In situ Activation of C_{sp^3} -S Bond by Tandem Nickel-catalysed Alkenation of 1-Aryl-1,3-bis(dithioacetals) with Me₃SiCH₂MgCl

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The aliphatic C–S bond is activated by the *in situ* generation of a double bond *via* tandem nickel-catalysed alkenation of 1-aryl-1,3-bisdithioacetals with Me_3SiCH_2MgCl .

Although transition metal-catalysed cross coupling reactions are highly versatile in carbon–carbon bond formation,¹ the applications of the corresponding process with the unactivated C_{sp} –X bond are limited.² It is noted that only neopentyl iodides undergo coupling reactions with aromatic Grignard reagents in the presence of a palladium catalyst.² The major impediment is the low reactivity of the C_{sp} –X bond towards oxidative addition with transition metals, and occasionally side reactions such as reduction, β -elimination, as well as homocoupling becoming predominant.^{2b-d} One possible way to solve this problem is to design a substrate which could, under the reaction conditions, *in situ* generate a double bond so that the originally unreactive C_{spⁱ⁻}X moiety becomes an allylic one. Consequently, further coupling with the Grignard reagent could take place. Our recent discovery on the nickel-catalysed alkenation of benzylic or allylic dithioacetals





Table 1 NiCl₂(PPh₃)₂-catalysed reaction of 1 with Me₃SiCH₂MgCl

1	Product			
	3	$\operatorname{Yield}(\%)(E:Z)$	4	Yield(%)(E:Z)
a	а	30 (20:80)	а	57 (60:40)
b	а	55 (14:86)	а	33 (60:40)
с	b	53 (10:90)	b	22 (68:32)
d	b	54 (10:90)	b	21 (60:40)
e	с	57 (12:88)	с	35 (60:40)
f	d	46 (14 : 86)	d	40 (60 : 40)

allylsilane is obtained predominantly when five-membered dithiolane is employed, and vinylsilane becomes the major product using six-membered dithiane as the substrate.⁵ The ring size of the nonbenzylic dithioacetal moiety in 1, however, had no effect on the product distribution. Thus, the reactions of 1c and d gave similar ratios of 3b and 4b.

Table 1 summarizes representative examples of the nickelcatalysed reactions of 1 with Me₃SiCH₂MgCl. Dienes 3 containing both vinyl- and allyl-silane functionalities were obtained in moderate yields.⁶ Separation of 3 from 4 was readily achieved by column chromatography on silica gel. The stereochemistry of these products was determined by nuclear Overhauser effect (NOE) experiments.[†] The stereoselectivity of 3 can be understood within the framework of steric requirements of the β -elimination process, the intermediate 5a being more stable than its conformer 5b.

In summary, these results have demonstrated the first example of the *in situ* generation of a double bond to activate an aliphatic C–S bond. The application of this tandem reaction has illustrated a novel approach leading to diene synthesis. Although, at this stage, we cannot avoid obtaining **4** as the side product, the method does provide a convenient synthesis of dienes **3** in moderate yields.

We thank the National Science Council of the Republic of China for support.

Received, 9th January 1992; Com. 2/00107A

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with Grignard reagents $[eqn. (1)]^3$ provides a useful model to test this viewpoint; the strategy is outlined in eqn. (2). Bis(dithioacetal) **1** contains one benzylic dithioacetal moiety and one aliphatic dithioacetal group located at the C-3 position relative to the benzylic dithioacetal functionality. In the presence of the nickel catalyst, the benzylic dithioacetal group would be expected to react first with the Grignard reagent generating intermediate **2** which continuously reacts with the Grignard reagent under the reaction conditions leading to diene **3**.

We have shown previously that the nickel-catalysed cross coupling reaction of the dithioacetals occurs *via* the first formation of the carbon–carbon bond followed by a formal elimination step.³ Thus, **4** may also be formed in addition to **2** depending on the orientation of β -elimination. In order to activate the aliphatic dithioacetal moiety in **1**, the first coupling reaction would require the formation of the double bond regioselectively; and only allylic dithioacetal **2** can further couple with the Grignard reagent, **4** being unreactive.

Bis(dithioacetals) were conveniently prepared according to modified literature procedures.⁴ At the beginning of this work, **1a** was treated with 6 equiv. of Me₃SiCH₂MgCl in the presence of 5 mol% of NiCl₂(PPh₃)₂ in refluxing benzene-diethyl ether for 16 h to afford a 35:65 ratio of **3a**⁺ (E: Z = 20:80) and **4a** (E: Z = 60:40) in 87% yield. On the other hand, the reaction of **1b** afforded in 88% yield a 63:37 mixture of **3a** (E: Z = 14:86) and **4a** (E: Z = 40:60). These results are compatible with our earlier findings where 565

[†] The *E* and *Z* isomers were readily separated by HPLC. ¹H NMR data (CDCl₃, 200 MHz): 1E,3Z-3a: δ -0.08 (s, 9 H), 0.15 (s, 9 H), 2.11 (s, 2 H), 3.78 (s, 3 H), 5.86 (d, J 18 Hz, 1 H), 6.28 (d, J 11 Hz, 1 H), 6.82 (dd, J11, 18 Hz, 1 H), 6.85 (d, J11 Hz, 2 H), 7.38 (d, J11 Hz, 2 H); $1E.3E-3a: \delta = -0.19 (s, 9 H), 0.00 (s, 9 H), 1.91 (s, 2 H), 3.81 (s, 3 H)$ H), 5.68 (d, J 18 Hz, 1 H), 5.96 (d, J 11 Hz, 1 H), 6.60 (dd, J 11, 18 Hz, 1 H), 6.83 (d, J 11 Hz, 2 H), 7.15 (d, J 11 Hz, 2 H); 1E, 3Z-3b: δ -0.12 (s, 9 H), 0.99 (s, 9 H), 2.19 (s, 2 H), 5.87 (d, J 18 Hz, 1 H), 6.26 (d, J 11 Hz, 1 H), 6.79 (dd, J 11, 18 Hz, 1 H), 7.20–7.40 (m, 5 H); 1E,3E-3b: δ -0.03 (s, 9 H), 0.18 (s, 9 H), 1.96 (s, 2 H), 5.68 (d, J 18 Hz, 1 H), 5.98 (d, J 11 Hz, 1 H), 6.58 (dd, J 11, 18 Hz, 1 H, 25% NOE enhancement upon irradiation at δ 2.19), 7.18-7.36 (m, 5 H); 1E,3Z-3c: δ -0.10 (s, 9 H), 0.09 (s, 9 H), 2.17 (s, 2 H), 2.31 (s, 3 H), 5.84 (d, J 18 Hz, 1 H), 6.25 (d, J 11 Hz, 1 H), 6.78 (dd, J 11, 18 Hz, 1 H), 7.08 (d, J 8 Hz, 2 H), 7.27 (d, J 8 Hz, 2 H); 1E,3E-3c: δ -0.17 (s, 9 H), -0.04 (s, 9 H), 1.92 (s, 2 H), 2.33 (s, 3 H), 5.68 (d, J 18 Hz, 1 H), 5.96 (d, J 11 Hz, 1 H), 6.60 (dd, J 11, 18 Hz, 1 H), 7.07 (d, J 8 Hz, 2 H), 7.30 (d, J 8 Hz, 2 H); 1E,3Z-3d: -0.08 (s, 9 H), 0.12 (s, 9 H), 2.22 (s, 2 H), 5.89 (d, J 18 Hz, 1 H), 6.34 (d, J 11 Hz, 1 H), 6.82 (dd, J 11, 18 Hz, 1 H), 7.31-7.62 (m, 9 H); 1E,3E-3d: δ -0.13 (s, 9 H), 0.01 (s, 9 H), 1.98 (s, 2 H), 5.74 (d, J 18 Hz, 1 H), 6.03 (d, J 11 Hz, 1 H), 6.65 (dd, J 11, 18 Hz, 1 H), 7.29-7.65 (m, 9 H).