**trans-Stilbene as a Starting Material for the Synthesis of Tamoxifen Based on Palladium-Catalyzed Cross-Coupling Reactions**

Carolina M. Nunes, Jones Limberger, Silvia Poersch, Marcus Seferin, Adriano L. Monteiro*

Laboratory of Molecular Catalysis, Instituto de Química – UFRGS, Av. Bento Gonçalves, 91501-970 – CP 15003, 9500 Porto Alegre, RS, Brazil
Fax +55(51)33087304; E-mail: adriano.monteiro@ufrgs.br
Received 2 April 2009; revised 24 April 2009

**Abstract:** (Z)-Tamoxifen was synthesized from a simple olefin (trans-stilbene) in 5 steps and 40% overall yield ($Z/E = 74:26$). The phenyl substituted group (4-Me$_2$NCH$_2$CH$_2$OC$_6$H$_4$) was attached by a bromination–dehydrobromination–Suzuki reaction sequence. Subsequently, the ethyl group was attached to the triarylated olefin by a bromination–Negishi reaction sequence. Both the Suzuki and Negishi cross-coupling processes are stereospecific, and the stereo-selectivity depends only on the bromination–dehydrobromination reactions. (Z)-Tamoxifen was also obtained from trans-stilbene in only 3 steps by using Heck reaction–bromination–Negishi reaction sequence in 57% overall yield ($Z/E = 65:35$).

**Key words:** tamoxifen, cross-coupling, stilbene, substituted olefins, palladium

The construction of tetrasubstituted olefins with a high degree of stereocontrol remains a significant challenge in organic synthesis.$^1$ One example of important tetrasubstituted olefin is (Z)-tamoxifen, which is a selective estrogen receptor modulator (SERM) used in the treatment of breast cancer.$^2,3$ It is important to mention that the antiestrogenic activity of tamoxifen is highly dependent on the olefin geometry, and several syntheses of tamoxifen and its derivatives have been reported. The basic approach for the synthesis of tamoxifen and derivatives is the coupling of functionalized ketones by low-valent titanium (McMurry reaction), which, unfortunately, results in a mixture of the desired hetero-ketone coupling and the undesired homo-ketone coupling.$^4$ Multi-step synthesis, involving dehydoration$^5$ and double-bond migration$^6,7$ reactions, has been used to produce tamoxifen ($Z/E = ~1:1$). Palladium-catalyzed reactions are versatile methods for carbon–carbon bond formation, and most of the selective syntheses of (Z)-tamoxifen have at least one step involving a Pd-catalyzed cross-coupling reaction.$^8–22$ One powerful strategy used to obtain tetrasubstituted olefin selectively is to create a substituted vinylic metal substrate by a selective carbometalation of disubstituted alkynes, followed by quenching with an electrophile (iodine or bromine), and then a Pd-coupling reaction or a direct cross-coupling reaction of the vinylic metal substrate.$^8–14$ On the other hand, Pd-catalyzed three-component coupling of aryl iodides, internal alkynes, and arylboronic acids provides a one-step, selective route to tetrasubstituted olefins including tamoxifen.$^{15}$ Disubstituted alkynes are also starting materials for the synthesis of tamoxifen, using a Ni-catalyzed ariallative carboxylation.$^{23}$ We have recently reported that tri- and tetrasubstituted olefins can be obtained in high yields and regioselectivities, using stilbene as the starting material and a Pd-catalyzed cross-coupling process.$^{24,25}$ *trans*-Stilbene is cheaper than alkynes and can be obtained by a Heck cross-coupling reaction of halobenzene and styrene. Therefore, we wish to report here the application of this approach for the synthesis of (Z)-tamoxifen (Scheme 1). The substituted phenyl group ($R_1 = 4$-Me$_2$NCH$_2$CH$_2$OC$_6$H$_4$) can be attached by a bromination–dehydrobromination–Suzuki reaction sequence or by a Heck reaction. Finally, the ethyl group ($R_2$) can be attached to the triarylated olefin by a bromination–Negishi reaction sequence. Alternatively, we also investigated the possibility of first inserting the ethyl group ($R_1$) by a Negishi reaction and then the phenyl substituted group ($R_2 = 4$-Me$_2$NCH$_2$CH$_2$OC$_6$H$_4$) by a Suzuki reaction.

**Scheme 1** Possible syntheses of (Z)-tamoxifen ($R_1 = 4$-Me$_2$NCH$_2$CH$_2$OC$_6$H$_4$ and $R_2 = Et$) from trans-stilbene

*trans*-Stilbene was submitted to a sequence of bromination–dehydrobromination to give the monobrominated product ($E$)-bromostilbene (Scheme 2). The bromination was performed in CH$_2$Cl$_2$ at 0 °C, affording the anti-addition product *meso*-1,2-dibromo-1,2-diphenylethane in good yield (ca. 71%).$^{26,27}$ The yield was improved to 92% by using room-temperature ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate (BMI·PF$_6$) as the...
A faster reaction was observed in BMI·PF₆, but the dibrominated product was obtained as a mixture of 88% meso and 12% rac. It is important to mention that after extraction of the products, the ionic liquid could be recovered and reused for further bromination reactions. The best compromise between yield and selectivity was obtained when the reaction was carried out in a water suspension with pyridinium hydrobromide perbromide as the brominating agent (84% yield and >98% meso compound, as judged by GC-MS analysis). Then, a screening of bases and solvents for the dehydrobromination of meso-1,2-dibromo-1,2-diphenylethane was performed. By using K₂CO₃ as the base and a mixture of THF and methanol as the solvent, (E)-bromostilbene was obtained in a yield of 88% (Scheme 2). The high stereoselectivity obtained for the dehydrobromination product (E/Z = 97:3) is related to the strong preference for the anti-elimination process. It is worthwhile to mention that the overall bromination–dehydrobromination process results in an inversion of the configuration of the two phenyl groups from trans to cis.

![Scheme 2 Synthesis of (E)-bromostilbene from trans-stilbene](image)

For the synthesis of triarylethene product by Pd-catalyzed Suzuki reaction, we chose the cross-coupling of (E)-bromostilbene with 4-methoxyphenylboronic acid as a reaction model. The optimization results are summarized in Table 1. As the initial condition, we used an optimized protocol obtained for the coupling of arylboronic acids with vinyl bromide, generated in situ from 1,2-dibromo-1,2-diphenylethane (Table 1, entry 1). (E)-Bromostilbene is more active than vinyl bromide, and the substrate was completely converted after 1 hour at room temperature, affording 1a in almost quantitative yield (Table 1, entry 2). In addition, lower catalyst loading was used, giving a turnover number of 1960 in 1 hour (Table 1, entries 1, 2, 5). The phosphine-free system also gave the expected coupling product in good yields (Table 1, entries 3 and 4). However, incomplete conversions were obtained even when using higher reaction times and palladium loadings. In all cases, the Suzuki reaction proceeded while retaining the configuration (97%). By using the best conditions, (E)-1-[4-[(dimethylamino)ethoxy]phenyl]-1,2-diphenylethene (1b) was obtained in 94% yield and 98% selectivity for the E-isomer (Table 1, entry 5).

The synthesis of triarylalkenes by Heck vinylation of aryl halides with stilbene is a very attractive alternative to bromination–dehydrobromination–Suzuki reaction sequence since it could produce the desired (E)-1-(4-methoxyphenyl)-1,2-diphenylethene from stilbene in only one step. This reaction was investigated by Doucet and Santelli, who used a catalyst composed of [Pd(C₅H₅)Cl]₂ and cis,cis,cis-1,2,3,4-tetakis(diphenylphosphinomethyl)cyclopentane (Tedicyp) as the phosphine ligand. The addition of 4-bromoanisole to trans-stilbene in the presence of 0.2% catalyst led to the corresponding coupled products in 75% yield with an E/Z ratio of 61:39. We decided to investigate the Heck reaction of 4-bromoanisole with stilbene, using a catalyst system composed of Pd(OAc)₂ and P(o-tol)₃ (Table 2). Classical bases for the Heck reaction, such as Et₃N or NaOAc, gave only moderate yields and selectivities (Table 2, entries 1 and 2). However, higher activity and stereoselectivity for the E-isomer was obtained by using K₂CO₃ (Table 2, entry 3). We were delighted to see that by replacing 4-bromoanisole with 1-bromo-4-[2-(dimethylamino)ethoxy]benzene and using this aryl bromide as limiting reagent, the coupling product 1 was obtained in almost quantitative yield with an E/Z ratio of 87:13 (Table 2, entry 4).

The bromination of triarylethenes directly produces the bromotritylarethenes, since dibrominated products are not stable, and undergo HBr elimination in the reaction media. A nonselective bromination of (E)-1a was observed when the reaction was carried out in CH₂Cl₂ at 0 °C (E/Z = 45:55, Table 3, entry 1). More interestingly, under the same conditions, bromination with a reasonable stereoselectivity was observed for the substrate (E)-1b possessing a 2-(dimethylamino)ethoxy group (E/Z = 73:27, Table 3, entry 2). In view of these results, we ex-

Table 1 Pd-Catalyzed Suzuki Cross-Coupling Reaction of (E)-Bromostilbene with Arylboronic Acids

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd (mol%)</th>
<th>L</th>
<th>Time (h)</th>
<th>Product</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5</td>
<td>Ph₂P</td>
<td>1</td>
<td>1a</td>
<td>100</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>0.05</td>
<td>Ph₂P</td>
<td>1</td>
<td>1a</td>
<td>99</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td></td>
<td>72</td>
<td>1a</td>
<td>92</td>
<td>93</td>
</tr>
<tr>
<td>4</td>
<td>0.05</td>
<td></td>
<td>72</td>
<td>1a</td>
<td>99</td>
<td>98</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>Ph₂P</td>
<td>1</td>
<td>1b</td>
<td>100</td>
<td>94</td>
</tr>
</tbody>
</table>

* Reaction conditions: (E)-bromostilbene (1 mmol), arylboronic acid (1.5 mmol), KOH (2 mmol), Pd(OAc)₂/L ratio = 2, MeOH (3 mL), THF (3 mL).
amined the effect of different bases on the bromination of \((E)\)-1a (Table 3, entries 1, 3–8). A stereoselectivity of 78% was obtained using \(\text{Et}_3\text{N}\) as the base (Table 3, entry 8), which has a structure similar to that of the (dimethylamino)ethoxy group. Indeed, \(\text{Et}_3\text{N}\) has no effect on the bromination reaction gave a mixture of regioisomers that discarded this sequence as an alternative to the selective synthesis of tamoxifen.

Alternatively, we also investigated the possibility of inserting the first ethyl group by Negishi reaction and then the aryl group by Suzuki reaction (Scheme 3). We examined the coupling of \((E)\)-bromostilbene with ethylzinc chloride in THF at room temperature using different catalyst precursors and phosphine ligands. Using \(\text{PdCl}_2(\text{PPh}_3)_2\) as a catalyst precursor at room temperature, the \((Z)\)-1,2-diphenylbut-1-ene was obtained in 90% isolated yield. Once again, the stereoselectivity was maintained in the cross-coupling reaction (\(EIZ = 97:3\)). Unfortunately, due to the presence of the ethyl group, the bromination reaction gave a mixture of regioisomers that discarded this sequence as a more attractive route, \((Z)\)-tamoxifen was obtained form a Negishi cross-coupling reaction between \((E)\)-2b and ethylzinc chloride (Scheme 4). The protocol obtained for the reaction of \((E)\)-bromostilbene with ethylzinc chloride was not directly transposable to the coupling of bromotriphenylethylene. As a more attractive route, \((Z)\)-tamoxifen was also obtained from \(\text{trans}\)-stilbene in only 3 steps by using Heck vinylation was less stereoselective (\(EIZ = 87:13\)), the corresponding brominated product \((E)\)-2b was

---

**Table 2** Pd-Catalyzed Heck Cross-Coupling Reaction of Aryl Bromides with \((E)\)-Bromostilbene

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Base</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
<th>E/Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>(\text{Et}_3\text{N})</td>
<td>51</td>
<td>47(^b)</td>
<td>73:27</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>(\text{NaOAc})</td>
<td>74</td>
<td>54(^b)</td>
<td>72:28</td>
</tr>
<tr>
<td>3</td>
<td>Me</td>
<td>(\text{K}_2\text{CO}_3)</td>
<td>100</td>
<td>79(^b)</td>
<td>83:17</td>
</tr>
<tr>
<td>4</td>
<td>(\text{CH}_3\text{CH}_2\text{NMe}_2)</td>
<td>(\text{K}_2\text{CO}_3)</td>
<td>100</td>
<td>98(^c)</td>
<td>87:13</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions (entries 1–3): 4-bromoanisole (1 mmol), \(\text{trans}\)-stilbene (0.5 mmol), base (1 mmol), \(\text{Pd(OAc)}_2\) (0.01 mmol), \(\text{P(o-tol)}_3\) (0.04 mmol), DMF (4 mL), 130 °C, 48 h.

---

**Table 3** Bromination of Triarylethylenes 1a, b

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Base</th>
<th>Product</th>
<th>Yield (%)</th>
<th>E/Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>–</td>
<td>2a</td>
<td>94</td>
<td>45:55</td>
</tr>
<tr>
<td>2</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>–</td>
<td>2b</td>
<td>88</td>
<td>73:27</td>
</tr>
<tr>
<td>3</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>(\text{NaOr-Bu})</td>
<td>2a</td>
<td>95</td>
<td>45:55</td>
</tr>
<tr>
<td>4</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>(\text{i-PrNH})</td>
<td>2a</td>
<td>88</td>
<td>48:52</td>
</tr>
<tr>
<td>5</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>(\text{i-PrNEt})</td>
<td>2a</td>
<td>87</td>
<td>47:53</td>
</tr>
<tr>
<td>6</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>(\text{DMAP})</td>
<td>2a</td>
<td>90</td>
<td>49:51</td>
</tr>
<tr>
<td>7</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>(\text{Et}_3\text{N})</td>
<td>2a</td>
<td>90</td>
<td>78:22</td>
</tr>
<tr>
<td>8(^\text{c})</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>(\text{Et}_3\text{N})</td>
<td>2a</td>
<td>90</td>
<td>78:22</td>
</tr>
<tr>
<td>9</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>(\text{Et}_3\text{N})</td>
<td>2b</td>
<td>73</td>
<td>73:27</td>
</tr>
<tr>
<td>10(^\text{a})</td>
<td>(\text{CH}_2\text{Cl}_2)</td>
<td>(\text{Et}_3\text{N})</td>
<td>2b</td>
<td>78</td>
<td>74:26</td>
</tr>
<tr>
<td>11</td>
<td>(\text{BMI·PF}_6)</td>
<td>–</td>
<td>2a</td>
<td>86</td>
<td>55:45</td>
</tr>
<tr>
<td>12</td>
<td>(\text{BMI·PF}_6)</td>
<td>(\text{Et}_3\text{N})</td>
<td>2a</td>
<td>82</td>
<td>55:45</td>
</tr>
<tr>
<td>13(^\text{c})</td>
<td>(\text{H}_2\text{O})</td>
<td>–</td>
<td>2a</td>
<td>82</td>
<td>56:44</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: \((E)\)-1-aryl-1,2-diphenylethene (2 mmol), base (8 mmol), \(\text{CH}_2\text{Cl}_2\) (20 mL), \(\text{Br}_2\) (3 mmol in 20 mL of \(\text{CH}_2\text{Cl}_2\)), 0 °C.

---

**Scheme 3** Synthesis and bromination of \((Z)\)-1,2-diphenylbut-1-ene

---

Synthesis 2009, No. 16, 2761–2765 © Thieme Stuttgart · New York
The synthesis of (Z)-tamoxifen by Negishi cross-coupling reaction is depicted in Scheme 4. The reaction sequence involves first bromination, then dehydrobromination, followed by a Suzuki coupling reaction.

Scheme 5 illustrates the trans-Stilbene as a starting material for the synthesis of (Z)-tamoxifen, obtained in only 65% selectivity. It is important to mention that a simple recrystallization of this product from hexanes afforded pure (E)-2b with 50% recovery.

In summary, we have demonstrated that (Z)-tamoxifen can be stereoselectively synthesized from trans-stilbene in 5 steps with 40% overall yield. The substituted phenyl group (R1 = 4-Me2NCH2CH2OC6H4) was attached by a bromination–dehydrobromination–Suzuki reaction sequence. The ethyl group was attached to the triarylated olefin by a bromination–Negishi reaction sequence. Both the Suzuki and Negishi cross-coupling processes are stereospecific, and the stereoselectivity depends only on the bromination–dehydrobromination reactions. (Z)-Tamoxifen was also obtained from trans-stilbene in only three steps by using Heck reaction–bromination–Negishi reaction sequence in 57% overall yield with a lower selectivity (Z/E = 65:35). The extension of this protocol for the selective synthesis of tetracyclic olefins is now under investigation in our group.

All reactions were carried out under argon in oven-dried resealable Schlenk tube. Iodobenzene was purchased from Acros and styrene was purchased from Aldrich and dried before to use. MeOH and THF were degassed and dried, respectively. Arylboronic acids were prepared according to the previously published procedure.15 Bromination reactions of trans-stilbene to afford meso-1,2-dibromo-1,2-diphenylethane were performed as described in the literature.23,26 Chemicals were used without purification. NMR spectra were recorded on a Varian XL300 spectrometer. IR spectra were recorded on a Shimadzu FTIR-8300 spectrometer. Mass spectra were obtained on a GC/MS Shimadzu QP-5050 (EI, 70 eV). Gas chromatography analyses were performed on a HP column DB-17 GC with a FID and 30 meter capillary column with a dimethylsiloxane stationary phase. ESI-(+) HRMS analyses were performed on a Q-Tof (Micromass) mass spectrometer.

**Suzuki Coupling of 1-Bromo-1,2-diphenylethene and Arylboronic Acids; General Procedure**

An oven-dried resealable Schlenk flask charged with 1-bromo-1,2-diphenylethene (259 mg, 1.0 mmol) was evacuated and back-filled with argon. Then, Pd(OAc)2 (1.1 mg, 0.005 mmol), Ph3P (2.6 mg, 0.01 mmol), aryloboronic acid (1.2 mmol), KOH (112 mg, 2 mmol), MeOH (2.5 mL), and THF (2.5 mL) were added. The reaction mixture was stirred at r.t. for 1 h. The solution was then taken up in Et2O (30 mL) and the Et2O layer was washed with aq 1 M NaOH (10 mL) and brine (2 × 5 mL). The organic layer was dried (MgSO4), filtered, concentrated under reduced pressure. The crude material was puriﬁed by flash chromatography on silica gel (Table 1).

**Heck Coupling Reaction of trans-Stilbene with Aryl Bromides; (E)-1-[(2-dimethylamino)ethoxy]phenyl]-1,2 diphenylethene (1b)**

Yield: 94%.

IR (Nujol): 3055, 3022, 1604, 1574, 1508, 1244, 756, 696 cm⁻¹.

1H NMR (300 MHz, CDCl3): δ = 2.32 (s, 6 H), 2.71 (t, J = 8 Hz, 2 H), 4.05 (t, J = 6 Hz, 2 H), 6.84 (s, 1 H), 6.87–7.31 (m, 14 H).

13C NMR (75.4 MHz, CDCl3): δ = 45.8, 58.2, 65.9, 114.1, 126.3, 126.4, 127.3, 127.8, 128.5, 128.6, 129.3, 130.3, 135.9, 137.5, 140.4, 142.0, 158.4.

GC-MS (EI, 70 eV): m/z (%): 343 (68, M⁺), 178 (100), 165 (91), 252 (89), 239 (88), 253 (67), 179 (57), 215 (54), 176 (52).

HRMS: m/z calcd for C25H19NO (M + H⁺): 344.2035; found: 344.2035.

**Bromination of Triarylethenes; 1-Bromo-2-[(2-dimethylamino)ethoxy]phenyl]-1,2 diphenylethene (2b)**

A solution of Br2 (575 mg, 3.6 mmol) in CH2Cl2 (10 mL) was added dropwise to a stirred solution of 1b (1.03 g, 3.3 mmol) and Et3N (1.20 g, 12 mmol) in CH2Cl2 (10 mL) at r.t. and the reaction mixture was kept overnight in the dark. The bromine color of the mixture was removed by an excess of aq NaHSO3 and the organic layer was washed with aq 10% KOH (20 mL). The organic layer was dried

---

C. M. Nunes et al.

Synthesis 2009, No. 16, 2761–2765 © Thieme Stuttgart · New York
(Na₂SO₄) and the solvent was evaporated to give 1.01 g (78%) of an E/Z mixture (74:26) of 2b as a white solid.

1H NMR (300 MHz, CDCl₃): δ (multiplet of diasteroisomers) = 2.25 (E-isomer, s, 6 H), 3.21 (Z-isomer, s, 6 H), 2.62 (E-isomer, t, J = 5.7 Hz, 2 H), 2.65 (Z-isomer, t, J = 5.7 Hz, 2 H), 2.72 (E-isomer, t, J = 5.7 Hz, 2 H), 3.90 (Z-isomer, t, J = 5.7 Hz, 2 H), 4.05 (Z-isomer, t, J = 5.7 Hz, 2 H), 6.53 (E-isomer, d, J = 8.7 Hz, 2 H), 6.77 (E-isomer, d, J = 8.7 Hz, 2 H), 6.83–7.34 (Z- and E-isomers, m, 10 H).

(E)-2b Recrystallization of the E/Z mixture of 2b from hexanes afforded the pure (E)-2b; mp 116–117 °C (Lit.² mp 116–117 °C).

1H NMR (300 MHz, CDCl₃): δ = 2.33 (s, 6 H), 2.72 (t, J = 5.7 Hz, 2 H), 3.96 (d, J = 8.9 Hz, 2 H), 6.53 (d, J = 8.9 Hz, 2 H), 6.77 (d, J = 8.9 Hz, 2 H), 7.08–7.34 (m, 10 H).

HRMS: m/z calcd for C₂₄H₂₅BrNO (M + H⁺): 422.1119; found: 422.1125.

Negishi Coupling of 1-Bromo-2-{4-[2-(dimethylamino)ethoxy]phenyl}-1,2 diphenylethene (2b) with Ethylzinc Chloride

An oven-dried resealable Schlenk flask was charged with ZnCl₂ (273 mg, 2 mmol), THF (3 mL), and Et₂Zn (2 mL of a 1 M solution in hexane, 2 mmol). The mixture was stirred at r.t. for 1 h before use. The mixture was transferred to an oven-dried resealable Schlenk flask containing 2b (630 mg, 1.5 mmol), THF (5 mL), and tol-BINAP (20.3 mg, 0.03 mmol) were added and the mixture was stirred at 30 °C for 2 h.

After removal of the solvent, the residue was chromatographed on silica gel (hexanes) to give 412 mg (74%) of an oil which was purified by flash chromatography (hexanes:EtOAc 98:2) to give a white solid. The diasteroisomeric ratio was determined by GCMS analysis and configuration of the major diasteroisomer established by NMR could be confirmed by GC-analysis of an authentic sample of (Z)-tamoxifen.¹⁷

1H NMR (300 MHz, CDCl₃): δ = 0.93 (Z-isomer, t, J = 7.3 Hz, 3 H), 0.95 (E-isomer, t, J = 7.3 Hz, 3 H), 2.29 (Z-isomer, s, 6 H), 2.36 (E-isomer, s, 6 H), 2.42–2.50 (Z- and E-isomers, m, 4 H), 2.65 (Z-isomer, t, J = 5.7 Hz, 2 H), 2.75 (E-isomer, t, J = 5.7 Hz, 2 H), 3.93 (Z-isomer, t, J = 5.7 Hz, 2 H), 4.09 (E-isomer, t, J = 5.7 Hz, 2 H), 6.66 (Z-isomer, d, J = 9 Hz, 2 H), 6.77 (Z-isomer, d, J = 9 Hz, 2 H), 6.89–7.37 (Z- and E-isomers, m, 10 H).

HRMS: m/z calcd for C₂₆H₃₀NO (M + H⁺): 372.2327; found: 372.2328.

Acknowledgment

We thank CNPq, FAPERGS, PRONEX and INCT-Catalise for partial financial support. We also thank CNPq (C.N.M and S.P.) and CAPES (J.L.) for scholarships.

References

(5) Yus, M.; Ramon, D. J.; Gomez, I. Tetrahedron 2003, 59, 3219.