

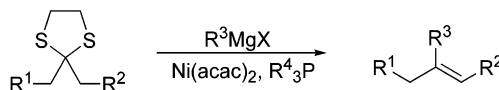
Nickel-Catalyzed Olefination of  
Unactivated Aliphatic DithioacetalsLi-Fu Huang,<sup>†,§</sup> Chih-Hao Huang,<sup>†</sup> Baldur Stulgies,<sup>§,⊥</sup> Armin de Meijere,<sup>⊥</sup> and  
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## ABSTRACT



Olefination of aliphatic dithioacetals with Grignard reagents is catalyzed by Ni(acac)<sub>2</sub> in the presence of an appropriate trialkylphosphine ligand.

There has been an increasing interest in the transition-metal-catalyzed cross coupling of aliphatic halides or related electrophiles with nucleophiles.<sup>1–4</sup> The use of electron-rich aliphatic phosphine ligands, inter alia, has provided a powerful access to these coupling reactions.<sup>2</sup> We have extensively studied the nickel-catalyzed cross-coupling reactions of benzylic or allylic dithioacetals with Grignard reagents.<sup>5,6</sup> In the absence of an auxiliary chelating group(s)<sup>6</sup> or specially de-

signed substrates,<sup>7</sup> aliphatic dithioacetals alone do not react with Grignard reagents, even in the presence of the typical nickel triarylphosphine catalyst. We envisaged that an increase of the nucleophilicity of the nickel catalyst by incorporation of a trialkylphosphine ligand might enhance the reactivity of the catalytic center toward the oxidative addition across the carbon–sulfur bond, and we now wish to document the first examples of such a nickel-catalyzed olefination of unactivated aliphatic dithioacetals with Grignard reagents.

In the beginning of this work, we examined the performance of different kinds of trialkylphosphine ligands in the olefination reaction of **1** with the Grignard reagent. Thus, treatment of 2-(2'-naphthyl)acetaldehyde dithioacetal **1** with 3 equiv of MeMgI in the presence of 5 mol % of Ni(acac)<sub>2</sub> and 12 mol % of trialkylphosphine in refluxing toluene for 20 h afforded a mixture of the naphthyl derivatives **2–4** (eq 1). The results are summarized in Table 1.

The reaction may proceed according to a mechanism similar to the one proposed for the benzylic substrates.<sup>5,6</sup> The two carbon–sulfur bonds in **1** may be cleaved at different stages and the overall reaction may involve a coupling process followed by an elimination step. The organonickel intermediate **5** would be expected to undergo nonselective

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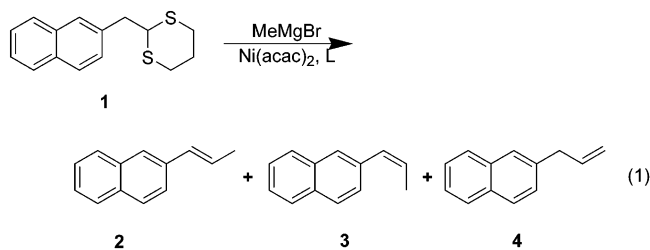
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**Table 1.** Ni(acac)<sub>2</sub>-Catalyzed Olefination of **1** in the Presence of Trialkylphosphine Ligand

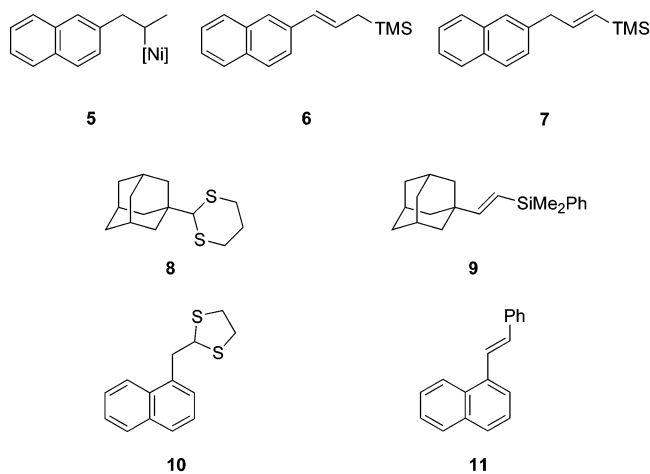


entry	ligand (mol %)	% yield	2/3/4 <sup>a</sup>
1	P(Cy) <sub>3</sub> ( <b>12</b> )	34	10/1/4
2	P( <i>n</i> -Bu) <sub>3</sub> ( <b>12</b> )	20	10/1/3
3	P( <i>t</i> -Bu) <sub>3</sub> ( <b>12</b> )	78	12/1/2.5
4	P( <i>t</i> -Bu) <sub>2</sub> Me ( <b>12</b> )	70	10/1/4

<sup>a</sup> Estimated by <sup>1</sup>H spectrum.

$\beta$ -hydride elimination giving a mixture of **2**–**4**. Although the product distributions were not much affected by the nature of the trialkylphosphine ligands, phosphines with a large cone angle may cause higher reactivity in these olefination reactions, and indeed, the best yield was obtained when P<sup>*t*</sup>Bu<sub>3</sub> was used.

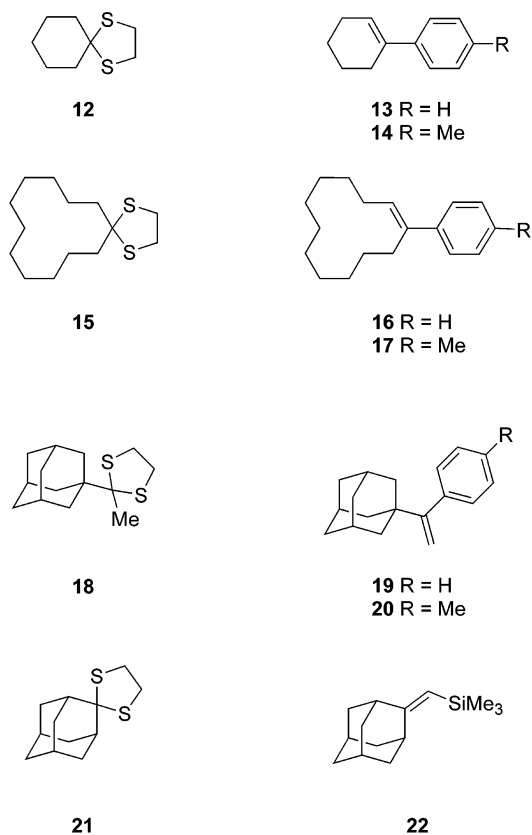
When **1** was treated with TMSCH<sub>2</sub>MgCl in the presence of 5 mol % of Ni(acac)<sub>2</sub> and 12 mol % of P<sup>*t*</sup>Bu<sub>3</sub> under the same conditions as just described, allylsilane **6** was obtained in 57% yield. Interestingly, only a trace amount of vinylsilane **7** was detected, which was easily removed from **6** by recrystallization. Vinylsilane **9** was obtained in 91% yield from the nickel-catalyzed reaction of **8** with PhMe<sub>2</sub>SiCH<sub>2</sub>MgCl under the same conditions. In a similar manner, reaction of **10** with PhMgBr afforded **11** (containing a trace amount of the *cis* isomer) in 50% yield. Apparently, the ring size of the dithioacetal moiety does not have any influence on the reactivity under these olefination conditions.



Ketone dithioacetals also reacted smoothly under similar conditions. Again, the nature of the ligand does influence the yield of the reaction. Thus, nickel-catalyzed reaction of cyclohexanone dithioacetal **12** with PhMgBr afforded **13** in 48% yield when P<sup>*t*</sup>Bu<sub>3</sub> was employed as the ligand. The yield

of **13** improved to 56% when P<sup>*t*</sup>Bu<sub>2</sub>Me was used. Similarly, the cyclododecanone derivative **15** was transformed into the corresponding olefination product **16** (*E/Z* = 10/1) in 52% and 67% yields, respectively, under the same conditions with P<sup>*t*</sup>Bu<sub>3</sub> and P<sup>*t*</sup>Bu<sub>2</sub>Me as the ligand. Since ketone dithioacetals in general are more sterically congested than aldehyde dithioacetals, a less bulky ligand may provide a more spacious environment to lead to the desired coupling product. Thus, by using P<sup>*t*</sup>Bu<sub>2</sub>Me as the ligand, the Ni(acac)<sub>2</sub>-catalyzed reactions of **12** and **15** with 4-MeC<sub>6</sub>H<sub>4</sub>MgBr afforded **14** and **17** in 59% and 63% yields, respectively. Dithioacetals derived from acyclic ketones behaved similarly. Treatment of **18** with PhMgBr under the same conditions, with P<sup>*t*</sup>Bu<sub>2</sub>Me as the ligand, gave the corresponding olefination product **19** in 61% yield. Olefin **20** was isolated in 55% yield from a similar reaction of **18** with 4-MeC<sub>6</sub>H<sub>4</sub>MgBr. Aliphatic Grignard reagent also reacted smoothly. For example, treatment of **21** with Me<sub>3</sub>SiCH<sub>2</sub>MgCl afforded the corresponding vinylsilane **22** in 73% yield by using the same procedure.

In summary, we have demonstrated the first example of the nickel-catalyzed cross-coupling reaction of the aliphatic dithioacetals derived from aldehydes and ketones with Grignard reagents. Our results document an additional application of trialkylphosphines to assist the activation of otherwise unactivated aliphatic carbon–sulfur bonds in the nickel-catalyzed cross-coupling reaction. The reaction may provide a useful procedure for a direct conversion of a dithioacetal-protected carbonyl group into the corresponding olefins. In particular, vinylsilanes are conveniently obtained by this route. Further investigation to improve the regioselectivity in the formation of the new double bond is in progress in our laboratory.



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**Supporting Information Available:** Experimental details of the nickel-catalyzed reactions of dithioacetals with Grignard reagents. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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