JOC Article

Synthesis of Functionalized Nitroarylmagnesium Halides via an Iodine−Magnesium Exchange

Ioannis Sapountzis, Henry Dube, Robert Lewis, Nina Gommermann, and Paul Knochel*

Department Chemie, Ludwig-Maximilians-University, Butenandtstrasse 5-13, 81377 Munich, Germany

paul.knochel@cup.uni-muenchen.de

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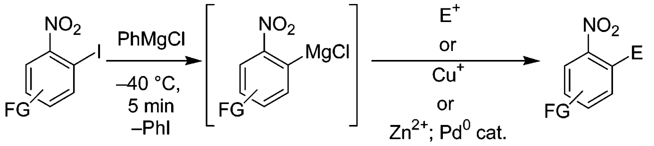

Various nitro-substituted aryl and heteroaryl iodides undergo an iodine−magnesium exchange reaction when treated with PhMgCl leading to nitro-containing magnesium organometallics. These Grignard reagents display an excellent stability at temperatures below −40 °C and do not undergo electron-transfer reactions. They react as expected with various electrophiles.

Introduction

Nitro compounds are key intermediates in organic synthesis. They are part-structures of numerous fine chemicals, dyes, high-energy materials, and biologically active substances. Also, many nitrogen substituents in an aromatic molecule are introduced by nitration,[1] and their easy transformation to a plethora of derivatives led to the application of nitro chemistry to several total syntheses.[2] The reduction of a nitro group to an amino function is also possible using a variety of catalysts and reagents.[3]

This high significance of the nitro group has made it an attractive target for organometallic chemists, but only a few successful attempts to prepare organometallics bearing a nitro function have been reported.[4] Most often, the metal of choice was lithium, which is precluding the presence of many functional groups and requires very low reaction temperatures (typically −100 °C) for the halide−lithium exchange. The direct oxidative addition of Mg and Zn into a carbon−halogen bond without reducing the nitro group could not be achieved.[5] The nitro group may prevent the oxidative addition by coordinating to the metal surface or by inhibiting electron-transfer reactions to the σ^*(C−X) orbitals.[6] Despite these unsuccessful attempts, nitro compounds have found numerous applications in organometallic chemistry as electrophiles. Several synthetically useful procedures have been reported, such as the 1,4- or 1,6-addition of alkylmagnesium halides,[7] the vicarious nucleophilic substitution of stabilized α-chlorocarbanions,[8] or the Bartoli indole synthesis.[9,10] Further applications are found in the selective 1,4-addition of carbanions to nitroalkenes.[11]

Recently, we found that the preparation of functionalized Grignard reagents through a halogen−magnesium exchange reaction enables the formation of a variety of new functionalized organometallic compounds.[12] Functional groups, which reacted with other organomagne-

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[1] Ono, N. *The nitro group in organic synthesis*; Wiley-VCH: New York, 2001.

[2] (a) Bondoch, J.; Sole, D.; Rubio, S. G.; Bosch, J. *J. Am. Chem. Soc.* **1997**, *119*, 7230. (b) Sole, D.; Bondoch, J.; Rubio, S. G.; Peidro, E.; Bosch, J. *Angew. Chem.* **1999**, *111*, 408; *Angew. Chem., Int. Ed.* **1999**, *38*, 395. (c) Sole, D.; Bonjoch, J.; Rubio, S. G.; Peidro, E.; Bosch, J. *Chem. Eur. J.* **2000**, *6*, 655. (d) Szantay, C.; Balogh, Z. K.; Moldvai, I.; Szantay, C.; Major, E. T.; Blasko, G. *Tetrahedron* **1996**, *52*, 11053.

[3] Ono, N. *The nitro group in organic synthesis*; Wiley-VCH: New York, 2001; pp 170−172 and literature cited herein.

[4] (a) Tucker, C. E.; Majid, T. N.; Knochel, P. *J. Am. Chem. Soc.* **1992**, *114*, 3983. (b) Cameron, J. F.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1991**, *113*, 4303. (c) Wiriyachitra, P.; Falcone, S. J.; Cava, M. P. *J. Org. Chem.* **1979**, *44*, 3957. (d) Köbrich, G.; Buck, P. *Chem. Ber.* **1970**, *103*, 1412. (e) Buck, P.; Gleiter, R.; Köbrich, G. *Chem. Ber.* **1970**, *103*, 1431 and references cited herein.

[5] Knochel, P. In *Metal-catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998.

[6] (a) Richey, H. G., Jr. *Grignard Reagents*; Wiley: New York, 2000. (b) Kharasch, M. S.; Reinmuth, O. *Grignard Reactions of Nonmetallic Substances*; Prentice-Hall: New York, 1954. (c) Hamdouchi, C.; Walborsky, H. M. In *Handbook of Grignard-Reagents*; Silverman, G. S., Rakita, P. E., Eds.; Marcel Dekker: New York, 1996; pp 145−218.

[7] (a) Severin, T. *Angew. Chem.* **1958**, *70*, 164. (b) Severin, T.; Adam, M. *Chem. Ber.* **1964**, *97*, 186. (c) Bartoli, G. *Acc. Chem. Res.* **1984**, *17*, 109.

[8] (a) Makosza, M.; Winiarski, J. *Acc. Chem. Res.* **1987**, *20*, 282. (b) Makosza, M. *Synthesis* **1991**, 103.

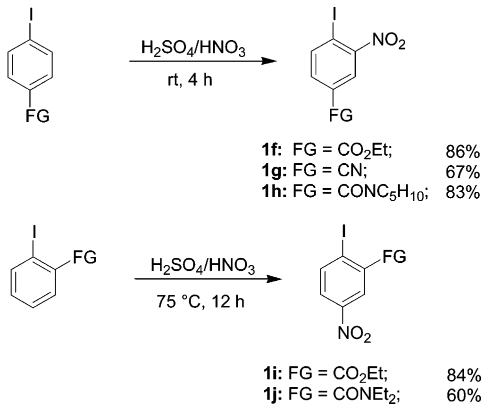
[9] Bartoli, G.; Palmieri, G.; Bosco, M.; Dalpozzo, R. *Tetrahedron Lett.* **1989,** *30,* 2129.

[10] For a highlight on nitro compounds and Grignard reagents see: Ricci, A.; Fochi, M. *Angew. Chem., Int. Ed.* **2003,** *42,* 1444.

[11] (a) Yao, C.-F.; Kao, K.-H.; Liu, J.-T.; Chu, C.-M.; Wang, Y.; Chen, W.-C.; Lin, Y.-M.; Lin, W.-W.; Yan, M.-C.; Liu, J.-Y.; Chuang, M.-C.; Shiue, J.-L. *Tetrahedron* **1998**, *54*, 791−822. (b) Ashwood, M. S.; Bell, L. A.; Houghton, P. G.; Wright, S. H. B. *Synthesis* **1988**, 379−81.

10.1021/jo048132o CCC: $30.25

SCHEME 1



1f: FG = CO_2Et; 86%
1g: FG = CN; 67%
1h: FG = $CONC_5H_{10}$; 83%

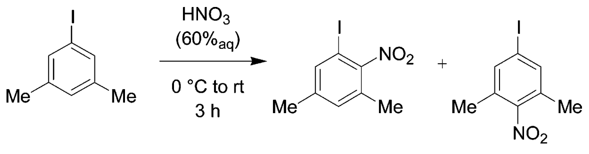
1i: FG = CO_2Et; 84%
1j: FG = $CONEt_2$; 60%

sium reagents, were tolerated at low temperatures. By using PhMgCl for the performance of the I/Mg exchange, aryl iodides bearing a nitro group in the ortho position could be converted in the corresponding *o*-nitro-substituted Grignard reagents.[13] Herein we wish to describe the full details of the selective formation of nitro-substituted aromatic Grignard reagents. Moreover, the application of these Grignard reagents in transition-metal catalyzed and mediated reactions is described. The extension to the preparation of *m*- and *p*-nitroarenes is also outlined.

Results and Discussion

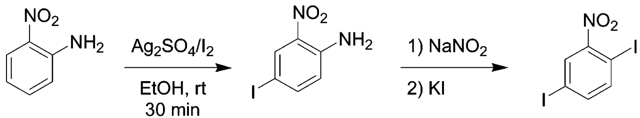
Preparation of Functionalized Iodonitrobenzenes (1). Only a few functionalized iodonitrobenzenes are commercially available, in particular 2-iodonitrobenzene (**1a**), 2,4-dinitroiodobenzene (**1b**), 3-iodo-4-nitroanisole (**1c**), 2-iodo-4-nitroaniline (**1d**), and 2,6-diiodo-4-nitrophenol (**1e**). All other derivatives were prepared according to literature procedures. The most general approach was the nitration of functionalized iodobenzenes. In the case of an electron-withdrawing group in the para position of the arene, like an ester, a cyano function, or an amide, the nitration occurred at ambient temperature under standard reaction conditions using a mixture of concentrated nitric acid and sulfuric acid, leading to compounds **1f**–**h** in good yields (Scheme 1). The nitration of ortho-functionalized iodobenzenes was performed at elevated temperatures (75 °C) and with longer reaction times (12 h) leading to the nitrated substrates **1i** and **1j** in good yields.

SCHEME 2



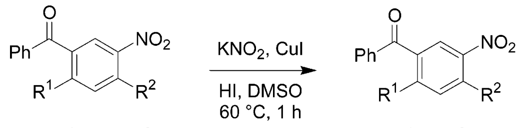
2 **1k**: 46% **1l:** 42%

SCHEME 3



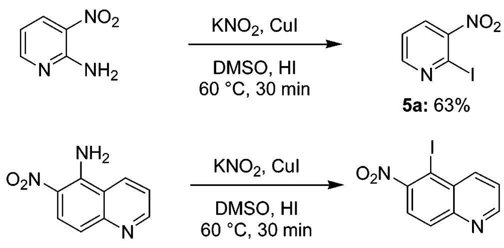
3: 80% **1m:** 95%

SCHEME 4



4a: R^1=NH_2, R^2=H
4b: R^1=H, R^2=NH_2
1n: R^1=I, R^2=H 90%
1o: R^1=H, R^2=I 94%

SCHEME 5



5a: 63%
5b: 84%

The preparation of less electron-poor nitrobenzenes required milder conditions since the above-mentioned conditions led to oxidative decomposition of these substrates. Thus, the nitration of 3,5-dimethyliodobenzene (**2**) with nitric acid $(60\%_{aq})$ gave both possible regioisomers **1k** and ***1l*** in 46% and 42% isolated yield (Scheme 2).

Unfortunately, the nitration of commercially available 1,4-diiodobenzene was not possible. Therefore, a sequential approach of iodination and Sandmeyer reaction was used to synthesize compound **1m**, as outlined in Scheme 3. First, a selective iodination of 2-nitroaniline at the 4-position was carried out with Ag_2SO_4/I_2,[14] leading to compound **3**, which was converted subsequently to 2,5-diiodonitrobenzene (**1m**) in a second step by diazotisation and replacement of the diazonium group with iodine, using KI in 95% yield (Scheme 3).

Finally, a modified Sandmeyer reaction developed by Baik and Wong[15] allowed the selective conversion of amino-nitrobenzophenones **4a**,**b** into the corresponding iodides **1n** and **1o**, as shown in Scheme 4. Standard diazotization and subsequent reaction with KI led to lower yields.

Similarly, the synthesis of the two nitro-functionalized heterocyclic iodides **5a** and **5b** was carried out using the same conditions as mentioned above (Scheme 5).

Finally, the iodination of 4-nitrophenol **6** led to a mixture of mono- and diiodinated products **1p** and **1e** which were easily separated by column chromatography. Conversion of the phenols **1p**,**e** under standard conditions furnished tosylates **1q** and **1r** in good yields (Scheme 6).

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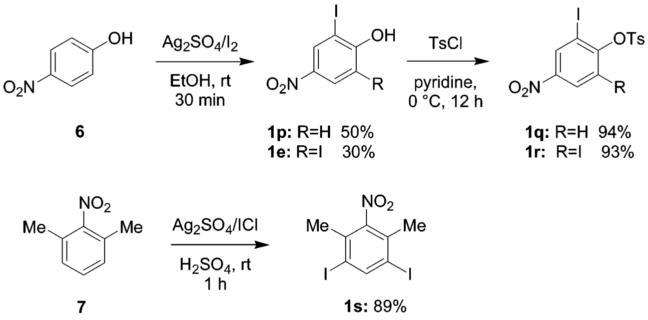
(12) (a) Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem.* **2003**, *115,* 4438; *Angew. Chem.*, *Int. Ed.* **2003**, *42*, 4302. (b) Boymond, L.; Rottländer, M.; Cahiez, G.; Knochel, P. *Angew. Chem.* **1998**, *110*, 1801; *Angew. Chem.*, *Int. Ed. Engl.* **1998**, *37*, 1701. (c) Jensen, A. E.; Dohle, W.; Sapountzis, I.; Lindsay, D. M.; Vu, V. A.; Knochel, P. *Synthesis*, **2002**, 565–569. (d) Krasovskiy, A.; Knochel P. *Angew. Chem.* **2004**, *116*, 3396; *Angew. Chem.*, *Int. Ed.* **2004**, *43*, 3333. For the preparation of functionalized Grignard reagents using lithium trialkyl-magnesiates, see: (a) Oshima, K. *J. Organomet. Chem.* **1999**, *575*, 1. (b) Kitagawa, K.; Inoue, A.; Shinokubo, H.; Oshima, K. *Angew. Chem.* **2000**, *112*, 2594; *Angew. Chem.*, *Int. Ed.* **2000**, *39*, 2481.

(13) Sapountzis, I.; Knochel, P. *Angew. Chem.* **2002**, *114*, 1680–1681; *Angew. Chem.*, *Int. Ed.* **2002**, *41*, 1610–1611.

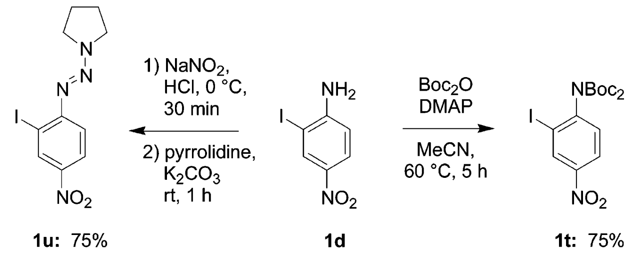
(14) Sy, W.-W. *Synth. Commun.* **1992**, *22*, 3215.

(15) Baik, W. P.; Kim, J. M.; Kim, Y. S.; Yoon, C. H.; Kim, S. J.; Lee, S. W. PCT Int. Appl. WO 2001-KR1586, 2002.

SCHEME 6



SCHEME 7



The iodination of 1,3-dimethyl-2-nitrobenzene (**7**) with the very active electrophilic iodination reagent, prepared in situ from ICl and Ag_2SO_4, provided diiodo compound **1s** in excellent yield (Scheme 6).[16] 2-Iodo-4-nitroaniline (**1d**) was converted into the di-Boc-protected aniline **1t**[17]and into its triazene derivative **1u**[18] under standard conditions (Scheme 7).

Preparation of Functionalized *o*-Nitroarylmagnesium Halides 8 via an Iodine−Magnesium Exchange Reaction. Reactions with Aldehydes. In a preliminary experiment, 2-iodonitrobenzene (**1a**) was treated with PhMgCl (1.1 equiv) in THF at −40 °C. A complete iodine−magnesium exchange was observed within 5 min, as indicated by GC analysis of the reaction mixture. The resulting nitro-substituted Grignard reagent **8a** reacted with benzaldehyde (**10a**, 1.5 equiv) within 30 min at −40 °C, leading to the expected benzhydryl alcohol **9a** in 87% isolated yield (entry 1, Table 1). A variety of functional groups including an ester, amide, cyano, and methoxy, as well as additional nitro or iodo functionalities, were tolerated, allowing the synthesis of a broad range of functionalized *o*-nitro-substituted arylmagnesium species (**8b**−**i**). These compounds reacted in good to excellent yields with aliphatic and aromatic aldehydes **10** (Scheme 8 and Table 1).

As shown in Table 1 a variety of nitro-substituted benzylic alcohols could be prepared with this method. Remarkably, a fast iodine−magnesium exchange was observed for 2,5-dinitroiodobenzene (**1b**). The I/Mg exchange was complete within 30 s at −40 °C. A smooth reaction was observed with aldehydes **10**, despite the presence of two nitro groups in the Grignard reagent, leading to alcohols **9b** and **9c** in 81% and 74% yield, respectively (entries 2 and 3 of Table 1). Substrates with strongly electron-donating functional groups, like a methoxy group in **1c** or like the two methyl substituents in compound **1k**, underwent a fast exchange reaction (<15 min for the exchange reaction), and the magnesiated products **8c** and **8g** were trapped with benzaldehyde (**10a**) in good yields (entries 4 and 11). Electron-withdrawing substituents such as an ester in **8d**, an amide in **8f**, and a cyano group in **8e** were also well tolerated under these reaction conditions, furnishing the addition products **9f**−**j** in good to excellent yields (entries 6−10). Remarkably, with 2,5-diiodonitrobenzene (**1m**), only the *o*-iodine atom underwent an iodine−magnesium exchange, furnishing after reaction with benzaldehyde (**10a**) or hexanal (**10c**) the corresponding alcohols ***9l*** and **9m** in 89% and 86% yield (entries 12 and 13). This selectivity can be explained by a chelation of the nitro functionality to the magnesium center. Electronic and inductive effects should also favor the *o*-iodine−magnesium exchange. By using PhMgCl for the I/Mg exchange reaction, even sensitive functional groups such as a ketone were tolerated (entry 14), leading at lower temperatures (−78 °C) to the magnesiated species **8i** and after addition to benzaldehyde (**10a**) to product **9n** in 93% yield. The iodine−magnesium exchange reaction was also applicable to heteroaromatic *o*-iodonitro compounds **5a** and **5b**, as shown in Scheme 9.

Thus, the reaction of 2-iodo-3-nitropyridine (**5a**) at −78 °C led to magnesiated heterocycle **11a** within 5 min, and subsequent reaction with benzaldehyde (**10a**) furnished alcohol **12a** in 55% yield. Similarly, the formation of magnesiated quinoline **11b** proceeded under mild conditions (−40 °C, 5 min) from the corresponding iodide **5b**. The reaction of **11b** with benzaldehyde (**10a**) led to alcohol **12b** in 78% yield.

Transmetalation to Copper Reagents of Type 13 and Further Reactions. The reactivity and selectivity of the Grignard reagents **8** was not appropriate for reactions with some electrophiles and a transmetalation to a transition metal derivative was required. Thus, for the reaction with allylic halides or acid halides the intermediate *o*-nitroarylmagnesium reagents of type **8** were treated with CuCN·2LiCl[19] (1 equiv, −40 °C, 5 min), resulting in the in situ formation of the arylcopper species **13a**−**i**, which smoothly reacted with a variety of electrophiles (Scheme 10 and Table 2).

As shown in Table 2, the transmetalation to organocopper derivatives considerably extends the field of application for these functionalized Grignard reagents.[20] Thus, an allylation was possible with either allyl bromide (**15**) (entries 1 and 10 of Table 2) or with the more reactive ethyl (2-bromomethyl)acrylate (**16**)[21] (entries 2, 3, 7, 8, 9, 11, and 12) furnishing the corresponding products in good to excellent yields. Furthermore, these copper reagents underwent acylation reactions with benzoyl bromide (**17**) leading to the highly functionalized ketone **14d** in good yield (entry 4). The use of less reactive

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[16] Chaikovski, V. K.; Kharlova, T. S.; Filimonov, V. D.; Saryucheva, T. A. *Synthesis* **1999**, 748.

[17] Grehn, L.; Gunnarsson, K.; Rugnarsson, U. *Acta Chem. Scand.* **1986**, *B40*, 745.

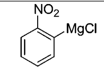
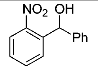
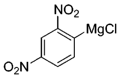
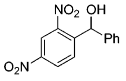
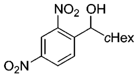
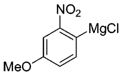
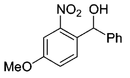
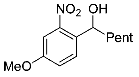
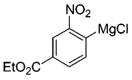
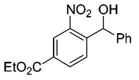
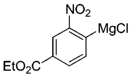
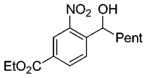
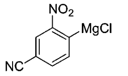
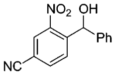
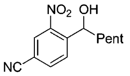
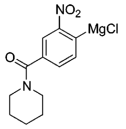
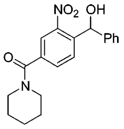
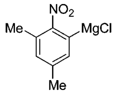
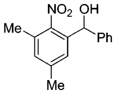
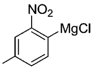
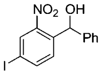
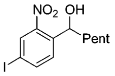
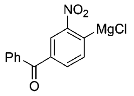
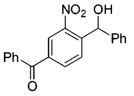
[18] Gross, M. L.; Blank, D. H.; Welch, W. M. *J. Org. Chem.* **1993**, *58*, 2104−2109.

[19] Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.

[20] The transmetalation of Grignard reagent **8b**, bearing two nitro groups, led to a copper species, which was no longer as stable as the corresponding Grignard reagent, showing the limitations of this methodology and allowing the conversion to the allylated compound in only 24% GC yield.

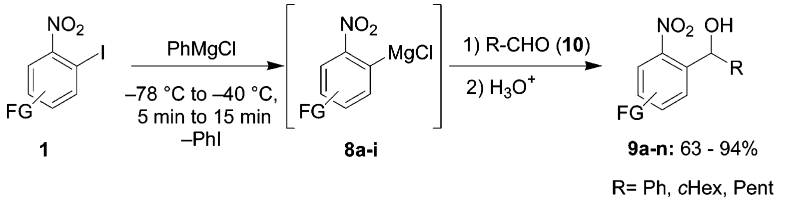
[21] Byun, H.-S.; Reddy, K. C.; Bittman, R. *Tetrahedron Lett.* **1994**, *35*, 1371.

TABLE 1. Products 9a−q Obtained by the Reaction of Functionalized *o*-Nitro-Substituted Arylmagnesium Compounds 8 with Aldehydes

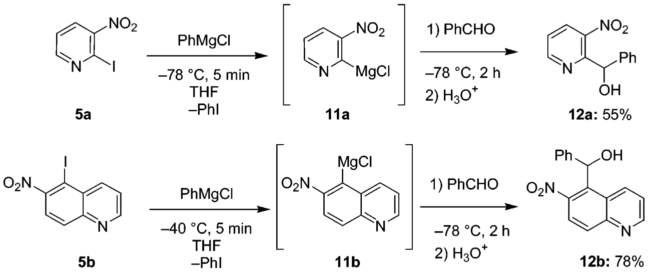
Entry	Arylmagnesium Reagent **8**	Aldehyde **10**	Product **9**	Yield (%)[a]
1	 **8a**[b]	PhCHO **10a**	 **9a**	87
2	 **8b**[c]	PhCHO **10a**	 **9b**	81
3	**8b**[c]	*c*HexCHO **10b**	 **9c**	74
4	 **8c**[b]	PhCHO **10a**	 **9d**	72
5	**8c**[b]	PentCHO **10c**	 **9e**	71
6	 **8d**[b]	PhCHO **10a**	 **9f**	94
7	 **8d**[b]	PentCHO **10c**	 **9g**	87
8	 **8e**[b]	PhCHO **10a**	 **9h**	94
9	**8e**[b]	PentCHO **10c**	 **9i**	63
10	 **8f**[b]	PhCHO **10a**	 **9j**	84
11	 **8g**[b]	PhCHO **10a**	 **9k**	74
12	 **8h**[b]	PhCHO **10a**	 **9l**	89
13	**8h**[b]	PentCHO **10c**	 **9m**	86
14	 **8i**[d]	PhCHO **10a**	 **9n**	93

[a] Yield of analytically pure product. [b] Iodine−magnesium exchange: −40 °C, 15 min. [c] Iodine−magnesium exchange: −40 °C, 0.5 min. [d] Iodine−magnesium exchange: −78 °C, 30 min.

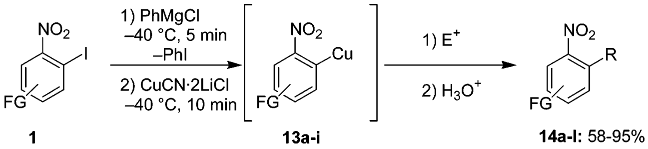
SCHEME 8



SCHEME 9



SCHEME 10



benzoyl chloride furnished product **14d** in only 45% yield, whereas the more reactive aliphatic propionyl chloride (**18**) afforded product **14e** in 61% yield (entry 5). Remarkably, copper derivative **13d** underwent an addition−elimination reaction with 3-iodo-2-methyl-2-cyclopentenone[22] (**19**) leading to product **14f** in 61% yield (entry 6).

Palladium-Catalyzed Cross-Coupling Reactions of *o*-Nitroarylzinc Halides 20. Transition-metal catalyzed cross-coupling reactions between Csp^2-centers are extensively used for preparing pharmaceuticals and agrochemical intermediates.[23] In particular, the Suzuki cross-coupling reaction has found many applications due to the high functional group compatibility of boronic acids and esters.[24] The Negishi cross-coupling,[25] involving the

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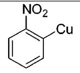
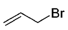
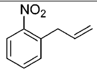
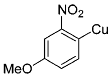
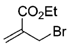
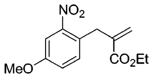
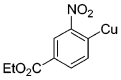
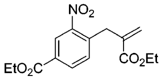
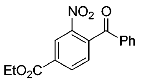
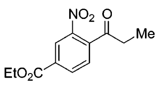
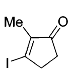
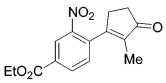
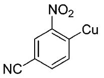
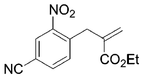
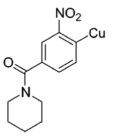
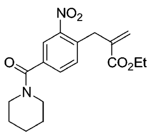
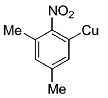
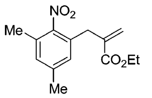
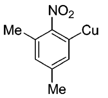
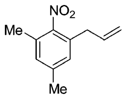
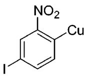
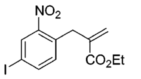
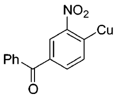
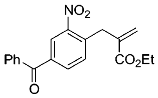
(22) Piers, E.; Nagakura, I. *Synth. Commun.* **1975**, *5*, 193.

TABLE 2. Products 14 Obtained by the Reaction of the Functionalized *o*-Nitro-Substituted Arylcopper Reagents 8 with Different Electrophiles

Entry	Arylcopper Reagent **13**	Electrophile	Product **14**	Yield (%)[a]
1	 **13a**	 **15**	 **14a**	75
2	 **13c**	 **16**	 **14b**	72
3	 **13d**	**16**	 **14c**	75
4	**13d**	PhCOBr **17**	 **14d**	76
5	**13d**	EtCOCl **18**	 **14e**	61
6	**13d**	 **19**	 **14f**	61
7	 **13e**	**16**	 **14g**	58
8	 **13f**	**16**	 **14h**	78
9	 **13g**	**16**	 **14i**	76
10	 **13g**	**15**	 **14j**	78
11	 **13h**	**16**	 **14k**	74
12	 **13i**	**16**	 **14l**	95

[a] Yield of analytically pure product.

reaction of organozinc reagents with organic halides in the presence of a palladium catalyst has been less well-utilized due to the water and air sensitivity of organozinc species. However, the excellent ability of organozinc species to undergo transmetalation reactions often allows Negishi cross-coupling reactions to be performed under exceedingly mild reaction conditions.[26] Since polyfunctionalized organozinc reagents can readily be prepared by direct insertion of zinc,[27] I/Zn exchange,[28] or transmetalation reactions,[4] a number of polyfunctionalized organozinc reagents are readily available for cross-coupling reactions.[29]

Organomagnesium reagents can be converted to the corresponding zinc species **20** by addition of $ZnBr_2$, allowing a palladium-catalyzed Negishi cross-coupling reaction to be performed. As shown in Scheme 11, the initially formed iodobenzene (**21a**) reacted as an electrophile, leading to cross-coupling product **22a** in 78% yield upon addition of bis(dibenzylideneacetone)palladium(0) ($Pd(dba)_2$, 5 mol %) and tris-*o*-furylphosphine (tfp; 10 mol %) at ambient temperature within 2 h.

Therefore, a more sterically hindered Grignard reagent was required, which would still allow a fast exchange reaction, but would be less reactive in the Negishi cross-coupling reaction. Performing the I/Mg exchange reactions with mesitylmagnesium bromide[30] was advantageous for the preparation of the starting organomagnesium species **8** (Scheme 12).

With mesitylmagnesium bromide, the iodine−magnesium exchange reaction produced mesityl iodide (**21b**), which is unreactive toward an insertion of palladium due to the steric hindrance of the methyl substituents. A variety of different iodoarenes of type **21** and 2-bromothiazole (**23**) were cross-coupled under these conditions as shown in Table 3.

To our delight, the 2,4-dinitro-substituted arylzinc compound **20a**, which was prepared according to our method using mesitylmagnesium bromide, showed a good thermal stability under the usual reaction conditions. The exchange reaction was very fast leading to Grignard

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[23] For general reviews see: (a) *Metal-catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998. (b) *Cross-Coupling Reactions. A Practical Guide*; Miyaura, N., Ed.; Springer-Verlag: Berlin, Germany, 2002. (c) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (d) Negishi, E. *Organometallics in Organic Synthesis*; Wiley: New York, 1980.

[24] (a) Tyrell, E.; Brookes, P. *Synthesis* **2003**, 469. (b) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633. (c) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem.* **2001**, *113*, 4676; *Angew. Chem., Int. Ed.* **2001**, *40*, 4544. (d) Suzuki, A. *J. Organomet. Chem.* **1999**, *576,* 305.

[25] (a) Negishi, E. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley: New York, 2002; Vol. 1, pp 229 and 767. (b) Anctil, E. J. G.; Snieckus, V. *J. Organomet. Chem.* **2002**, *653*, 150. (c) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263. (d) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340. (e) Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* **1980**, *102*, 3198. (f) Kobayashi, M.; Negishi, E. *J. Org. Chem.* **1980**, *45*, 5223. (g) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Tetrahedron Lett.* **1986**, *27*, 955.

[26] Bonnet, V.; Mongin, F.; Trécourt, F.; Breton, G.; Marsais, F.; Knochel, P. *Synlett* **2002**, 1008.

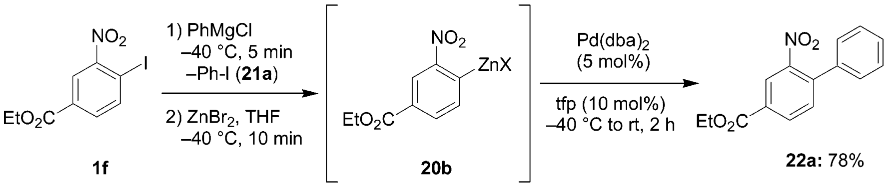
[27] (a) Majid, T.; Knochel, P. *Tetrahedron Lett.* **1990**, *31*, 4413. (b) Fillon, H.; Gosmini, C.; Périchon, J. *J. Am. Chem. Soc.* **2003**, *125*, 3867. (c) Rieke, R. D. *Science* **1998**, *246*, 1260. (d) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, *56*, 1445.

[28] Kneisel, F. F.; Dochnahl, M.; Knochel, P. *Angew. Chem.* **2004**, *116*, 1032; *Angew. Chem., Int. Ed.* **2004**, *43*, 1017.

[29] For Pd-catalyzed cross-coupling reactions using nitroaryl stannanes and nitroaryl boronic esters see: (a) Li, D.; Zhao, B.; LaVoie, E. J. *J. Org. Chem.* **2000**, *65*, 2802. (b) Ghosez, L.; Franc, C.; Denonne, F.; Cuisinier, C.; Touillaux, R. *Can. J. Chem.* **2001**, *79*, 1827.

[30] Hawkins, R. T.; Lennarz, W. J.; Snyder, H. R. *J. Am. Chem. Soc.* **1960**, *82*, 3053.

SCHEME 11



SCHEME 12

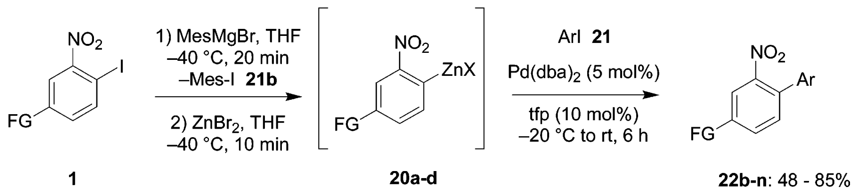
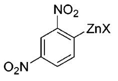
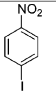
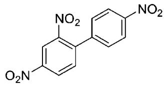
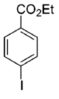
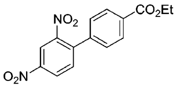
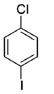
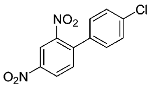
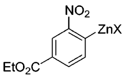
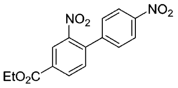
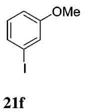
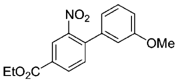
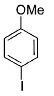
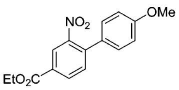
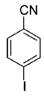
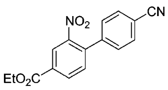
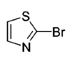
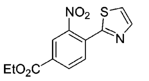
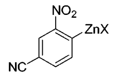
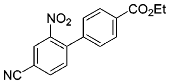
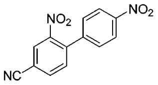
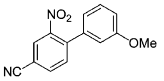
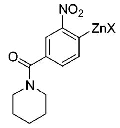
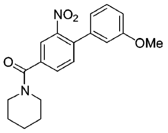
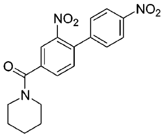


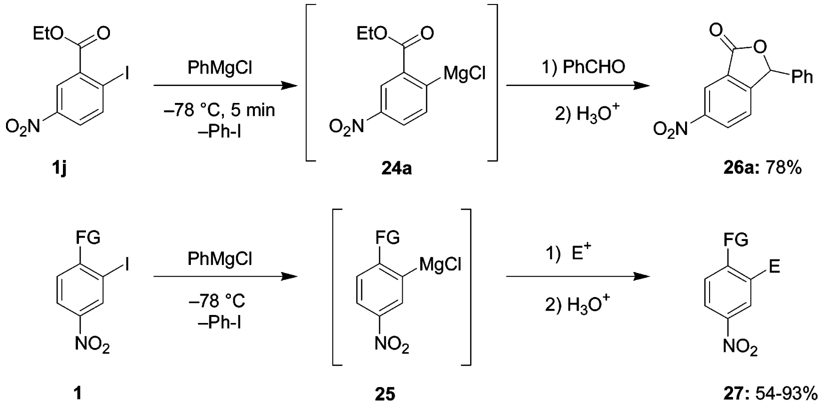
TABLE 3. Polyfunctional Biphenyls 22, Obtained by Pd-Catalyzed Cross-Couplings of Nitro-Substituted Arylzinc Compounds 20

Entry	Arylzinc reagent **20**	Aryl iodide **21**	Biphenyl **22**	Yield (%)[a]
1	 **20a**[b]	 **21c**	 **22b**	55
2	**20a**[b]	 **21d**	 **22c**	68
3	**20a**[b]	 **21e**	 **22d**	55
4	 **20b**[c]	**21c**	 **22e**	85
5	**20b**[c]	 **21f**	 **22f**	80
6	**20b**[c]	 **21g**	 **22g**	53
7	**20b**[c]	 **21h**	 **22h**	53
8	**20b**[c]	 **23**	 **22i**	48
9	 **20c**[c]	**21d**	 **22j**	73
10	**20c**[c]	**21c**	 **22k**	68
11	**20c**[c]	**21f**	 **22l**	75
12	 **20d**[d]	**21f**	 **22m**	67
13	**20d**[d]	**21c**	 **22n**	74

[a] Yield of analytically pure product. [b] Iodine–Magnesium exchange: MesMgCl, −40 °C, 1 min, then $ZnBr_2$, −40 °C, 10 min. [c] Iodine–Magnesium exchange: MesMgCl, −40 °C, 15 min, then $ZnBr_2$, −40 °C, 10 min. [d] Iodine–Magnesium exchange: MesMgCl, −40 °C, 20 min, then $ZnBr_2$, −40 °C, 10 min.

reagent **8b** within 1 min at −40 °C. After transmetalation with zinc bromide to zinc reagent **20a**, its cross-coupling with several functionalized aryl iodides furnished the expected biphenyls **22b**–**d** in 55–68% yield (entries 1–3 of Table 3). Especially interesting was the synthesis of biphenyl **22b**, which bears three nitro groups but did not undergo any electron-transfer processes under the reaction conditions, showing that Negishi cross-coupling reactions are compatible with the presence of reagents bearing several nitro functionalities. The reaction of ethyl 4-iodo-3-nitrobenzoate (**1e**) with mesitylmagnesium bromide (1.05 equiv) in THF at −40 °C furnished within 15 min the desired arylmagnesium species **8d**, which was immediately transmetalated to the corresponding zinc

SCHEME 13

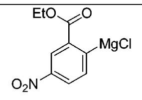
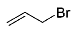
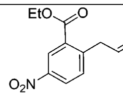
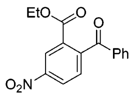
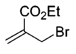
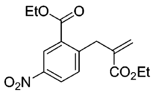
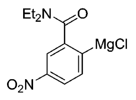
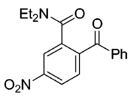


derivative **20b** by the reaction with zinc bromide at −40 °C (10 min). The resulting organozinc species **20b** was perfectly stable at 20 °C and reacted with a broad range of aryl iodides in the presence of Pd(dba)$_2$ (5 mol %) and tfp (10 mol %) within 6 h at 20 °C. Aromatic halides such as 4-nitro-1-iodobenzene reacted especially well, furnishing the desired biphenyl **22e** in 85% yield (entry 4). An aryl iodide bearing an electron-withdrawing group, like 3-methoxy-1-iodobenzene, reacted similarly with **20b** affording the corresponding biphenyl **22f** in 80% yield (entry 5). Interestingly, 4-iodobenzonitrile gave biphenyl **22g** only in 53% yield (entry 7). A heterocyclic bromide such as 2-bromothiazole (**23**) provided the desired cross-coupling product **22i** in 48% yield (entry 8). Similarly, the cyano-substituted zinc reagent **20c** reacted with aryl iodides as expected leading to polyfunctional biphenyls **22j**−***l*** in 68−75% yield (entries 9−11). The amide-substituted organozinc compound **20d** led to the Negishi cross-coupling products **22m** and **22n** in 67 and 74%, respectively (entries 12 and 13).

One major drawback of the sterically hindered mesitylmagnesium bromide was its reduced reactivity for undergoing the I/Mg exchange reaction. Therefore, only electron-poor arenes underwent a straightforward I/Mg exchange reaction. Electron-donating substituents such as in compounds **1a**, **1c**, and **1k** gave mixtures of the exchange product and products generated through addition to the nitro group when mesitylmagnesium bromide was used for the I/Mg exchange.[31]

Preparation of Functionalized *m*- and *p*-Nitroarylmagnesium Halides of Type 24 and 25 via an Iodine−Magnesium Exchange. While the preparation of *o*-nitroarylmagnesium halides **8** was possible, the formation of arylmagnesium halides bearing a nitro group in the meta and para position turned out to be much more difficult. The chelation of the nitro group reduced significantly the reactivity of the resulting Grignard reagent and therefore no intermolecular addition to the nitro group was observed. The presence of an *o*-nitro group also accelerated significantly the exchange reaction by the inductive effect of the nitro group. Therefore *m*- and *p*-nitroarylmagnesium halides were more difficult to prepare in comparison to the *o*-nitroarylmagnesium halides and side reactions often took place during the I/Mg exchange reaction. Thus, the addition of PhMgCl to 3- and 4-iodonitrobenzene did not lead to any exchange product, but instead led only to the nitro group reduction, resulting in the formation of 3- and 4-ioddiphenylhydroxylamine as indicated by GC-MS analysis.[31] We envisioned that the introduction of another chelating or electron-withdrawing group could facilitate the exchange. Adding an additional chelating substituent, such as an ester, on the aromatic ring proved successful, as shown in Scheme 13. Treatment of ethyl 2-iodo-4-nitrobenzoate (**1i**) with PhMgCl (1.1 equiv) in THF at −78 °C led to a fast exchange reaction (10 min), as indicated by GC analysis of reaction aliquots. The resulting nitro-substituted Grignard reagent **24a** was reacted subsequently with benzaldehyde (**10a**) (1.5 equiv) furnishing lactone **26** in 78% isolated yield (Scheme 13 and Table 4).

TABLE 4. *p*-Nitro-Functionalized Aromatic Compounds 26, Obtained by Reaction of *p*-Nitro-Substituted Arylmagnesium Reagents 24

Entry	Arylmagnesium Reagent 24	Electrophile	Product 26	Yield (%)[a]
1	 **24a**	 **15**	 **26b**	87[b]
2	**24a**	PhCOBr **17**	 **26c**	94[b]
3	**24a**	 **16**	 **26d**	67[b]
4	 **24b**	**17**	 **26e**	68[b]

[a] Yield of analytically pure product. [b] The Grignard reagent was transmetalated with CuCN·2LiCl to the corresponding copper reagent before reaction with the electrophile

Similarly, *m*-nitro-substituted compounds of type **1** were converted into the corresponding Grignard reagents **25** using PhMgCl (Scheme 13 and Table 5). Depending on the nature of the group ortho to the iodide, different

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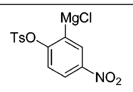
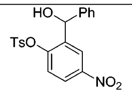
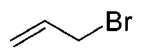
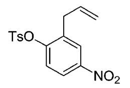
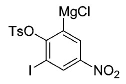
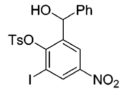
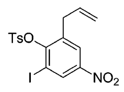
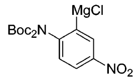
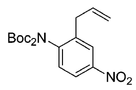
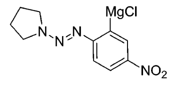
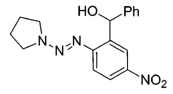
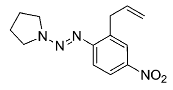
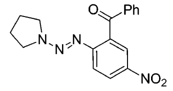
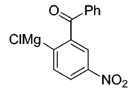
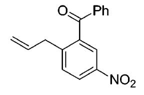
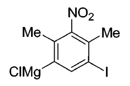
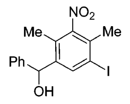
[31] Sapountzis, I.; Knochel, P. *J. Am. Chem. Soc.* **2002**, *124*, 9390−9391.

TABLE 5. *m*-Nitro-Functionalized Aromatic Compounds 27, Obtained by Reaction of *m*-Nitro-Substituted Arylmagnesium Reagents 25

Entry	Arylmagnesium Reagent **25**	Electrophile	Product **27**	Yield (%)[a]
1	 **25a**[c]	PhCHO **10a**	 **27a**	80
2	**25a**[c]	 **15**	 **27b**	93[b]
3	 **25b**[d]	PhCHO **10a**	 **27c**	78
4	**25b**[d]	**15**	 **27d**	87[b]
5	 **25c**[e]	**15**	 **27e**	64[b]
6	 **25d**[f]	**10a**	 **27f**	58
7	**25d**[f]	**15**	 **27g**	61[b]
8	**25d**[f]	PhCOBr **17**	 **27h**	75[b]
9	 **25e**[g]	**15**	 **27i**	54[b]
10	 **25f**[e]	**10a**	 **27j**	71

[a] Yield of analytically pure product. [b] The Grignard reagent was transmetalated with $CuCN\cdot 2LiCl$ to the corresponding copper reagent before reaction with the electrophile. [c] Iodine−magnesium exchange: −78 °C, 15 min. [d] Iodine−magnesium exchange: −78 °C, 10 min. [e] Iodine−magnesium exchange: −78 °C, 30 min. [f] Iodine−magnesium exchange: −55 °C, 30 min in THF/NMP= 3:1. [g] Iodine−magnesium exchange: −40 °C, 30 min.

reactivities were observed, showing that these Grignard reagents represent clearly the limits of our approach. Tables 4 and 5 display the products of type **26** and **27** prepared by directly reacting the Grignard reagent or after subsequent transmetalation to an organocopper derivative.

The carbonyl group stabilized the Grignard reagent **24a** well, leading to a fast reaction with PhMgCl even at low reaction temperatures (−78 °C). Transmetalation to the corresponding organocopper derivative with the soluble copper salt $CuCN\cdot 2LiCl$ allowed reactions with allyl bromide (**15**), ethyl (2-bromomethyl)acrylate (**16**), and benzoyl bromide (**17**) (entries 1−3 of Table 4) in good to excellent yields. Similarly, the amido function in compound **1j** and the corresponding Grignard reagent **24b** reacted after transmetalation with benzoyl bromide (**17**), affording compound **26e** in 68% yield (entry 4).

To facilitate the I/Mg exchange reaction, the phenols **1e** and **1p** were converted to the corresponding tosylates **1q** and **1r**.[32] Thus, the exchange of 2-iodo-4-nitrophenyl tosylate **1q** was complete within 15 min and the Grignard reagent **25a** was reacted subsequently with benzaldehyde (**10a**), leading to benzhydryl alcohol **27a** in 80% yield (entry 1, Table 5). The 2,6-diiodo compound **1r** underwent the mono-exchange reaction even faster, leading after reaction with benzaldehyde (**10a**) to polyfunctional alcohol **27c** in 78% yield (entry 3). Both Grignard reagents **25a** and **25b** could be transmetalated with $CuCN\cdot 2LiCl$ and reaction with allyl bromide (**15**) furnished the expected allylated products **27b** and **27d** in 93% and 87% yield, respectively (entries 2 and 4). A di-Boc protection was most suitable in the case of aniline **1d**, allowing the I/Mg exchange reaction to occur at −78 °C within 30 min. Subsequent transmetalation of Grignard reagent **25c** to the copper derivative and reaction with allyl bromide (**15**) led to compound **27e** in 64% yield (entry 5). Trapping with an aldehyde led to partial transfer of the Boc group from nitrogen to oxygen, which could not be avoided even at low temperatures. In contrast, the formation of triazene-protected Grignard reagent **25d** required elevated temperatures (−55 °C) and a more polar solvent mixture (THF:NMP = 3:1) to ensure a better solubility and faster reaction. However, Grignard reagent **25d** reacted with benzaldehyde (**10a**) yielding alcohol **27f** in 58% yield (entry 6). Transmetalation with $CuCN\cdot 2LiCl$ and reaction with allyl bromide (**15**) or benzoyl bromide (**17**) furnished compounds **27g** and **27h** in 61% and 75% yield, respectively (entries 7 and 8). Remarkably, a keto group was also compatible leading to the new organomagnesium compound **25e**, which was reacted after transmetalation with $CuCN\cdot 2LiCl$ with allyl bromide (**15**) affording compound **27i** in 54% yield (entry 9). Finally, the sterical hindrance of two methyl groups in nitro compound **1s** allowed the synthesis of Grignard reagent **25f**, which was reacted with benzaldehyde (**10a**) furnishing compound **27j** in 75% yield (entry 10).

Palladium-Catalyzed Cross-Coupling Reactions of Magnesiated 4-Nitroarenes 24. A transmetalation to the corresponding zinc derivative was also possible allowing the application of the new Grignard reagents to the wide field of palladium-catalyzed cross-coupling reactions. As shown in Scheme 14, the transmetalation to arylzinc reagent **28**, followed by the addition of

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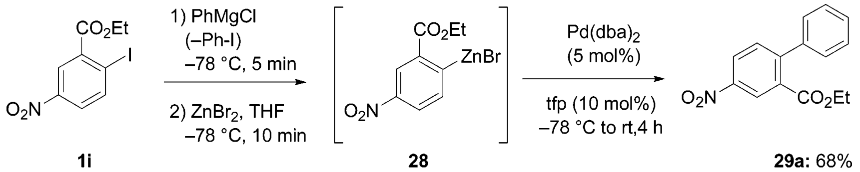
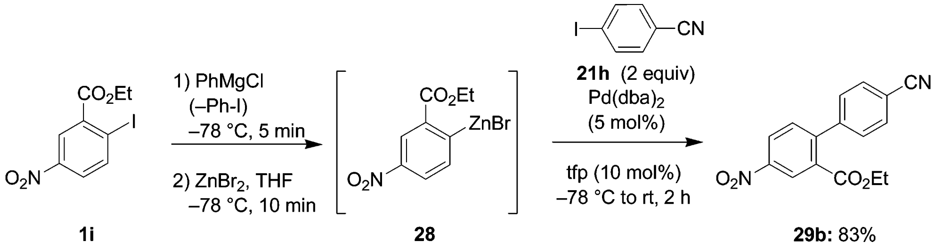
(32) We prepared several other protected phenols. While the trifluoromethylsulfonyl substituent has facilitated the exchange reaction, the corresponding Grignard reagent **14** had a strong tendency to eliminate and formed benzyne, even at low temperatures. The same behavior was observed for the corresponding pivalate or carbonate. Protecting phenol **1p** as an ethoxymethyl ether led to a very slow I/Mg exchange reaction at −78 °C (4 h) and the isolated yield for the reaction with benzaldehyde was moderate (32%).

SCHEME 14



SCHEME 15



Pd(dba)$_2$ (5 mol %) and tfp (10 mol %) furnished biphenyl **29a** at ambient temperature within 2 h in 68% yield (Scheme 14).

Mesitylmagnesium bromide did not lead to the desired Grignard species, but to the reductive addition to the nitro group, hampering further reactions. However, the use of an excess of an electron-poor aryl iodide, such as 4-iodobenzonitrile (**21h**), led to the formation of biaryl **29b** in 83% isolated yield (Scheme 15).

In summary, we have shown that the I/Mg exchange is a very powerful tool for the preparation of functionalized aromatic and heteroaromatic Grignard reagents bearing a nitro group. The reaction conditions for this exchange are compatible with the presence of a broad variety of other functional groups, allowing the preparation of highly functionalized arylmagnesium halides bearing nitro groups. Moreover, the reactivity of these Mg reagents is fine-tuned by transmetalations with transition metal salts expanding the scope of this reaction considerably. Further applications of this methodology are currently underway in our laboratories.

Experimental Section

Representative Procedure for the Performance of an Iodine−Magnesium Exchange Reaction on Functionalized *o*-Iodonitroarenes: Synthesis of 1-(4-iodo-2-nitrophenyl)-1-hexanol (9m): A dry and argon-flushed 25-mL flask equipped with a magnetic stirrer and a septum was charged with 2,5-diiodonitrobenzene (**1m**) (562 mg, 1.50 mmol). Dry THF (5 mL) was added, the mixture was cooled to −40 °C, and PhMgCl (0.80 mL, 1.6 mmol, 2.0 M in THF) was added dropwise. On completion of the I/Mg exchange (5 min, checked by GC analysis of reaction aliquots), hexanal (**10c**; 201 mg, 2.00 mmol) was added dropwise. The reaction mixture was stirred for 30 min at −40 °C, the cooling bath was removed, and the mixture was stirred for an additional 30 min at room temperature. The reaction mixture was quenched with saturated NH$_4$Cl$_{(aq)}$ (2 mL) and poured into water (25 mL) and the aqueous phase was extracted with ethyl acetate (2 × 40 mL). The collected organic phases were washed with brine (30 mL), dried (Na$_2$SO$_4$), and concentrated in vacuo. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded the title compound **9m** (480 mg, 86%) as a pale yellow oil. ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C) δ 8.21 (d, ^4J(H,H) = 1.8 Hz, 1 H), 7.96 (dd, ^3J(H,H) = 8.4 Hz, ^4J(H,H) = 1.8 Hz, 1 H), 7.55 (d, ^3J(H,H) = 8.4 Hz 1 H), 5.22−5.18 (m, 1 H), 2.47 (s−br, 1 OH), 1.83−1.27 (m, 8 H), 0.92−0.88 (m, 3 H). ^{13}C NMR (75 MHz, CDCl$_3$, 25 °C) δ 148.1, 142.3, 140.0, 132.7, 129.8, 91.4, 69.1, 38.1, 31.4, 25.7, 22.5, 14.0. MS (70 eV, EI), *m/z* (%) 349 (not detectable), 332 (2) [M − OH]$^+$, 278 (100), 261 (16), 229 (24), 203 (4), 76 (3). IR (KBr) $\tilde{\nu}$ 1529, 1466, 1347, 1054, 869, 832. HRMS for C$_{12}$H$_{16}$INO$_3$ (332.0148 [M − OH]$^+$) found 332.0169 [M − OH]$^+$. C$_{12}$H$_{16}$INO$_3$ required: C, 41.28; H, 4.62; I, 36.35; N, 4.01. Found: C, 41.66, H, 4.32; I, 36.76; N, 4.00.

Representative Procedure for the Performance of an Iodine−Magnesium Exchange Reaction on Functionalized *m*- and *p*-Iodonitroarenes: Synthesis of Ethyl 2-Allyl-5-nitrobenzoate (26b): A dry argon-flushed 25-mL flask, equipped with a magnetic stirrer and a septum, was charged with ethyl 2-iodo-5-nitrobenzoate (**1i**) (321 mg, 1.00 mmol). Dry THF (4 mL) was added, the mixture was cooled to −78 °C, and PhMgCl (0.66 mL, 1.1 mmol, 1.6 M in THF) was added dropwise. On completion of the I/Mg exchange (10 min, checked by GC analysis of reaction aliquots) CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 m in THF) was added dropwise. The reaction mixture was stirred for 5 min and allyl bromide (240 mg, 2.00 mmol) was added. The reaction mixture was stirred for 2 h at −78 °C, the cooling bath was removed, and the reaction mixture was quenched with saturated NH$_3$/NH$_4$Cl$_{(aq)}$ (5 mL) and poured into water. The aqueous phase was extracted with ethyl acetate (2 × 40 mL). The collected organic phases were washed with brine (30 mL), dried (Na$_2$SO$_4$), filtered, and concentrated in vacuo. Purification by flash chromatography (pentane/diethyl ether = 29:1) yielded the title compound **26b** (204 mg, 87%) as a yellow oil. ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C) δ 8.70 (d, ^4J(H,H) = 2.7 Hz, 1 H), 8.24 (dd, ^3J(H,H) = 8.9 Hz, ^4J(H,H) = 2.7 Hz, 1 H), 7.46 (d, ^3J(H,H) = 8.9 Hz, 1 H), 6.03−5.89 (m, 1 H), 5.12−5.00 (m, 2 H), 4.39 (q, ^3J(H,H) = 7.1 Hz, 2 H), 3.84 (d, ^3J(H,H) = 6.6 Hz, 2 H), 1.40 (t, ^3J(H,H) = 7.1 Hz, 3 H). ^{13}C NMR (75 MHz, CDCl$_3$, 25 °C) δ 165.5, 148.9, 146.2, 135.6, 132.0, 131.2, 126.1, 125.7, 117.1, 61.8, 38.2, 14.2. MS (70 eV, EI), *m/z* (%) 235 (23) [M$^+$], 220 (35), 207 (34), 192 (100), 179 (11), 160 (12), 144 (8), 115 (42), 89 (5). IR (KBr) $\tilde{\nu}$ 1727, 1525, 1479, 1445, 1350, 1252. HRMS for C$_{12}$H$_{13}$NO$_4$ (235.0845) found 235.0845.

Representative Procedure for Synthesis of Nitro-Substituted Polyfunctional Biphenyls by Negishi Cross-Coupling of *o*-Nitroarylzinc Reagents: Synthesis of Ethyl 2′,4′-Dinitrobiphenyl-4-carboxylate (22c): A dry argon-flushed 25-mL flask, equipped with a magnetic stirrer and a septum, was charged with 1-iodo-2,4-dinitrobenzene (**1b**; 441 mg, 1.50 mmol), dry THF (6 mL) was added, the mixture was cooled to −40 °C, and mesitylmagnesium bromide (2.5 mL, 1.7 mmol, 0.72 M in THF) was then added dropwise. On completion of the I/Mg exchange (1 min, checked by GC analysis of reaction aliquots) zinc bromide (1.6 mL, 1.6 mmol, 1.0 M in THF) was added dropwise and the reaction mixture was stirred for 5 min. In the meantime, another dry twonecked flask equipped with a magnetic stirrer and a septum was charged with bis(dibenzylideneacetone)palladium(0) (Pd(dba)$_2$; 39.5 mg, 0.075 mmol, 5 mol %) and tris-*o*-furylphosphine (tfp; 35 mg, 0.15 mmol, 10 mol %) followed by THF (2 mL). The initial red color disappeared after 2 min leading to a yellow solution and ethyl 4-iodobenzoate (455 mg, 1.65 mmol) was added. This solution was added after 10 min of stirring via cannula to the reaction mixture at −40 °C and the cooling bath was removed. The reaction mixture was stirred for 3 h at room temperature, treated with ethanol (2 mL), and poured into water (25 mL). The aqueous phase was extracted with ethyl acetate (3 × 40 mL), and the collected organic phases were washed with brine (30 mL), dried (Na$_2$SO$_4$), filtered, and concentrated in vacuo. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded biphenyl **22c** as a pale yellow solid (320 mg, 68%). Mp 121−122 °C. ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C) δ 8.77 (d, ^4J(H,H) = 2.4 Hz, 1 H), 8.46 (dd, ^3J(H,H) = 8.4 Hz, ^4J(H,H) = 2.4 Hz, 1 H), 8.14 (d, ^3J(H,H) = 8.2 Hz, 2 H), 7.67 (d, ^3J(H,H) = 8.4 Hz, 1 H), 7.39 (d, ^3J(H,H) = 8.2 Hz, 2 H), 4.41 (q, ^3J(H,H) = 7.1 Hz, 2 H), 1.41 (t, ^3J(H,H) = 7.1 Hz, 3 H). ^{13}C NMR (75 MHz, CDCl$_3$, 25 °C) δ 164.7, 147.9, 146.3, 140.4, 138.6, 132.1, 130.5, 129.2, 126.8, 125.7, 118.9, 60.4, 13.3. MS (70 eV, EI), *m/z* (%) 316 (2) [M$^+$], 288 (50), 271 (100), 260 (22), 242 (12), 225 (32), 215 (20), 179 (53), 169 (16), 151 (33), 139 (20). IR (KBr) $\tilde{\nu}$ 1717, 1602, 1530, 1352, 1298, 1286, 1106. HRMS for C$_{15}$H$_{12}$N$_2$O$_6$ (316.0695) found 316.0685. C$_{15}$H$_{12}$N$_2$O$_6$ required: C, 56.96; H, 3.82; N, 8.86. Found: C, 56.66; H, 3.92; N, 8.69.

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Supporting Information Available: Detailed experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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