PREPARATION OF 4-IODO-β-CARBOLINE-3-CARBOXAMIDE VIA ORTHO-METALATION AND ITS USE IN PALLADIUM-CATALYZED CARBON-CARBON BOND FORMING REACTIONS WITH UNSATURATED SUBSTRATES

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Abstract - The 4-iodo derivative of N-9 protected β-carboline-3-(N-methyl)-3-(N-phenyl)carboxamide (12) was prepared by sequential treatment of N-9 protected β-carboline-3-(N-phenyl)carboxamide (2) with methylthiium, iodine and methyl iodide. Compound (12), in the presence of catalytic palladium acetate and tri-o-toly1phosphine in acetonitrile and triethylamine, reacted with a variety of unsaturated substrates (styrenes, acrylate, tributyl(vinyl)tin, trimethylsilyl-acetylene) to give the corresponding C-4 coupled adducts (13a-g).

INTRODUCTION

While very few 4-substituted 3-carboxy-β-carbolines have been isolated from natural sources,¹ the main interest in this class of compounds stems from their potent interactions with the benzodiazepine receptor of the central nervous system.² Indeed, the nature of the substituent at C-4 of 3-carboxy-β-carbolines has an important bearing on the type of pharmacological activity exhibited by this class of compounds in vivo. Most of the synthetic methods toward these compounds have generally relied on introduction of the C-4 substituent during the course of the construction of the β-carboline nucleus.³-⁸ An alternative, and more efficient, procedure would allow introduction of a C-4 substituent directly on a pre-formed 3-carboxy-β-carboline moiety. To this purpose, we have recently applied the technique of ortho-directed metalation to β-carboline-3-carboxamides (1 or 2).⁹,¹⁰ This has allowed the synthesis, in one step and in high yield, of a wide variety of 4-substituted derivatives (3 or 4, Scheme 1), depending on the electrophile
(E⁺) used to quench the anion generated at C-4 by methyllithium. During the course of these studies,

it was also discovered that the N,N-dimethylsulfonamide moiety served as an excellent protecting group for the indolic NH. Thus, this protecting group was found to be perfectly stable under the strongly basic conditions of the metalation reaction, it facilitated proton abstraction at C-4 due to its electron-withdrawing properties and, finally, it could be efficiently removed using either samarium diiodide or triflic acid in trifluoroacetic acid (to give 5).

In order to further increase the versatility of this procedure, we describe in this paper the first synthesis of a 4-iodo derivative of β-carboline (2) and its use in palladium-catalyzed C-C cross-coupling reactions with a variety of unsaturated substrates.

RESULTS AND DISCUSSION

We first investigated the possibility of directly using the 4-iodo derivative of 2 for palladium-catalyzed Heck-type reactions. This key compound (6) was obtained in 76% yield by treatment of 2 in THF at -78 °C with 2.2 eq of methyllithium for 45 min followed by reaction with 2.5 eq of iodine for 30 min at -78 °C and then 2 h at 20 °C (Scheme 2).

However, attempts to couple compound (6) with styrene under Heck conditions gave at best less than 5% of the desired coupled product (7), the starting material (6) being almost completely recovered. Use of a different unsaturated substrate such as methyl acrylate gave similar low yields of coupled product which, in addition, underwent cyclization to 8 via 1,4-Michael addition of the amide NH to the acrylate double
bond, as clearly shown by $^1$H-NMR spectroscopy of the final product.\textsuperscript{13}

Such inertness of aromatic halides to palladium-catalyzed coupling reactions has previously been observed in the case of carboxamide-combining substrates.\textsuperscript{14} Lack of reactivity was attributed to complexation of the inserted palladium catalyst with the amide NH, preventing further reaction. Methylation of the amide function was found to prevent this phenomenon and thereby promote coupling with the unsaturated substrate. Therefore, in order to circumvent similar problems arising from the free amide NH of substrate (6), it was decided to prepare the $N$-methyl derivative of the latter. This was attempted by first methylating 2 using sodium hydride and methyl iodide in THF to give 9 and subjecting the latter to the standard ortho-metalation conditions with iodine as the electrophile (Scheme 3).
Surprisingly, no trace of the desired 4-iodo derivative could be found in the reaction mixture. Instead, products corresponding to the methyl ketone (10) and the tertiary alcohol (11) were observed, indicating that, in contrast to the aniline group, the N-methylanilide function tends to react with methyl lithium rather than promote ortho-metalation.

An alternative procedure was thus devised to prepare the N-methylated 4-iodo derivative, as depicted in Scheme 4. This consisted of first treating 2 with methyl lithium and then with iodine exactly as before. However, at the end of the reaction period, the reaction mixture was quenched with a large excess of methyl iodide (6 eq) and left to stir at 20 °C for 5 h. The major product formed was the desired 4-iodo-N-methylamide derivative (12) (66%) together with a minor amount of the non-methylated analogue (6) (16%). These two products could be easily separated by chromatography.

With compound (12) in hand, palladium-catalyzed coupling reactions with styrene were re-attempted using a variety of conditions (Table 1). It was found that use of 0.1 eq of palladium acetate in the presence of 0.2 eq of tri-o-tolylphosphine and 3 eq of triethylamine in acetonitrile at 80 °C gave excellent yields (85%) of the C-4 styryl-β-carboline (13a). Use of other solvents (DMF, toluene, triethylamine) led to considerably lower yields of 13a. Interestingly, and as observed by Heck in analogous coupling reactions, the tri-o-tolylphosphine ligand is vastly superior to triphenylphosphine and triphenylarsine in promoting coupling. On the other hand, use of Pd2(dba)3 as catalyst rather than Pd(OAc)2 gave only slightly lower yields (79%) of coupled product (13a).

These reaction conditions were successfully extended to other unsaturated substrates, as shown in Table 2. Thus, o-fluorostyrene, allylbenzene, acrylonitrile and methyl acrylate reacted with the 4-iodo-β-carboline (12) to give 60-75% yields of the expected coupled products (13b-e), respectively. Moreover, with trimethylsilylacetylene, high yields (93%) of the 4-acetylenic β-carboline (13f) were obtained.
Table 1: Optimization of the palladium-catalyzed coupling reaction of 12 with styrene

<table>
<thead>
<tr>
<th>Ligand</th>
<th>solvent</th>
<th>yield (%)</th>
</tr>
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<tbody>
<tr>
<td>P(o-toly)₃</td>
<td>MeCN</td>
<td>85</td>
</tr>
<tr>
<td>P(o-toly)₃</td>
<td>DMF</td>
<td>26</td>
</tr>
<tr>
<td>P(o-toly)₃</td>
<td>toluene</td>
<td>5</td>
</tr>
<tr>
<td>P(o-toly)₃</td>
<td>Et₃N</td>
<td>11</td>
</tr>
<tr>
<td>PPh₃</td>
<td>MeCN</td>
<td>5</td>
</tr>
<tr>
<td>AsPh₃</td>
<td>MeCN</td>
<td>25</td>
</tr>
<tr>
<td>Pd(OAc)₂</td>
<td>MeCN</td>
<td>79</td>
</tr>
</tbody>
</table>

Finally, a Stille reaction between 12 and tributyl(vinyl)tin provided in one step and in 98% yield the 4-vinyl derivative (13g). This type of compound has previously only been available via a multistep, low yielding process starting from indole.

Table 2: Palladium acetate-catalyzed coupling of 12 with various unsaturated substrates to give 13b-13g.

<table>
<thead>
<tr>
<th>substrate</th>
<th>Pd N°</th>
<th>R</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzene F</td>
<td>13b</td>
<td>F</td>
<td>70</td>
</tr>
<tr>
<td>benzene</td>
<td>13c</td>
<td></td>
<td>60</td>
</tr>
<tr>
<td>COOMe</td>
<td>13d</td>
<td>COOMe</td>
<td>75</td>
</tr>
<tr>
<td>CN</td>
<td>13e</td>
<td>CN</td>
<td>73</td>
</tr>
<tr>
<td>SiMe₃</td>
<td>13f</td>
<td>SiMe₃</td>
<td>93</td>
</tr>
<tr>
<td>Bu₃Sn</td>
<td>*</td>
<td></td>
<td>98</td>
</tr>
</tbody>
</table>

* : coupling reaction performed without Et₃N
In conclusion, the ortho-directed metalation process we have developed for β-carboline-3-carboxamides allows efficient preparation of the corresponding 4-iodo derivative which, in turn, allows application of a wide range of palladium-catalyzed coupling reactions with unsaturated substrates. This process, much more efficient than previously described methods for the introduction of substituents at C-4 of the neuroactive 3-carboxy-β-carbolines, thereby permits access to a great structural diversity of substituents at this position.

**EXPERIMENTAL**

**General** - Melting points were determined on a Büchi apparatus and are uncorrected. IR spectra of samples were obtained either as films or as KBr pellets with a Nicolet 205 FT-IR spectrophotometer. $^1$H-NMR and $^{13}$C-NMR spectra were determined on Bruker 200 MHz, 250 MHz or 300 MHz instruments. Chemical shifts are given as δ values with reference to Me$_4$Si as internal standard. Electron impact and chemical ionization MS spectra were recorded on an AEI MS-50 and AEI MS-9 spectrometer, respectively. High resolution MS spectra were obtained using a Kratos MS-80 spectrometer. Thin-layer chromatography was performed on Merck silica gel 60 plates with fluorescent indicator. The plates were visualized with UV light (254 nm). All column chromatography was conducted on Merck 60 silica gel (230-400 mesh) at medium pressure (200 mbar). Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette, France.

9-(N,N-Dimethylsulfamoyl)-4-iodo-3-N-phenyl-β-carboline-3-carboxamide (6) - A solution of compound (2)$^{10}$ (1.26 g, 3.2 mmol) in anhydrous THF (150 mL) was treated dropwise at -78 °C under argon with a solution of methylithium in THF (7 mL of a 1.0 M solution, 7 mmol). After completion of the addition, the resulting violet-colored reaction mixture was stirred for 45 min at -78 °C and a solution of iodine (2 g, 8 mmol) in THF (15 mL) was added dropwise. The reaction mixture was then stirred for 30 min at -78 °C and then for 2 h at rt. At the end of the reaction period, the solution was cooled to 0 °C, water (20 mL) was added and the volume was reduced by three-quarters under reduced pressure. Ethyl acetate (150 mL) was added and the solution was washed successively with saturated aqueous sodium thiosulfate (2 x 50 mL), water (50 mL) and saturated aqueous sodium chloride (50 mL). The organic phase was dried (Na$_2$SO$_4$) and the solvents were evaporated under reduced pressure, leaving a residue which was purified by column chromatography on silica gel (ethyl acetate - heptane 1:2). Compound (6),
obtained as a white solid (1.26 g, 76%) was crystallized in methanol, mp 199 °C. IR (KBr) 3326, 1671, 1529, 1170 cm⁻¹. CIMS m/z 521 (MH⁺). ¹H-NMR (250 MHz, DMSO-d₆) δ : 3.00 (s, 6H, N(CH₃)₂), 7.25 (dd, 1H, J = 8.0 and 7.6 Hz, H-6), 7.89 (d, 2H, J = 8.0 Hz, ArH), 7.98 (dd, 1H, J = 7.6 and 8.4 Hz, H-7), 8.37 (d, 1H, J = 8.4 Hz, H-5), 9.34 (s, 1H, H-1), 10.77 (s, 1H, exchangeable with D₂O, NH). Anal. Calcd for C₂₀H₁₇N₄O₃S.0.25H₂O: C, 45.77; H, 3.36; N, 10.67; I, 24.18; S, 6.11. Found: C, 45.84; H, 3.58; N, 10.58; I, 24.28; S, 6.15.

9-(N,N-Dimethylsulfamoyl)-3-N-methyl-3-N-phenyl-β-carboline-3-carboxamide (9) - A solution of compound (2) (1 g, 2.53 mmol) in anhydrous THF (150 mL) was treated at 0 °C under argon with sodium hydride (182 mg of a 50% dispersion in oil; 3.8 mmol). The reaction mixture was stirred for 30 min at 0 °C and then for 1.5 h at rt. Methyl iodide (315 µL, 5.1 mmol) was added and the reaction mixture was stirred for a further 2 h at rt. The solution was then cooled to 0 °C, ice-cold water (10 mL) was added and the volume was reduced by three-quarters under reduced pressure. Ethyl acetate (150 mL) was added and the solution was washed successively with water (50 mL) and with saturated aqueous NaCl (50 mL). The organic phase was dried (Na₂SO₄) and evaporated in vacuo leaving a crude product which was purified by column chromatography on silica gel (ethyl acetate-heptane 3:1), affording compound (9) as a white powder (908 mg, 88%), mp 156 °C (MeOH). IR (KBr) 1646, 1170 cm⁻¹. CIMS m/z 409 (MH⁺). ¹H-NMR (200 MHz, DMSO-d₆) δ : 2.87 (s, 6H, N(CH₃)₂), 3.57 (s, 3H, CONCH₃), 7.16-7.36 (m, 5H, ArH), 7.62 (pseudo t, 1H, J = 7.6 Hz, H-6), 7.83 (pseudo t, 1H, J = 7.6 Hz, H-7), 8.21 (d, 1H, J = 8.5 Hz, H-8), 8.50 (d, 1H, J = 8.0 Hz, H-5), 8.63 (s, 1H, H-4), 9.07 (s, 1H, H-1). ¹³C-NMR (62.5 MHz, DMSO-d₆) δ : 37.7, 38.1, 114.4, 115.2, 122.3, 122.6, 123.8, 125.9, 126.5, 128.6, 130.3, 130.8, 133.9, 134.4, 139.1, 144.2, 147.7, 168.0. Anal. Calcd for C₂₁H₂₀N₄O₃S : C, 61.75 ; H, 4.94 ; N, 13.72 ; S, 7.85. Found: C, 61.56 ; H, 4.53 ; N, 13.87 ; S, 7.64.

9-(N,N-Dimethylsulfamoyl)-4-iodo-3-N-methyl-3-N-phenyl-β-carboline-3-carboxamide (12) - A solution of compound (2) (5 g, 12.7 mmol) in anhydrous THF (400 mL) was treated dropwise under argon at -78 °C with a solution of methyllithium in THF (31.7 mL of a 1.0 M solution; 31.7 mmol). The reaction mixture was stirred for 45 min and a solution of iodine (9.7 g, 38.1 mmol) in THF (20 mL) was added dropwise. The reaction mixture was stirred for a further 30 min at -78 °C and then for 2 h at rt. At the end of the reaction period, freshly distilled methyl iodide (4.8 mL, 76.1 mmol) was added and stirring
was maintained at rt for 5 h. Work-up of the reaction mixture in the same manner as for the preparation of compound (6) afforded a crude product which was purified by column chromatography on silica gel (ethyl acetate-heptane 1:1). Compound (6) (1.03 g, 16%) was the first product to be eluted. Further elution of the column afforded the major product (12) as a white solid (4.7 g, 66%), mp 237 °C (MeOH). IR 1649, 1173 cm⁻¹. CIMS m/z 535 (MH)+. ¹H-NMR (200 MHz, CDCl₃) δ : 2.74 (s, 6H, N(CH₃)₂), 3.59 (s, 3H, CONCH₃), 7.01-7.15 (m, 3H, ArH), 7.30 (d, 2H, J = 7.6 Hz, ArH), 7.46 (dd, 1H, J = 8.0 and 7.7 Hz, H-6), 7.65 (dd, 1H, J = 7.7 and 8.5 Hz, H-7), 8.18 (d, 1H, J = 8.5 Hz, H-8), 9.04 (d, 1H, J = 8.0 Hz, H-5), 9.25 (s, 1H, H-1). ¹³C-NMR (75 MHz, DMSO-d₆) δ : 37.2, 38.7, 114.7, 122.5, 122.9, 124.0, 125.9, 127.0, 127.1, 128.8, 129.3, 130.6, 130.9, 134.6, 135.0, 136.0, 142.8, 168.9. Anal. Calcd for C₂₁H₁₉N₄O₃S : C, 47.20; H, 3.58; N, 10.48; I, 23.75; S, 6.00. Found : C, 47.25; H, 3.51; N, 10.31; I, 23.45; S, 5.96.

**General procedure for the palladium-catalyzed coupling of compound (12) with olefins** - A solution of compound (12) (100 mg, 0.2 mmol), palladium (II) acetate (5 mg, 0.02 mmol), tri-o-tolylphosphine (12 mg, 0.04 mmol), triethylamine (80 μL, 0.6 mmol) and the olefin (2 mmol) in acetonitrile (10-15 mL) was placed in a sealed tube and degassed with argon for 5 min. The solution was then heated at 80 °C for 5 h, cooled to rt and diluted with ethyl acetate (100 mL). The solution was washed successively with aqueous HCl (50 mL of a 5% solution), water (50 mL) and saturated aqueous NaCl (50 mL). The organic phase was dried (Na₂SO₄), evaporated to dryness under reduced pressure and the residue was purified by column chromatography on silica gel (dichloromethane-ethyl acetate 3:1). The following compounds were prepared using this procedure:

9-(N,N-Dimethylsulfamoyl)-3-N-methyl-3-N-phenyl-4-(2-phenylethylene)-β-carboline-3-carboxamide (13a) - Using the general procedure described above, compound (13a) was obtained as an amorphous white solid in 85% yield from compound (12) and styrene. IR (KBr) 1651, 1171 cm⁻¹. ¹H-NMR (200 MHz, CDCl₃) δ : 2.80 (s, 6H, N(CH₃)₂), 3.45 (s, 3H, CONCH₃), 6.89-7.64 (m, 14H, ArH), 7.99 (d, 1H, J = 8.0 Hz, H-5), 8.18 (d, 1H, J = 8.4 Hz, H-8), 9.36 (s, 1H, H-1). HRCIMS calcd for C₂₉H₂₇N₄O₃S m/z 511.1804 found 511.1790.
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9-(N,N-Dimethylsulfamoyl)-3-N-methyl-3-N-phenyl-4-(3-phenyl-1,2-propenyl)-β-carboline-3-carboxamide (13b) - Using the general procedure described above, compound (13b) was obtained as an amorphous white solid in 70% yield from compound (12) and o-fluorostyrene: IR (KBr) 1654, 1173 cm⁻¹. CIMS m/z 529 (MH)⁺. ¹H-NMR (300 MHz, CDCl₃) δ : 2.79 (s, 6H, N(CH₃)₂), 3.45 (s, 3H, CONCH₃), 6.76-7.05 (m, 5H, ArH), 7.15-7.39 (m, 6H, ArH), 7.57 (pseudo t, 1H, J = 8.3 Hz, H-7), 7.63 (m, 1H, ArH), 8.07 (d, 1H, J = 8.1 Hz, H-5), 8.18 (d, 1H, J = 8.3 Hz, H-8), 9.34 (s, 1H, H-1). Anal. Calcd for C₂₉H₂₅N₄O₃FS.0.5H₂O: C, 64.80; H, 4.84; N, 10.43; S, 5.96. Found: C, 64.62; H, 5.07; N, 10.66; S, 6.28.

9-(N,N-Dimethylsulfamoyl)-3-N-methyl-3-N-phenyl-4-(3-phenyl-1,2-propenyl)-β-carboline-3-carboxamide (13c) - Using the general procedure described above, compound (13c) was obtained as an amorphous white solid in 60% yield from compound (12) and allylbenzene: IR (KBr) 1651, 1172 cm⁻¹. CIMS m/z 525 (MH)⁺. ¹H-NMR (300 MHz, CDCl₃) δ : 2.75 (s, 6H, N(CH₃)₂), 3.58 (s, 3H, CONCH₃), 4.22 (d, 2H, J = 4.0 Hz, CH₂Ar), 6.38 (d, 1H, J = 4.0 Hz, CH₂CH), 6.97-7.26 (m, 10H, ArH), 7.39 (dd, 1H, J = 7.6 and 8.0 Hz, H-6), 7.47 (m, 1H, ArH), 7.57 (dd, 1H, J = 7.6 and 8.5 Hz, H-7), 8.13 (d, 1H, J = 8.0 Hz, H-5), 8.20 (d, 1H, J = 8.5 Hz, H-8), 9.16 (s, 1H, H-1). Anal. Calcd for C₃₀H₂₈N₄O₃S: 0.1 CH₃CO₂C₂H₅ : C, 68.45 ; H, 5.44 ; N, 10.50 ; S, 6.01. Found : C, 68.83 ; H, 5.62 ; N, 10.43 ; S, 5.94.

4-(2-Carboxmethoxyethylene)-9-(N,N-dimethylsulfamoyl)-3-N-methyl-3-N-phenyl-β-carboline-3-carboxamide (13d) - Using the general procedure described above, compound (13d) was obtained as an amorphous white solid in 75% yield from compound (12) and methyl acrylate: IR (KBr) 1716, 1644, 1175 cm⁻¹. CIMS m/z 493 (MH)⁺. ¹H-NMR (300 MHz, CDCl₃) δ : 2.77 (s, 6H, N(CH₃)₂), 3.50 (s, 3H, CONCH₃), 3.93 (s, 3H, CO₂CH₃), 6.57 (d, 1H, J = 16.1 Hz, OCCH=CH), 6.98-7.10 (m, 5H, ArH), 7.37 (dd, 1H, J = 7.6 and 8.0 Hz, H-6), 7.59 (dd, 1H, J = 7.6 and 8.5 Hz, H-7), 7.91-7.96 (m, 2H, J = 8.5 and 16.1 Hz, H-8, OCCH=), 8.16 (d, 1H, J = 8.0 Hz, H-5), 9.34 (s, 1H, H-1). Anal. Calcd for C₂₅H₂₄N₄O₅S. 0.6 CH₃CO₂C₂H₅ : C, 60.34 ; H, 5.32 ; N, 10.27 ; S, 5.88. Found : C, 60.04 ; H, 5.21 ; N, 10.48 ; S, 5.96.

4-(2-Cyanethylene)-9-(N,N-dimethylsulfamoyl)-3-N-methyl-3-N-phenyl-β-carboline-3-carboxamide (13e) - Using the general procedure described above, compound (13e) was obtained as an amorphous white solid in 73% yield from compound (12) and acrylonitrile: IR (KBr) 2223, 1648, 1174 cm⁻¹. ¹H-NMR (250 MHz, CDCl₃) δ : 2.77 (s, 6H, N(CH₃)₂), 3.54 (s, 3H, CONCH₃), 6.16 (d, 1H, J =
16.6 Hz, NCCH=CH), 7.00-7.10 (m, 5H, ArH), 7.41 (dd, 1H, J = 7.6 and 8.0 Hz, H-6), 7.62 (dd, 1H, J = 7.6 and 8.0 Hz, H-7), 7.68 (d, 1H, J = 16.6 Hz, NCCH=), 7.91 (d, 1H, J = 8.0 Hz, H-8), 8.17 (d, 1H, J = 8.0 Hz, H-5), 9.35 (s, 1H, H-1). HRCIMS calcd for C_{24}H_{22}N_{5}O_{3}S m/z 460.1443 found 460.1431.

9-(N,N-Dimethylsulfamoyl)-3-N-methyl-3-N-phenyl-4-trimethylsilylacetylene-β-carboline-3-carboxamide (13f) - Using the general procedure described above, compound (13f) was obtained as an amorphous yellow solid in 93% yield from compound (12) and trimethylsilylacetylene. IR (KBr) 2245, 1654, 1175. CIMS m/z 505 (MH)^+. ^1H-NMR (250 MHz, CDCl$_3$) δ: 0.42 (s, 9H, Si(CH$_3$)$_3$), 2.73 (s, 6H, N(CH$_3$)$_2$), 3.57 (s, 3H, CONCH$_3$), 7.00-7.23 (m, 5H, ArH), 7.41 (pseudo t, 1H, J = 7.6 Hz, H-6), 7.61 (pseudo t, 1H, J = 8.5 Hz, H-7), 8.13 (d, 1H, J = 8.5 Hz, H-8), 8.62 (d, 1H, J = 8.0 Hz, H-5), 9.22 (s, 1H, H-1). Anal. Calcd for C$_{26}$H$_{28}$N$_4$O$_3$Si: C, 61.57; H, 5.74; N, 10.64; S, 6.09. Found: C, 61.93; H, 5.88; N, 10.42; S, 6.06.

9-(N,N-Dimethylsulfamoyl)-4-ethylene-3-N-methyl-3-N-phenyl-β-carboline-3-carboxamide (13g) - Using the general procedure described above, with the exception that the addition of triethylamine was omitted, compound (13g) was obtained as an amorphous white solid in 98% yield from compound (12) and tributyl(vinyl)tin. IR (film) 1652, 1175 cm$^{-1}$. ^1H-NMR (300 MHz, CDCl$_3$) δ: 2.77 (s, 6H, N(CH$_3$)$_2$), 3.51 (s, 3H, CONCH$_3$), 5.82 (d, 1H, J = 11.3 Hz, =CH$_3$), 5.84 (d, 1H, J = 17.8 Hz, =CH$_2$), 6.88-700 (m, 2H, J = 11.3 and 17.8 Hz, CH=CH$_2$, ArH), 7.06 (m, 4H, ArH), 7.35 (dd, 1H, J = 7.6 and 8.0 Hz, H-6), 7.57 (dd, 1H, J = 7.6 and 8.5 Hz, H-7), 8.10 (d, 1H, J = 8.5 Hz, H-8), 8.17 (d, 1H, J = 8.0 Hz, H-5), 9.28 (s, 1H, H-1). HRCIMS calcd for C$_{23}$H$_{23}$N$_4$O$_3$Si m/z 435.1490 found 435.1461.

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REFERENCES AND NOTES


1992, 12, 484.


12. 1H-NMR spectral data for compound (7) (300 MHz, CDCl₃) δ : 2.92 (s, 6H, N(CH₃)₂), 6.88 (d, 1H, J = 16.7 Hz, CH=CH), 7.00-7.47 (m, 9H, ArH), 7.61 (dd, 1H, J = 7.6 and 8.5 Hz, H-7), 7.67 (d, 1H, J = 7.8 Hz, ArH), 7.76 (d, 1H, J = 7.8 Hz, ArH), 8.24 (d, 1H, J = 8.5 Hz, H-8), 8.26 (d, 1H, J = 16.7 Hz, CH=CH), 8.50 (d, 1H, J = 8.2 Hz, H-5), 9.42 (s, 1H, H-1), 10.29 (s, 1H, exchangeable with D₂O, NH); CIMS m/z 497 (MH)+.

13. 1H-NMR spectral data for compound (8) (300 MHz, CDCl₃) δ : 2.91 (s, 6H, N(CH₃)₂), 3.02 (ddd, 2H, J = 2.5, 7.2 and 15.8 Hz, CH₂CH), 3.39 (s, 3H, CH₃O), 6.20 (dd, 1H, J = 2.5 and 7.2 Hz, CH₂CH), 7.32 (t, 1H, J = 7.6 Hz, ArH), 7.49 (t, 2H, J = 7.6 Hz, ArH), 7.56 (ddd, 1H, J = 7.6 and 8.0 Hz, H-8), 7.63 (d, 1H, J = 7.6 Hz, ArH), 7.73 (dd, 1H, J = 7.6 and 8.4 Hz, H-7), 8.13 (d, 1H, J = 8.4 Hz, H-6), 8.32 (d, 1H, J = 8.0 Hz, H-9), 9.72 (s, 1H, H-4); CIMS m/z 479 (MH)+.


15. By 1H-NMR spectroscopy of the crude reaction mixture. Compounds (10) and (11) were not isolated.


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