in no case was the reaction allowed to evaporate to dryness. The green reaction mixture was diluted with $CHCl_3$ (20 mL), and the solution was poured onto 50 mL of dilute aqueous H_2S; the biphasic system was vigorously stirred for 1 h and filtered through Celite to remove the insoluble inorganic species. The pale yellow $CHCl_3$ layer was dried over Na_2SO_4 and evaporated, and the residue was chromatographed on silica gel using the mobile phase indicated in each case.

1-(*p*-Tolyl)pyrazole (2): yield, 86% after 4 h at 90 °C using CH_2Cl_2 (10 mL) and DMF (5 mL) as solvent and chromatography eluting with $CHCl_3$; mp 30–31 °C; IR (KBr) 3050, 2950, 1525, 1390 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.87 (d, 1H, J = 2.4 Hz); 7.70 (d, 1H, J = 1.8 Hz); 7.56 (d, 2H, J = 8.1 Hz); 7.25 (d, 2H, J = 8.1 Hz); 6.44 (m, 1H); 2.37 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 140.8; 138.0; 136.2; 129.9; 126.7; 119.2; 107.3; 20.9. Anal. Calcd for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.70. Found: C, 75.59; H, 6.35; N, 17.26.

1-(*p*-Tolyl)-1*H*-indazole (3) and 2-(*p*-tolyl)-2*H*-indazole (4): yield, 59% of **3** and 15% of **4** (88% overall) after 15 min at 65 °C and 16 h at rt and chromatography eluting with CH_2Cl_2.

Data for 3: mp 63–65 °C; IR (KBr) 3050, 2935, 1540 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.17 (d, 1H, J = 1.2 Hz); 7.77 (dt, 1H, J = 8.1 and 0.9 Hz); 7.70 (dq, 1H, J = 8.4 and 0.9 Hz); 7.59 (d, 2H, J = 8.4 Hz); 7.39 (td, 1H, J = 8.7 and 1.2); 7.31 (d, 2H, J = 8.4 Hz); 7.19 (td, 1H, J = 8.1 and 0.9 Hz); 2.42 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 138.7; 137.6; 136.4; 134.9; 129.8; 126.8; 125.0 ; 122.6; 121.2; 121.1; 110.25; 20.9. Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.80; N, 13.45. Found: C, 80.66; H, 6.09; N, 13.12.

Data for 4: mp 92–94 °C. IR (KBr) 3050, 2920, 1525 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.37 (d, 1H, J = 0.9 Hz); 7.81–7.76 (m, 3H); 7.70 (dt, 1H, J = 8.7 and 0.9 Hz); 7.34–7.28 (m, 3H); 7.11 (ddd, 1H, J = 8.7, 6.6, 0.9 Hz); 2.42 (s, 3H); ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 138.2; 137.8; 130.0; 126.6; 122.6; 122.2; 120.8; 120.2; 117.8; 21.0. Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.80; N, 13.45. Found: C, 80.46; H, 6.02; N, 13.09.

1-(*p*-Tolyl)imidazole (5): yield, 82% after 6 h at 90 °C, as an oil that was chromatographed on silica gel, eluting with $CHCl_3$; IR (NaCl) 3120, 3040, 2930, 1525, 1390 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.60–7.10 (m, 5H); 6.99 (m, 1H); 6.83 (m, 1H); 2.40 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 137.6; 130.3; 129.7; 121.4; 115.4; 20.8. Anal. Calcd for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.70. Found: C, 75.56; H, 6.40; N, 17.32.

1-(*p*-Tolyl)benzimidazole (6): yield, 98%, after 4.5 h at 90 °C, as an oil that was chromatographed on silica gel, eluting with CH_2Cl_2; IR (NaCl) 3050, 1520, 1485, 1450 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.07 (m, 1H); 7.79 (m, 1H); 7.42 (m, 1H); 7.26 (m, 6H); 2.44 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 144.1; 138.1; 133.6; 130.5; 123.8; 123.6; 122.7; 120.3; 110.5. Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.80; N, 13.45. Found: C, 80.37; H, 5.96; N, 13.11.

2-Phenyl-1-(*p*-tolyl)benzimidazole (7): yield, 75% after 4.5 h at 90 °C, using CH_2Cl_2 (2 mL) and DMF (0.5 mL) as the reaction medium, and chromatography eluting with petroleum ether–AcOEt (99:1); mp 95–97 °C; IR (KBr) 3040, 1600, 1505 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.88 (m, 1H); 7.58 (dd, 2H, J = 7.8 and 2.0 Hz); 7.34–7.12 (m, 6H); 7.31 (d, 2H, J = 8.4); 7.18 (d, 2H, J = 8.5 Hz); 2.44 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 152.4; 142.9; 138.5; 134.3; 130.9; 130.4; 129.4; 129.3; 128.2; 127.1; 126.4; 123.2; 122.8; 119.8; 110.5; 21.2. Anal. Calcd for $C_{20}H_{16}N_2$: C, 84.51; H, 5.63; N, 9.86. Found: C, 84.43; H, 5.51; N, 9.77.

1-(*p*-Tolyl)-1*H*-1,2,4-triazole (8) and 4-(*p*-tolyl)-4*H*-1,2,4-triazole (9): Yield, 18% of **8**, and 5% of **9** after 24 h at 80 °C and chromatography eluting with petroleum ether–ether (9:1).

Data for 8: mp 57–59 °C; IR (NaCl, $CHBr_3$) 1575, 1400 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.55 (s, 1H); 8.11 (s, 1H); 7.55 (d, 2H, J = 8.5 Hz); 7.31 (d, 2H, J = 8.5 Hz); 2.42 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$) δ 152.3; 140.6; 138.2; 134.6; 130.2; 119.9; 21.0. Anal. Calcd for $C_9H_9N_3$: C, 67.92; H, 5.66; N, 26.41. Found: C, 68.19; H, 5.89; N, 26.12.

Data for 9: oil; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.37 (s, 2H); 6.91 (d, 2H, J = 8.4 Hz,); 6.72 (d, 2H, J = 8.4 Hz); 2.55 (s, 3H).

1-(*p*-Tolyl)-1*H*-1,2,3-benzotriazole (10) and 2-(*p*-tolyl)-2*H*-1,2,3-benzotriazole (11): yield, 23% of **10** and 6% of **11** after 38 h at 140 °C in DMF and chromatography eluting with petroleum ether–ether (9:1).

Data for 10: mp 89–91 °C. IR (KBr) 1525, 1460 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.13 (d, 1H, J = 8.4 Hz); 7.72 (d, 1H, J = 8.4 Hz); 7.64 (d, 2H, J = 8.4 Hz); 7.53 (t, 1H, J = 8.4 Hz); 7.45–7.39 (m, 3H); 2.47 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 146.2; 138.7; 134.2; 132.1; 130.2; 127.9; 124.1; 122.7; 120.1; 110.2; 21.1. Anal. Calcd for $C_{13}H_{11}N_3$: C, 74.64; H, 5.26; N, 20.09. Found: C, 74.37; H, 5.34; N, 20.29.

Data for 11: mp 108–110 °C; IR (KBr) 1512, 1455 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 8.23 (d, 2H, J = 8.5 Hz); 7.93–7.89 (m, 2H); 7.41–7.37 (m, 2H); 7.34 (d, 2H, J = 8.5 Hz); 2.38

(s, 3H); ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 144.8; 139.1; 133.3; 129.9; 126.9; 120.4; 118.2; 21.1.

***N*-Arylation of Azole Anions. General Procedure.** A solution or suspension of the starting azole (0.38 to 2.10 mmol) in CH_2Cl_2 (1 to 5 mL) was added to a suspension of NaH (17 to 93 mg of a commercial 60% suspension in paraffin, prewashed with 2 × 10 mL of dry petroleum ether, 0.42 to 2.31 mmol of NaH) in CH_2Cl_2 (3 mL). After 10 min at rt, hydrogen evolution had ceased and a solution of *p*-tolyllead triacetate (0.34 to 2.31 mmol) and copper(II) acetate (10 mg) in CH_2Cl_2 (2 to 5 mL) was added. The reaction mixture was heated at the temperatures and for the times indicated in each case (CH_2Cl_2 slowly boiled off during heating, although in no case was the reaction allowed to evaporate to dryness) and was then cooled and diluted with $CHCl_3$ (20 mL). This solution was poured onto 50 mL of dilute aqueous H_2S, and the biphasic system was vigorously stirred for 1 h and filtered through Celite to remove the insoluble inorganic species. The $CHCl_3$ layer was dried over Na_2SO_4 and evaporated, and the residue was chromatographed on silica gel eluting with the solvent system indicated in each case.

Arylation of 1,2,4-Triazole. Starting from 50 mg (0.72 mmol) of 1,2,4-triazole, 93 mg (81%) of compound **8** (see data above) were obtained after 24 h at 85 °C and column chromatography eluting with CH_2Cl_2.

Arylation of 1,2,3-Benzotriazole. Starting from 250 mg (2.10 mmol) of benzotriazole, the following compounds were obtained: 177 mg of recovered starting material; 60 mg (14%, 47% based on recovered starting material) of **10**, 7 mg (2%, 6% based on recovered starting material) of **11**, 150 mg (46%) of **12**, and 20 mg (8%) of **13** after 48 h at 85 °C and chromatography eluting with a gradient from (99:1) petroleum ether–CH_2Cl_2 to neat CH_2Cl_2.

Data for 12: mp 240–242 °C, lit.[36] 238–239 °C.

Data for 13: mp 194–195 °C; lit.[37] 192–193 °C. For spectral data, see reference 38.

Arylation of 3-Methylindole. Starting from 30 mg (0.38 mmol) of 3-methylindole, 35 mg of a mixture of **14** and bis(*p*-tolyl) ether **15** (**14**:**15** = 1:1.35 by ^{1}H-NMR, 19% of **14**, 24% based on recovered starting material) and 10 mg of recovered 3-methylindole were obtained after 16 h at 50 °C. Silica gel column chromatography, eluting with neat petroleum ether, allowed the isolation of a sample of pure **15** from the mixture.[39]

Data for 14: ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.61 (dd, 1H, J = 7.0 and 1.5 Hz); 7.52 (dd, 1H, J = 6.9 and 1.3 Hz); 7.36 (d, 2H, J = 8.4 Hz); 7.29 (dd, 2H, J = 8.4 Hz); 7.23 (td, 1H, J = 7.0 and 1.5 Hz); *ca.* 7.10 (s, 1H, partially hidden by a signal of compound **15**); 7.20 (td, 1H, J = 6.7 and 1.3 Hz); 2.42 (s, 3H); 2.38 (d, 3H, J = 1.0 Hz); ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 137.4; 135.9; 135.7; 130.0; 129.5; 125.5; 123.9; 122.1; 119.5; 119.0; 112.3; 110.3; 21.0; 9.6. MS, *m/z* (%) 221 (M^+, 100); 204 (14); 128 (12); 91 (5); 77 (15); 65 (10); 51 (8).

2-Phenyl-6(5)-nitro-1*H*-benzimidazole (18). Method A. A solution of 2-phenylbenzimidazole **16**[34] (10 g, 51.5 mmol) in fuming nitric acid (25 mL) was stirred at rt for 3 min. The reaction mixture was poured on crushed ice (150 g) and the yellow precipitate was filtered and washed with 1% aqueous NH_4OH. The solid, containing **18** and some unreacted **16**, was dissolved in the minimum amount of refluxing AcOH (*ca.* 20 mL), and this solution was poured on crushed ice (100 g). The precipitate of crude **18** was filtered and recrystallized from EtOH, yielding 8.62 g (70%) of yellow needles of **18**: mp 213–215 °C (EtOH), lit.[34] 196 °C; IR (KBr) 3500–2400, 1630, 1510, 1340 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 300 MHz) δ 8.49 (br s, 1H); 8.24 (d, 1H, J = 2.2 Hz); 8.35–8.20 (m, 1H); 8.15 (dd, 1H, J = 8.8 and 2.2 Hz); 7.78 (br d, 1H, J = 8.8 Hz); 7.66–7.58 (m, 4H). Anal. Calcd for $C_{13}H_9N_3O_2$: C, 65.27; H, 3.76; N, 17.57. Found: C, 65.03; H, 3.71; N, 17.49.

Method B. A solution of 4-nitro-1,2-phenylenediamine (550 mg, 3.6 mmol) and benzaldehyde (0.38, 3.6 mmol) in EtOH (10 mL) was refluxed for 90 min and then stirred at rt for 12 h. The yellow precipitate of 2-(benzylideneamino)-4-nitroaniline (**17**) (650 mg) was filtered and washed with EtOH. A part of this precipitate (500 mg) was dissolved in nitrobenzene (4.5 mL) and refluxed for 2.5 h in an oil bath at 210 °C. A precipitate was formed, which was filtered, joined with the residue left by evaporation of nitrobenzene under reduced pressure, and purified by column chromatography on silica gel, eluting with $CHCl_3$, followed by recrystallization from EtOH. Yield, 200 mg of **18** (40%).

2-Phenyl-1*H*-benzimidazol-6(5)-amine (19). A suspension of **18** (2 g, 8.36 mmol) and stannous chloride dihydrate (7.66 g, 40 mmol of $SnCl_2$) in 35% aqueous HCl (20 mL) was heated at 100 °C for 4.5 h, while magnetically stirred. The cooled reaction mixture was basified with 20% aqueous NaOH and extracted with $CHCl_3$ (4 × 80 mL). Concentration gave a residue which was washed with AcOEt (15 mL), leaving 1.20 g (69%) of pure amine **19**: mp 291–293 °C (AcOEt); IR (KBr) 3470, 3380, 3300–2300, 1635, 1610 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 270 MHz) δ 8.34 (s, 1H); 8.10 (dd, 2H, J = 7.1 and 1.2 Hz); 7.60–7.25 (m, 3H); 7.28 (d, 1H, J = 8.5 Hz); 6.70 (br s, 1H); 6.55 (dd, 1H, J = 8.5 and 1.6 Hz); 4.91 (s, 2H). Anal. Calcd for $C_{13}H_{11}N_3$: C, 74.64; H, 5.26; N, 20.09. Found: C, 74.58; H, 5.19; N, 20.01.

2-Phenyl-6(5)-(*p*-tolylamino)benzimidazole (20). A solution of amine **19** (380 mg, 1.81 mmol), *p*-tolyllead triacetate (1.12 g, 2.35 mmol), and copper(II) acetate (40 mg) in CH_2Cl_2 (15 mL) and DMF (20 mL) was stirred at rt for 6 h. The reaction mixture was filtered through a layer of alumina, the filtrate was evaporated, and the residue was purified by chromatography on silica gel, eluting with a gradient from 8:2 AcOEt–petroleum ether to neat AcOEt, yielding 265 mg (50%) of **20**. Alternatively, the solution was poured onto 50 mL of dilute aqueous H_2S and the biphasic system was vigorously stirred for 1 h and filtered through Celite to remove the insoluble inorganic species. The aqueous phase was extracted with $CHCl_3$ (3 × 50 mL), and the combined organic layers were dried over Na_2SO_4 and evaporated. The residue was purified by chromatography as above, affording essentially the same yield of **20**. IR (KBr) 3370, 3100–2700, 1610, 1510 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 300 MHz) δ 8.11 (dd, 1H, J = 7.1 and 1.5 Hz); 7.96 (brs, 1H); 7.58–7.44 (m, 5H); 7.23 (brs, 1H); 7.06 (d, 2H, J = 8.7 Hz); 7.00 (d, 2H, J = 8.6 Hz); 6.95 (dd, 1H, J = 8.6 and 1.5 Hz); 2.25 (s, 3H, CH_3). Anal. Calcd for $C_{20}H_{17}N_3$: C, 80.26; H, 5.68; N, 14.04. Found: C, 80.14; H, 5.53; N, 14.09.

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(39) Compound **15**, which was identified by its NMR and mass spectral data, is commercially available (Aldrich Chemical Co.).