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Deprotonation of Benzoxazole and Oxazole Using Lithium Magnesates

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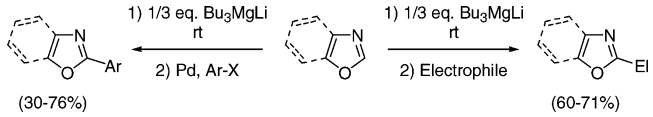

The first deprotonations of oxazole and benzoxazole using lithium magnesates are described. The reactions occurred in tetrahydrofuran at room temperature using 1/3 equiv of lithium tributylmagnesate. As 2-lithiooxazole and 2-lithiobenzoxazole, lithium tri(2-oxazolyl)magnesate and lithium tri(2-benzoxazolyl)magnesate very rapidly and completely isomerized to the more stable 2-(isocyano)enolate and 2-(isocyano)phenolate type structures, respectively, a result shown by NMR analysis. The isolation of 2-substituted oxazoles and benzoxazoles in medium to good yields after electrophilic trapping was interpreted in two ways: (1) the equilibration between the open and closed structures is faster than the trapping of the open isomers, and the closed isomers are more reactive than the open ones, or (2) the open isomers react with electrophiles in a intramolecular Passerini type reaction. The nonreactivity of the 2-(isocyano)enolate type structure toward anisaldehyde in the absence of lithium bromide makes the intramolecular Passerini type reaction more plausible.

Introduction

The preparation of functional heterocycles is an important synthetic goal because of the multiple applications of these molecules.[1] Deprotonation using alkyllithiums or lithium dialkylamides has been developed as one of the major tools since lithiated derivatives display a high reactivity toward many electrophilic functions.[2] Nevertheless, this methodology often requires low temperatures, which can be difficult to realize on an industrial scale. In addition, unlike organoboron, organotin, organozinc, and organomagnesium compounds, organolithiums can hardly be involved in cross-coupling reactions.[3]

More recently, organomagnesium compounds have been prepared by deprotonation at higher temperatures, but the uses of such reactions have barely been explored. The pioneering work of Marxer and Siegrist in 1974 showed EtMgBr was capable of deprotonating 1-phenylpyrazole at the ortho position of the phenyl ring.[4] Eaton reported in 1989 the deprotonation of both methyl benzoate and *N*,*N*-diethylbenzamide with Hauser bases (^{i}Pr$_2$NMgBr or TMPMgBr, TMP = 2,2,6,6-tetramethylpiperidino) or magnesium diamides ((^{i}Pr$_2$N)$_2$Mg or TMP$_2$-Mg).[5] In 1995, Schlecker extended this methodology to the regioselective magnesiation of pyridine carboxamides and carbamates,[6] alkylmagnesium halides and dialkylmagnesiums rarely deprotonating such substrates because of easier 1,4-addition reactions.[7] Next, Kondo and Sakamoto described the regioselective magnesiation of

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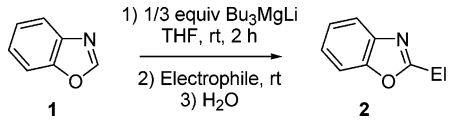
SCHEME 1



2a: El= D, 68%
2b: El= I, 60%
2c: El= CH(OH)-4-anisyl, 70%
2d: El= CH(OH)-3,4,5-trimethoxyphenyl, 71%

N-substituted indoles,[8] thiophenes,[9] and thiazole[9] using $(^{i}Pr_2N)_2Mg$, $^{i}Pr_2NMgBr$, and $^{i}Pr_2NMgCl$. Nevertheless, because of the limited reactivity of these bases, an excess, in general, has to be used to ensure good yields. Pyrrole rings of numerous 1-phenyldipyrromethanes did not require a protection step to be deprotonated at the position adjacent to the nitrogen atom using EtMgBr.[10]

Ten years after Eaton, Kondo achieved the deprotonation of methyl benzoate and other activated benzenes through the formation of an arylzincate using lithium di-*tert*-butyl(2,2,6,6-tetramethylpiperidino)zincate as a base, a methodology extended to pyridine and its bromo derivatives, quinoline, isoquinoline, and ethyl thiophenecarboxylates.[11]

Because arylmagnesates react with a wider range of electrophiles than arylzincates, we have been interested in deprotonation reactions using lithium magnesates. Mulvey documented in 1999 the preparation of a mixed-metal sodium−magnesium macrocyclic amide which behaves like a template for the site selective dideprotonation of benzene and toluene.[12] This process cannot be used, as it is for synthetic purposes because it involves a large excess of arene (5 mmol out of the 5 mL used are consumed in the reaction). Richey observed in 2004 that treating benzene halides with magnesates partially results in benzyne formation.[13] Even if the organometallic precursors of benzyne have not been intercepted by electrophiles, the results show magnesates are capable of abstracting aromatic protons. Very recently, we studied the deprotonation of fluoro aromatics,[14] chloropyridines,[15] and thiophenes[16] using lithium magnesates, the obtained arylmagnesates being either trapped with electrophiles or involved in palladium-catalyzed cross-couplings.

Herein, we describe the first deprotonation reactions of benzoxazole and oxazole using lithium magnesates and the reactivity of the species obtained toward electrophiles or in transition metal-catalyzed cross-coupling reactions with aryl halides. To obtain more information on the position of the equilibrium between the 2-metalated benzoxazole or oxazole and the open isomers, the mixed lithium−magnesium species were analyzed using NMR spectroscopy.

Results and Discussion

Although benzoxazole and oxazole can be readily metalated by alkyllithiums at C2, the 2-metalated species are in equilibrium with the corresponding lithium phenolate and enolate, respectively.[17] In addition, NMR studies have shown the equilibria were completely on the side of the open isomers.[18] From oxazole, depending on the nature of the electrophile used to trap, 2-substituted derivatives (e.g. using DMF, benzophenone, and ethyl formate), 4-substituted derivatives (using more reactive aldehydes) or acyclic isomers (using oxophilic electrophiles such as TMSCl or D_2O) are obtained, the acyclic isomers cyclizing during the workup and/or by heating.[19] The precomplexation of oxazoles with borane proved efficient to overcome this problem;[20] nevertheless, the reaction has to be carried out at −78 °C. Transmetalation to the organozinc derivatives favors the ring closure, a result evidenced by NMR studies[18] and attributed to the strong covalent carbon−zinc bond along with zinc's low oxophilicity, allowing Negishi cross-couplings.[21]

The deprotonation of benzoxazole (**1**) was attempted using 1/3 equiv of lithium tributylmagnesate (Bu_3MgLi)[22] in tetrahydrofuran (THF) at room temperature. Trapping the intermediate magnesate with heavy water, iodine, or 4-anisaldehyde afforded the deuterated compound **2a**, the iodide **2b**, and the alcohol **2c**, respectively, in good yields. Deprotonation of thiophenes using Bu_3MgLi being favored in the presence of TMEDA,[16] the reaction was attempted using this additive. Any positive effect was noted in this case, since the alcohol **2d** prepared in the presence of TMEDA was isolated in a similar yield (Scheme 1).

The intermediate magnesate of benzoxazole was next involved in cross-couplings with various aromatic halides

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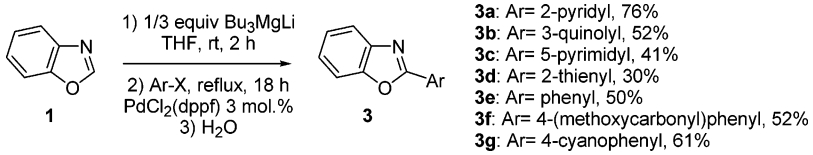
SCHEME 2



under palladium catalysis using 1,1′-bis(diphenylphosphino)ferrocene (dppf) as ligand.[16,23] Moderate to good yields were obtained when it was subjected to the reaction with π-deficient substrates such as 2-bromopyridine, 3-bromoquinoline, and 5-bromopyrimidine, giving the biaryl compounds **3a**−**c**. A lower yield was noted with less activated 2-bromothiophene (compound **3d**). Medium to good results were recorded with halides of the benzene series, affording **3e**−**g**, even when a reactive function such as ester or nitrile was present. The nature of the halogen of the halide, bromine or iodine, seems to have little impact on the outcome of the reaction (Scheme 2).

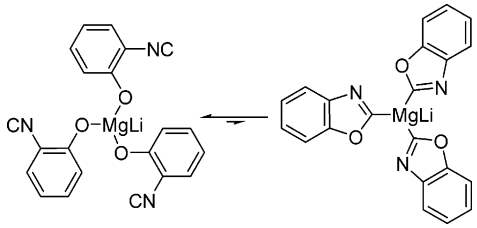
It is of primary interest to ascertain whether the 2-metalated heterocycle is in equilibrium with the corresponding 2-(isocyano)phenolate. Since it is impossible to determine the ratio of 2-metalated to its open counterpart solely from trapping reactions, NMR spectroscopy studies were undertaken. Therefore, the ^{1}H and ^{13}C (JMOD) NMR spectra of the reaction mixture obtained after the deprotonation step were recorded. The spectra (Figure 1) indicated very clearly that the deprotonation using 1/3 equiv of Bu_3MgLi in THF at room temperature essentially provided the thermodynamically more stable 2-(isocyano)phenolate, in particular with JMOD spectra signals at 164.5, 164.4, and 116.8 ppm attributed to its phenolate α-C, isocyanide, and phenolate β-C atoms, respectively. The isolation of 2-substituted benzoxazoles after trapping could be explained by a faster equilibration between the open and closed structures (Scheme 3) than the quenching of the open isomer, associated with a greater reactivity of the closed isomer. Note that such an explanation was proposed to explain the formation of 2-metalated (benz)oxazoles by trapping the lithio derivatives with zinc halides.[18]

Since NMR measurements showed the open species was the only observable product at room temperature, an alternative could be an intramolecular Passerini type reaction[24] of the open isomer with electrophiles, involving the α-addition of the electrophilic site and the nucleophilic oxygen atom of the phenolate to the isocyanide carbon (Scheme 4).

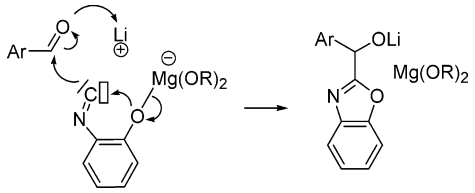
The reaction was next extended to oxazole (**4**). Under the conditions employed for benzoxazole, the iodide **5a** and the alcohol **5b** were provided in good yields. Cross-couplings with 2-bromopyridine and iodobenzene afforded the expected 2-aryloxazole **6a**,**b** in medium yields (Scheme 5).

To gain greater understanding of the nature of the species in solution after the deprotonation step, the ^{1}H NMR spectrum of the reaction mixture was recorded. It indicated that the thermodynamically more stable 2-(isocyano)enolate predominated in the equilibrium with the 2-metalated oxazole: the ^{1}H NMR spectra signals at 6.88 and 4.48 ppm (Figure 2c) attributed to the enolate α-H and β-H atoms, respectively, proved to be close to those of the corresponding lithio derivative (6.95 and 4.42 ppm, Figure 2b). 2-Substituted oxazoles were formed in limited yields, probably due to the crystallization of the deprotonated species as its 2-(isocyano)enolate form in the reaction mixture. As in the benzoxazole series, one can interpret the formation of 2-substituted oxazoles in two ways: (1) the closed isomer is more reactive than the open one, and its consumption displaces the equilibrium, or (2) the open isomer reacts with electrophiles in an intramolecular Passerini type reaction, involving the α-addition of the electrophile site and the nucleophilic oxygen atom of the enolate to the isocyanide carbon.

SCHEME 3



SCHEME 4



Since lithium bromide catalyzes Passerini type reactions,[25] its absence from the reaction mixture could give information about the mechanism involved.[26] Consequently, the 2-(isocyano)enolate was isolated from the reaction mixture containing LiBr by filtration and treated with a THF solution of anisaldehyde. Under these conditions, no reaction was observed, a result that gives weight to the Passerini type approach.

Conclusions

Benzoxazole was deprotonated using 1/3 equiv of Bu_3MgLi in THF at room temperature. As 2-lithiobenzoxazole, lithium tri(2-benzoxazolyl)magnesate very rapidly and completely isomerized to the more stable 2-(isocyano)phenolate type structure, a result evidenced by NMR analysis. The isolation of 2-substituted benzoxazoles in medium to good yields after electrophilic trapping was

(23) Concerning cross-couplings with lithium arylmagnesates, see: (a) Dumouchel, S.; Mongin, F.; Trécourt, F.; Quéguiner, G. *Tetrahedron Lett.* **2003**, *44*, 3877−3880. (b) Dumouchel, S.; Mongin, F.; Trécourt, F.; Quéguiner, G. *Tetrahedron* **2003**, *59*, 8629−8640.

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(26) LiBr is present in all the other reaction mixtures since it is formed during the synthesis of Bu_3MgLi from BuLi and $MgBr_2$.

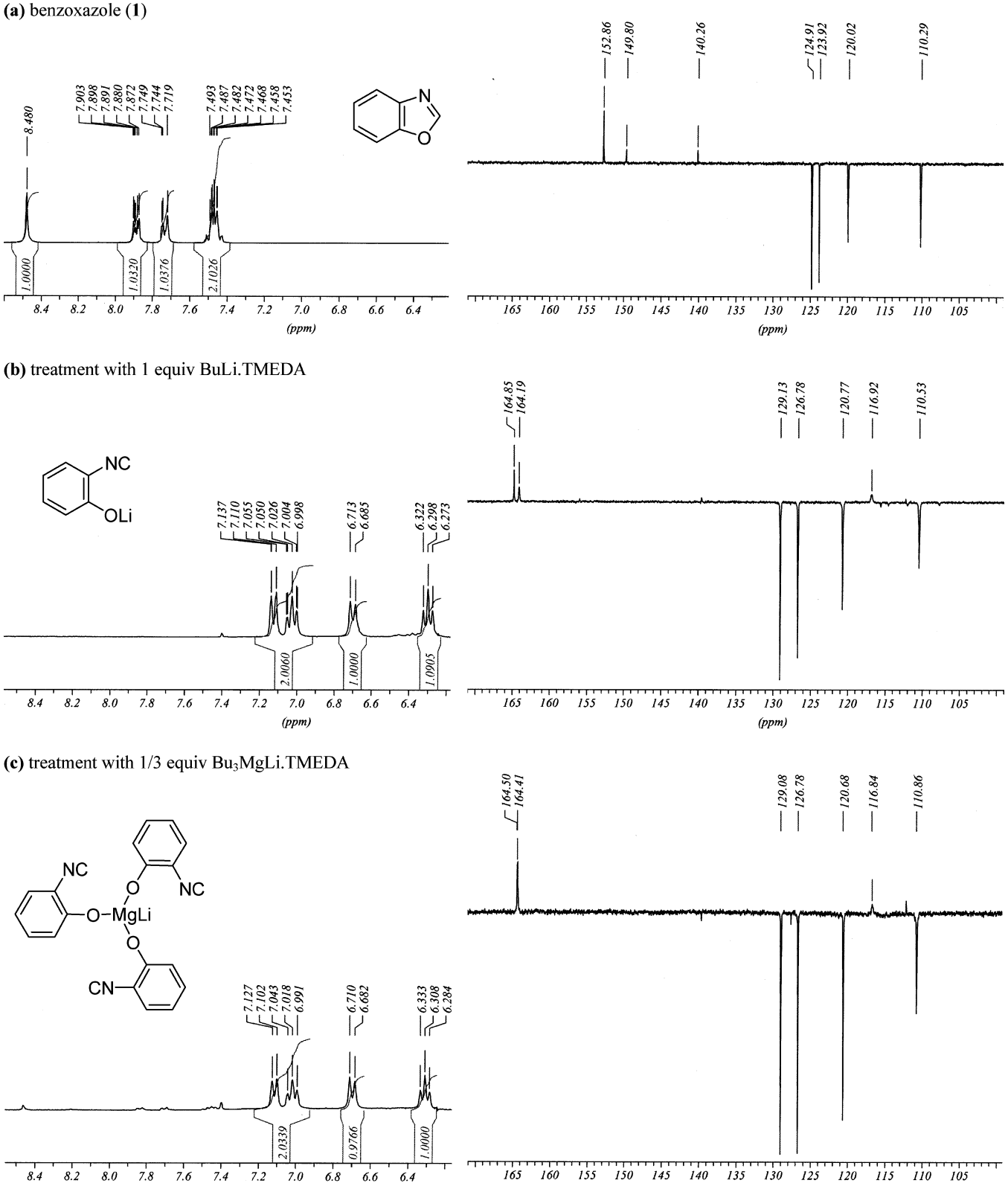


FIGURE 1. ^{1}H and ^{13}C NMR (JMOD) spectra of benzoxazole (**1**) and the derivatives obtained after deprotonation in THF (rt).

interpreted in two ways: (1) the equilibration between the open and closed structures is faster than the trapping of the open isomer, and the closed isomer is more reactive than the open one, or (2) the open isomer reacts with electrophiles in a intramolecular Passerini type reaction.

Similar results were observed starting from oxazole. The non reactivity of the 2-(isocyano)enolate type structure toward anisaldehyde in the absence of lithium bromide makes the intramolecular Passerini type reaction more plausible.

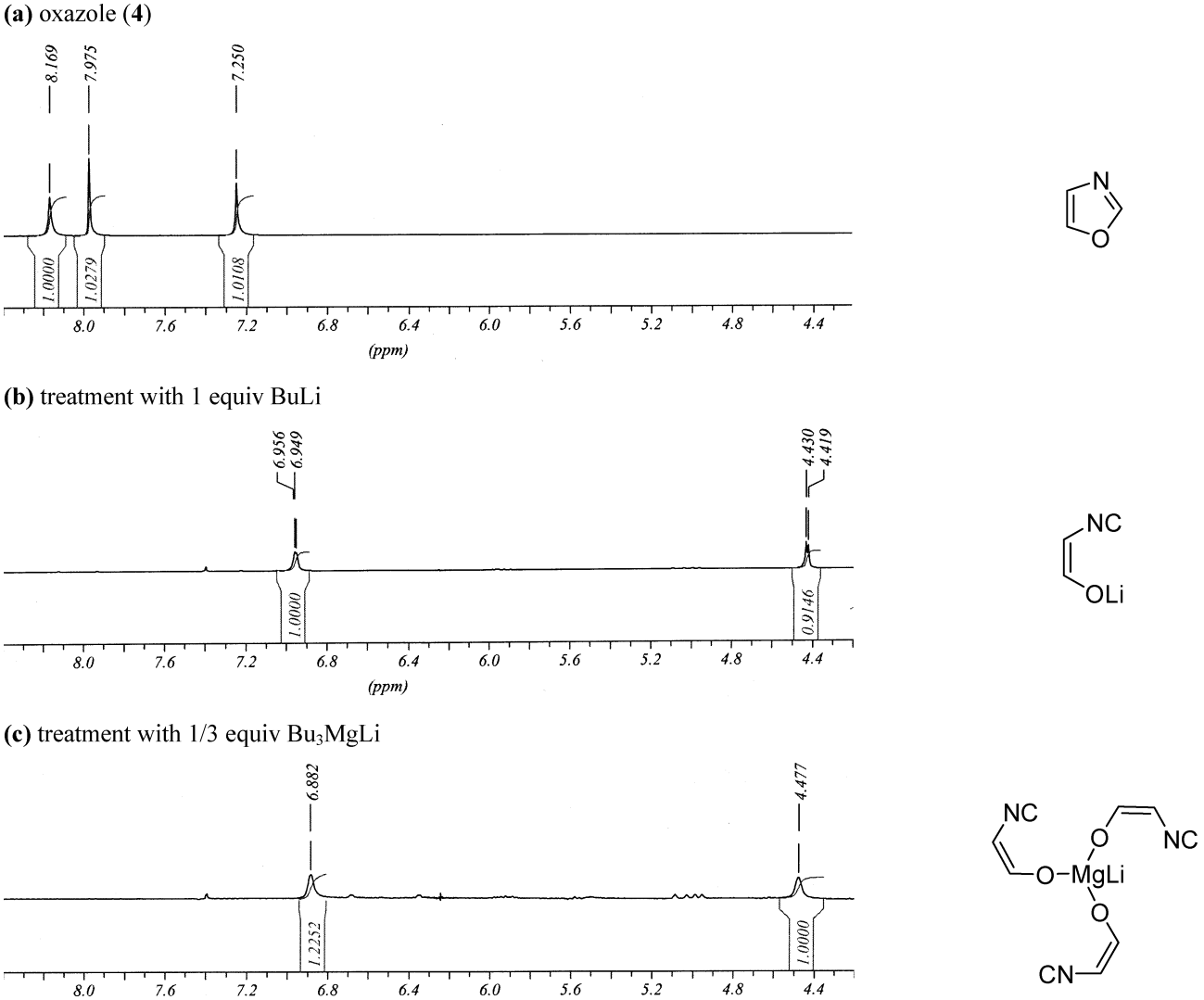
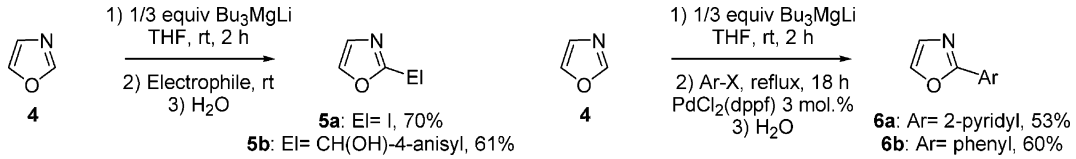


FIGURE 2. ^{1}H NMR spectra of oxazole (**4**) and the derivatives obtained after deprotonation in THF (rt).

SCHEME 5



In conclusion, lithium magnesates are suitable for hydrogen−magnesium exchange reactions on oxazole and benzoxazole at room temperature, whereas corresponding hydrogen−lithium exchanges have generally to be performed at lower temperatures. Compared to the lithio species, the organometallics here obtained can also either react with electrophiles, but without recourse to precomplexation with borane in the case of oxazole, or undergo palladium-catalyzed cross-couplings, but without the transmetalation step.

Experimental Section

General Procedures. The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. For the intermediate species resulting from deprotonation reactions, the ^{1}H and JMOD (*J*-modulated spin−echo experiment) NMR spectra were recorded at room temperature after addition of 20% d_8-THF (to provide a lock signal) to a fraction (0.6 mL) of the reaction mixture. The deuterium incorporation was determined from the ^{1}H NMR integration values. The main absorptions of the IR spectra are given.

Starting Materials. THF was distilled from benzophenone/Na. The water content of the solvents was estimated to be lower than 45 ppm by the modified Karl Fischer method.[27] Metalation and cross-coupling reactions were carried out under dry N_2. $MgBr_2$ was freshly prepared in THF using a described procedure.[28] Petrol refers to petroleum ether (bp 40−60 °C).

Unless otherwise noted, the reaction mixture was diluted with CH_2Cl_2 (50 mL) after the reaction. The organic layer was dried over $MgSO_4$, the solvents were evaporated under reduced

pressure, and the crude product was chromatographed on a silica gel column (eluent is given in the product description).

2-Deuteriobenzoxazole (2a). BuLi (6.0 mmol) was added to a solution of $MgBr_2$ (2.0 mmol) in THF (3 mL) at −10 °C. After stirring for 1 h at −10 °C, benzoxazole (0.71 g, 6.0 mmol) was introduced. After 2 h at room temperature, D_2O (1 mL) was added and the mixture was stirred for 18 h at room temperature before addition of water saturated with NH_4Cl (1 mL). Yield: 75% (90% *d*) (eluent CH_2Cl_2). The ^1H and ^{13}C NMR data of this product showed the replacements of 2-H by 2-D, and 2-CH by 2-CD, respectively; IR (KBr) ν 3431, 3062, 1557, 1472, 1455, 1425, 1316, 1291, 1267, 1070, 1014, 874, 829, 800, 759, 729, 668. Anal. Calcd for C_7H_4DNO (120.13): C, 69.99; "H",[29] 4.29; N, 11.66. Found: C, 69.60; "H", 4.36; N, 11.27.

2-Iodobenzoxazole (2b).[30] The procedure is as described for **2a** but using a solution of I_2 (1.5 g, 6.0 mmol) in THF (3 mL) instead of D_2O (in this case, the reaction mixture was treated with $Na_2S_2O_3$ until bleaching): yield 57% (eluent: CH_2Cl_2/petrol 90:10); ^1H NMR δ 7.70 (m, 1H), 7.53 (m, 1H), 7.30 (m, 2H); ^{13}C NMR δ 153.9 (q), 142.5 (q), 125.2 (t), 124.6 (t), 119.2 (t), 110.0 (t), 108.2 (q); IR (KBr) ν 3066, 1686, 1648, 1632, 1575, 1486, 1474, 1447, 1238, 1115, 1077, 743. Anal. Calcd for C_7H_4INO (245.02): C, 34.31; H, 1.65; N, 5.72. Found: C, 34.60; H, 1.97; N, 5.75.

2-Iodooxazole (5a). The procedure is as described above but using oxazole (0.39 mL) instead of benzoxazole: yield 70% (eluent: CH_2Cl_2); yellow oil; ^1H NMR δ 7.77 (s, 1H), 7.10 (s, 1H); ^{13}C NMR δ 144.8 (q), 129.8 (q), 101.3 (t); IR (KBr) ν 2961, 2924, 2853, 1731, 1714, 1463, 1454, 1261, 1094, 1022, 801. Anal. Calcd for C_3H_2INO (194.96): C, 18.48; H, 1.03; N, 7.18. Found: C, 18.16; H, 1.14; N, 6.89.

α-(4-Methoxyphenyl)-2-benzoxazolemethanol (2c). The procedure is as described for **2a** but using 4-anisaldehyde (0.73 mL, 6.0 mmol) instead of D_2O: yield 70% (eluent: CH_2Cl_2/AcOEt 80:20); ^1H NMR δ 7.71 (m, 1H), 7.45 (m, 3H), 7.33 (m, 2H), 6.92 (d, 2H, J = 6.8 Hz), 5.98 (s, 1H), 3.82 (s, 3H), 3.42 (s, 1H); ^{13}C NMR δ 166.9 (q), 159.9 (q), 150.9 (q), 140.3 (q), 131.1 (q), 128.3 (t, 2C), 125.2 (t), 124.5 (t), 120.1 (t), 114.2 (t, 2C), 110.9 (t), 70.2 (t), 55.3 (p); IR (KBr) ν 3236, 2929, 2836, 1612, 1574, 1510, 1456, 1440, 1244, 1177, 1164, 1107, 1067, 1030, 1002, 972, 864, 840, 819, 749, 596. Anal. Calcd for $C_{15}H_{13}NO_3$ (255.28): C, 70.58; H, 5.13; N, 5.49. Found: C, 70.21; H, 5.52; N, 5.31.

α-(4-Methoxyphenyl)-2-oxazolemethanol (5b). The procedure is as described above but using oxazole (0.39 mL) instead of benzoxazole: yield 61% (eluent: CH_2Cl_2); mp 105−110 °C; ^1H NMR δ 7.54 (s, 1H), 7.33 (d, 2H, J = 8.7 Hz), 6.98 (s, 1H), 6.85 (d, 2H, J = 8.7 Hz), 5.82 (s, 1H), 4.92 (s, 1H), 3.77 (s, 3H); ^{13}C NMR δ 164.9 (q), 159.7 (q), 132.3 (t), 131.5 (q), 128.0 (t, 2C), 126.8 (t), 114.1 (t, 2C), 69.7 (t), 55.4 (p); IR (KBr) ν 3436, 2961, 2838, 1652, 1611, 1513, 1252, 1173, 1030, 765, 588. Anal. Calcd for $C_{11}H_{11}NO_3$ (205.22): C, 64.38; H, 5.40; N, 6.83. Found: C, 64.33; H, 5.42; N, 6.45.

Note that when the 2-(isocyano)enolate was isolated from the reaction mixture containing LiBr by filtration under an air-free atmosphere (nitrogen), and treated with a THF solution of anisaldehyde, no reaction was observed after 18 h at room temperature.

α-(3,4,5-Trimethoxyphenyl)-2-benzoxazolemethanol (2d). BuLi (6.0 mmol) was added to a solution of $MgBr_2$ (2.0 mmol) in THF (3 mL) at −10 °C. After stirring for 1 h at −10 °C, TMEDA (0.30 mL, 2 mmol) and, 1 h later, benzoxazole (0.71 g, 6.0 mmol) were introduced. After 2 h at room temperature, 3,4,5-trimethoxybenzaldehyde (1.2 g, 6.0 mmol) was added and the mixture was stirred for 18 h at room temperature before addition of water saturated with NH_4Cl (1 mL). Yield: 71% (eluent: cyclohexane/AcOEt 70:30); mp 110−112 °C; ^1H NMR δ 7.68 (m, 1H), 7.48 (m, 1H), 7.32 (m, 2H), 6.77 (s, 2H), 5.97 (s, 1H), 4.39 (broad s, 1H), 3.82 (s, 9H); ^{13}C NMR δ 166.9 (q), 153.9 (q, 2C), 151.3 (q), 140.6 (q), 138.5 (q), 134.8 (q), 125.8 (t), 125.0 (t), 120.5 (t), 111.3 (t), 104.1 (t, 2C), 71.0 (t), 61.2 (p), 56.5 (p, 2C); IR (KBr) ν 3196, 3092, 2937, 2836, 1592, 1565, 1506, 1456, 1418, 1333, 1236, 1139, 1098, 1080, 993, 840, 821, 748. Anal. Calcd for $C_{17}H_{17}NO_5$ (315.33): C, 64.75; H, 5.43; N, 4.44. Found: C, 64.63; H, 5.35; N, 4.39.

2-(2-Pyridyl)benzoxazole (3a). BuLi (6.0 mmol) was added to a solution of $MgBr_2$ (2.0 mmol) in THF (3 mL) at −10 °C. After stirring for 1 h at −10 °C, benzoxazole (0.71 g, 6.0 mmol) was introduced. After 2 h at room temperature, the mixture thus obtained was added dropwise to a solution of 2-bromopyridine (0.58 mL, 6.0 mmol) and $PdCl_2$(dppf) (49 mg, 60 μmol) at reflux and the mixture was heated at reflux for 18 h before addition of water saturated with NH_4Cl (1 mL) Yield: 76% (eluent: CH_2Cl_2/Et_2O 95:5); mp 109−110 °C (lit.[31] 108 °C); ^1H NMR δ 8.62 (d, 1H, J = 4.5 Hz), 8.13 (d, 1H, J = 7.9 Hz), 7.65 (m, 2H), 7.48 (m, 1H), 7.20 (m, 3H); ^{13}C NMR δ 160.5 (q), 150.1 (q), 149.4 (t), 145.0 (q), 140.9 (q), 136.2 (t), 125.2 (t), 124.7 (t), 124.1 (t), 122.6 (t), 119.8 (t), 110.3 (t); IR (KBr) ν 3059, 1553, 1452, 1439, 1347, 1243, 1077, 1039, 934, 811, 762, 740, 703. Anal. Calcd for $C_{12}H_8N_2O$ (196.21): C, 73.46; H, 4.11; N, 14.28. Found: C, 73.43; H, 4.19; N, 14.33.

2-(2-Pyridyl)oxazole (6a). The procedure is as described above but using oxazole (0.39 mL) instead of benzoxazole: yield 53% (eluent: CH_2Cl_2); IR (KBr) ν 3417, 3127, 2190, 1644, 1591, 1557, 1513, 1461, 1445, 1275, 1148, 1096, 1077, 916, 797, 715. Anal. Calcd for $C_8H_6N_2O$ (146.15): C, 65.75; H, 4.14; N, 19.17. Found: C, 65.69; H, 4.36; N, 18.89. The other analyses were found identical to those previously described.[32]

3-(2-Benzoxazolyl)quinoline (3b).[33] The procedure is as described for **3a** but using 3-bromoquinoline (0.83 mL) instead of 2-bromopyridine: yield 52% (eluent: CH_2Cl_2); mp 184 °C; ^1H NMR δ 9.75 (d, 1H, J = 1.9 Hz), 9.02 (d, 1H, J = 1.9 Hz), 8.19 (d, 1H, J = 8.3 Hz), 7.98 (d, 1H, J = 8.3 Hz), 7.77 (m, 2H), 7.65 (m, 2H), 7.42 (m, 2H); ^{13}C NMR δ 160.4 (q), 150.3 (q), 148.4 (q), 148.0 (t), 141.4 (q), 134.9 (t), 131.0 (t), 129.0 (t), 128.4 (t), 127.4 (t), 126.8 (q), 125.4 (t), 124.6 (t), 119.9 (q), 119.9 (t), 110.4 (t); IR (KBr) ν 3021, 1573, 1556, 1491, 1454, 1245, 1182, 967, 918, 786, 763, 747, 475. Anal. Calcd for $C_{16}H_{10}N_2O$ (246.26): C, 78.03; H, 4.09; N, 11.38. Found: C, 77.81; H, 4.11; N, 11.29.

2-(5-Pyrimidyl)benzoxazole (3c).[34] The procedure is as described for **3a** but using 5-bromopyrimidine (0.95 g) instead of 2-bromopyridine: yield 41% (eluent: CH_2Cl_2/AcOEt 80:20); mp 168 °C; ^1H NMR δ 9.56 (s, 2H), 9.37 (s, 1H), 7.83 (m, 1H), 7.65 (m, 1H), 7.44 (m, 2H); ^{13}C NMR δ 159.7 (t), 157.7 (q), 155.1 (t, 2C), 150.3 (q), 141.1 (q), 126.1 (t), 125.0 (t), 121.8 (q), 120.3 (t), 110.7 (t); IR (KBr) ν 3089, 3042, 2955, 1618, 1567, 1459, 1436, 1410, 1352, 1307, 1187, 1129, 1064, 1032, 765, 751, 715, 632, 623. Anal. Calcd for $C_{11}H_7N_3O$ (197.19): C, 67.00; H, 3.58; N, 21.31. Found: C, 66.84; H, 3.77; N, 21.07.

2-(2-Thienyl)benzoxazole (3d). The procedure is as described for **3a** but using 2-bromothiophene (0.49 g) instead of 2-bromopyridine: yield 30% (eluent: CH_2Cl_2/petrol 80:20); mp 102−103 °C (lit.[35] 104.5 °C); ^1H NMR δ 7.92 (dd, 1H, J = 3.8 and 1.1 Hz), 7.74 (m, 1H), 7.56 (m, 2H), 7.35 (m, 2H), 7.20 (dd, 1H, J = 4.9 and 3.8 Hz); ^{13}C NMR δ 159.5 (q), 149.9 (q),

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141.6 (q), 129.9 (t), 129.5 (t), 129.2 (q), 127.8 (t), 124.6 (t), 124.3 (t), 119.3 (t), 110.0 (t); IR (KBr) ν 3062, 1615, 1570, 1494, 1451, 1419, 1245, 1227, 1049, 1007, 852, 794, 760, 743, 716. Anal. Calcd for $C_{11}H_7NOS$ (201.24): C, 65.65; H, 3.51; N, 6.96; S, 15.93. Found: C, 65.69; H, 3.34; N, 6.94; S, 15.81.

2-Phenylbenzoxazole (3e). The procedure is as described for **3a** but using iodobenzene (0.67 mL) instead of 2-bromopyridine: yield 50% (eluent: CH_2Cl_2). The physical and spectral data are analogous to those obtained for a commercial sample.

2-Phenyloxazole (6b). The procedure is as described above but using oxazole (0.39 mL) instead of benzoxazole: yield 60% (eluent: CH_2Cl_2). The analyses were found identical to those previously described.[36]

Methyl 4-(2-Benzoxazolyl)benzoate (3f). The procedure is as described for **3a** but using methyl 4-iodobenzoate (1.6 g) instead of 2-bromopyridine: yield 52% (eluent: CH_2Cl_2); mp 198 °C (lit.[37] 197−198 °C); ^{1}H NMR δ 8.34 (d, 1H, J = 8.3 Hz), 8.20 (d, 1H, J = 8.7 Hz), 7.81 (m, 1H), 7.62 (m, 1H), 7.40 (m, 2H), 3.97 (s, 3H); ^{13}C NMR δ 166.2 (q), 161.8 (q), 150.7 (q), 141.8 (q), 132.4 (q), 130.9 (q), 130.0 (t, 2C), 127.4 (t, 2C), 125.6 (t), 124.8 (t), 120.2 (t), 110.7 (t), 52.3 (p); IR (KBr) ν 3420, 2954, 1454, 1436, 1410, 1278, 1245, 1195, 1110, 1054, 1012, 828, 762, 746, 713. Anal. Calcd for $C_{15}H_{11}NO_3$ (253.25): C, 71.14; H, 4.38; N, 5.53. Found: C, 70.98; H, 4.51; N, 5.32.

4-(2-Benzoxazolyl)benzonitrile (3g). The procedure is as described for **3a** but using methyl 4-bromobenzonitrile (1.1 g) instead of 2-bromopyridine: yield 61% (eluent: CH_2Cl_2/petrol 80:20); mp 204−205 °C (lit.[38] 207−209 °C). The other analyses are in accordance with those of the literature.[38]

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