Organic Letters
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Multicomponent Coupling Reaction of Perfluoroarenes with 1,3-Butadiene and Aryl Grignard Reagents Promoted by an Anionic Ni(II) Complex

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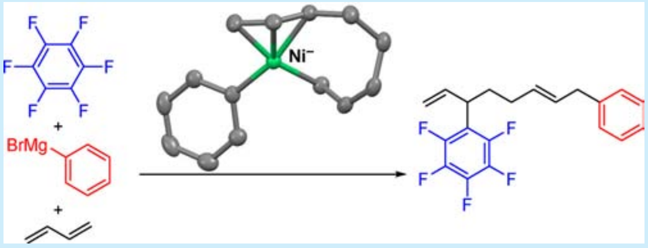
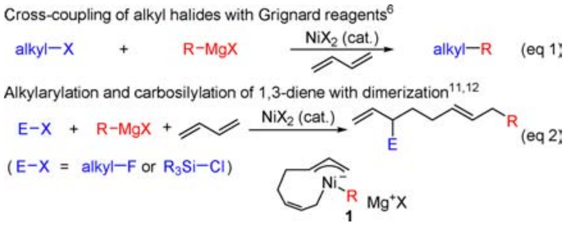
Supporting Information

ABSTRACT: An anionic Ni complex was isolated and its structure determined by X-ray crystallography. With such an anionic complex as a key intermediate, a regio- and stereoselective multicomponent coupling reaction of perfluoroarenes, aryl Grignard reagents, and 1,3-butadiene in a 1:1:2 ratio was achieved, resulting in the formation of 1,6-octadiene derivatives containing two aryl groups, one from the perfluoroarene and the other from the aryl Grignard reagent, at the 3- and 8-positions, respectively.



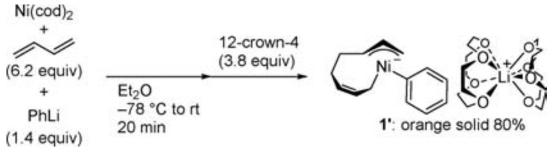
An anionic organoplatinum complex (Zeise's salt) was prepared almost two centuries ago as the first example of an organometallic complex.[1] Despite such a long history of anionic complexes of transition metals, they are not often employed in synthetic reactions as catalysts,[2−5] except for the case of Cu.[3] This is in contrast to the well-developed and still growing use of neutral or cationic transition metal catalysts in organic synthesis. While anionic transition metal complexes have been occasionally proposed as key catalytic intermediates in C−C bond-forming reactions,[2,4,5] their structures as well as their chemical characteristics have rarely been clarified.[5] During the course of our studies on C−C bond-forming reactions using anionic late transition metal complexes, we developed catalytic reactions in which nickelate,[6] palladate,[7] cobaltate,[8] rhodate,[9] and ferrate[10] complexes are thought to play important roles as key catalytic intermediates. For example, the anionic nickel complex **1**, generated by the reaction of Ni(0) with a Grignard reagent in the presence of 1,3-butadiene, has been proposed to catalyze C(sp^3)−C(sp^3) as well as C(sp^3)−C(sp^2) cross-coupling reactions (Scheme 1, eq 1).[6] When chlorosilanes or alkyl fluorides are employed as electrophiles in the presence of an appropriate Grignard reagent, dimerization of the 1,3-diene with concomitant carbosilylation[11] or alkylarylation,[12] respectively, takes place to give double-functionalized 1,6-octadienes (Scheme 1, eq 2). In the present study, the anionic Ni complex **1**[13] was structurally characterized for the first time, and as a synthetic application, a multicomponent coupling reaction[14] of perfluoroarenes with aryl Grignard reagents and two molecules of 1,3-butadiene was developed.

Scheme 1. Nickelate-Catalyzed Transformations



After screening a series of organometallic reagents and additives, we successfully isolated the simple complex NiPh(η^1,η^3-C_8H_{12})·Li(12-crown-4)$_2$ (**1′**) as a thermally unstable orange solid in 80% yield by treating Ni(cod)$_2$ with PhLi and 1,3-butadiene in Et$_2$O followed by the addition of 12-crown-4 (Scheme 2).

Scheme 2. Synthesis of Nickelate Complex 1′



When the nickelate complex **1′** was recrystallized from THF and pentane at −25 °C, a crystalline product suitable for X-ray diffraction analysis was obtained. The molecular structure of **1′** is shown in Figure 1.[15,16] The asymmetric unit consists of an anionic Ni moiety and a Li cation carrying two molecules of 12-crown-4. The octadienediyl moiety arising from the dimerization of 1,3-butadiene is coordinated to the Ni center in an η^1,η^3-fashion with a square-planar geometry including the Ph group.

Treatment of Ni(cod)$_2$ with 1,3-butadiene and PhMgBr in THF-d_8 resulted in a material that showed essentially the same signals[16] as those of the anionic Ni complex **1′**, supporting the formation of the corresponding Mg complex **1b**. We then

Received: August 6, 2016
Published: September 9, 2016

DOI: 10.1021/acs.orglett.6b02343
Org. Lett. 2016, 18, 4868−4871

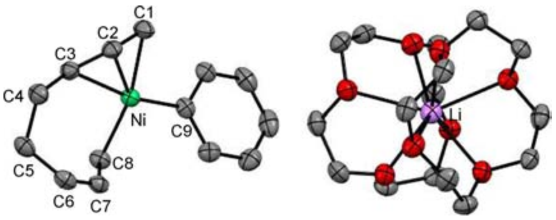
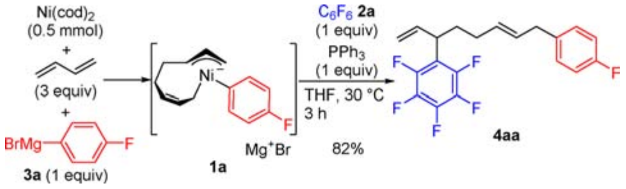


Figure 1. ORTEP drawing of NiPh(η^1,η^3-C_8H_{12})·Li(12-crown-4)$_2$ (**1′**) with thermal ellipsoids at the 50% probability level. H atoms and disordered 12-crown-4 have been omitted for clarity.

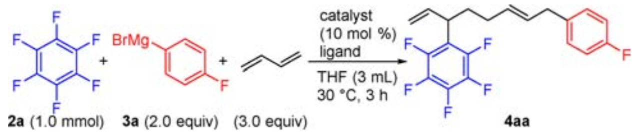
generated nickelate complex **1a** in the same manner from *p*-fluorophenyl Grignard reagent **3a** and examined its reactivity. Hexafluorobenzene (**2a**) reacted with **1a** at the γ-carbon atom of the σ-allyl group to give the four-component coupling product **4aa** in 82% yield in the presence of PPh_3 (Scheme 3). The isolated Ni complex **1′** also catalyzed the multicomponent coupling reaction efficiently.[16]

Scheme 3. Reaction of Nickelate Complex 1a with 2a



Although transition-metal-catalyzed cross-coupling reactions of perfluoro(hetero)arenes with organometallic reagents through C−F bond cleavage have been reported,[17−21] in some cases the reaction requires the assistance of directing groups[18e,21] or strongly electron-withdrawing groups.[18f,g,19,20] The transformations include arylation,[18] alkenylation,[19] alkynylation,[20] and methylation[21] reactions. The multicomponent coupling reaction of perfluoroarenes has not been reported to date,[14,17] and therefore, the present reaction provides a useful synthetic tool for functionalization of perfluoroarenes.[17] We then ran catalytic reactions using **2a** and *p*-fluorophenyl Grignard reagent **3a**. When **2a**, 2 equiv of **3a**, and 3 equiv of 1,3-butadiene were stirred in THF at 30 °C for 3 h in the presence of 10 mol % $NiBr_2$(dme), the four-component coupling product **4aa** was obtained in 33% yield exclusively as a sole regio- and stereoisomer with an *E* configuration (Table 1, entry 1). The addition of PPh_3 improved the yield to 75% (Table 1, entry 2). P(*p*-Tol)$_3$, a more electron-rich phosphine derivative, showed a similar effect, although the sterically hindered P(*o*-Tol)$_3$ and electron-deficient P(*p*-FC_6H_4)$_3$ resulted in lower yields (Table 1, entries 3−5). A bidentate phosphine ligand (dppe) suppressed the reaction (Table 1, entry 6). In the reaction in entry 2, the further reaction of **4aa** with 1,3-butadiene took place to depress the yield of **4aa**. When the amounts of the Grignard reagent and PPh_3 were reduced and $NiCl_2$ was employed, the yield improved to 92% (Table 1, entries 7 and 8). No evidence of the direct cross-coupling between **2a** and **3a** was observed.

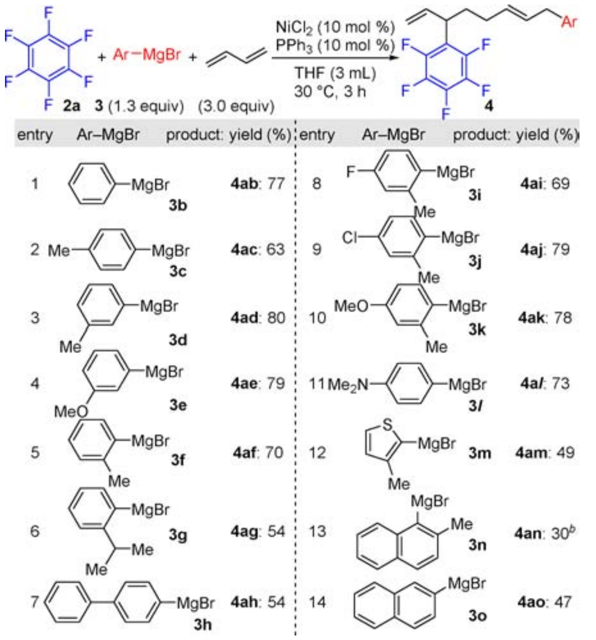
Table 1. Ni-Catalyzed Four-Component Coupling of C_6F_6, *p*-FC_6H_4MgBr, and 1,3-Butadiene



entry	catalyst	ligand (mol %)	yield (%)[a]
1	$NiBr_2$(dme)[b]	none	33
2	$NiBr_2$(dme)	PPh_3 (20)	75
3	$NiBr_2$(dme)	P(*p*-Tol)$_3$ (20)	75
4	$NiBr_2$(dme)	P(*o*-Tol)$_3$ (20)	32
5	$NiBr_2$(dme)	P(*p*-FC_6H_4)$_3$ (20)	44
6	$NiBr_2$(dme)	dppe (10)	2
7[c]	$NiCl_2$	PPh_3 (20)	88
8[c]	$NiCl_2$	PPh_3 (10)	92 (81)

[a] Determined by GC. Isolated yield is in parentheses. [b] dme = 1,2-dimethoxyethane. [c] 1.3 equiv of **3a**.

Table 2. Ni-Catalyzed Four-Component Coupling Using Various Grignard Reagents[a]



entry	Ar–MgBr	product: yield (%)
1	3b	4ab: 77
2	3c	4ac: 63
3	3d	4ad: 80
4	3e	4ae: 79
5	3f	4af: 70
6	3g	4ag: 54
7	3h	4ah: 54
8	3i	4ai: 69
9	3j	4aj: 79
10	3k	4ak: 78
11	3l	4al: 73
12	3m	4am: 49
13	3n	4an: 30[b]
14	3o	4ao: 47

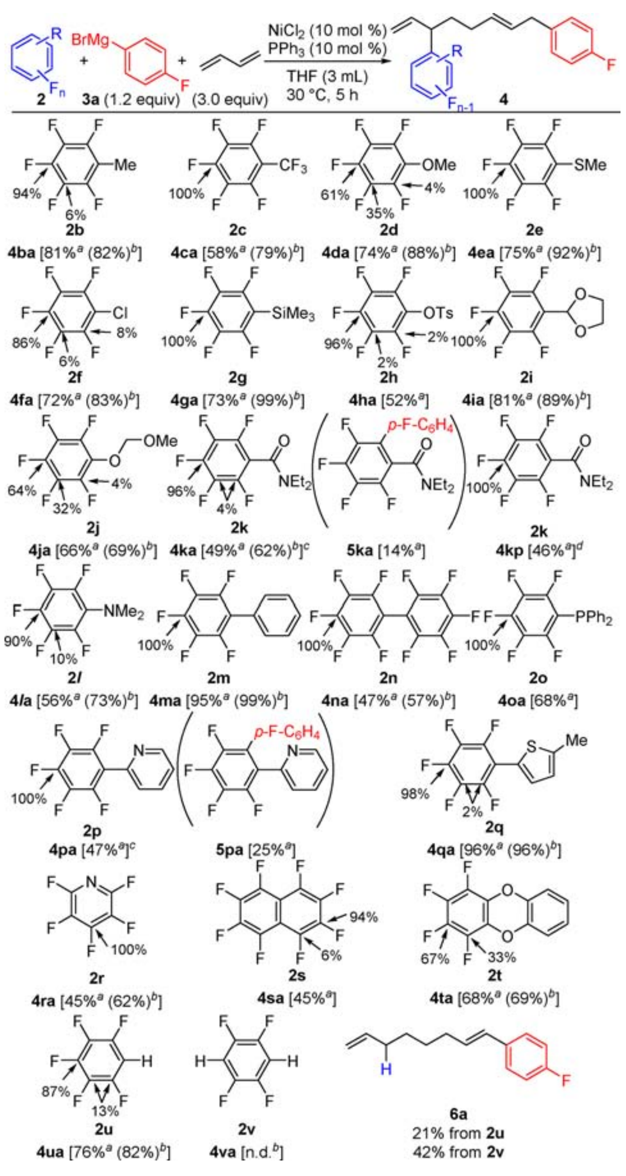
[a] Reaction conditions are the same as in Table 1, entry 8. Isolated yields are shown. [b] Reaction in 10 mL of THF for 18 h.

With the optimal conditions shown in entry 8 in hand, we investigated the scope of the aryl Grignard reagents (Table 2). Phenyl Grignard reagent **3b** reacted with **2a** and 1,3-butadiene to give the corresponding four-component coupling product **4ab** in 77% isolated yield (Table 2, entry 1). Substituents at the *para*, *meta*, and *ortho* positions did not affect the reaction, and the corresponding products **4ac−ah** were produced in good yields (Table 2, entries 2−7). When the sterically hindered *i*-Pr group was introduced at the *ortho* position, the yield was slightly reduced (Table 2, entry 6). Grignard reagents having an electron-withdrawing and/or -donating group(s) at the *para* position participated efficiently in the four-component coupling reaction (Table 2, entries 8−11). Thienyl as well as 1- and 2-naphthyl Grignard reagents resulted in somewhat lower yields (Table 2, entries 12−14).

The scope of the reaction with respect to perfluoroarenes is shown in Scheme 4. The reaction of pentafluorotoluene (**2b**) proceeded smoothly at the *para* position predominantly (94% selectivity), giving **4ba** in 81% total yield. Octafluorotoluene (**2c**) also selectively reacted at the *para* position, but the regioselectivity of the reaction of **2d** was relatively low, and *para*, *meta*, and *ortho* substitution took place competitively in a

DOI: 10.1021/acs.orglett.6b02343
Org. Lett. 2016, 18, 4868−4871

Scheme 4. Ni-Catalyzed Four-Component Coupling Reaction of Perfluoroarenes, 3a, and 1,3-Butadiene

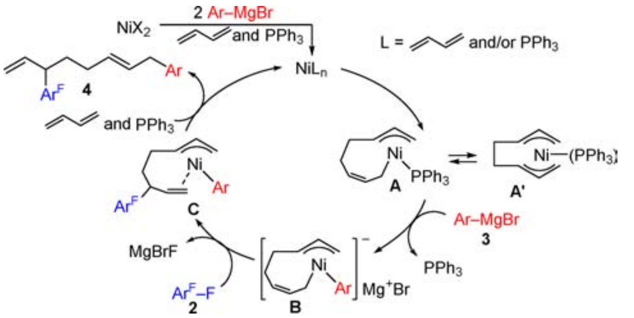


[a]Isolated yields. [b]GC yields. Regioselectivities were determined by GC or NMR (see the SI for details) and are shown in percent. [c]Cross-coupling product **5** was formed. [d]2,6-Dimethylphenyl Grignard reagent **3p** was used instead of **3a**.

61:35:4 ratio in 74% combined yield. These regioselectivities could be explained by the electron density of the perfluoroaryl group, with the present reaction preferably occurring at the more electron-deficient position. The C−S, C−Cl, and C−Si bonds of **2e**−**g** as well as the sulfonyl ester moiety in **2h** remained intact, and only Ar−F bond cleavage was observed. The protecting groups of aldehyde **2i** and phenol **2j** were both tolerated. The reactions of **2k** with Grignard reagents **3a** and **3p** afforded the corresponding products in moderate yields, along with a 14% yield of the direct cross-coupling product **5ka** in the former case. Interestingly, this direct cross-coupling reaction took place only at the *ortho* position, probably as a result of coordination of the amide group to the Mg of the Grignard reagent, thus facilitating the S_NAr reaction as a directing group. This is in contrast to the present four-component coupling, which prefers the *para* position. Indeed, even when perfluoroarenes containing a coordinating group such as Me_2N-, Ph_2P-, or pyridyl were employed, the reaction took place selectively at the *para* position, as in the cases of noncoordinating phenyl- and pentafluorophenyl-substituted arenes **2m** and **2n**. The lower yield of the reaction of **2p** can be attributed to the competing direct coupling reaction with the Grignard reagent **3a** to give **5pa**. The reaction of perfluoropyridine **2r** took place exclusively at the 4-position to give **4ra**, albeit in moderate yield (45%). Octafluoronaphthalene (**2s**) reacted preferably at the 2-position over the 1-position to give **4sa**, although the site selectivity of **2t** was as low as ca. 1:2. Pentafluorobenzene (**2u**) gave the corresponding product **4ua** in 76% yield accompanied by a 21% yield of the protonated product **6a**. In addition, the reaction using **2v** exclusively gave **6a** in 42% yield via protonation of an intermediate by the acidic C−H bond of **2v**.

A plausible reaction pathway is shown in Scheme 5. The Ni precatalyst is initially reduced to Ni(0) by the aryl Grignard reagent. The thus-formed Ni(0) causes the oxidative dimerization of 1,3-butadiene in the presence of PPh_3 to form bis(allyl)nickel intermediate **A** along with its isomer **A′**.[22] Although the neutral Ni species **A** and **A′** are inert toward perfluoroarene **2**,[16] the corresponding ate complex **B** reacts with **2** via an S_NAr mechanism,[23] probably aided by coordination of the Mg cation to activate a C−F bond,[24] resulting in the formation of a new C−C bond at the γ-position of the σ-allyl moiety. Subsequent reductive elimination gives the desired product **4** and Ni(0). Kinetic studies revealed that the S_NAr reaction of **B** with the perfluoroarene is relatively fast in the catalytic cycle.[16]

Scheme 5. Proposed Catalytic Cycle



In conclusion, we have reported the structural characterization of the anionic nickel complex **1′** as the corresponding Li salt of **1** and its use in a multicomponent reaction of perfluoroarenes with aryl Grignard reagents and two molecules of 1,3-butadiene. In this reaction, perfluoroaryl and aryl groups are selectively introduced at the 3- and 8-positions of 1,6-octadiene, respectively. A C−F bond in the perfluoroarene is cleaved with high *para* selectivity via a rapid S_NAr mechanism by the reaction with anionic Ni(II) complex **1**, in sharp contrast to previously reported reactions of perfluoroarenes, which involve oxidative addition of C−F bonds to zero-valent metal catalysts.[18−20] The proposed mechanism would provide a new strategy for the catalytic transformation of perfluoroarenes.

DOI: 10.1021/acs.orglett.6b02343
Org. Lett. 2016, 18, 4868−4871

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02343.

Additional results, procedures, characterization data, and NMR spectra (PDF)
Crystallographic data for **1′** (CIF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by JSPS KAKENHI Grants JP25248025, JP16H06039, JP25105734, and JP16H01150. We thank JSPS for the Japanese−German Graduate Externship. T.I. thanks The Sumitomo Foundation.

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(15) CCDC-1478800 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the CCDC via www.ccdc.cam.ac.uk/data_request/cif.

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