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Thieno[2',3':5,6]azepino[2,1-a]isoindolones from Hydroxylactam-alcohols via *N*-Acyliminium Ion Olefin Cyclization

Pascal Pigeon, Mohamed Othman and Bernard Decroix*

URCOM, Université du Havre, 25 rue Philippe Lebon, BP 540, 76058 Le Havre Cedex,
France

A one pot synthesis of thienoazepinoisoindolones from the reaction of hydroxylactam-alcohols, under acidic treatment, is described *via* an *N*-acyliminium olefin cyclization.

Heterocyclization involving *N*-acyliminium ions (intramolecular α -amidoalkylation reaction), although known for some time [1] have been examined in the major cases with hydroxylactams having a secondary hydroxy group [2,3]. Nevertheless, it has been reported for some cyclizations with an angular alkyl (methyl [4], ethyl [5], *t*-butyl [6], *n*-butyl [6]) or aromatic (phenyl [5]) group. An *N*-acyliminium ion was generated in acidic medium, which reacted with a nucleophile, olefin or aromatic, to give the cyclized product. We wish to report herein our results concerning the reactivity of hydroxylactam-alcohol of type **I**, and the *in situ* generation of both *N*-acyliminium ion, from hydroxylactam, and olefin as a π nucleophile from tertiary alcohol. As expected cyclization gave a 7-membered ring included in tetracyclic compounds of type **II** with a double bond where the position depends both on the nature of the alkyl groups R_1 and R_2 and on the conditions of the reaction (nature of the acid, and solvent).

Compounds of type **II** are structurally related to some natural isoindolo (or pyrrolo) benzazepine alkaloids [7] and derivatives isolated from Chilean *Berberidaceae*, *Berberis darwinii* Hook and *Taxus baccata* [8]. Furthermore it was found that prominent examples of structures which bear a benzazepine moiety exhibit significant clinical antidepressant effects [9-11]. Because of their potential biological properties condensed arylisoindoloazepines as aporphoeadane [7,12] were interesting to synthesize. To this end a strategy was designed which rests upon the construction of the C₁-C₄ link between isoindole and aryl moieties in structure **II**. Recently we have reported different approaches to analogs of azepines **II** [2,13,14]. Herein we wish to report another strategy depicted in Schemes I, II, III.

Scheme I

Scheme II

The hydroxylactam-alcohols of type **I** which are the precursors of cyclized products of type **II** were prepared according to Scheme I from the previously reported phthalimidoester **1** [14]. Reduction of **1** using sodium borohydride [15] followed by addition of a Grignard reagent led to compounds **3a,c** via the hydroxylactam **2**. Diols **3b,d** were obtained directly from **1** by addition of Grignard reagent. Hydroxylactam-alcohols **3a-d** are precursors of *N*-acyliminium ions (from hydroxylactam) and olefins (from alcohol) and an *N*-acyliminium-olefin cyclization [1] could be considered. Actually when **3a-d** were heated under reflux in toluene with a catalytic amount of *p*-toluenesulfonic acid and azeotropic elimination of water we observed the formation of three different products **7-9**. All of these compounds corresponded to an *N*-acyliminium-olefin cyclization. The possible *N*-acyliminium- aromatic cyclization leading to a five membered ring did not work according to our previous observation [5].

The reaction occurred probably via the intermediate **4a-d** that added to the olefin leading to a stable carbocation **6a-d** (Scheme I). The loss of a proton gave compounds **7-9** depending of the nature of R_1 and R_2 in the starting molecule. It is noteworthy that in the cases of R_1 is a methyl or ethyl (**3b** or **3d**) the enamide-olefin **5b** or **5d** could be observed. Examination of the reaction after 1 hour of heating by NMR showed the presence of the characteristic olefinic proton signals. A NOE difference experiment indicated *E* geometry for both olefins in **5d**.

In the case of **3c** ($R_1 = \text{H}$, $R_2 = \text{Methyl}$), after 30 minutes of reflux, compound **7c** was obtained as a single *E* isomer (Scheme II). However, when the reaction time was increased, inseparable unknown products and degradation began to appear. The less reactive compound **3d** ($R_1 = \text{Ethyl}$, $R_2 = \text{Methyl}$) needed one night of reflux, and led to an inseparable mixture of isomers **7d** (*Z,E*). The *Z/E* ratio of **7d** changed during the reaction time. The major *E* isomer partially

isomerized into *Z* isomer until equilibrium was reached (5 days 42/58 *Z/E* ratio). The stereochemistry of the C_{10b} and C₁₁ carbons was evident from the ¹H NMR spectrum analysis of **7c** (R₁ = H) which revealed a *cis* coupling constant of J = 2 Hz between H_{10b} and H₁₁. This observation allowed us to assign a *cis* relationship to R₁ (H, Ethyl) and H₁₁ in **7c,d**. The *trans* position of R₁ (methyl) at carbon C₁₁ was in accordance with the stereochemistry observed during a *N*-acyl-iminium-olefin cyclization process [1]. NOE difference experiments were used to distinguish the geometry (*E* or *Z*) of the double bond of **7c,d**. No trace of compound with an endocyclic double bond as **8** or **9** was detected.

Under similar acidic condition as above compound **3b** (R₁ = Methyl, R₂ = H) afforded a mixture of compounds **7b** (30%) and **8b** (70%) (Scheme III). This latter could be isolated as pure product by a recrystallization from ethanol. It is interesting to note that the minor product **7b** was the single product when the thiophene ring was changed for a furan or a benzene ring [16]. The loss of a proton in **6b** gave preferentially an endocyclic double bond (**8b**) rather than an unsubstituted exocyclic one (**7b**).

Finally, in the case of **3a** (R₁ = H, R₂ = H) the azepine **9a** was obtained (Scheme III). This compound was likely formed *via* the azepine isomer **8a**, which isomerized to give the more stable compound **9a**. We have already observed, in the isoindolo[2,1-*a*]quinoline series [17,18], a similar shift corresponding to this double bond that results from the presence of a particularly labile proton at the junction carbon C_{10b}. This mobility of the hydrogen atom at C_{10b} avoided the formation of an exocyclic double bond as in **7b**.

To confirm that **8a** was the intermediate, we treated the hydroxylactam-alcohol **3a** with *p*-toluenesulfonic acid in dichloromethane at room temperature. After 24 hours, the thienoazepine **8a** was obtained as the single product. A similar result was observed when **3a** reacted with thionyl chloride in dichloromethane at room temperature during one hour. Under acidic treatment (*p*-toluenesulfonic acid + toluene + reflux) **8a** was completely isomerized into the azepine **9a**.

The results presented here indicate that generation of both *N*-acyliminium ion and olefin from hydroxylactam-alcohol can provide a means for annulating seven membered rings. The formation of an exocyclic double bond is observed when the junction carbon C_{10b} of the thienoazepinoisoindolones is substituted, and in the other cases an endocyclic double bond is observed. Furthermore, when the junction carbon bears an hydrogen atom, a migration of that double bond can occur.

EXPERIMENTAL.

Melting points are uncorrected. The infrared spectra of solids (potassium bromide) were recorded on a Perkin Elmer FTIR paragon 1000 spectrometer. The ^1H and ^{13}C nmr spectra were recorded on a Bruker AC-200 (200 MHz) instrument in deuteriochloroform solution and the chemical shifts (δ) are expressed in ppm relative to internal tetramethylsilane. Ascending thin layer chromatography was performed on precoated plates of silica gel 60 F 254 (Merck) and the spots visualized using an ultraviolet lamp or iodine vapor. E. Merck silica gel 60 F (70-300 mesh) was used for column chromatography. The elemental analyses were carried out by the microanalysis laboratory of INSA at Rouen, F 76130 M^t. S^t. Aignan, France. Phthalimide **1** [14] and hydroxylactam **2** [15] were synthesized as previously described.

Preparation of Diols **3a-d**.

Phthalimide **1** or hydroxylactam **2** (10 mmol) were dissolved in 100 ml of dry dichloromethane with stirring. This solution was added dropwise to a stirred solution of Grignard reagent (ethyl(or methyl)magnesium iodide, 6 equivalents in ether) and stirring was continued for 3 hours. The mixture was then poured into a dilute aqueous solution of ammonium chloride and was extracted with dichloromethane. The aqueous layer was extracted with dichloromethane and the organic layers were combined. The solution was dried and concentrated under reduced pressure. The resulting solids were chromatographed (silica gel - dichloro- methane) and were not recrystallized to avoid dehydration. These compounds were used in the next step without further purification, and the microanalyses have not been attempted.

2,3-Dihydro-3-hydroxy-2-[2'-(1-hydroxy-1-methyl)ethylthien-3'-ylmethyl]-1*H*-isoindol-1-one (**3a**).

This compound was obtained in a yield of 91%, starting from hydroxylactam **2**; ^1H nmr: δ 1.63 (s, 6H, 2CH₃), 4.69 (d, $J = 15$ Hz, 1H, CH₂N), 4.99 (d, $J = 15$ Hz, 1H, CH₂N), 4.78 (s, 1H, OH), 5.02 (s, 1H, OH), 5.63 (s, 1H, CH), 6.82 (d, $J = 5$ Hz, 1H, H_{thiophene}), 6.98 (d, $J = 5$ Hz, 1H, H_{thiophene}), 7.32-7.77 (m, 4H, H_{arom}).

2,3-Dihydro-3-hydroxy-3-methyl-2-[2'-(1-hydroxy-1-methyl)-ethylthien-3'-ylmethyl]-1*H*-isoindol-1-one (**3b**).

This compound was obtained in a yield of 94%, starting from phthalimide **1**; ^1H nmr: δ 1.43 (s, 3H, CH₃), 1.62 (s, 6H, 2CH₃), 4.72 (d, $J = 16$ Hz, 1H, CH₂N), 4.84 (d, $J = 16$ Hz, 1H, CH₂N),

6.75 (d, $J = 5$ Hz, 1H, $H_{\text{thiophene}}$), 7.10 (d, $J = 5$ Hz, 1H, $H_{\text{thiophene}}$), 7.45-7.76 (m, 4H, H_{arom}).

2,3-Dihydro-3-hydroxy-2-(2'-(1-ethyl-1-hydroxypropyl)thien-3'-ylmethyl)-1*H*-isoindol-1-one (**3c**).

This compound was obtained in a yield of 95%, starting from hydroxylactam **2**; ^1H nmr: δ 0.81 (t, $J = 7$ Hz, 6H, 2CH_3), 1.78 (q, $J = 7$ Hz, 4H, 2CH_2), 4.68 (d, $J = 14$ Hz, 1H, NCH_2), 4.97 (d, $J = 14$ Hz, 1H, NCH_2), 4.97 (s, 1H, OH), 5.63 (s, 1H, CH), 6.80 (d, $J = 5$ Hz, $H_{\text{thiophene}}$), 7.03 (d, $J = 5$ Hz, 1H, $H_{\text{thiophene}}$), 7.32-7.54 (m, 3H, H_{arom}), 7.63 (d, $J = 7$ Hz, 1H, H_{arom}).

2,3-Dihydro-3-hydroxy-3-ethyl-2-[2'-(1-ethyl-1-hydroxypropyl)thien-3'-ylmethyl]-1*H*-isoindol-1-one (**3d**).

This compound was obtained in a yield of 92%, starting from phthalimide **1**; ^1H nmr: δ 0.43 (t, $J = 7$ Hz, 3H, CH_3), 0.79-0.90 (m, 6H, 2CH_3), 1.70-1.90 (m, 4H, 2CH_2), 2.10-2.25 (m, 2H, CH_2), 4.31 (s, 1H, OH), 4.67 (d, $J = 15$ Hz, 1H, CH_2N), 4.92 (d, $J = 15$ Hz, 1H, CH_2N), 6.98 (d, $J = 5$ Hz, 1H, $H_{\text{thiophene}}$), 7.03 (d, $J = 5$ Hz, 1H, $H_{\text{thiophene}}$), 7.33-7.56 (m, 3H, H_{arom}), 7.64 (d, $J = 7$ Hz, 1H, H_{arom}).

Dehydration of Diols **3b,d** into Dienes **5b,d**.

Diols **3b,d** (10 mmol), a catalytic amount of *p*-toluenesulfonic acid and toluene were stirred and refluxed with elimination of water using a Dean-Stark apparatus for 1 hour. The solution was cooled, washed with an aqueous sodium hydrogen carbonate solution, dried on magnesium sulfate, then concentrated under reduced pressure. The solid was recrystallized from ethanol.

2,3-Dihydro-3-methylidene-2-(2'-(1-methylvinyl)thien-3'-ylmethyl)-1*H*-isoindol-1-one (**5b**).

Dehydration of **3b** gave **5b** in 84% yield, mp: 112° ; ir: $1696 (\text{C}=\text{O}) \text{ cm}^{-1}$; ^1H nmr: δ 2.19 (s, 3H, CH_3), 4.64 (d, $J = 2$ Hz, 1H, $=\text{CH}_2$), 5.02 (s, 2H, NCH_2), 5.08 (d, $J = 2$ Hz, 1H, $=\text{CH}_2$), 5.11 (s, 1H, $=\text{CH}_2$), 5.35 (s, 1H, $=\text{CH}_2$), 6.76 (d, $J = 5$ Hz, 1H, $H_{\text{thiophene}}$), 7.06 (d, $J = 5$ Hz, 1H, $H_{\text{thiophene}}$), 7.40-7.68 (m, 3H, H_{arom}), 7.85 (d, $J = 7$ Hz, 1H, H_{arom}); ^{13}C NMR: δ 25.2 (CH_3), 37.9 (CH_2), 89.6 ($=\text{CH}_2$), 116.8 ($=\text{CH}_2$), 119.8 (CH), 123.3 (CH), 123.4 (CH), 128.0 (CH), 129.2 (C), 129.4 (CH), 132.0 (CH), 133.3 (C), 136.3 (C), 137.4 (C), 141.3 (C), 141.5 (C), 167.0 (CO).

Anal. Calcd. for $\text{C}_{17}\text{H}_{15}\text{NOS}$: C, 72.57; H, 5.37; N, 4.97. Found: C, 72.69; H, 5.48; N, 5.16.

2,3-Dihydro-3-ethylidene-2-(2'-(1-ethylprop-1-enyl)thien-3'-ylmethyl)-1*H*-isoindol-1-one (**5d**).

Dehydration of **3d** gave **5d** in a 80% yield, mp: 125° ; ir: $1694 (\text{C}=\text{O}) \text{ cm}^{-1}$; ^1H nmr: δ 1.05 (t, $J = 7$ Hz, 3H, CH_3), 1.82 (d, $J = 7$ Hz, 3H, $\text{CH}_3\text{-C}=\text{}$), 2.06 (d, $J = 7$ Hz, 3H, $\text{CH}_3\text{-C}=\text{}$), 2.45 (q,

J = 7 Hz, 2H, CH₂), 4.91 (s, 2H, NCH₂), 5.31 (q, J = 7 Hz, 1H, =CH), 5.59 (q, J = 7 Hz, 1H, =CH), 6.71 (d, J = 5 Hz, 1H, H_{thiophene}), 7.00 (d, J = 5 Hz, 1H, H_{thiophene}), 7.40-7.60 (m, 2H, H_{arom}), 7.78 (d, J = 7 Hz, 1H, H_{arom}), 7.90 (d, J = 7 Hz, 1H, H_{arom}); ¹³C NMR: δ 12.8 (CH₃), 13.1 (CH₃), 13.8 (CH₃), 25.8 (CH₂), 37.8 (CH₂), 106.7 (CH enamide), 122.7 (CH), 123.3 (CH), 123.4 (CH), 126.8 (CH), 127.6 (CH), 128.3 (CH), 130.3 (C), 131.6 (CH), 133.3 (C), 135.2 (C), 135.4 (C), 135.6 (C), 142.0 (C), 166.1 (CO).

Anal. Calcd. for C₂₀H₂₁NOS: C, 74.27; H, 6.54; N, 4.33. Found: C, 73.99; H, 6.48; N, 4.36.

Cyclization of Diol **3a** into Azepine **8a**.

A solution of diol **3a** (10 mmol) and thionyl chloride (1.5 ml, 3 equivalents), in dry dichloromethane (50 ml) was stirred for 2 hours (monitoring by TLC). The solution was poured into water and the organic layer was washed with an aqueous sodium hydrogen carbonate solution, dried with magnesium sulfate, then concentrated under reduced pressure at room temperature to furnish pure azepine **8a**. This unstable compound was obtained in 94% yield but was not purified because it evolved to **9a**. ¹H nmr: δ 2.17 (s, 3H, CH₃), 4.72 (d, J = 15 Hz, 1H, H₄), 5.84 (d, J = 15 Hz, 1H, H₄), 5.22 (s broad, 1H, H_{10b}), 5.86 (s broad, 1H, H₁₁), 7.03 (d, J = 5 Hz, 1H, H₃), 7.22 (d, J = 5 Hz, 1H, H₂), 7.38-7.62 (m, 3H, H_{8,9,10}), 7.80 (d, J = 7 Hz, 1H, H₇); ¹³C NMR: δ 24.5 (CH₃), 41.4 (CH₂), 60.5 (CH), 121.9 (CH), 122.7 (CH), 123.4 (CH), 124.5 (CH), 128.1 (CH), 128.7 (CH), 131.5 (CH), 132.1 (C), 132.8 (C), 135.7 (C), 140.0 (C), 144.2 (C), 166.7 (CO).

Cyclization of Diols **3a-d** into Azepines **7b,c,d, 8b** or **9a**

Using conditions described above for preparation of **5**, the diols **3a-d** or dienes **5b,d** led to azepines **7b,c,d, 8b**, or **9a**.

4,10_b-Dihydro-10_b-methyl-12-methyl-thieno[2',3':5,6]azepino-[2,1-*a*] isoindol-6-one (**9a**).

The azepine **9a** was obtained as the single product in a yield of 86% (calculated from **2**) after 1 hour of reflux. This compound has mp 157° (ethanol); ir: 1693 (C=O) cm⁻¹; ¹H nmr: δ 1.64 (d, J = 7 Hz, 3H, CH₃), 4.15-4.32 (m, 1H, H₁₂), 4.92 (d, J = 15 Hz, 1H, H₄), 5.19 (d, J = 15 Hz, 1H, H₄), 5.76 (d, J = 5 Hz, 1H, H₁₁), 7.00 (s, 2H, H_{2,3}), 7.34-7.62 (m, 3H, H_{8,9,10}), 7.78 (d, J = 7 Hz, 1H, H₇); ¹³C NMR: δ 21.9 (CH₃), 31.1 (CH), 38.4 (CH₂), 109.6 (=CH), 118.8 (CH), 120.7 (CH), 123.1 (CH), 127.7 (C), 128.8 (CH), 129.0 (CH), 131.5 (C), 131.6 (CH), 135.9 (C), 136.8 (C), 145.5 (C), 166.3 (CO).

Anal. Calcd. for C₁₆H₁₃NOS: C, 71.88; H, 4.90; N, 5.24. Found: C, 72.31; H, 4.75; N, 5.28.

4,10_b-Dihydro-11*H*-10_b-methyl-12-methylidene-thieno[2',3':5,6]azepino[2,1-*a*]isoindol-6-one (**7b**) and 4,10_b-Dihydro-10_b-methyl-12-methyl-thieno[2',3':5,6]azepino[2,1-*a*]isoindol-6-one (**8b**).

From **3b** (or **5b**) after one night of reflux a 70/30 mixture of isomer azepines **8b** and **7b** was obtained in a yield of 72% (calculated starting from **1**). Recrystallization from ethanol furnished a small amount of pure **8b**.

Compound **7b** had a ¹H nmr: δ 1.58 (s, 3H, CH₃-C_{10b}), 2.87 (d, J = 13 Hz, 1H, H₁₁), 3.07 (d, J = 13 Hz, 1H, H₁₁), 4.21 (d, J = 17 Hz, 1H, H₄), 4.59 (s, 1H, H₂C=C₁₂), 5.04 (s, 1H, H₂C=C₁₂), 5.33 (d, J = 17 Hz, 1H, H₄), 6.93 (d, J = 5 Hz, 1H, H₃), 7.00 (d, J = 5 Hz, 1H, H₂), 7.32-7.62 (m, 3H, H_{8,9,10}), 7.74 (d, J = 7 Hz, 1H, H₇).

Compound **8b** had a mp: 168°; ir: 1687 (C=O) cm⁻¹; ¹H nmr: δ 1.67 (s, 3H, CH₃-C_{10b}), 2.09 (s, 3H, CH₃-C₁₂), 4.31 (d, J = 17 Hz, 1H, H₄), 5.44 (d, J = 17 Hz, 1H, H₄), 5.78 (s, 1H, H₁₁), 7.05 (d, J = 5 Hz, 1H, H₃), 7.15 (d, J = 5 Hz, 1H, H₂), 7.33-7.62 (m, 3H, H_{8,9,10}), 7.75 (d, J = 7 Hz, 1H, H₇); ¹³C NMR: δ 25.7 (CH₃), 26.7 (CH₃), 38.4 (CH₂), 66.2 (C), 120.9 (CH), 123.6 (CH), 123.8 (CH), 126.9 (C), 126.8 (CH), 128.1 (CH), 128.4 (CH), 129.5 (C), 131.8 (CH), 136.1 (C), 138.1 (C), 149.1 (C), 166.4 (CO).

Anal. Calcd. for C₁₇H₁₅NOS: C, 72.57; H, 5.37; N, 4.98. Found: C, 72.36; H, 5.32; N, 5.12.
4,10_b-Dihydro-11*H*-12-ethylidene-11-methyl-thieno[2',3':5,6]-azepino[2,1-*a*]isoindol-6-one (**7c**).

Starting from **3c** after 30 minutes of reflux the azepine **7c** (*E* configuration) was obtained in 82% yield as an oil (calculated from **2**). This compound had a ¹H nmr: δ 0.44 (d, J = 7 Hz, 3H, CH₃-C₁₁), 1.91 (d, J = 7 Hz, 3H, CH₃-C=C₁₂), 3.57 (qd, J = 7 and 2 Hz, 1H, H₁₁), 4.24 (d, J = 16 Hz, 1H, H₄), 4.70 (d, J = 2 Hz, 1H, H_{10b}), 5.30 (d, J = 16 Hz, 1H, H₄), 5.89 (q, J = 7 Hz, 1H, HC=C₁₂), 6.91 (d, J = 5 Hz, 1H, H₃), 7.00 (d, J = 5 Hz, 1H, H₂), 7.33-7.60 (m, 3H, H_{8,9,10}), 7.82 (d, J = 7 Hz, 1H, H₇); ¹³C NMR: δ 11.2 (CH₃), 13.6 (CH₃), 35.9 (CH), 41.0 (CH₂), 65.1 (CH), 121.3 (CH), 122.2 (CH), 123.4 (CH), 125.7 (CH), 127.9 (CH), 128.6 (CH), 130.7 (C), 131.4 (CH), 132.1 (C), 136.6 (C), 140.7 (C), 144.0 (C), 167.8 (CO); MS (IE, 70 ev) m/e: 295 (M⁺).

4,10_b-Dihydro-11*H*-10_b-ethyl-12-ethylidene-11-methyl-thieno[2',3':5,6]azepino[2,1-*a*]isoindol-6-one (**7d**).

From **3d** (or **5d**) an oily *E/Z* mixture of azepine **7d** was obtained in a yield of 68% (calculated starting from **1**). The *E/Z* ratio was 80/20 after 12 hours and became 58/42 after five days of reflux. The *E* and *Z* isomers were separated by GC-MS analysis.

The *E* Isomer has ^1H nmr: δ 0.25-0.40 (m, 6H, $\text{CH}_3\text{-C-C}_{10\text{b}}$ and $\text{CH}_3\text{-C}_{11}$), 1.85-1.95 (m, 1H, $\text{CH}_2\text{-C}_{10\text{b}}$), 1.89 (d, $J = 7$ Hz, 3H, $\text{CH}_3\text{-C=C}_{12}$), 2.35-2.55 (m, 1H, $\text{CH}_2\text{-C}_{10\text{b}}$), 3.42 (q, $J = 7$ Hz, 1H, H_{11}), 3.87 (d, $J = 16$ Hz, 1H, H_4), 5.52 (d, $J = 16$ Hz, 1H, H_4), 5.95 (q, $J = 7$ Hz, 1H, HC=C_{12}), 6.91 (d, $J = 5$ Hz, 1H, H_3), 6.99 (d, $J = 5$ Hz, 1H, H_2), 7.35-7.62 (m, 3H, $\text{H}_{8,9,10}$), 7.84 (d, $J = 7$ Hz, 1H, H_7); ^{13}C NMR: δ 6.9 (CH_3), 13.8 (CH_3), 14.1 (CH_3), 26.5 (CH_2), 37.9 (CH_2), 41.1 (CH), 71.0 (C), 120.2 (CH), 122.4 (CH), 123.8 (CH), 127.3 (CH), 128.0 (CH), 128.8 (CH), 131.3 (C), 131.9 (CH), 132.8 (C), 135.5 (C), 140.3 (C), 147.9 (C), 168.1 (CO); MS (IE, 70 eV) m/e : 135, 267, 323 (M^+), 164, 91, 172.

The *Z* Isomer has ^1H nmr: δ 0.20-0.41 (m, 6H, $\text{CH}_3\text{-C-C}_{10\text{b}}$ and $\text{CH}_3\text{-C}_{11}$), 1.85-1.95 (m, 1H, $\text{CH}_2\text{-C}_{10\text{b}}$), 1.90 (d, $J = 7$ Hz, 3H, $\text{CH}_3\text{-C=C}_{12}$), 2.31-2.56 (m, 1H, $\text{CH}_2\text{-C}_{10\text{b}}$), 2.85 (q, $J = 7$ Hz, 1H, H_{11}), 3.82 (d, $J = 16$ Hz, 1H, H_4), 5.38 (d, $J = 16$ Hz, 1H, H_4), 5.77 (q, $J = 7$ Hz, 1H, HC=C_{12}), 6.98 (d, $J = 5$ Hz, 1H, H_3), 7.12 (d, $J = 5$ Hz, 1H, H_3), 7.26-7.61 (m, 3H, $\text{H}_{8,9,10}$), 7.78 (d, $J = 7$ Hz, 1H, H_7); ^{13}C NMR: δ 6.7 (CH_3), 13.7 (CH_3), 15.3 (CH_3), 27.2 (CH_2), 36.9 (CH_2), 50.3 (CH), 70.9 (C), 120.3 (CH), 123.6 (CH), 123.6 (CH), 127.7 (CH), 127.8 (CH), 128.5 (CH), 131.6 (C), 132.6 (CH), 133.8 (C), 133.8 (C), 135.3 (C), 147.8 (C), 167.8 (CO); MS (IE, 70 eV) m/e : 135, 267, 323 (M^+), 164, 91, 172.

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