## LETTER

## Direct Carbon–Carbon Bond Formation from Alcohols and Active Methylenes using NaHSO<sub>4</sub>/SiO<sub>2</sub>

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**Abstract:** A simple and efficient procedure for carbon–carbon bond formation has been developed starting from alcohols and active methylene-containing compounds using silica gel supported sodium hydrogen sulfate (NaHSO<sub>4</sub>/SiO<sub>2</sub>) under mild conditions. NaHSO<sub>4</sub>/SiO<sub>2</sub> can be reused without loss of catalytic activity at least ten times.

Key words: carbon–carbon coupling, silica gel, alcohol, supported catalysts

The C–C bond formation reactions are fundamental in organic synthesis. General procedures for C–C bond formation reactions typically involve using reactive nucleophiles (NuH) or organometallic compounds (R<sup>1</sup>M) and halides (R<sup>2</sup>X) or related species. These species are often prepared from active methylenes and alcohols. However, the general method for C–C bond formation using R<sup>1</sup>M and R<sup>2</sup>X generates stoichiometric amounts of unwanted MX. Direct substitution of the hydroxyl group in an alcohol by nucleophiles could be considered as an ideal process because of the generation of H<sub>2</sub>O as an only byproduct and because of the wide availability of starting materials (Figure 1).



Figure 1

Khalaf et al.<sup>1</sup> have reported such a transformation using an excess of  $H_2SO_4$  and either  $H_3PO_4$  or a stoichiometric amount of AlCl<sub>3</sub>. The catalytic activation of alcohols is considered to be difficult due to the poor leaving ability of the OH group. In 2006, Yasuda et al.<sup>2</sup> reported C–C bond formation from alcohols and active methylene-containing compounds mediated by indium trichloride, and Sanz et al.<sup>3</sup> reported the metal-free catalytic substitution of alcohols using a catalytic amount of Brønsted acid such as

*SYNLETT* 2011, No. 20, pp 2971–2976 Advanced online publication: 28.11.2011 DOI: 10.1055/s-0031-1290083; Art ID: U06611ST © Georg Thieme Verlag Stuttgart · New York PTS and polymer-supported PTS. Similar reactions have been reported using Lewis or Brønsted acid as a catalyst in recent years.<sup>4-9</sup> Moreover, Brønsted acid ionic liquid also catalyzed the reaction of 1,3-dicarbonyl compounds with alcohols.<sup>10</sup> However, these reactions require long reaction times, high temperatures and large amounts of nucleophilic species. In the course of our study of synthetic methods using inorganic solid-supported reagents, we have found that NaHSO<sub>4</sub>/SiO<sub>2</sub> catalyzes the direct nucleophilic substitution of alcohols. The advantages of the procedure using inorganic-supported reagents are: (i) the supported reagents could be separated after use from the reaction mixture by simple filtration; (ii) used supported reagents could be regenerated extensively by drying in vacuo. Similar reactions using supported reagents, HClO<sub>4</sub>/SiO<sub>2</sub>, have been reported very recently,<sup>11</sup> however, excess amounts of material and long reaction times were needed to complete the reactions. Furthermore, the  $HClO_4/SiO_2$  system could not be reused for subsequent reactions.

In this paper we describe direct C–C bond formation from alcohols and active methylenes using a reusable  $NaHSO_4/SiO_2$  system (Scheme 1).



Scheme 1 Direct C-C bond formation using NaHSO<sub>4</sub>/SiO<sub>2</sub>

The reaction of acetyl acetone (1a) with benzhydrol (2a) was investigated as a model reaction to determine the optimum reaction conditions for the synthesis of 3; the results are summarized in Table 1.

When a mixture of **1a** (10 mmol), **2a** (2 mmol), and NaHSO<sub>4</sub>/SiO<sub>2</sub> (2.1 mmol) was stirred in dichloroethane (DCE) at 80 °C for 180 minutes, **3aa** was obtained in 95% yield. Although the amount of **1a** was reduced until equivalent to the amount of **2a** in the same reaction, the yields of **3aa** did not decrease; however, the yield of **3aa** did decrease when the reaction time was shortened (Table 1, entries 4 and 5). In the reaction using an equivalent amount of **1a** and **2a**, as the reaction temperature was decreased,

the yield of **3aa** decreased along with increasing amounts of by-product (Table 1, entries 4 and 6–8). The structure of the by-product was deduced to be dibenzhydryl ether (**4**) on the basis of its NMR spectroscopic data and by HRMS. When the reaction was carried out with reduced amounts of NaHSO<sub>4</sub>/SiO<sub>2</sub>, the yield of **3aa** decreased and that of **4** increased (Table 1, entries 9–11). When other solvents such as toluene, chloroform and cyclohexane were used instead of DCE for this reaction, each solvent gave **3aa** in moderate to excellent yields (Table 1, entries 12–14). Among the acid catalysts tested, NaHSO<sub>4</sub>/SiO<sub>2</sub> was the most effective system.

Silica gel supported polyphosphoric acid (PPA/SiO<sub>2</sub>) and silica sulfuric acid (SSA)<sup>12</sup> also catalyzed this reaction to afford moderate yields of **3aa** (Table 1, entries 15–19). The reaction using silica gel supported zinc chloride (ZnCl<sub>2</sub>/SiO<sub>2</sub>) gave **3aa** in good yield. Silica gel did not

promote the reaction. When granular NaHSO<sub>4</sub> was used, no **3aa** was generated, but 8% yield of **4** was isolated. Formation of **4** suggests a reaction pathway shown in Scheme 2. When the reaction was carried out in the absence of **1a** at 0 °C, **4** was quantitatively formed. Reaction of **4** with two equivalents of **1a** was carried out in the presence of NaHSO<sub>4</sub>/SiO<sub>2</sub> at 60 °C to give **3aa** (>99%). The coupling probably proceeds through the formation of a stabilized carbocation, which can react with **1a** to produce **3aa**, or with **2a** to give **4**. Ether **4** could be an intermediate of a reaction that proceeds in two steps: formation of carbocation and alkylation of active methylenes. NaHSO<sub>4</sub>/ SiO<sub>2</sub> accelerates both steps in the reaction of **1a** with **2a**.

We checked the reusability of NaHSO<sub>4</sub>/SiO<sub>2</sub> in advance of reactions by using a series of various active methylenes. NaHSO<sub>4</sub>/SiO<sub>2</sub> was recovered from the reaction mixture by filtration, regenerated by drying in vacuo at

 Table 1
 Optimization of Reaction Conditions for the Reaction of Acetyl Acetone and Benzhydrol<sup>a</sup>

$ \begin{array}{c} O \\ H \\$								
1a	2a	1		Ph´ `Ph <b>3aa</b>				
Entry	1a (mmol)	2a (mmol)	Solvent	Catalyst	Amount (g)	Time (min)	Temp (°C)	Yield (%) <sup>b,c</sup>
1	10	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	180	80	95
2	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	180	80	94
3	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	60	80	93
4	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	30	80	98
5	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	15	80	87
6	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	30	60	98
7	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	30	30	43 (25)
8	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	30	0	2 (36)
9	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	0.8	30	60	92 (4)
10	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	0.5	30	60	76 (11)
11	2	2	DCE	NaHSO <sub>4</sub> /SiO <sub>2</sub>	0.1	30	60	39 (19)
12	2	2	toluene	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	30	60	98
13	2	2	CHCl <sub>3</sub>	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	30	60	98
14	2	2	cyclohexane	NaHSO <sub>4</sub> /SiO <sub>2</sub>	1.0	30	60	61 (11)
15	2	2	DCE	PPA/SiO <sub>2</sub>	1.0	30	60	38 (31)
16	2	2	DCE	SSA	1.0	30	60	72
17	2	2	DCE	ZnCl <sub>2</sub> /SiO <sub>2</sub>	1.0	30	60	88
18	2	2	DCE	NaHSO <sub>4</sub>	2.1 (mmol)	30	60	0 (8)
19	2	2	DCE	SiO <sub>2</sub>	1.0	30	60	0

<sup>a</sup> In all reactions NaHSO<sub>4</sub>/SiO<sub>2</sub> (2.1 mmol/g, 1.0 g) was used.

<sup>b</sup> Isolated yield.

<sup>c</sup> The yield of **4** is given in parentheses.

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120 °C for two hours, and used for the subsequent reaction. As can be seen from Table 2, NaHSO<sub>4</sub>/SiO<sub>2</sub> could be recycled at least ten times without loss of catalytic activity, and **3aa** was obtained in satisfactory yields.

Table 2 Reuse of NaHSO<sub>4</sub>/SiO<sub>2</sub> for the Synthesis of 3aa

1. 0.	NaHSO <sub>4</sub> /SiO <sub>2</sub>			
1a <sub>+</sub> 2a	DCE 60 °C, 30 min			
Reuse	Catalyst	Yield (%) <sup>a</sup>		
0	NaHSO <sub>4</sub> /SiO <sub>2</sub>	98		
1	NaHSO <sub>4</sub> /SiO <sub>2</sub>	97		
2	NaHSO <sub>4</sub> /SiO <sub>2</sub>	99		
3	NaHSO <sub>4</sub> /SiO <sub>2</sub>	99		
4	NaHSO <sub>4</sub> /SiO <sub>2</sub>	99		
6	NaHSO <sub>4</sub> /SiO <sub>2</sub>	99		
8	NaHSO <sub>4</sub> /SiO <sub>2</sub>	98		
10	NaHSO <sub>4</sub> /SiO <sub>2</sub>	98		

<sup>a</sup> Isolated yield.

A series of active methylene-containing compounds were used for this reaction. Reactions of alkyl acetoacetates **1b**, **1c**, and **1d** with **2a** gave the corresponding product, **3ba**, **3ca**, and **3da**, in moderate to good yields, respectively (Table 3, entries 1–3). When these reactions were carried out at 80 °C, the corresponding products, **3ba–da**, were obtained in excellent yields. *tert*-Butyl acetoacetate did not give 3ea, but instead 3ea' and an unexpected product 5 were formed in 50 and 40% yields, respectively (Scheme 3). A more detailed investigation on the pathway of formation of 5 is underway. Benzoyl acetoacetic acid ethyl ester 1f gave 3fa in excellent yield at 60 °C for 30 minutes, whereas 4,4-dimethyl-3-oxopentanoic acid ethyl ester (1g) and 4-chloro-3-oxobutanoic acid ethyl ester (1h) needed longer reaction times and higher temperature than 1f (1 h and 2 h at 80 °C), to obtain 3ga and 3ha in excellent yields, respectively (Table 3, entries 6 and 7).  $\beta$ -Diketones also gave **3** in excellent yields. Benzoyl acetone 1k and dibenzoylmethane 1l gave 3ka and 3la, respectively, quantitatively. In the reaction of 11, twice the amount of DCE was used because 3la did not dissolve completely in 10 mL DCE; the mixture of solidified 3la and a NaHSO<sub>4</sub>/SiO<sub>2</sub> was separated by filtration.



Reaction of trifluoro acetyl acetone **1j** was carried out at 80 °C for two hours to give **3ja** in 79% yield. In the reactions of  $\alpha$ -methyl- $\beta$ -diketone **1m** and  $\alpha$ -methyl- $\beta$ -keto ester **1i**, the latter gave **3ia** in 83% yield, whereas the former did not react under similar conditions (Table 4, entries 8 and 12).  $\beta$ -Ketoamide and cyclic diketone also underwent a similar reaction. For instance, **1n** and **1o** reacted with **2a** to give **3na** in 97% yield and **3oa** in 92%, respectively.

Various alcohols were used for the reaction of 1a (Table 4). The reaction using p-chlorobenzhydrol (2b) gave 3ab quantitatively (80 °C for 0.5 h), whereas pmethoxybenzhydrol (2c) gave 3ac in 62% yield along with the corresponding ether. Compound 2d produced 1-(2-methyl-4-phenyl-4*H*-chromen-3-yl)ethanone (6) quantitatively, instead of **3ad** (Table 4, entry 4 and Scheme 4). Secondary benzylic alcohol 2e-g also reacted with 1a, and **3ae-ag** were obtained in moderate to good yields. In these reactions, 1-(4-chlorophenyl)ethanol (2f) required five hours reaction time to give **3af** in satisfactory yield. When benzyl alcohol 2h was used for the reaction, 3ah was not formed. In the reactions of allylic alcohols, 3-hydroxy-1,3-diphenyl propene (2i) gave 3ai in good yield, and 3-hydroxy-1-phenyl-1-butene (2j) gave 3aj in moderate yield. Cinnamic alcohol 2k and *tert*-butyl alcohol 2l, however, did not yield the expected product **3ak** and **3al**. Reaction of tert-butyl alcohol with 2a did not proceed under similar conditions.



Scheme 4

In conclusion, we have developed a simple and efficient method for C–C bond formation from alcohols and active methylene-containing compounds using NaHSO<sub>4</sub>/SiO<sub>2</sub> as an acid catalyst.<sup>13–15</sup> This new method for the formation of C–C bonds has the advantage of mild reaction conditions,

high yield, simplicity of operation, and utilization of inexpensive and reusable catalyst.

## **References and notes**

(1) Khalaf, A. A.; Roberts, R. M. J. Org. Chem. 1972, 37, 4227.

R <sup>1</sup> R <sup>2</sup>	+ OH NaHS + Ph Ph D 60 °C	$\begin{array}{ccc} O_4/SiO_2 \\ CE \\ , 30 \text{ min} \end{array} \begin{array}{c} R^1 \\ Ph \end{array} \begin{array}{c} R^2 \\ Ph \end{array}$				
Entry	Substrate (1)		Temp (°C)	Time (h)	3	Yield (%) <sup>a</sup>
1	1b	OEt	60	0.5	3ba	80 (98) <sup>b</sup>
2	1c	OAlivi	60	0.5	3ca	66 (99) <sup>b</sup>
3	1d	OBn	60	0.5	3da	84 (92) <sup>b</sup>
4	1e	O O Ot-Bu	80	0.5	3ea	0°
5	1f		60	0.5	3fa	97
6	1g		80	1	3ga	98
7	1h		80	2	3ha	91
8	1i	OEt	80	1	3ia	83
9	1j	F <sub>3</sub> C O	80	2	3ja	79
10	1k	O O Ph	60	0.5	3ka	99
11	11	Ph Ph	60	0.5	3la	50 (99) <sup>d</sup>
12	1m	Ph Ph	80	4	3ma	-(99) <sup>e</sup>
13	1n	O O NMe2	80	3	3na	97
14	10		80	3	<b>3</b> 0a	92

Table 3 Reaction of 2a with 1 Using NaHSO<sub>4</sub>/SiO<sub>2</sub>

<sup>a</sup> Isolated yield.

<sup>b</sup> Reaction was performed at 80 °C.

<sup>c</sup> See Scheme 3.

<sup>d</sup> DCE (20 mL) was used.

<sup>e</sup> The recovery of **1m** is given in parentheses.

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Table 4Reaction of 1a with 2 using NaHSO4/SiO2

	+ $R^1$ $R^2$ $R^2$	HaHSO <sub>4</sub> /SiO <sub>2</sub>				
1a Entry	2 Alcohol (2)	R <sup>17</sup> R <sup>2</sup> 3	Temp (°C)	Time (h)		Yield (%) <sup>a</sup>
1	2a	OH	60	0.5	3aa	98
2	2b	OH	80	0.5	3ab	99
3	2c		80	0.5	3ac	62
4	2d	OH OH	60	0.5	3ad	0 (94) <sup>b</sup>
5	2e	OH	80	0.5	3ae	57
6	2f	OH CI	80	5	3af	67 (11) <sup>c</sup>
7	2g	OH	80	0.5	3ag	79
8	2h	ОН	80	3	3ah	0
9	2i	OH	80	0.5	3ai	83
10	2j	OH	80	0.5	3aj	62
11	2k	ОН	80	0.5	3ak	0
12	21	он	80	3	3al	0

<sup>a</sup> Isolated yield. <sup>b</sup> See Scheme 4.

<sup>c</sup> The yield of the corresponding ether is given in parentheses.

- (2) Yasuda, M.; Somyo, T.; Baba, A. Angew. Chem. Int. Ed. 2006, 45, 793.
- (3) Sanz, R.; Martínez, A.; Miguel, D.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. Adv. Synth. Catal. 2006, 348, 1841.
- (4) Motokura, K.; Fujita, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. Angew. Chem. Int. Ed. 2006, 45, 2605.
- (5) Sanz, R.; Miguel, D.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. Org. Lett. 2007, 9, 2027.
- (6) Noji, M.; Konno, Y.; Ishii, K. J. Org. Chem. 2007, 72, 5161.
- (7) Rueping, M.; Nachtsheim, B. J.; Kuenkel, A. Org. Lett. 2007, 9, 825.
- (8) Motokura, K.; Nakagiri, N.; Mizugaki, T.; Ebitani, K.; Kaneda, K. J. Org. Chem. **2007**, 72, 6006.
- (9) Kischel, J.; Mertins, K.; Michalik, D.; Zapf, A.; Beller, M. Adv. Synth. Catal. 2007, 349, 865.
- (10) Funabiki, K.; Komeda, T.; Kubota, Y.; Matsui, M. *Tetrahedron* **2009**, *65*, 7457.
- (11) Liu, P. N.; Dang, L.; Wang, Q. W.; Zhao, S. L.; Xia, F.; Ren, Y. J.; Gong, X. Q.; Chen, J. Q. J. Org. Chem. 2010, 75, 5017.
- (12) Salehi, P.; Zolfigol, M. A.; Shirini, F.; Baghbanzadeh, M. *Curr. Org. Chem.* **2006**, *10*, 2171.
- (13) Preparation of NaHSO<sub>4</sub>/SiO<sub>2</sub>: SiO<sub>2</sub> [Wakogel C-200 (Wako Pure Chemical Ind. Ltd.), 10 g] was added to a solution of NaHSO<sub>4</sub>·H<sub>2</sub>O (30 mmol, 4.14 g) in distilled water, and the mixture was stirred at room temperature for 0.5 h. The water was removed by rotary evaporation under reduced pressure, and the resulting reagent was dried in vacuo (10 mmHg) at 120 °C for 5 h
- (14) Typical procedure: A mixture of 1 (2.0 mmol), 2 (2.0 mmol), and NaHSO<sub>4</sub>/SiO<sub>2</sub> (2.1 mmol, 1.0 g) in DCE (10 mL) was stirred at 60 °C for 0.5 h, and then the used supported reagent was removed by filtration. The filtrate was concentrated and dried in vacuo to obtain 3 (>98% by GC).
- (15) **Compound 3ca**: White solid; mp 68–70 °C. IR (neat): 1739, 1707 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta = 2.09$  (s, 3 H), 4.42 (dt, J = 6.0, 1.4 Hz, 2 H), 4.56 (d, J = 12.4 Hz, 1 H), 4.78 (d, J = 12.4 Hz, 1 H), 5.07–5.13 (m, 2 H), 5.57–5.67 (m, 1 H), 7.14–7.36 (m, 10 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta = 30.1, 50.9, 65.1, 66.0, 118.7, 126.9, 127.0, 127.7, 127.8, 128.6, 128.8,$

131.2, 141.1, 141.4, 167.3, 201.6. HRMS (EI): m/z [M]+ calcd for C<sub>20</sub>H<sub>20</sub>O<sub>3</sub>: 308.1412; found: 308.1417. Anal. Calcd for C<sub>20</sub>H<sub>20</sub>O<sub>3</sub>: C, 77.90; H, 6.54. Found: C, 78.07; H, 6.58. Compound 3da: White solid; mp 95–97 °C. IR (neat): 1740, 1709 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 2.05 (s, 3 H), 4.58 (d, J = 12.1 Hz, 1 H), 4.78 (d, J = 12.1 Hz, 1 H), 4.93 (d, J = 12.1 Hz, 1 Hz, 1 H), 4.93 (d, J = 12.1 Hz, 1 Hz, 1 Hz), 4.93 (d, J = 12.1 Hz),J = 13.7 Hz, 1 H), 4.96 (d, J = 13.7 Hz, 1 H), 7.03–7.29 (m, 15 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 30.0, 50.9, 65.1, 67.2, 126.8, 127.0, 127.6, 127.8, 128.1, 128.2, 128.5, 128.7, 128.8, 135.0, 141.1, 141.4, 167.5, 201.4. HRMS (EI): m/z [M]+ calcd for  $C_{24}H_{22}O_3$ : 358.1569; found: 358.1569. Anal. Calcd for C<sub>24</sub>H<sub>22</sub>O<sub>3</sub>: C, 80.42; H, 6.19. Found: C, 80.16; H, 5.82. **Compound 3ga**: White solid; mp 101–102 °C. IR (neat): 1729, 1705 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 0.91 (s, 9 H), 0.94 (t, J = 7.1 Hz, 3 H), 3.84–3.99 (m, 2 H), 4.86 (d, J = 12.1 Hz, 1 H), 4.89 (d, J = 12.1 Hz, 1 H), 7.09–7.37 (m, 10 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 13.7, 25.9, 45.7, 52.0, 58.8, 61.2, 126.7, 126.8, 128.1, 128.4, 128.5, 141.3, 141.7, 167.6, 207.4. HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>22</sub>H<sub>26</sub>O<sub>3</sub>: 338.1882; found: 338.1879. Anal. Calcd for  $C_{22}H_{26}O_3$ : C, 78.07; H, 7.74. Found: C, 77.96; H, 7.73. Compound 3ja: White solid; mp 99–101 °C. IR (neat): 1769, 1716 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 1.92 (s, 3 H), 4.83 (d, J = 11.9 Hz, 1 H), 5.16 (d, J = 11.9 Hz, 1 H), 7.17–7.32 (m, 10 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 31.1, 51.6, 65.9, 115.2 (q, *J* = 291.9 Hz, CF<sub>3</sub>), 127.3, 127.3, 127.6, 128.1, 129.0, 129.1, 139.7, 140.2, 184.2 (q, J = 36.9 Hz, COCF<sub>3</sub>), 199.0. HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub>: 320.1024; found: 320.1033. Anal. Calcd for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub>: C, 67.50; H, 4.72. Found: C, 67.27; H, 4.48.

**Compound 3na**: White solid; mp 138–139 °C. IR (neat): 1704, 1636 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 2.09 (s, 3 H), 2.77 (s, 3 H), 2.91 (s, 3 H), 4.63 (d, *J* = 11.9 Hz, 1 H), 4.96 (d, *J* = 11.9 Hz, 1 H), 7.13–7.33 (m, 10 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 27.7, 36.1, 37.6, 51.5, 63.2, 126.8, 127.0, 127.8, 128.1, 128.5, 128.9, 141.1, 142.0, 167.1, 204.9. HRMS (EI): *m/z* [M]<sup>+</sup> calcd for C<sub>19</sub>H<sub>21</sub>NO<sub>2</sub>: 295.1572; found: 295.1571. Anal. Calcd for C<sub>19</sub>H<sub>21</sub>NO<sub>2</sub>: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.34; H, 7.17; N, 4.70 Copyright of Synlett is the property of Georg Thieme Verlag Stuttgart and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.