

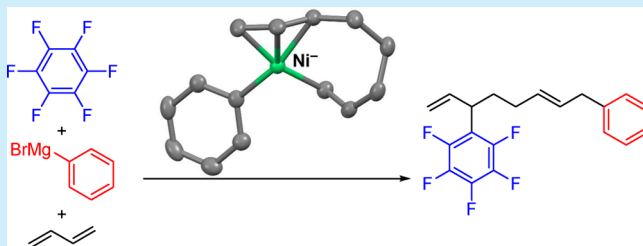
Multicomponent Coupling Reaction of Perfluoroarenes with 1,3-Butadiene and Aryl Grignard Reagents Promoted by an Anionic Ni(II) Complex

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S 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.

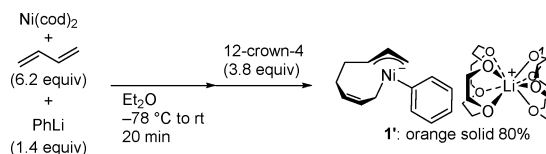


An anionic organoplatinum complex (Zeise's salt) was prepared almost two centuries ago as the first example of an organometallic complex.¹ Despite such a long history of anionic complexes of transition metals, they are not often employed in synthetic reactions as catalysts,^{2–5} except for the case 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 ferrate¹⁰ 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(sp³)–C(sp³) as well as C(sp³)–C(sp²) 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 carbosilylation¹¹ 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 reaction¹⁴ of perfluoroarenes with aryl Grignard reagents and two molecules of 1,3-butadiene was developed.

After screening a series of organometallic reagents and additives, we successfully isolated the simple complex NiPh(η¹,η³-C₈H₁₂)·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 Et₂O followed by the addition of 12-crown-4 (Scheme 2).

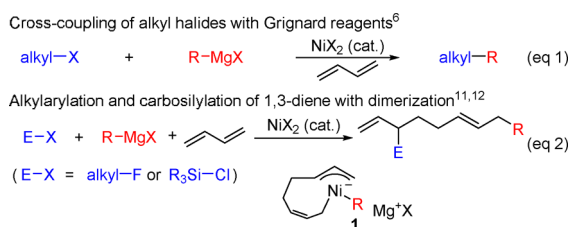
Scheme 2. Synthesis of Nickelate Complex **1'**



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 η¹,η³-fashion with a square-planar geometry including the Ph group.

Treatment of Ni(cod)₂ with 1,3-butadiene and PhMgBr in THF-d₈ resulted in a material that showed essentially the same signals¹⁶ as those of the anionic Ni complex **1'**, supporting the formation of the corresponding Mg complex **1b**. We then

Scheme 1. Nickelate-Catalyzed Transformations



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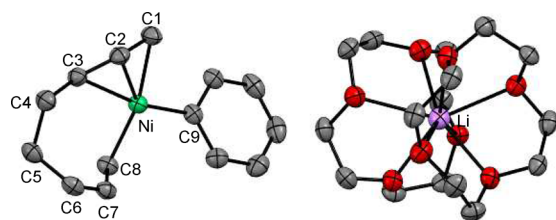
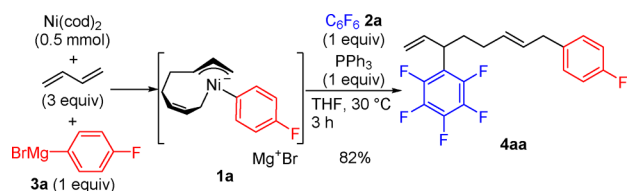


Figure 1. ORTEP drawing of $\text{NiPh}(\eta^1, \eta^3\text{-C}_8\text{H}_{12})\cdot\text{Li}(12\text{-crown-4})_2$ (**1'**) with thermal ellipsoids at the 50% probability level. H atoms and disordered 12-crown-4 have been omitted for clarity.

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

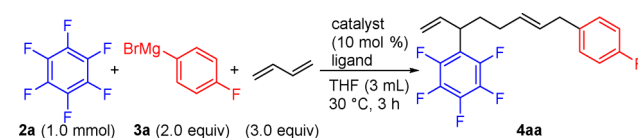
Scheme 3. Reaction of Nickelate Complex **1a** with **2a**



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 alkylation,²⁰ and methylation²¹ 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 % $\text{NiBr}_2(\text{dme})$, 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). $\text{P}(p\text{-Tol})_3$, a more electron-rich phosphine derivative, showed a similar effect, although the sterically hindered $\text{P}(o\text{-Tol})_3$ and electron-deficient $\text{P}(p\text{-FC}_6\text{H}_4)_3$ 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.

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

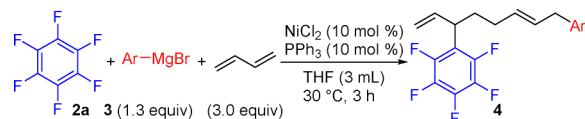
Table 1. Ni-Catalyzed Four-Component Coupling of C_6F_6 , $p\text{-FC}_6\text{H}_4\text{MgBr}$, and 1,3-Butadiene



entry	catalyst	ligand (mol %)	yield (%) ^a
1	$\text{NiBr}_2(\text{dme})^b$	none	33
2	$\text{NiBr}_2(\text{dme})$	PPh_3 (20)	75
3	$\text{NiBr}_2(\text{dme})$	$\text{P}(p\text{-Tol})_3$ (20)	75
4	$\text{NiBr}_2(\text{dme})$	$\text{P}(o\text{-Tol})_3$ (20)	32
5	$\text{NiBr}_2(\text{dme})$	$\text{P}(p\text{-FC}_6\text{H}_4)_3$ (20)	44
6	$\text{NiBr}_2(\text{dme})$	<i>dppe</i> (10)	2
7 ^c	NiCl_2	PPh_3 (20)	88
8 ^c	NiCl_2	PPh_3 (10)	92 (81)

^aDetermined by GC. Isolated yield is in parentheses. ^b*dme* = 1,2-dimethoxyethane. ^c1.3 equiv of **3a**.

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

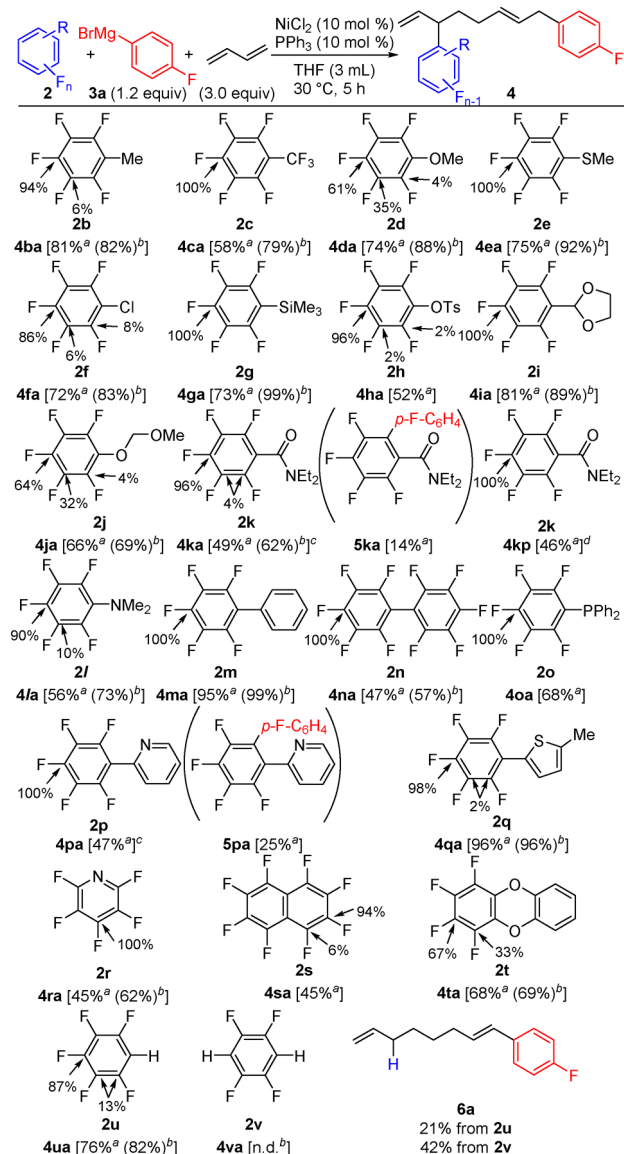


entry	Ar–MgBr	product	yield (%)	entry	Ar–MgBr	product	yield (%)
1	3b	4ab	77	8	3i	4ai	69
2	3c	4ac	63	9	3j	4aj	79
3	3d	4ad	80	10	3k	4ak	78
4	3e	4ae	79	11	3l	4al	73
5	3f	4af	70	12	3m	4am	49
6	3g	4ag	54	13	3n	4an	30 ^b
7	3h	4ah	54	14	3o	4ao	47

^aReaction conditions are the same as in Table 1, entry 8. Isolated yields are shown. ^bReaction in 10 mL of THF for 18 h.

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

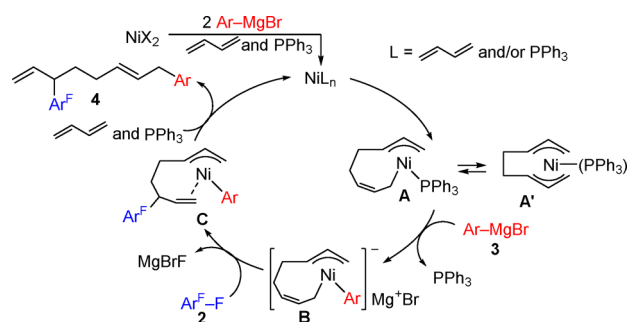
Scheme 4. Ni-Catalyzed Four-Component Coupling Reaction of Perfluoroarenes, 3a, and 1,3-Butadiene


^aIsolated yields. ^bGC yields. Regioselectivities were determined by GC or NMR (see the SI for details) and are shown in percent. ^cCross-coupling product 5 was formed. ^d2,6-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

Scheme 5. Proposed Catalytic Cycle


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

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.

■ ASSOCIATED CONTENT

S 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.

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