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NICKEL-CATALYZED CROSS-COUPLING OF ARYL PHOSPHATES WITH GRIGNARD AND ORGANOALUMINIUM REAGENTS. SYNTHESIS OF ALKYL-, ALKENYL-, AND ARYLBENZENES FROM PHENOLS

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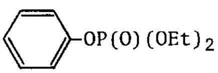
Summary: Aryl phosphates derived from phenols were converted into alkyl-, alkenyl-, and arylbenzenes in high yields by cross-coupling with various kinds of Grignard and organoaluminium reagents in the presence of nickel(II) catalysts.

Synthesis of aromatic compounds with alkyl, alkenyl, or aryl substituents from phenols by conversion of the carbon-oxygen bond into the carbon-carbon bond is an important and necessary synthetic objective. Recently, Wenkert et al. have succeeded in the preparation of biaryls from aryl methyl ethers by reaction with a Grignard reagent in the presence of a nickel-phosphine complex, though the method suffers from disadvantages that the yields are usually low even under drastic conditions and only the phenyl Grignard reagent can be used.[1] We now report herein an effective procedure with wide applicability for the preparation, which has been achieved by nickel-catalyzed cross-coupling of aryl phosphates with various types of organometallic reagents under mild reaction conditions.

$$\underset{\mathbf{1}}{\text{Ar-OH}} \xrightarrow[\text{2) ClP(O)(OEt)}_2]{\text{1) NaH/THF}} \underset{\mathbf{2}}{\text{Ar-OP(O)(OEt)}_2} \xrightarrow[\text{[Ni]}]{\text{RM } (\mathbf{3})} \underset{\mathbf{4}}{\text{Ar-R}}$$

2a:

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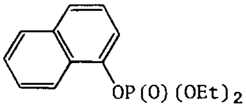
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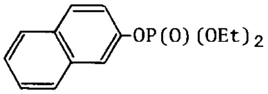

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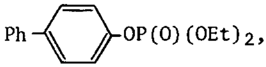
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2e:

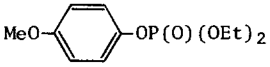
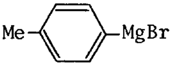
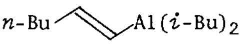
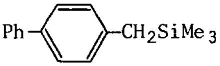
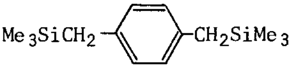
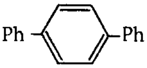
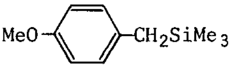

2f:


Table 1. Cross-Coupling of Aryl Phosphates with Grignard Reagents and Organoaluminium Reagents in the Presence of Nickel Catalysts[a]

Entry	Aryl phosphate **2**	RM **3**	Catalyst	Product[b] **4**	Yield[c] (%)
1	**2a**	Me_3SiCH_2MgCl (**3a**)	$Ni(acac)_2$	$Ph-CH_2SiMe_3$	(77)
2	$P(O)(OPh)_3$	Me_3SiCH_2MgCl (**3a**)[d]	$Ni(acac)_2$	$Ph-CH_2SiMe_3$	(98)
3	**2a**	 (**3b**)	$Ni(acac)_2$		(91)
4	**2b**	Me_3SiCH_2MgCl (**3a**)	$Ni(acac)_2$	$1-Np-CH_2SiMe_3$	79
5	**2b**	PhMgBr (**3c**)	$Ni(acac)_2$	1-Np-Ph	(77)
6	**2b**	$PhCH_2MgCl$ (**3d**)	$NiCl_2(PPh_3)_2$	$1-Np-CH_2Ph$	80
7	**2b**	*n*-BuMgCl (**3e**)[e]	$NiCl_2(dppp)$	1-Np-*n*-Bu	82
8	**2b**	Et_3Al (**3f**)	$NiCl_2(dppp)$	1-Np-Et	95
9	**2b**	 (**3g**)[f]	$Ni(acac)_2$		99
10	**2c**	PhMgBr (**3c**)	$Ni(acac)_2$	2-Np-Ph	75
11	**2d**	Me_3SiCH_2MgCl (**3a**)	$Ni(acac)_2$		56
12	**2e**	Me_3SiCH_2MgCl (**3a**)[d]	$Ni(acac)_2$		52
13	**2e**	PhMgBr (**3c**)[d]	$Ni(acac)_2$		80
14	**2f**	Me_3SiCH_2MgCl (**3a**)[e]	$Ni(acac)_2$		54

[a] The reaction was carried out in ether at room temperature for 6∿16 h unless otherwise noted. **2** : **3** : catalyst = 1 : 2∿3 : 0.05. [b] 1-Np and 2-Np stand for 1-naphthyl and 2-naphthyl, respectively. [c] Isolated yields based on the amount of aryl phosphate used. Yields determined by GLC are given in parentheses. [d] Five equivalents of the Grignard reagent was used. [e] Reflux in ether for 6 h. [f] The organoaluminium reagent was prepared from 1-hexyne and diisobutylaluminium hydride in THF. The coupling reaction was carried out in refluxing THF for 6 h.

Aryl diethyl phosphates **2** were prepared by treatment of 1 equiv of a phenol **1** with 1.2 equiv of sodium hydride and 1.1 equiv of diethyl phosphorochloridate in dry THF.[2]

Catalytic activities of several transition metal complexes were examined for the coupling of phenyl diethyl phosphate (**2a**) with trimethylsilylmethylmagnesium chloride (**3a**). Nickel acetylacetonate [$Ni(acac)_2$] was found to be the most active catalyst giving rise to benzyltrimethylsilane in 77% yield under mild reaction conditions (at room temperature for 15 h) (entry 1 in Table 1). Nickel bromide was a little less active giving 40% yield of the coupling product. Nickel(II) complexes with tertiary phosphines such as triphenylphosphine or 1,3-bis(diphenylphosphino)propane (dppp) were almost inactive for the reaction of **3a** at room temperature while they gave 20∿50% yields at ether reflux. Tetrakis(triphenylphosphine)-palladium(0) did not catalyze the cross-coupling at all, though the palladium(0) complex has been reported to be an effective catalyst for the reaction of alkenyl phosphates with organoaluminium or Grignard reagents.[3,4,5] Palladium(II) chloride, cobalt(II) chloride, iron(III) acetylacetonate, and copper(I) bromide were all inactive.

The reaction of triphenyl phosphate with five-fold excess of the Grignard reagent **3a** gave one equiv of the coupling product (entry 2), showing that the diphenyl phosphate anion formed is not subject to the cross-coupling any more. Phenyl, *p*-tolyl, and benzyl groups as well as trimethylsilylmethyl group can be introduced into phenyl, 1-naphthyl, and 2-naphthyl diethyl phosphates (**2a**,**b**,**c**) in high yields by use of $Ni(acac)_2$ or $NiCl_2(PPh_3)_2$ (entries 3∿6 and 10).[6]

In a typical experiment (entry 4), to a mixture of $Ni(acac)_2$ (13 mg, 0.05 mmol) and trimethylsilylmethylmagnesium chloride (**3a**) (3.0 mmol) in ether (5 ml) was added 1-naphthyl diethyl phosphate (**2b**) (280 mg, 1.0 mmol). The mixture was stirred at room temperature for 10 h, and then hydrolyzed with dilute hydrochloric acid. After work-up in the usual manner, medium pressure column chromatography on silica gel eluting with hexane gave 1-trimethylsilylmethylnaphthalene (169 mg, 79% yield).

Nickel acetylacetonate catalyzed the reaction of *E*-1-hexenyldiisobutylaluminium[7] with 1-naphthyl phosphate **2b** to give stereoselectively *E*-1-(1-naphthyl)-1-hexene in quantitative yield (entry 9). Cross-coupling of organometallic reagents containing labile β-hydrogens was not effected by $Ni(acac)_2$, but use of $NiCl_2(dppp)$ as catalyst enables the reaction to proceed, giving rise to *n*-butyl- and ethylnaphthalene from reaction of **2b** with *n*-butylmagnesium chloride (**3e**) and triethylaluminium (**3f**), respectively (entries 7 and 8). 1,4-Bis(trimethylsilylmethyl)benzene[6] and *p*-terphenyl could be obtained from the diphosphate **2e** derived from hydroquinone, both of the phosphinoxy groups being substituted (entries 12 and 13). Reaction of 4-methoxyphenyl phosphate (**2f**) with the Grignard reagent **3a** in the presence of Ni(acac)$_2$ gave (4-methoxyphenylmethyl)trimethylsilane,[6] leaving the methoxy group intact (entry 14).

In general, aryl phosphates are similar to aryl chlorides in reactivity toward cross-coupling catalyzed by transition metal complexes. They are less reactive than aryl bromides or iodides which undergo catalysis by palladium as well as nickel complexes, whereas the chlorides do enter only into nickel-catalyzed coupling.[8,9] But aryl phosphates are more reactive than aryl tosylates, methyl ethers, and silyl ethers, none of which underwent the Grignard cross-coupling under the present reaction conditions.

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