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N-ARYLATION OF AZOLES AND THEIR BENZO DERIVATIVES BY *p*-TOLYLLEAD TRIACETATE

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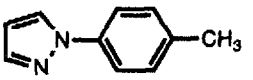
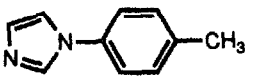
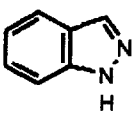
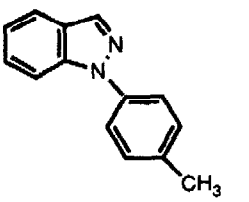
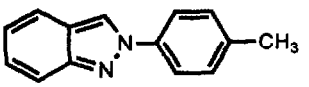
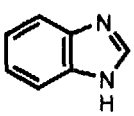
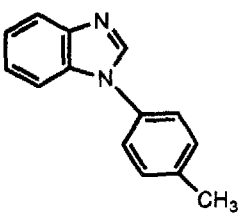
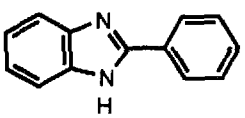
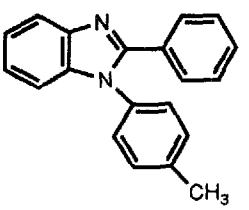
Abstract. *The N-arylation of a variety of azoles and their benzo derivatives was achieved by treatment at 90-100 °C with p-tolyllead triacetate in the presence of copper (II) acetate.*

The development of methods for the mild and efficient arylation of organic compounds continues to be an important synthetic challenge[1]. Among the recently described reagents, aryllead (IV) triacetates[2] are very useful for the C-arylation of a variety of substrates[3-5]. These reagents, like arylbismuth derivatives[1,6], act as aryl cation equivalents and effect the arylation of certain types of carbon atoms under mild conditions. It has been recently shown that other nucleophiles, such as iodide and azide anions[7], are also able to displace lead from aryllead triacetates.

Although no reaction occurs when amines are treated with aryllead triacetate alone, the discovery that copper species catalyze the reaction betwen amines and pentavalent organobismuth reagents[8] and the well known similarities in the chemical behaviour of organobismuth and organolead compounds led Barton *et al.* to investigate the effect of copper catalysis on the arylation of amines by aryllead reagents. Their results[9,10] show that addition of a small amount of copper (II) allows the room-temperature phenylation of amines with *p*-tolyllead triacetate.

Arylation of heterocyclic nitrogen is a long-standing problem, which is far from being satisfactorily solved. Traditional procedures, such as the Ulmann reaction[11], although useful for reactions starting from activated aryl halides[12], usually require harsh experimental conditions and very often give poor yields. Other procedures, such as the use of arynes[13], diaryliodonium salts[14], photochemical reactions[15] and organobismuth reagents[16] have also been reported, but the yields described are usually moderate and the scope of the examples known is limited, since these studies have commonly been restricted to indole-related substrates. Therefore, the preparation of N-arylated heterocycles has often relied on multi-step syntheses where the heterocyclic unit was built over an aromatic amino group[17].

Starting cmpd.	Eqs. of 1	Time/h	Temp./°C	Solvent	Yield/%[a]	Product(s)
	1.1	4	90	CH_2Cl_2-DMF(2:1)	86	
	1.1	6	90	CH_2Cl_2-DMF(2:1)	82	
	1.1	16	25	CH_2Cl_2	58	
					29	
	1.5	4.5	95	CH_2Cl_2-DMF(10:1)	98	
	1.5	4.5	90	CH_2Cl_2-DMF(10:1)	75	

[a] Yields are given for isolated, purified products

To our knowledge, the only results reported so far on the use of organolead reagents for the N-arylation of aromatic heterocycles are the failure of indole and carbazole to react under the reaction conditions employed for the arylation of aromatic amines[9]. Therefore, we wish to describe here our findings on this subject, proving that a variety of aromatic heterocycles can be efficiently N-arylated by these reagents. As shown in Table 1, treatment of either pyrazole and imidazole or their benzo derivatives, *i.e*, indazole and benzimidazole, with 1.1-1.5 equivalents of *p*-tolyllead triacetate (**1**)[2b], in the presence of a catalytic amount of copper diacetate, typically at 90-100 °C for 4-6 h, except in the case of indazole, which reacted at room temperature, and at a scale varying between 0.25 and 2.5 mmole of the starting azole, afforded excellent yields of the desired N-aryl derivatives. A single reaction product was obtained in all cases except for indazole, which gave a 3:1 mixture of the expected 1- and 2-substituted derivatives, this ratio being in agreement with the general features of indazole reactivity[18]. Steric hindrance and electronic effects in the vicinity of the reacting heterocyclic nitrogen caused the arylation to be only slightly less effective, as shown by the comparison of the results obtained for benzimidazole and 2-phenylbenzimidazole (entries 3 and 4 of Table 1, respectively).

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