Microwave-Assisted Molybdenum-Catalyzed Reductive Cyclization of *o*-Nitrobenzylidene Amines to 2-Aryl-2*H*-indazoles

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Received: 29.03.2013; Accepted after revision: 20.05.2013

Abstract: The reductive cyclization of *o*-nitrobenzylidene amines under microwave conditions employing $MoO_2Cl_2(dmf)_2$ as catalyst and Ph_3P as reducing agent delivers 2-aryl-2*H*-indazoles with yields ranging from 61–92%.

Key words: catalysis, cyclization, indazoles, molybdenum, Schiff bases

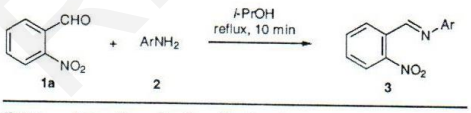
Indazoles are an important class of heterocyclic compounds that possess diverse biological and pharmacological activities, including anti-inflammatory, antitumor, antiviral, antidepressant, and contraceptive activities.[1] It is thus not surprising that a number of methods for the preparation of indazoles exist.[2] However, the majority has been developed for the preparation of 1*H*-indazoles. The number of approaches to 2*H*-indazoles is still scarce. Among the classical methods for the preparation of 2*H*-indazoles are the unselective N-arylation and N-alkylation of indazoles,[3] the reductive cyclization of secondary 2-nitrobenzylamines with Sn, $SnCl_2$, Zn, $TiCl_4$/Zn, and Fe[4] or under electrochemical conditions,[5] as well as the reductive cyclization of *o*-nitrobenzylidene amines with an excess of $(EtO)_3P$.[6]

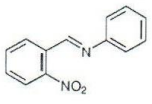
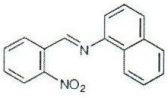
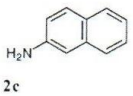
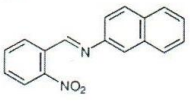
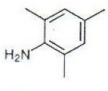
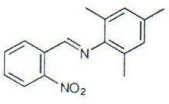
Recently, a few methods for the transition-metal-catalyzed synthesis of 2*H*-indazoles have been reported. Among them are the palladium-catalyzed reaction between 2-halophenyl acetylenes and hydrazines,[7] the palladium-catalyzed intramolecular amination of *N*-aryl-*N*-(*o*-bromobenzyl)hydrazines,[8] the iron-catalyzed N,N-bond formation of 2-azidophenyl ketoximes,[9] the copper-catalyzed reaction of 2-bromobenzaldehydes with primary amines and NaN_3,[10] the copper-catalyzed reaction of 2-azidobenzaldehydes and anilines,[11] and the palladium-catalyzed reaction of 2-nitrobenzylidene amines with CO in the presence of $SnCl_2$ under high pressure.[12] However, most of them suffer from some drawbacks, such as limited substrate scope, requirement for expensive catalysts and ligands, long reaction times, and unsatisfactory yields. This is why the development of new methods for the preparation of 2*H*-indazoles based on catalytic transformations is subject to current research.

Here, we report the first molybdenum-catalyzed synthesis of the 2*H*-indazole skeleton. The highly selective and high-yielding approach towards the synthesis of 2-aryl-2*H*-indazoles is based on the reductive heterocyclization of easily available *o*-nitrobenzylidene amines using a combination of $MoO_2Cl_2(dmf)_2$ as a catalyst [13] and Ph_3P as a reducing agent under several conditions.

The synthesis of the substrates, the *o*-nitrobenzylidene amines **3a–m** could easily be achieved by heating equimolar amounts of *o*-nitrobenzaldehyde (**1a**) and aromatic amines **2a–m** in *i*-PrOH (Table 1). The Schiff bases were obtained in crystalline form and purified by flash chromatography to deliver the compounds in analytically pure form with yields in the range between 84–97%.[14]

Table 1 Synthesis of 2-Nitrobenzylidene Amines **3a–m**



Entry	Aromatic amine **2**	Product **3**	Yield (%)[a]
1	 **2a**	 **3a**	90
2	 **2b**	 **3b**	97
3	 **2c**	 **3c**	95
4	 **2d**	 **3d**	90

SYNLETT 2013, 24, 1573–1577
Advanced online publication: 27.06.2013
DOI: 10.1055/s-0033-1339195; Art ID: ST-2013-D0283-L