Diastereoselective Access to Chiral Non-Racemic [1,3]Oxazolo-[2,3-*a*]isoindol-5-one Ring Systems *via O*-Cationic Cyclization.

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Dedicated to Professor Jean Morel for his retirement

The title compounds **4** have been prepared from suitable β–amino- alcohol **2** and phthalic anhydride (**5**) in a three-step sequence in moderate to good yields (58-94%). The key step of this methodology is based on an intramolecular *O*-cationic cyclization involving *N*-acyliminium species. The high levels of the observed chemoselectivity during the intermolecular or intramolecular cyclization were also discussed.

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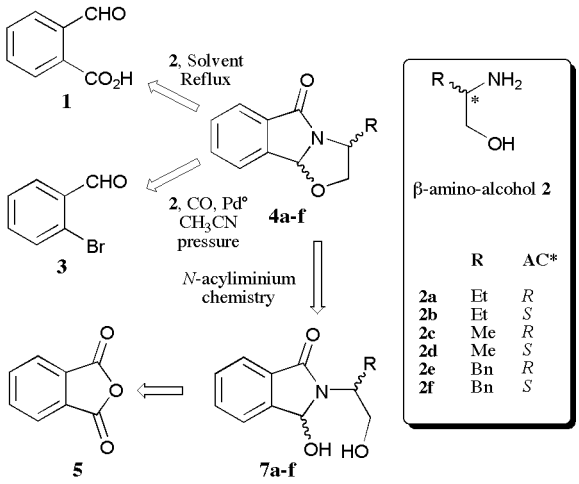
As reviewed recently by Meyers *et al*. [1], the bicyclic *N,O*-acetal product, commonly known as the bicyclic lactam, has proven to be an exceptional chiral building block for the asymmetric construction of a wide variety of natural and unnatural carbocyclic and heterocyclic compounds containing one or more stereogenic center(s) [1]. However, structurally related aromatic tricyclic lactams are little explored in the literature, a fact that is reflected in the few reports of synthetic applications of nitrogen heterocycles [2-6].

As a consequence of the greater potential of these bicyclic lactams, notable advances concerning the synthesis and reactivity of these species continue to be made. So, three general methods have been developed to accede to these polycyclic systems: 1°)- The most frequently used method to achieve this reaction, was the cyclodehydration process between an optically pure amino-alcohol **2** and a ketoacid **1** (Scheme 1) under azeotropic removal of water with a catalytic amount of *p*-toluenesulfonic acid [5] or not [1-4,6]; 2°)-The aromatic tricyclic lactam unit was also reported recently according to this second route: a palladium-catalyzed stereoselective synthesis *via* carbonylative cyclization process between amino alcohol **2** and 2-bromobenzaldehyde (**3**) under controlled pressure [6]; 3°)-The third way developed to obtain these lactams **4** was related to the extensive work involving *N*-acyliminium species [7,8]. In all these reported methods, the corresponding isoindolinones **4** were isolated in moderate to good yields. Another method based on an intramolecular nucleophilic substitution was also described for preparation of similar lactams with oxygen atom as nucleophile. The yields reported were low and in all cases the starting materials were recovered [9a]. But with a nitrogen atom as an internal nucleophile, the azacyclic products were isolated in good yields [9b].

Scheme 1

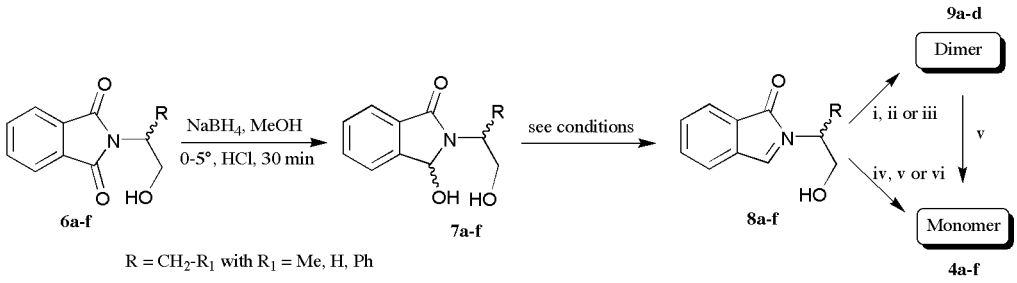


Key: Retrosynthetic sequence leading to chiral bicyclic lactams **4a-f**; *AC: Absolute configuration of the starting amino-alcohol **2a-f**.

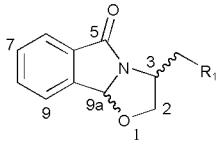
Because of the flexibility and versatility of the latter strategy allied with our general interest in development of synthetic utility on *N*-acyliminium ion chemistry, we present in this paper a facile approach to chiral monosubstituted oxazoloisoindolinones **4**.

Recently, Kumar *et al*. [10] have reported the dimerization of α-hydroxylactam **7a** into **9a** in acidic medium (*i.e.* catalytic trifluoroacetic acid, dichloromethane, room temperature, 16h: Method A) *via* an unexpected intermolecular cyclization (Scheme 2). During these investigations the formation of the *N,O*-acetal monomer product **4a** was not detected. Based on these observations, our first target was to re-examine the cationic cyclization to identify the best formulation to achieve the intramolecular cyclization leading to the oxa-tricyclic lactam **4a**.

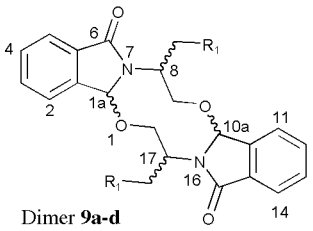
Scheme 2



Key: (i) **Method A:** TFA cat., CH_2Cl_2, rt, 16 h (reference [10]); (ii) **Method B:** excess AcOH, CH_2Cl_2, rt, 36 h; (iii) **Method C:** PTSA cat., CH_2Cl_2, rt, 24 h; (iv) **Method D:** excess TFA, CH_2Cl_2, rt, 2 h; (v) Method E: HCl cat., $CHCl_3$, rt, 24 h; (vi) **Method F:** H_2SO_4 cat., CH_2Cl_2, rt, 12 h.



Monomer **4a-f**



Dimer **9a-d**

So, the requisite *N*-acyliminium ion precursor **7a** was obtained in 2 steps from phthalimide (**5**), by thermal amino-anhydride condensation at 200° (95%) (Method I) or by condensation under azeotropic conditions (89%) (Method II) [11], followed by sodium borohydride reduction under mild conditions with regular addition of ethanolic hydrogen chloride solution (3 drops of concentrated hydrochloric acid in 5 ml of ethanol) (*i.e.*, 3 equivalents of sodium borohydride, methanol, 0-5°, 30 minutes, hydrochloric acid in ethanol, about 75% in all cases) [10,12].

The subjection of α-hydroxylactam **7a** to weak acetic acid (Method B) or catalytic *p*-toluenesulfonic acid (Method C) in dichloromethane at room temperature for 36 hours or 24 hours (Table 1, entry 2 or 3) afforded only the dimeric product **9a** which showed a (1a*S*,8*R*,10a*S*,17*R*) configuration in 42 or 82% yield, respectively. This product, which resulted from an intermolecular cyclization of the *N*-acyliminium ion intermediate **8a**, is identical to that reported earlier by using conditions i [10]. Thus, we examined the effect of an R group substituent and its absolute configuration in the intermolecular cyclization process.

Table 1

Screening of the Reaction Conditions of *O*-Cationic Cyclization of the Ions *N*-Acyliminium Ion Precursors **7** Leading to Monomer **4** and Dimer **9** Produced *via* Scheme 2

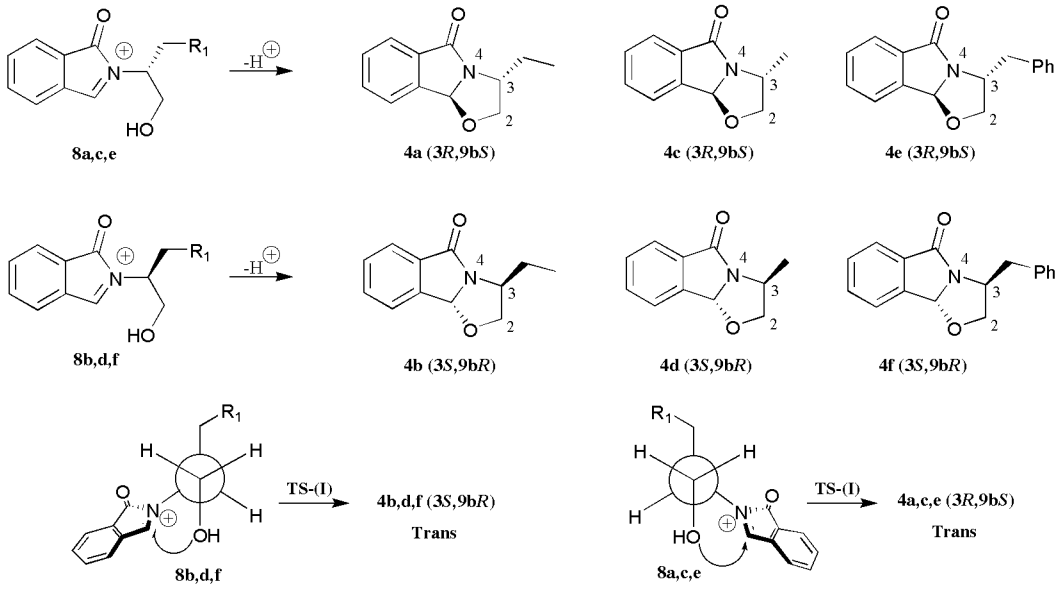
Entry	β-amino-alcohol [a]	conditions	Product [b]	mp°/oil	Yield %	Method
1	**2a** R = Et (*R*)	i	**9a** [10]	non indicated	40	**A**
2		ii	**9a**	242-243	42	**B**
3		iii	**9a**	" " "	82	**C**
4		iv	**4a**	colourless oil	58	**D**
5		v	**4a**	" " "	71	**E**
6		vi	**4a**	" " "	61	**F**
7	**2b** R = Et (*S*)	ii	**9b**	228-231	75	**B**
8		iv	**4b**	colourless oil	84	**D**
9		v	**4b**	" " "	88	**E**
10	**2c** R = Me (*R*)	ii	**9c**	199-203	70	**B**
11		v	**4c**	colourless oil	89	**E**
12	**2d** R = Me (*S*)	ii	**9d**	211-214	84	**B**
13		v	**4d**	colourless oil	94	**E**
14	**2e** R = Bn (*R*)	iv	**4e**	130-132	79	**D**
15		v	**4e**	" " "	82	**E**
16	**2e** R = Bn (*S*)	iv	**4f**	78-81	69	**D**
17		v	**4f**	" " "	74	**E**

[a] Absolute configuration of amino-alcohol; [b] Solids were purified by recrystallization as indicated in experimental part while liquids were purified by chromatography on silica gel column using *iso*-hexane/ethyl acetate 10/3 as eluent.

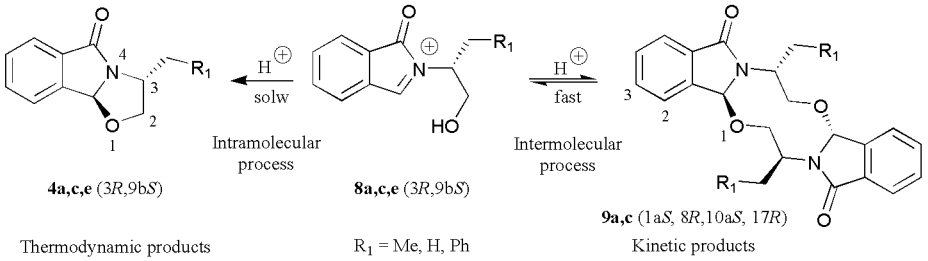
Thus, α-hydroxylactams **7b-d** upon treatment according method B outlined above (Table 1, entries 7, 10 and 12), produced after recrystallization (ethanol/water) in the same manner the dimers **9b-d** as a lone reaction products in comparable yields of 75%, 70%, and 84%, respectively. Invariably, the cyclization products resulted from an intermolecular *O*-cationic cyclization of the *N*-acyliminium ion intermediates **8b-d**.

all starting material was consumed (monitored by TLC) and the expected monomer **4a** was obtained in an excellent yield (95%). These results were comparable to these reported in the literature [3,4] in which, just now, only Lewis acids such as titanium tetrachloride, tin tetrachloride, boron trifluoride diethyl etherate, trimethylsilyl triflate and alkyl aluminum dichloride were used intensively as CH-O activator for the generation of *N*-acyliminium cation from bicyclic lactams.

Scheme 3



Scheme 4



On the basis of our precedent work in this area [11] and to avoid the dimerization process, other reaction conditions were tested. So, as shown in Table 1 the intramolecular cyclization leading to tricyclic lactam **4a** as a single diastereosomer (3*R*,9b*S*) occurred when excess trifluoroacetic acid (Method D) (Table 1, entry 4, 58%), catalytic concentrated hydrochloric acid (Method E) (Table 1, entry 5, 71%), or catalytic concentrated sulfuric acid (Method F) (Table 1, entry 6, 61%) was used as a proton source. Furthermore, since the bicyclic lactams could generate *N*-acyliminium species under acid catalysis [1], we envisaged the treatment of the dimeric product **9a** with hydrochloric acid (Method E) (Table 1, conditions v). Under these conditions, interestingly,

In order to rationalize the stereochemical outcome of these cyclization reactions, we have invoked the kinetic versus thermodynamic control [13] using the formal *N*-acyliminium species as intermediates (Scheme 4).

In fact, under mild conditions such as in the presence of catalytic trifluoroacetic acid, catalytic *p*-toluenesulfonic acid or neat acetic acid (Methods A, B and C), the *N*-acyliminium ion **8a** lead to the dimeric product **9a** as a single isomer [11] under kinetic process (fast reaction). Similarly, under harsher conditions such as excess of trifluoroacetic acid, or a catalytic amount of strong mineral acid (Methods D, E and F), **8a** led in an alternate way to the monomeric product **4a** under thermodynamic control. This latter,

(3*R*,9b*S*)-3-ethyl-2,3-dihydro-9b*H*-oxazolo[2,3-*a*]isoindol-5-one (**4a**), which is the result of a "disfavored" 5-endo-trigonal cyclization process [14], was also obtained from corresponding dimer under strong acidic conditions (Method E). In this scenario, the CH-O linkage of the kinetic product **9** is cleaved under protic acid activation into *N*-acyliminium ion congener **8**, which lead thermodynamically to the monomer **4** without epimerization. This fact, suggests that the kinetic product **9** is formed reversibly depending on the acid conditions, and under strong acid influence there is enough energy for the kinetic product to get back to the starting *N*-acyliminium ion **8**. In this case, there will be enough energy for some thermodynamic product **4** to be formed.

Furthermore, in both intermolecular and intramolecular *O*-cyclization process, the reaction proceed under mild conditions, cleanly and afforded the desired cyclic lactams **4a** and **9a** with moderate to good yields, and with high stereocontrol (during this process only one diastereosomer was obtained).

The diastereoselectivity observed during the *O*-cationic cyclization of α-hydroxylactam **7a** in acidic medium seems to proceed probably through Cram's rule (Scheme 3). This, can be explained by assuming that the transition state **TS-(I)** is the more one, in which the oxygen atom attacks the iminium ion **8a** (Scheme 3) when the OH group is anti the R (-CH_2-R_1 with R_1 = Me) one [15] to produce in all cases the expected isoindolinone **4a** as a single diastereosomer (EIMS *m/z* 203 ($M^{+\bullet}$) [11b].

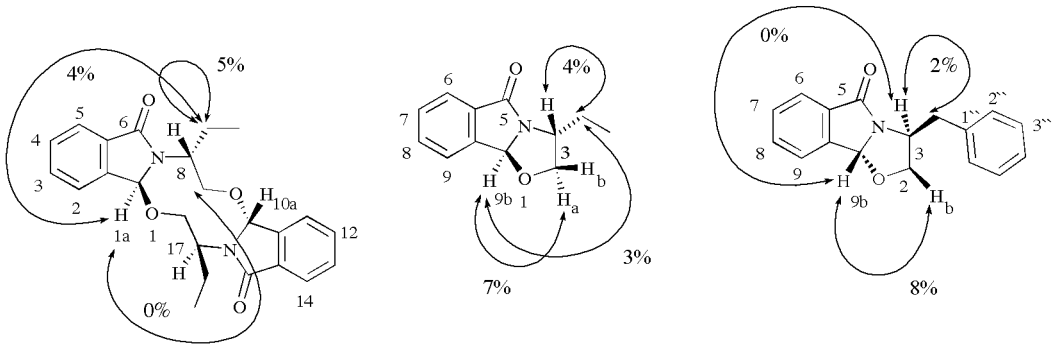
Since it was possible that imides **6a-f** could generate chiral cyclic lactams **4** *via* an intramolecular α-oxoamidoalkylation cyclization, we explored the elaboration of different aromatic imide models, substituted by ethyl, methyl and benzyl groups with *R* and *S* absolute configuration at the carbon adjacent to nitrogen atom, to establish the generality and versatility of the synthetic sequence highlighted in Schemes 1 and 2.

For this end and in the same way, α-hydroxylactams **7b-f** readily obtained by procedure as outlined for their analogous ω-carbinol lactam **7a**, were treated under conditions iv (Method D) and/or v (Method E) (see Table 1 for details) and led to the cyclization products **4b**, **4c**, **4d**, **4e** and **4f** in appreciable yields. Structures **4b-d**, were also obtained in good yields (70-84%) from the dimer **4b-d** by a consecutive ring opening-ring closure process (RO-RC) involving *N*-acyliminium ion intermediates. No epimerization of the angular stereogenic center C_{9b} was observed during these transformations.

Structure assignments of all compounds are based on their IR, NMR (^{1}H and ^{13}C-NMR experiments include NOE Difference and DEPT experiments, respectively), and GC-MS spectra. In the case of solids, their elemental analyses were also performed. Finally, for the known products, their characteristics were compared to those reported in the literature.

In summary, we have shown that chiral imides **6a-f**, as *N*-acyliminium ion precursors in an interrupted intermolecular *O*-cationic cyclization depending on the acidic conditions, could produce efficiently under thermodynamic control the expected chiral tricyclic lactams **4a-f** in good yields and an excellent stereocontrol. These latter, were also obtained from the dimeric products **9** obtained reversibly as kinetic isomers. Finally, because of the greater synthetic potential of these bicyclic lactams, the extension to elaboration of more fused isoindolinones is possible. Investigation in this way is underway.

Scheme 5



9a (1a*S*, 8*R*, 10a*S*, 17*R*) **4a** (3*R*, 9b*S*) **4f** (3*S*, 9b*R*)

NOE Difference experiments for the dimer **9a** and the monomers **4a,f**

The absolute configuration of the newly created stereo center at the 9b-position for the monomer **4a** was determined by NOE difference experiments. In fact, when H_{9b} (singlet at δ = 5.86 ppm) was irradiated, no significant NOE effect was detected for H_3 (quadruplet at δ = 4.07 ppm), but a strong NOE effect was observed between H_{9b} and the angular ethyl group -*C*H_2-CH_3 (quadruplet at δ = 1.73 ppm). These results demonstrate the *trans*-orientation of H_{9b} and H_3 as shown in Scheme 3.

EXPERIMENTAL

General.

All melting points were measured on a Boetius micro hot-stage and are uncorrected. The infrared spectra of solids (potassium bromide) were recorded on a Perkin Elmer FT-IR paragon 1000 spectrometer. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 (200 MHz) instrument in deuteriochloroform and chemical shifts (δ) are expressed in ppm relative to TMS as internal standard. Ascending thin layer chromatography was performed on pre-coated plates of silica gel 60 F 254 (Merck) and the spots visualized using an ultraviolet lamp or iodine vapor. Optical rotations were measured with a Perkin Elmer 241 polarimeter in a 10 cm cell in chloroform at 25°. Mass spectral measurements were recorded on an AEI MS 902 S spectrophotometer. The elemental analyses were carried out by the microanalysis laboratory of INSA, F-76130 Mt. St. Aignan, France.

General Procedure for Synthesis of Imides (**6a-f**).

Method I.

A mixture of powdered phthalic anhydride (**5**) (1.48 g, 10 mmoles) and (*R* or *S*)-β-amino-alcohol **2** (10 mmoles) was heated without solvent under vigorous stirring at 200° for 3 hours. The reaction mixture was cooled, poured on crushed ice (50 ml) and extracted twice with dichloromethane (2x50 ml). After separation, the organic layer was washed with water, brine, dried over magnesium sulfate and concentrated *in vacuo*. The resulting liquid was purified by distillation under reduced pressure to give imides **6a** (95%) and **6b** (92%) as colourless oil. The resulting solid was recrystallized from toluene (water or ethanol) to give suitable imides **6c-f** in 90-94% yield.

Method II.

A mixture of (*R* or *S*)-β-amino-alcohol **2** (10 mmoles), phthalic anhydride (**5**) (1.48 g, 10 mmoles) and triethylamine (0.5 ml, 3.6 mmoles) in toluene (50 ml) was refluxed with a Dean-stark apparatus for 12 hours. The reaction mixture was cooled, then was concentrated under reduced pressure. The residue was dissolved into dichloromethane, washed with 10% hydrochloric acid solution then with a sodium hydrogen carbonate solution. The organic layer was dried over magnesium sulfate, concentrated under reduced pressure, and distillation or recrystallization of the residue from toluene (water or ethanol) gave imides **6c-f** same as above in 85-93% yield.

(1'*R*)-*N*-(2'-Ethyl-1'-hydroxyethyl)-1*H*-isoindole-1,3(2*H*)-dione (**6a**).

This product was obtained as a colourless oil in 89% (Method II) and 95% (Method I) yields; bp 205°/10 torr; ir (neat): ν 3495 (OH), 1706 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.90 (t, J = 7.5Hz, 3H, CH_3), 1.86 (m, J = 7.6Hz and J = 7.7Hz, 2H, CH_2), 3.83 (dd, $J_{1',1'}$ = 11.7Hz, $J_{1',2'}$ = 3.5Hz, 1H, $H_{1'}$), 4.05 (dd, $J_{1',1'}$ = 11.7Hz, $J_{1',2'}$ = 7.7Hz, 1H, $H_{1'}$), 4.22 (m, $J_{2',1'}$ = 3.5Hz and $J_{2',1'}$ = 7.5Hz, 1H, $H_{2'}$), 4.26 (s, broad, 1H, OH), 7.82-7.69 (m, 4H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 10.7 (CH_3), 21.7 (CH_2), 55.5 ($C_{2'}$), 62.7 ($C_{1'}$), 123.2 (C_5 and C_6), 131.7 (C_{3a} and C_{7a}), 134.0 (C_4 and C_7), 169.1 (C_1 and C_3); EIMS *m/z* 219 ($M^{+\bullet}$).

Anal. Calcd. for $C_{12}H_{13}NO_3$ (219.24): C, 65.74; H, 5.97; N, 6.39. Found: C, 65.63; H, 5.88; N, 6.17.

(1'*S*)-*N*-(2'-Ethyl-1'-hydroxyethyl)-1*H*-isoindole-1,3(2*H*)-dione (**6b**).

This product was obtained as a colourless oil in 91 (Method II) and 92% (Method I) yields; bp 218°/9 torr; ir (neat): ν 3502 (OH), 1700 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.92 (t, J = 7.5Hz, 3H, CH_3), 1.88 (m, J = 7.5Hz and J = 7.8Hz, 2H, CH_2), 3.02 (s, broad, 1H, OH), 3.86 (dd, $J_{1',1'}$ = 11.7Hz and $J_{1',2'}$ = 3.6Hz, 1H, $H_{1'}$), 4.08 (dd, $J_{1',1'}$ = 11.7Hz and $J_{1',2'}$ = 7.8Hz, 1H, $H_{1'}$), 4.28 (dd, $J_{2',1'}$ = 3.6Hz and $J_{2',1'}$ = 7.5Hz, 1H, $H_{2'}$), 7.71-7.83 (m, 4H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 10.8 (CH_3), 21.7 (CH_2), 55.6 ($C_{2'}$), 62.8 ($C_{1'}$), 123.2 (C_5 and C_6), 131.7 (C_{3a} and C_{7a}), 134.0 (C_4 and C_7), 169.2 (C_1 and C_3); EIMS *m/z* 219 ($M^{+\bullet}$).

Anal. Calcd. for $C_{12}H_{13}NO_3$ (219.24): C, 65.74; H, 5.97; N, 6.39. Found: C, 65.58; H, 5.82; N, 6.11.

(1'*R*)-*N*-(1'-hydroxyethyl-2'-methyl)-1*H*-isoindole-1,3(2*H*)-dione (**6c**).

This product was obtained as a white yellow solid in 88 (Method II) and 90% (Method I) yields; mp 99-101° (toluene, water or ethanol); ir (potassium bromide): ν 3462 (OH), 1739 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.43 (d, J = 7.2Hz, 3H, CH_3), 3.19 (s broad, 1H, OH), 3.85 (dd, $J_{1',1'}$ = 11.7Hz, $J_{1',2'}$ = 3.9Hz, 1H, H-1'), 4.05 (dd, $J_{1',1'}$ = 11.7Hz, $J_{1',2'}$ = 8.0Hz, 1H, $H_{1'}$), 4.48 (m, $J_{2',1'}$ = 3.9Hz, $J_{2',1'}$ = 7.8Hz, 1H, $H_{2'}$), 7.68-7.73 (m, 2H, H_{arom}), 7.79-7.82 (m, 2H, H_{arom}); ^1H nmr (deuteriochloroform): δ 14.7 (CH_3), 49.4 ($C_{2'}$), 64.0 ($C_{1'}$), 123.2 (C_5 and C_6), 131.9 (C_3 and C_{7a}), 134.0 (C_4 and C_7), 168.9 (C_1 and C_3); EIMS *m/z* 205 ($M^{+\bullet}$).

Anal. Calcd. for $C_{11}H_{11}NO_3$ (205.21): C, 64.38; H, 5.40; N, 6.82. Found: C, 64.24; H, 5.19; N, 6.71.

(1'*S*)-*N*-(1'-hydroxyethyl-2'-methyl)-1*H*-isoindole-1,3(2*H*)-dione (**6d**).

This product was obtained as a white yellow solid in 91 (Method II) and 93% (Method I) yields; mp 97-100° (toluene, water or ethanol); ir (potassium bromide): ν 3451 (OH), 1723 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.42 (d, J = 7.1Hz, 3H, CH_3), 3.21 (s broad, 1H, OH), 3.87 (dd, $J_{1',1'}$ = 11.5Hz, $J_{1',2'}$ = 4.1Hz, 1H, H-1'), 4.02 (dd, $J_{1',1'}$ = 11.5Hz, $J_{1',2'}$ = 7.6Hz, 1H, $H_{1'}$), 4.52 (m, $J_{2',1'}$ = 4.1Hz, $J_{2',1'}$ = 7.6Hz, 1H, $H_{2'}$), 7.69-7.75 (m, 2H, H_{arom}), 7.77-7.84 (m, 2H, H_{arom}); ^1H nmr (deuteriochloroform): δ 14.6 (CH_3), 49.5 ($C_{2'}$), 64.1 ($C_{1'}$), 123.1 (C_5 and C_6), 131.5 (C_3 and C_{7a}), 134.1 (C_4 and C_7), 168.8 (C_1 and C_3); EIMS *m/z* 205 ($M^{+\bullet}$).

Anal. Calcd. for $C_{11}H_{11}NO_3$ (205.21): C, 64.38; H, 5.40; N, 6.82. Found: C, 64.29; H, 5.21; N, 6.66.

(1'*R*)-*N*-(2'-Benzyl-1'-hydroxyethyl)-1*H*-isoindole-1,3(2*H*)-dione (**6e**).

This product was obtained as a white yellow solid in 89 (Method II) and 91% (Method I) yields; mp 89° (toluene, water or ethanol); ir (potassium bromide): ν 3456 (OH), 1768 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.20 (d, J = 7.5Hz, 2H, CH_2-Ph), 3.85 (s, broad, 1H, OH), 3.90 (dd, $J_{1',1'}$ = 17.5Hz and $J_{1',2'}$ = 5.0Hz, 1H, $H_{1'}$), 4.08 (dd, $J_{1',1'}$ = 17.5Hz and $J_{1',2'}$ = 9.0Hz, 1H, $H_{1'}$), 4.62 (m, $J_{2',1'}$ = 4.9Hz, and $J_{2',1'}$ = 8.9Hz, 1H, $H_{2'}$), 7.12-7.21 (m, 5H, H_{arom}), 7.69-7.80 (m, 4H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 34.8 (CH_2), 55.1 ($C_{2'}$), 62.6 ($C_{1'}$), 123.2 (C_5 and C_6), 126.8 ($C_{4''}$), 128.4 ($C_{2''}$ and $C_{6''}$), 128.9 ($C_{3''}$ and $C_{5''}$), 132.0 (C_{3a} and C_{7a}), 134.0 (C_4 and C_7), 137.3 ($C_{1''}$), 169.0 (C_1 and C_3); EIMS *m/z* 281 ($M^{+\bullet}$).

Anal. Calcd. for $C_{17}H_{15}NO_3$ (281.31): C, 72.58; H, 5.37; N, 4.98. Found: C, 72.49; H, 5.38; N, 4.85.

(1'*S*)-*N*-(2'-Benzyl-1'-hydroxyethyl)-1*H*-isoindole-1,3(2*H*)-dione (**6f**).

This product was obtained as a white-yellow solid in 85 (Method II) and 94% (Method I) yields; mp 107-108° (toluene or water); ir (potassium bromide): ν 3446 (OH), 1752 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.19 (d, J = 7.7Hz, 2H, CH_2-Ph), 3.51 (s, broad, 1H, OH), 3.91 (dd, $J_{1',1'}$ = 11.9Hz and $J_{1',2'}$ = 3.7Hz, 1H, $H_{1'}$), 4.08 (dd, $J_{1',1'}$ = 12.0Hz and $J_{1',2'}$ = 7.5Hz, 1H, $H_{1'}$), 4.62 (m, $J_{2',1'}$ = 3.7Hz and $J_{2',1'}$ = 7.7Hz, 1H, $H_{2'}$), 7.13-7.21 (m, 5H, H_{arom}), 7.64-7.76 (m, 4H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 34.7 (CH_2), 55.2 ($C_{2'}$), 62.6 ($C_{1'}$), 123.2 (C_5 and C_6), 126.6 ($C_{4''}$), 128.4 ($C_{2''}$ and $C_{6''}$), 128.9 ($C_{3''}$ and $C_{5''}$), 131.9 (C_{3a} and C_{7a}), 133.9 (C_4 and C_7), 137.3 ($C_{1''}$), 168.9 (C_1 and C_3); EIMS *m/z* 281 ($M^{+\bullet}$).

Anal. Calcd. for $C_{17}H_{15}NO_3$ (281.31): C, 72.58; H, 5.37; N, 4.98. Found: C, 72.44; H, 5.28; N, 4.91.

General Procedure for the Synthesis of ω-Carbinol Lactams (**7a-f**).

To a stirred solution of chiral *N*-alkylated phthalimide **6a-f** (10 mmoles) in dry methanol (40 ml) at 0–5° was added by portions 3 equivalents of sodium borohydride (1.135 g, 30 mmoles). After addition of sodium borohydride, 3 drops of ethanolic hydrochloric acid solution was added during 10 minutes (prepared from 9 drops of concentrated hydrochloric acid in 15 ml of ethanol) until the reaction was complete (30 minutes to 2 hours, monitored by TLC). The excess of sodium borohydride was decomposed by careful addition of 10% hydrochloric acid solution to pH = 2. After removal of the solvent, the residue was diluted with water (40 ml) and the whole was extracted with 30 ml of dichloromethane. The organic layers were washed with water, brine, dried over sodium sulfate and evaporated under reduced pressure. The resulting oil was purified by chromatography on silica gel column using dichloromethane/acetone (5/1) as eluent to give pure ω-carbinol lactams **7a-f**.

(1'*R*,3*R* and 1'*R*,3*S*)-2,3-Dihydro-2-(2'-ethyl-1'-hydroxyethyl)-3-hydroxy-1*H*-isoindol-1-one (**7a**).

This product was obtained as a inseparable mixture of two diastereosomers (1/1) as a colourless oil in 75% yield; ^{1}H nmr (deuteriochloroform): δ 0.82 (1.01) (t, J = 7.3Hz, 3H, CH_3), 1.71 (1.92) (m, J = 7.0Hz, 2H, CH_2), 2.74 (2.97) (s, broad, 1H, $OH_{1'}$), 3.60 (3.83) (dd, J = 9.0Hz, 1H, $H_{1'}$), 3.80 (3.99) (dd, J = 12.0Hz, 1H, $H_{1'}$), 4.14 (4.49) (m, $J_{2',CH2-CH3}$ = 7.2Hz and $J_{2',1'}$ = 8.7Hz, 1H, $H_{2'}$), 4.93 (5.93) (s, broad, 1H, OH_3), 5.81 (5.86) (s, 1H, H_3), 7.32-7.54 (7.51-7.82) (m, 4H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 10.7 (10.9) (CH_3), 21.7 (27.4) (CH_2), 55.2 (56.3) ($C_{2'}$), 63.7 (64.1) ($C_{1'}$), 80.1 (90.7) (C_3), 123.2 (123.9) (C_6), 123.2 (124.4) (C_5), 129.5 (130.5) (C_7), 132.3 (132.8) (C_4), 130.9 (133.4) (C_{7a}), 143.2 (143.9) (C_{3a}), 168.8 (169.2) (C_1).

(1'*S*,3*R* and 1'*S*,3*S*)-2,3-Dihydro-2-(2'-ethyl-1'-hydroxyethyl)-3-hydroxy-1*H*-isoindol-1-one (**7b**).

This product was obtained as an inseparable mixture of two diastereosomers (2/1) as a colourless oil in 84% yield.

Major product: ^{1}H nmr (deuteriochloroform): δ 0.88 (t, J = 7.3Hz, 3H, CH_3), 1.74 (m, J = 7.5Hz, 2H, CH_2), 3.50 (s, broad, 1H, $OH_{1'}$), 3.64 (dd, $J_{1',1'}$ = 14.1Hz and $J_{1',2'}$ = 7.2Hz, 2H, $H_{1'}$), 4.22 (m, 1H, $H_{2'}$), 4.78 (s, broad, 1H, OH_3), 5.83 (s, 1H, H_3), 7.32-7.62 (m, 4H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 10.9 (CH_3), 21.6 (CH_2), 56.3 ($C_{2'}$), 64.2 ($C_{1'}$), 80.0 (C_3), 123.2 (C_6), 123.3 (C_5), 129.6 (C_7), 130.9 (C_4), 132.3 (C_{7a}), 143.1 (C_{3a}), 168.8 (C_1).

Minor product: ^{1}H nmr (deuteriochloroform): δ 1.17 (t, J = 7.1Hz, 3H, CH_3), 1.74 (m, J = 7.5Hz, 2H, CH_2), 3.50 (s, broad, 1H, $OH_{1'}$), 3.75 (dd, $J_{1',1'}$ = 14.1Hz and $J_{1',2'}$ = 7.2Hz, 2H, $H_{1'}$), 4.54 (m, 1H, $H_{2'}$), 4.88 (s, broad, 1H, OH_3), 5.79 (s, 1H, H_3), 7.32-7.62 (m, 4H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 10.0 (CH_3), 27.4 (CH_2), 53.7 ($C_{2'}$), 64.6 ($C_{1'}$), 83.3 (C_3), 123.1 (C_6), 123.5 (C_5), 129.7 (C_7), 130.6 (C_4), 132.2 (C_{7a}), 143.9 (C_{3a}), 170.5 (C_1).

(1'*R*,3*R* and 1'*R*,3*S*)-2,3-Dihydro-2-(1'-hydroxyethyl-2'-methyl)-3-hydroxy-1*H*-isoindol-1-one (**7c**).

This product was obtained as an inseparable mixture of two diastereosomers (1.5/1) as a colourless oil in 88% yield; ^{1}H nmr (DMSO-d_6): δ 1.35 (1.41) (d, J = 7.2Hz, 3H, CH_3), 3.44 (4.40) (q, J = 7.2Hz, 1H, $H_{1'}$), 3.65 (4.11) (q, J = 6.4Hz, 1H, $H_{1'}$), 4.19-4.25 (4.98-5.12) (m, 1H, $H_{2'}$), 5.94 (6.14) (d, J = 8.8Hz, 1H, H_3), 6.59 (6.63) (d, J = 8.8Hz, 1H, OH_3), 6.88 (s, broad, 1H, OH), 7.66-7.72 (m, 4H, H_{arom}); ^{13}C nmr (DMSO-d_6): δ 14.5 (16.2) (CH_3), 51.2 (51.0) ($C_{2'}$), 62.5 (64.0) ($C_{1'}$), 81.3 (81.7) (C_3), 122.7 (122.8) (C_5), 123.2 (123.6) (C_4), 129.7 (129.5) (C_7), 131.6 (131.2) (C_{7a}), 132.9 (132.0) (C_6), 145.9 (146.2) (C_{3a}), 166.1 (167.8) (C_1).

(1'*S*,3*R* and 1'*S*,3*S*)-2,3-Dihydro-2-(1'-hydroxyethyl-2'-methyl)-3-hydroxy-1*H*-isoindol-1-one (**7d**).

This product was obtained as an inseparable mixture of two diastereosomers (1.2/1) as a colourless oil in 82% yield; ^{1}H nmr (DMSO-d_6): δ 1.31 (1.39) (d, J = 6.9Hz, 3H, CH_3), 3.45 (4.33) (q, J = 6.9Hz, 1H, $H_{1'}$), 3.61 (4.21) (q, J = 6.6Hz, 1H, $H_{1'}$), 4.20-4.24 (4.96-5.02) (m, 1H, $H_{2'}$), 5.92 (6.04) (d, J = 9.0Hz, 1H, H_3), 6.56 (6.63) (d, J = 9.0Hz, 1H, OH_3), 6.71 (s, broad, 1H, OH), 7.59-7.65 (m, 4H, H_{arom}); ^{13}C nmr (DMSO-d_6): δ 15.0 (16.7) (CH_3), 50.0 (50.2) ($C_{2'}$), 62.9 (64.2) ($C_{1'}$), 81.2 (81.4) (C_3), 122.6 (122.9) (C_5), 123.1 (123.7) (C_4), 129.5 (129.6) (C_7), 131.0 (131.9) (C_{7a}), 132.4 (132.2) (C_6), 145.4 (145.6) (C_{3a}), 166.6 (167.4) (C_1).

(1'*R*,3*R* and 1'*R*,3*S*)-2-(2'-Benzyl-1'-hydroxyethyl)-2,3-dihydro-3-hydroxy-1*H*-isoindol-1-one (**7e**).

This product was obtained as a inseparable mixture of two diastereosomers (1/1) as a colourless oil in 94% yield; ^{1}H nmr (deuteriochloroform): δ 3.06 (3.24) (m, 2H, CH_2-Ph), 3.67 (3.79) (m, 1H, $H_{2'}$), 3.99 (4.50) (m, 2H, $H_{1'}$), 4.75 (4,88) (s, broad, 1H, $OH_{1'}$), 5.10 (5.65) (s, 1H, H_3), 5.62 (6.28) (s, broad, 1H, OH_3), 7.06-7.50 (m, 9H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 34.7 (35.1) (CH_2), 55.3 (58.1) ($C_{2'}$), 62.8 (63.0) ($C_{1'}$), 81.6 (82.8) (C_3), 122.7 (123.0) (C_5), 126.6 (126.8) (C_4), 128.5 (128.7) ($C_{2''}$ and $C_{6''}$), 128.8 (128.9) ($C_{4''}$), 129.0 (129.1) ($C_{3''}$ and $C_{5''}$), 129.4 (129.6) (C_7), 130.5 (131.2) (C_{7a}), 132.3 (132.4) (C_6), 137.3 (138.4) ($C_{1''}$), 143.9 (144.4) (C_{3a}), 168.8 (169.1) (C_1).

(1'*S*,3*R* and 1'*R*,3*S*)-2-(2'-Benzyl-1'-hydroxyethyl)-2,3-dihydro-3-hydroxy-1*H*-isoindol-1-one (**7f**).

This product was obtained as an inseparable mixture of two diastereosomers (1/1) as a colourless oil in 78% yield; ^{1}H nmr (deuteriochloroform): δ 2.94 (3.12) (m, 2H, CH_2-Ph), 3.65 (3.76) (m, 1H, $H_{2'}$), 3.95 (4.54) (m, 2H, $H_{1'}$), 4.75 (4.95) (s, broad, 1H, $OH_{1'}$), 5.10 (5.80) (s, 1H, H_3), 5.56 (6.18) (s, broad, 1H, OH_3), 7.12-7.57 (m, 9H, H_{arom}); ^{13}C nmr (deuteriochloroform): δ 34.7 (34.9) (CH_2), 54.3 (58.0) ($C_{2'}$), 62.7 (63.1) ($C_{1'}$), 80.7 (83.4) (C_3), 122.8 (123.1) (C_5), 126.5 (126.6) (C_4), 128.5 (128.6) ($C_{2''}$ and $C_{6''}$), 128.6 (128.8) ($C_{4''}$), 129.0 (129.1) ($C_{3''}$ and $C_{5''}$), 129.2 (129.5) (C_7), 130.7 (131.3) (C_{7a}), 132.3 (132.4) (C_6), 137.4 (138.3) ($C_{1''}$), 143.8 (144.1) (C_{3a}), 168.5 (168.7) (C_1).

General Procedure for *O*-Cationic Cyclization (**9a**) and (**4a-f**).

To a stirred solution of hydroxylactam **7a-f** (10 mmoles) as a mixture of two diastereosomers was added neat acid (10 ml of acetic acid (Method B) or trifluoroacetic acid Method D) in 10 ml of dichloromethane) or catalytic amount of acid (*p*-toluenesulfonic acid (Method C), concentrated hydrochloric acid (Method E) or sulfuric acid (Method F)) in 10 ml of dichloromethane or chloroform and allowed to react over times as indicated in Scheme 2. In the case of concentrated hydrochloric acid and sulfuric acid, only two to three drops were necessary. After complete reaction at room temperature under stirring, the reaction mixture was diluted with water (30 ml) and neutralized with 10% sodium hydroxide aqueous solution. The solution was extracted twice with dichloromethane or chloroform (20 ml). The organic layer was washed with water, brine, separated, dried over magnesium sulfate and evaporated under reduced pressure. The resulting crude residue was purified by chromatography on silica gel column for oils or recrystallization for solids to give the tricyclic product **4a-f** and the dimer product **9a** in moderate to good yields.

(3*R*,9b*S*)-Bis-3-ethyl-2,3-dihydro-9b*H*-oxazolo[2,3-*a*]isoindol-5-one (**9a**).

This product was obtained as white solids in 42% (Method B) or 82% (Method C) yield; mp 242-243° (ethanol/*N*,*N*-dimethylformamide); ir (potassium bromide): ν 1700 (CO) cm^{-1}; $[\alpha]_D^{35}$ = -300.00 (c 1*M*, $CHCl_3$) ($[\alpha]_D^{25}$ = -14.00 (c 0.5*M*, $CHCl_3$), reference [10]); UV (λ_{max} nm, (logε)): 250 (2.96); ^{1}H nmr (deuteriochloroform): δ 0.91 (t, J = 7.3Hz, 3H, CH_3), 1.83 (m, 2H, CH_2), 3.42 (d, J = 5.1Hz, 2H, H_2), 4.37 (m, 1H, H_3), 6.00 (s, 1H, H_{9b}), 7.51-7.60 (m, 3H, H_{arom}), 7.82 (d, J = 7.5Hz, 1H, H_9); ^{13}C nmr (deuteriochloroform): δ 10.8 (CH_3), 22.1 (CH_2), 52.0 (C_3), 64.1 (C_2), 84.6 (C_{9b}), 123.1 (C_7), 123.8 (C_9), 129.8 (C_6), 131.8 (C_{5a}), 132.2 (C_8), 141.1 (C_{9a}), 168.1 (C_5); EIMS *m/z* $1/2M^{+\bullet}$+2 = 205 (11%), $1/2M^{+\bullet}$+1 = 204 (100%), $1/2M^{+\bullet}$-CH_3 = 190 (5%), $1/2M^{+\bullet}$-OH = 188 (2%), 172 (35%), 132 (29%), 117 (3%), 104 (5%).

Anal. Calcd. for $C_{24}H_{26}N_2O_4$ (406.46): C 70.92%, H 6.45%, N 6.89%. Found: C 71.1%, H 6.58%, N 6.99%.

(3*R*,9b*S*)-3-Ethyl-2,3-dihydro-9b*H*-oxazolo[2,3-*a*]isoindol-5-one (**4a**).

This product was obtained as a colourless oil in 58% (Method D), 61% (Method E) or 71% (Method B) yield; ir (neat): ν 1712 (CO) cm^{-1}; $[\alpha]_D^{25}$ = -58.70 (c 1*M*, $CHCl_3$); UV (λ_{max} nm, (logε)): 245 (2.71); ^{1}H nmr (deuteriochloroform): δ 1.10 (t, J = 7.2Hz, 3H, CH_3), 1.73 (q, J = 7.3Hz, 2H, CH_2), 3.90 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 6.6Hz, 1H, H_2), 4.07 (q, $J_{3,2}$ = 6.6Hz and $J_{3,2}$ = 7.2Hz, 1H, H_3), 4.50 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 7.2Hz, 1H, H_2), 5.86 (s, 1H, H_{9b}), 7.53-7.61 (m, 3H, H_{arom}), 7.79 (d, J = 6.9Hz, H_9); ^{13}C nmr (deuteriochloroform): δ 10.7 (CH_3), 27.4 (CH_2), 56.3 (C_3), 76.2 (C_2), 90.7 (C_{9b}), 123.9 (C_7), 124.3 (C_9), 130.6 (C_6), 132.8 (C_8), 133.4 (C_{5a}), 142.2 (C_{9a}), 173.6 (C_5); EIMS *m/z* 203 ($M^{+\bullet}$)

Anal. Calcd. for $C_{12}H_{13}NO_2$ (203.24): C, 70.91; H, 6.45; N, 6.89. Found: C, 70.79; H, 6.38; N, 6.82.

(3*S*,9b*R*)-3-Ethyl-2,3-dihydro-9b*H*-oxazolo[2,3-*a*]isoindol-5-one (**4b**).

This product was obtained as a colourless oil in 84% (Method D) or 88% (Method E) yield; ir (neat): ν 1708 (CO) cm^{-1}; $[\alpha]_D^{25}$ = +63.90 (c 1*M*, $CHCl_3$); UV (λ_{max} nm, (logε)): 245 (2.71); ^{1}H nmr (deuteriochloroform): δ 1.10 (t, J = 7.2Hz, 3H, CH_3), 1.73 (q, J = 7.3Hz, 2H, CH_2), 3.90 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 6.6Hz, 1H, H_2), 4.07 (q, $J_{3,2}$ = 6.6Hz and $J_{3,2}$ = 7.2Hz, 1H, H_3), 4.50 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 7.2Hz, 1H, H_2), 5.86 (s, 1H, H_{9b}), 7.53-7.61 (m, 3H, H_{arom}), 7.79 (d, J = 6.9Hz, H_9); ^{13}C nmr (deuteriochloroform): δ 10.7 (CH_3), 27.4 (CH_2), 56.3 (C_3), 76.2 (C_2), 90.7 (C_{9b}), 123.9 (C_7), 124.3 (C_9), 130.6 (C_6), 132.8 (C_8), 133.4 (C_{5a}), 142.2 (C_{9a}), 173.6 (C_5); EIMS *m/z* 203 ($M^{+\bullet}$).

Anal. Calcd. for $C_{12}H_{13}NO_2$ (203.24): C, 70.91; H, 6.45; N, 6.89. Found: C, 70.66; H, 6.41; N, 6.79.

(3*R*,9b*S*)-2,3-Dihydro-3-methyl-9b*H*-oxazolo[2,3-*a*]isoindol-5-one (**4c**).

This product was obtained as a colourless oil in 89% yield (Method B); ir (neat): ν 1705 (CO) cm^{-1}; $[\alpha]_D^{25}$ = -24.30 (c 1*M*, $CHCl_3$); ^{1}H nmr (deuteriochloroform): δ 1.41 (d, J = 6.3Hz, 3H, CH_3), 3.86 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 6.3Hz, 1H, H_2), 4.21-4.29 (m, $J_{3,2}$ = 6.3Hz and $J_{3,2}$ = 7.1Hz, 1H, H_3), 4.52 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 7.1 Hz, 1H, H_2), 5.93 (s, 1H, H_{9b}), 7.57-7.66 (m, 3H, H_{arom}), 7.81 (d, J = 7.2 Hz, 1H, H_9); ^{13}C nmr (deuteriochloroform): δ 19.9 (CH_3), 50.1 (C_3), 77.5 (C_2), 90.4 (C_{9b}), 124.4 (C_8), 124.5 (C_9), 130.1 (C_6), 132.2 (C_7), 133.0 (C_{5a}), 142.2 (C_{9a}), 173.3 (C_5); EIMS *m/z* 189 ($M^{+\bullet}$).

Anal. Calcd. for $C_{11}H_{11}NO_2$ (189.21): C, 69.82; H, 5.86; N, 7.40. Found: C, 69.77; H, 5.59; N, 7.29.

(3*S*,9b*R*)-2,3-Dihydro-3-methyl-9b*H*-oxazolo[2,3-*a*]isoindol-5-one (**4d**).

This product was obtained as a colourless oil in 94% yield (Method E); ir (neat): ν 1702 (CO) cm^{-1}; $[\alpha]_D^{25}$ = +22.30 (c 1*M*, $CHCl_3$); ^{1}H nmr (deuteriochloroform): δ 1.43 (d, J = 6.6Hz, 3H, CH_3), 3.82 (dd, $J_{2,2}$ = 8.4Hz and $J_{2,3}$ = 6.6Hz, 1H, H_2), 4.23-4.30 (m, $J_{3,2}$ = 6.6Hz and $J_{3,2}$ = 6.9Hz, 1H, H_3), 4.50 (dd, $J_{2,2}$ = 8.4Hz and $J_{2,3}$ = 6.9Hz, 1H, H_2), 5.91 (s, 1H, H_{9b}), 7.55-7.61 (m, 3H, H_{arom}), 7.79 (d, J = 6.9Hz, 1H, H_9); ^{13}C nmr (deuteriochloroform): δ 19.7 (CH_3), 50.5 (C_3), 77.7 (C_2), 90.6 (C_{9b}), 124.0 (C_8), 124.4 (C_9), 130.6 (C_6), 132.8 (C_7), 133.4 (C_{5a}), 142.2 (C_{9a}), 173.5 (C_5); EIMS *m/z* 189 ($M^{+\bullet}$).

Anal. Calcd. for $C_{11}H_{11}NO_2$ (189.21): C, 69.82; H, 5.86; N, 7.40. Found: C, 69.77; H, 5.59; N, 7.29.

(3*R*,9b*S*)-3-Benzyl-2,3-dihydro-9b*H*-oxazolo[2,3-*a*]isoindol-5-one (**4e**).

This product was obtained as a white solids in 79% (Method D), or 82% (Method E) yield; mp 130-132° (diethyl ether/hexane) (non indicated in reference [4a]); ir (potassium bromide): ν 1706 (CO) cm^{-1}; $[\alpha]_D^{25}$ = -38.50 (c = 1, $CHCl_3$) ($[\alpha]_D^{25}$ = -44.20 (c 3.48 *M*, dichloromethane), reference [4a]); ^{1}H nmr (deuteriochloroform): δ 2.98 (dd, J = 13.9Hz and J = 7.9Hz, 1H, CH_2), 3.16 (dd, J = 13.9Hz and J = 5.6Hz, 1H, CH_2), 3.98 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 6.4Hz, 1H, H_2), 4.31 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 6.9Hz, 1H, H_2), 4.44-7.49 (m, $J_{3,2}$ = 6.9Hz and J = 13.4Hz, 1H, H_3), 5.74 (s, 1H, H_{9b}), 7.30-7.32 (m, 5H, H_{arom}), 7.52-7.57 (m, 3H, H_{arom}), 7.76 (d, J = 6.9Hz, 1H, H_9); ^{13}C nmr (deuteriochloroform): δ 39.7 (CH_2), 55.4 (C_3), 75.1 (C_2), 90.9 (C_{9b}), 123.9 (C_8), 124.4 (C_9), 126.8 ($C_{4''}$), 128.6 ($C_{2''}$ and $C_{6''}$), 129.5 ($C_{3''}$ and $C_{5''}$), 130.6 (C_6), 132.8 (C_7), 133.2 (C_{5a}), 136.8 ($C_{1''}$), 142.3 (C_{9a}), 173.42 (C_5); EIMS *m/z* 265 ($M^{+\bullet}$).

Anal. Calcd. for $C_{17}H_{15}NO_2$ (265.13): C, 76.96; H, 5.70; N, 5.28. Found: C, 76.88; H, 5.61; N, 5.19.

(3*S*,9b*R*)-3-Benzyl-2,3-dihydro-9b*H*-oxazolo[2,3-*a*]isoindol-5-one (**4f**).

This product was obtained as a white solids in 69% (Method D) or 74% (Method E) yield; mp 79-81° (ethanol/tetrahydrofuran) (86-87°, reference [4a]); ir (potassium bromide): ν 1703 (CO) cm^{-1}; $[\alpha]_D$ = +44.00 (c 1 *M*, $CHCl_3$) (($[\alpha]_D^{25}$ = +43.90 (c 2 *M*, $CHCl_3$), see reference [4a]); ^1H nmr (deuteriochloroform): δ 2.98 (dd, J = 13.9Hz and J = 7.9Hz, 1H, CH_2), 3.16 (dd, J = 13.9Hz and J = 5.6Hz, 1H, CH_2), 3.98 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 6.4Hz, 1H, H_2), 4.31 (dd, $J_{2,2}$ = 8.7Hz and $J_{2,3}$ = 6.9Hz, 1H, H_2), 4.44-4.49 (m, $J_{3,2}$ = 6.9Hz and J = 13.4Hz, 1H, H_3), 5.74 (s, 1H, H_{9b}), 7.30-7.32 (m, 5H, H_{arom}), 7.52-7.57 (m, 3H, H_{arom}), 7.76 (d, J = 6.9Hz, 1H, H_9); ^{13}C nmr (deuteriochloroform): δ 39.7 (CH_2), 55.4 (C_3), 75.1 (C_2), 90.9 (C_{9b}), 123.9 (C_8), 124.4 (C_9), 126.8 ($C_{4''}$), 128.6 ($C_{2''}$ and $C_{6''}$), 129.5 ($C_{3''}$ and $C_{5''}$), 130.6 (C_6), 132.8 (C_7), 133.2 (C_{5a}), 136.8 ($C_{1''}$), 142.3 (C_{9a}), 173.42 (C_5); EIMS *m/z* 265 ($M^{+\bullet}$).

Anal. Calcd. for $C_{17}H_{15}NO_2$ (265.13): C, 76.96; H, 5.70; N, 5.28. Found: C, 76.90; H, 5.56; N, 5.21.

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