A Two-Stage Synthesis of 8,10a-Epoxypyrido[2,1-*a*]isoindoles: Stereochemistry of the [4+2] Cycloaddition of Maleic Anhydride with 2,6-Difurylpiperidin-4-ones

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Abstract: A new straightforward synthesis of 8,10a-epoxypyrido[2,1-*a*]isoindoles and their 7-carboxylic acids from 2,6-difuryl-substituted piperidin-4-ones and maleic anhydride or acryloyl chloride via the intramolecular Diels–Alder reaction has been demonstrated. It has been shown that a one-stage synthesis of the title compounds can be performed under mild conditions and with high levels of regio- and stereoselectivity from easily accessible 2-furylpiperidines.

Key words: intramolecular Diels–Alder furan reaction, IMDAF, stereoselective synthesis, furans, 2,6-difurylpiperidin-4-ones, pyrido[2,1-*a*]isoindoles

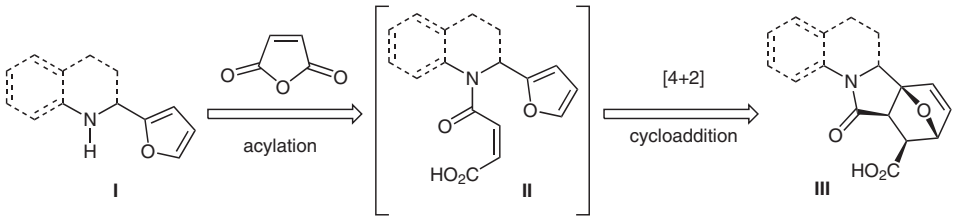
The chemistry and methods for the synthesis of hydrogenized pyrido[2,1-*a*]isoindoles are well known in organic chemistry,[1] but there are very few references to their 8,10a-epoxy-substituted analogues.[2] Nevertheless, these derivatives of 3a,6-epoxyisoindolones[3] are essential intermediates for the synthesis of polyfunctional-substituted isoindoles,[4] many of which can be widely used in practice.

The reactions of furfurylamines and unsaturated 2-furyl-substituted azaheterocycles **I** (Scheme 1) with maleic anhydride and α,β-unsaturated acid chlorides were systematically investigated by our research group.[5] It was established that the reactions proceed via N-acylation of furfurylamine **I** followed by a spontaneous intramolecular [4+2] cycloaddition of the olefinic fragment with the furan ring (in amide **II**), resulting in substituted and/or condensed 2,3,7,7a-tetrahydro-3a,6-epoxyisoindolones **III**.

Therefore, we recently developed an efficient approach for the synthesis of hydrogenated hydroxyisoquinolines,[6] isoindolo[2,1-*a*]quinoline,[7] isoindolo[2,1-*b*]benzazepine,[8] and isoindolo[1,2-*a*]isoquinoline[9] carboxylic acids.

Here we report a study of the cycloaddition of α,β-unsaturated acid derivatives with compounds containing the furfurylaminic fragment; 2-furyl-substituted piperidines.

The starting materials, 2,6-difurylpiperidin-4-ones **2a–l**, were easily prepared from commercially available ketones **1a–g,i,j** and furfural or 5-methylfurfural in one step (Scheme 2). The commercially unavailable ketone, diethyl 4-oxoheptanedioate (**1h**), was obtained as previously described.[10] The reaction to form **2** was performed according to the literature procedure,[11] but without heating the reaction mixture; a solution of ketone, furfural or 5-methylfurfural (2 equiv), and ammonium acetate (2 equiv) in ethanol was allowed to react at room temperature for three days. After standard workup, the target products, piperidinones **2a–l**, were isolated in moderate yields. The best results were obtained for the symmetric and phenyl-substituted compounds **2f,g,i,l** that crystallize well (Table 1).



Scheme 1

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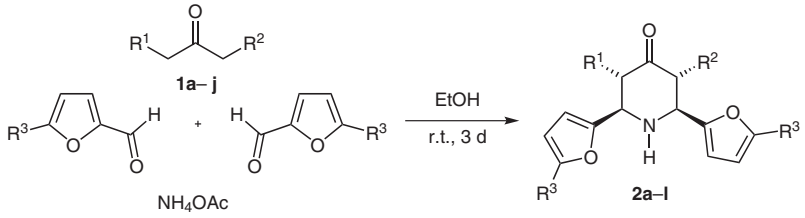


Scheme 2

Table 1 Yields of 2,6-Di-2-furylpiperidin-4-ones **2a–l**

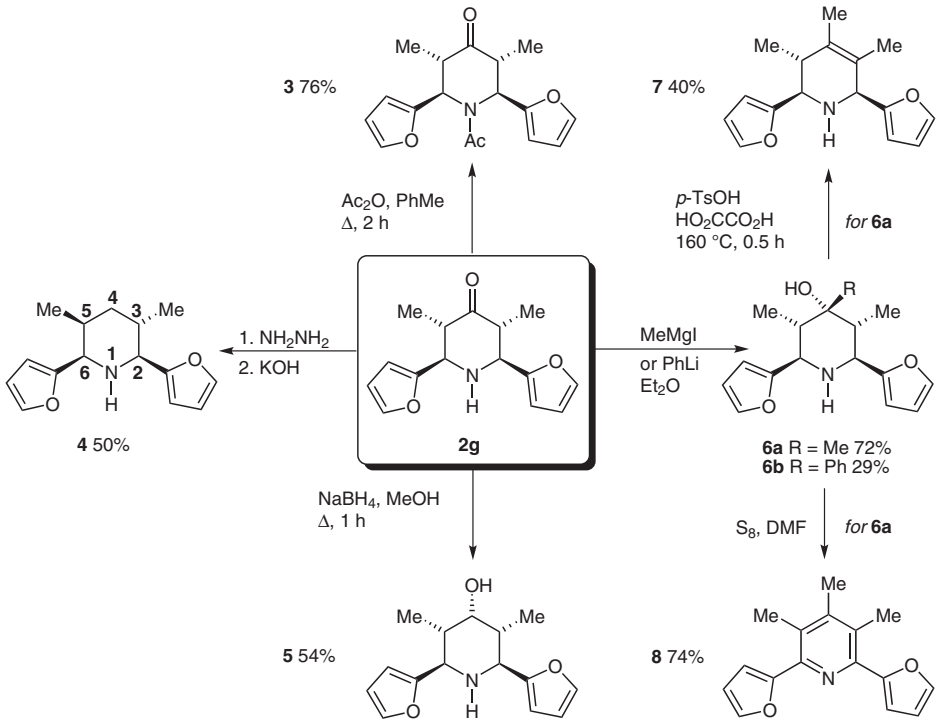
Product	R^1	R^2	R^3	Yield[a] (%)
2a	H	Me	H	34
2b	H	Et	H	33
2c	H	Pr	H	28
2d	H	*i*-Pr	H	31
2e	H	$CH_2CH{=}CH_2$	H	28
2f	Ph	Ph	H	62
2g	Me	Me	H	66
2h	CH_2CO_2Et	CH_2CO_2Et	H	30
2i	Me	Ph	H	56
2j	Et	Ph	H	31
2k	H	Me	Me	27
2l	Me	Me	Me	41

[a] The averaged yields for 3 optimal syntheses.

According to LC-MS data 2,6-difuryl-3-phenylpiperidinone is not generated under the aforementioned conditions. Likewise, we established that condensation of acetone and cyclohexanone with furfural and ammonium acetate does not proceed under the described conditions.[12] It was found that, in the case of acetone, high-molecular products of condensation (m/z = 271 [M^+], 309 and above) were obtained. The reaction with cyclohexanone leads to 2,6-bis(2-furylmethylene)cyclohexanone only. All attempts to carry out the synthesis in alternative solvents, such as *N*,*N*-dimethylformamide and acetic acid, via isolation of the α,α′-bis(2-furylmethylene)cyclohexanone were unsuccessful.

Based on the high values of the coupling constants of the pairs of the axial protons H2(a), H3(a), and H5(a), H6(a) (10.5–13 Hz), it was determined that all piperidinones **2a–l** obtained were isolated as individual *all*-equatorial isomers. The minor isomers of the compounds **2a–c**,**e**,**g**,**k** with the 3(a)-substituent detected in the crude reaction mixture (LC-MS) could not be isolated.

Modification of the easily accessible 2,6-difuryl-3,5-dimethylpiperidin-3-one **2g** was performed by the follow-



Scheme 3

ing chemical transformations. The *N*-acetyl-substituted **3** and deoxo derivative **4**, piperidinols **5**, **6** were obtained according to standard procedures (Scheme 3).

It should be noted that, under the conditions of the Kishner–Wolff reduction (Huang–Minlon modification) of all-equatorial piperidinone **2g**, we isolated 2(e),6(e)-difuryl-3(e),5(a)-dimethylpiperidine **4** only ($^3J_{5,6}$ = 2.7 Hz and $^3J_{2,3}$ = 10.5 Hz). This surprising fact was observed previously,[13] but requires careful consideration and will be the subject of a later publication.

It is interesting also that toluene was used as the solvent in the synthesis of the *N*-acetylpiperidinone **3**. Thus, boiling (140 °C, 1 h) the amine **2g** in excess of acetic anhydride yielded amide **3** in 30% yield, which, probably, can be explained by the ring opening of the piperidine ring at the C–N bond under these conditions.[14] The alcohols **5** and **6** were isolated as individual 4(a)-OH diastereomers. The preferred formation of the 4(a)-OH piperidinols of the type **5** and **6a** after reduction by sodium borohydride or the reaction of methyl- or phenylmagnesium iodide with the 2,6-diarylpiperidinones are wellknown in the literature.[15] The reaction of the compound **2g** with phenylmagnesium bromide does not afford the target piperidinone **6b**. Using phenyllithium instead of the Grignard reagent, the corresponding alcohol **6b** was obtained in low yield. The axial orientation of the protons H2 and H6 and of 4-OH in the amino alcohols **5** and **6a** was confirmed by comparison[15] and additionally by the absence of cross peaks between protons H2(H6)/H4 (in **5**) and H2(H6)/4-Me (in **6a**) in the NOESY spectra.

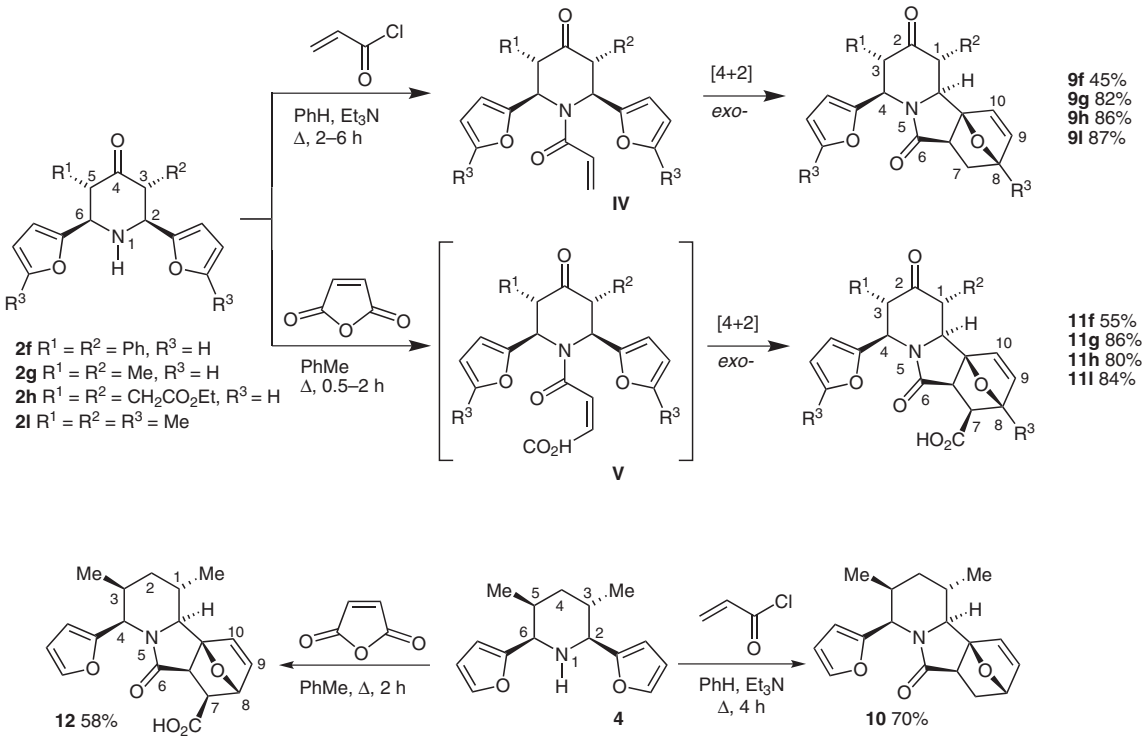
The dehydration and oxidation of the piperidinol **6a** afforded the 1,2,5,6-tetrahydropyridine **7** and the 2,6-difurylpyridine **8**, respectively (Scheme 3).

The next step of our study describes the reaction between piperidines **2** and **4** and derivatives of α,β-unsaturated acids. Both reactions went smoothly and under mild reaction conditions (Scheme 4).

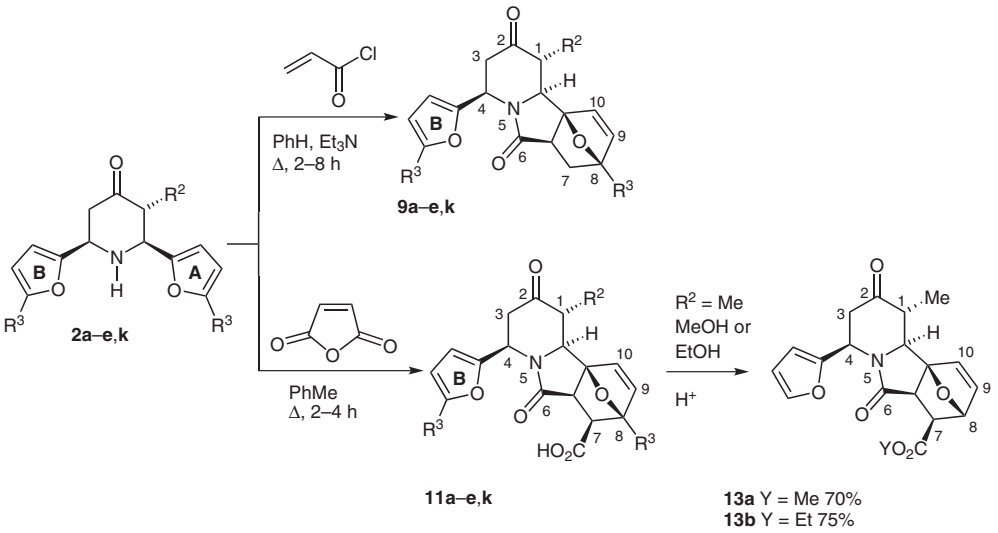
We suppose that the acylation of the symmetric piperidines **2f–h,l** with acryloyl chloride and maleic anhydride proceeds via acylation of the nitrogen atom and leads to the intermediate amides **IV** and **V**. The formation of the *N*-acryloyl derivative **IV** was monitored by TLC and LC-MS of the crude reaction mixture. The intermediate maleic acid monoamides **V** were not detected. When boiled in benzene or toluene, the intermediate acetyl derivatives **IV** and **V** undergo spontaneous intramolecular Diels–Alder reaction with a furan (IMDAF). Thus, the [4+2] cycloaddition proceeds between the furan ring and the double bond of the *N*-acetyl fragment and yields corresponding adducts **9f–h,l** and **11f–h,l**. It was found that the reaction time is significantly shorter in the case of maleic anhydride (from 2–8 h for acryloyl chloride to 1–2 h for maleic anhydride). This fact may be explained by the electron-withdrawing effect of the carboxylic group in the dienophilic fragment of the intermediate **V**.

It should be noted, that in all cases the IMDAF process was carried out under thermodynamic control (heating until no changes occurs by TLC or in LC-MS spectrum of the reaction mixture).

The reaction of acryloyl chloride and maleic anhydride with 3(e),5(a)-dimethylpiperidine **4** is regioselective and



Scheme 4



Scheme 5

affects the 2-furyl substituent only. Solely one regioisomer of compounds **10** and **12** was isolated from the reaction mixture in moderate yield. The configuration of the adducts **10** and **12** shown in Scheme 4 follows from consideration of the vicinal spin-spin coupling constants $^3J_{1,10b}$ = 11.8 Hz and $^3J_{3,4}$ = 4.4 Hz as compared with the same constants of the adducts **9g**,**h**,**l** and **11g**,**h**,**l** ($^3J_{1,10b}$ = 10.8–12.4 Hz, $^3J_{3,4}$ = 0–2.8 Hz). As the coupling constants ($^3J_{3,4}$) of compounds **10** and **12** and **9** and **11** have the same values, the spatial positions of 1-methyl group in these compounds are equal.

It is notable that the cycloaddition proceeds with only one furan ring of the 2,6-difurylpiperidines **2** and **4** even when a threefold excess of acylating agent (acryloyl chloride or maleic anhydride) was used. The cycloaddition proceeds neither for the *N*-acetyl derivative **3** nor for the pyridine **8** even in boiling xylene.

In all instances the cycloaddition proceeds in a stereoselective manner, where *exo* addition of the furan core to the dienophile prevails and leads to a single diastereomer of the hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindoles **9f–h**,**l** and **10** or their 7-carboxylic acids **11f–h**,**l** and **12**.

The reaction of acryloyl chloride or maleic anhydride with the asymmetric 3-R^2-2,6-difurylpiperidin-4-ones **2a–e**,**k** has the same mechanism and yields adducts **9a–e**,**k** and **11a–e**,**k** (Scheme 5, Table 2).

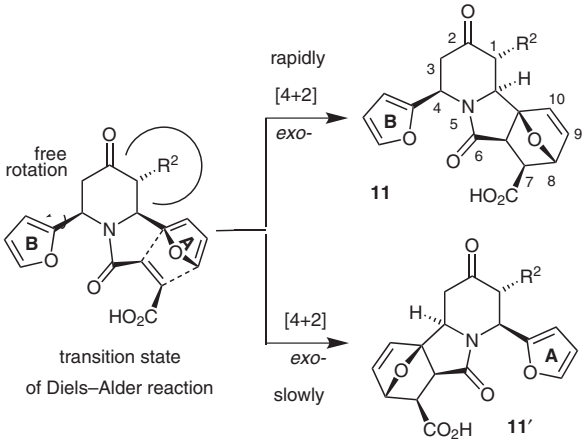
In this case, the reaction proceeds not only stereospecifically, but also regioselectively. It means that the IMDAF proceeds with the furan ring in position 2 only (labeled **A** in Scheme 5). The reaction is believed to depend on the steric interaction between the alkyl groups R^2 in position 3 and the 2-furyl fragment (Scheme 6) in the transition state. It causes a preferred conformation of furyl ring **A** in the position favoring the [4+2] cycloaddition (in compounds **2a–e**,**k**, the plane of furan fragment **A** and the plane of the piperidine cycle are orthogonal[16]), while the furan ring in position 6 **B** experiences free rotation about the C6–2-furyl-**B** bond.

Table 2 Yields of Hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindoles **9a–e**,**k** and **11a–e**,**k**

Substrate	R^2	R^3	Yield (%)	
			9	**11**
2a	Me	H	67	84
2b	Et	H	63	82
2c	Pr	H	45	67
2d	*i*-Pr	H	55	40
2e	$CH_2CH{=}CH_2$	H	45	70
2k	Me	Me	57	87

Thus, the adducts of cycloaddition **9a–e**,**k** obtained after crystallization have no impurities. However, the corresponding adducts **11a–e** have 4–8% impurity of the minor isomer **11′** (Scheme 6) in accordance with the ^{1}H NMR data.

Using the reaction of 3-isopropyl-2,6-difurylpiperidinone **2d** and maleic anhydride as an example, it was shown that



Scheme 6

the regioselectivity of the process greatly depends on the temperature of the synthesis. Piperidinone **2d** (as well as the other corresponding compounds) reacts with an equimolar amount of maleic anhydride in benzene at 22 °C slowly. According to ^{1}H NMR data, the residue obtained after 72 hours in the course of the reaction (44% yield) contains an approximately 1:2 mixture of isomers **11d′/11d**. The ratio of the isomers decreases to ~1:4 in boiling benzene (2 h, 40% yield). Using toluene as the solvent, we isolated the adduct in 39% yield, which contained a small amount of the minor isomer (**11d′/11d** ~1:9). Boiling the reaction mixture at 140 °C (*o*-xylene, 2 h), we obtained solely regioisomer **11d** in 32% yield.

The carboxylic acids **11a–e**,**k** are fine-grained powders poorly soluble in most organic solvents including dimethyl sulfoxide. Consequently it has been difficult to determine their spatial structure by NMR spectroscopy alone. In particular, the orientation of the 8,10a-epoxy bridge in Diels–Alder adducts **9** and **11** was ambiguous. It was necessary to obtain the corresponding methyl or ethyl esters **13** in order to determine their structures. The esters **13** are well soluble and crystallized readily. Their conformation was studied by ^{1}H and ^{13}C NMR spectroscopy in detail. Moreover, in the case of methyl ester **13a**, a single crystal suitable for the X-ray analysis was obtained by slow crystallization from ethanol–chloroform (Figure 1).

Based on the X-ray crystal structure data, it was possible to assign the signals in the NMR spectra of the adducts **9a–h**,**k**,**l**, **11a–h**,**k**,**l**, and **12**. The signals of the proton H10b with δ = 4.2–4.9 ($J_{10b,1}$ = 11.7–12.3 Hz) and of the low-field proton H4 (δ = 5.0–5.9) with $J_{4,3a}$ = 0–2.5 Hz are the most characteristic. The values of these coupling constants give a good fit with the dihedral angles H10b–C10b–C1H1 = 169.7° and H4–C4–C3–H3A = 67.8° ascertained using X-ray diffraction analysis. The *exo*-orientation of the substituent in the oxabicyclo[2.2.1]heptene fragment is confirmed by the value of the spin-spin coupling constant $J_{6a,7endo}$ = 8.9–9.3 Hz and the absence of a coupling constant $J_{8,7endo}$ (~ 0 Hz). It is interesting to mention some special characteristics of the ^{13}C NMR spectra:

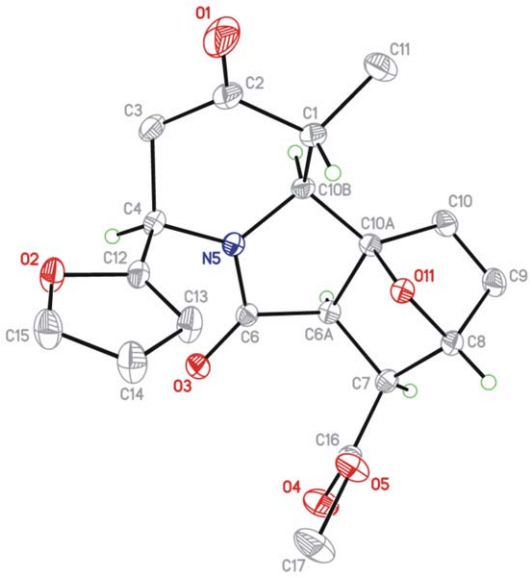
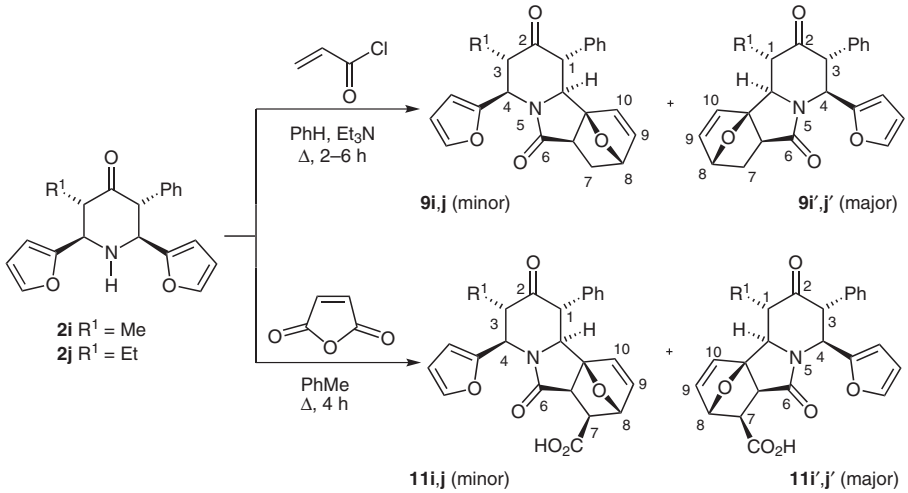


Figure 1 Molecular structure of ester **13a**; thermal ellipsoids are shown at 50% probability level

well-identifiable signals of C8 (δ = 78.5–81.5) and C10a (δ = 90.0–90.5) of the oxabicyclo[2.2.1]heptene fragment. The chemical shifts of these carbon atoms depend neither on the solvents used ($CDCl_3$ and DMSO-d_6), nor on the substituents on the ring.

It was also interesting to investigate the cycloaddition of unsaturated acid anhydrides with the asymmetric disubstituted 5-alkyl-3-phenylpiperidinones **2i**,**j** (Scheme 7). Similarly to the synthesis of **9** and **11** described above (Scheme 5), the reaction proceeds stereospecifically as an *exo*-[4+2] cycloaddition, but, in this case, it is difficult to make a conclusion about regioselectivity.

Adducts **9i**,**j**/**9i′**,**j′** were isolated from the reaction mixtures in ratios **9i/9i′** 1:4 (77% total yield) and **9j/9j′** 1:1.3 (78%). The ratio of isomers can be explained by the similar size of the 3-phenyl and the 5-methyl or 5-ethyl groups in the starting piperidinones **2i**,**j**. Obviously, the effective volume of the ethyl group in the compound **2j** is greater



Scheme 7

than that of the methyl group in piperidinone **2i**, which influences the isomeric composition of the adducts **9i**,**j**. When R = Me, isomer **9i′** prevails, in the case of the adduct from **2j** (R = Et) the isomeric ratio between **9j** and **9j′** is essentially 1:1. All adducts **9i**,**j** and **9i′**,**j′** were isolated after fractional crystallization or column chromatography.

Acids **11i**,**j** and **11i′**,**j′** were obtained as mixtures of isomers, whose ratio were determined as **11i/11i′** 1:4 and **11j/11j′** 1:6 by ^{1}H NMR spectroscopy. Unfortunately, it was not possible to run the chromatographic separation of these isomers due to their poor solubility. After fractional crystallization of the tetracycles **11i**,**j** and **11i′**,**j′** from ethanol–*N*,*N*-dimethylformamide mixtures, we isolated the predominant isomers **11i′**,**j′** only.

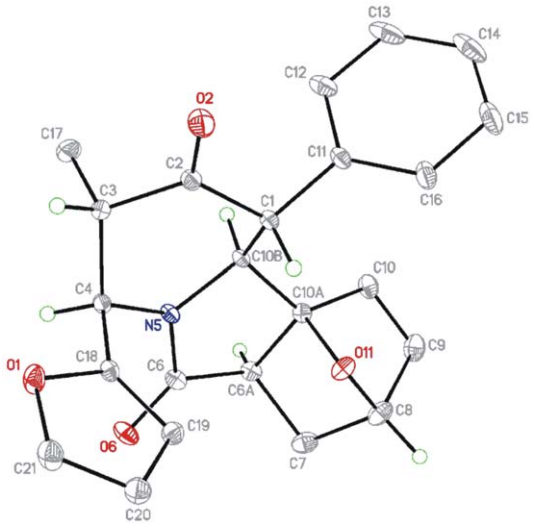


Figure 2 Molecular structure of the minor regioisomer **9i**

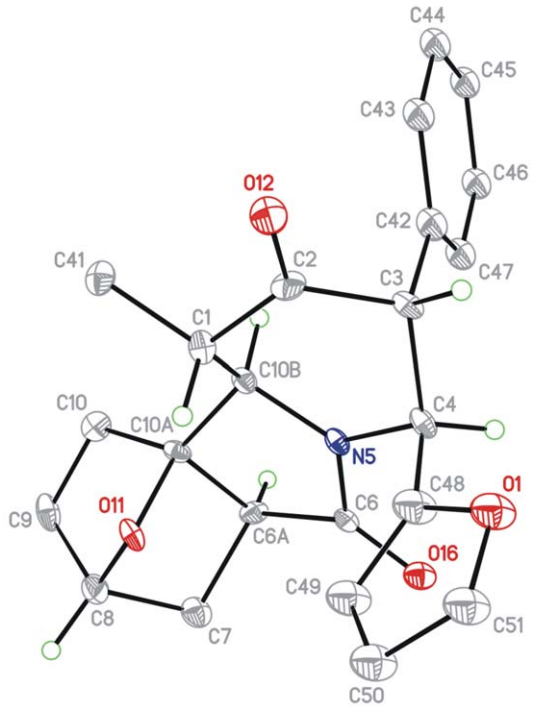


Figure 3 Molecular structure of major regioisomer **9i′**

It was not possible to determine the structure of regioisomers **9** obtained from **2i**,**j** using NMR data. The single crystals of adducts **9i** and **9i′** were obtained by slow crystallization from a mixture of heptane–ethyl acetate. The molecular structures of **9i** and **9i′** were established by X-ray diffraction analysis (Figures 2 and 3).

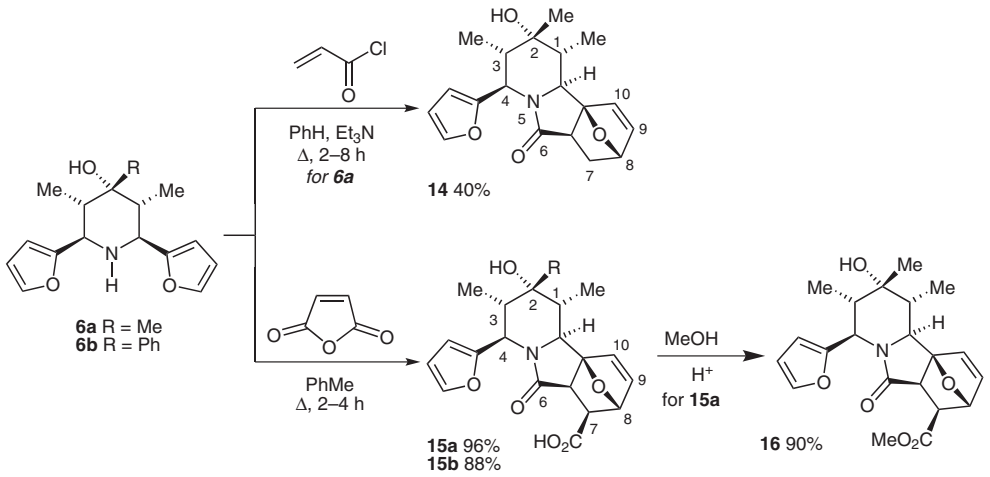
The unit cell of **9i′** contains four crystallographically independent molecules differing by only the rotation angle of the furyl substituent about the *exo*-C4–C(furyl) bond. Therefore, only the average geometrical parameters of the **9i′** molecules are discussed below.

Compounds **9i**, **9i′**, and **13a** comprise fused tetracyclic systems containing three five-membered rings (pyrrolidinone and tetrahydro- and dihydrofurans) and one six-membered (piperidinone) ring and are distinguished by substituents at C1, C3, and C7 (Figures 1– 3). Five-membered rings have the usual envelope conformations. The central six-membered ring adopts a twist-boat conformation (the C3 and $C10_B$ carbon atoms are out of the mean plane defined by the other atoms of the ring by 0.511 and 0.503; 0.587 and 0.529; and 0.578 and 0.521 Å for **9i**, **9i′**, and **13a**, respectively). The N5 nitrogen atom has a trigonal-planar geometry (the sums of the bond angles about N5 are 359.4°, 359.9°, and 360.0° for **9i**, **9i′** and **13a**, respectively). The dihedral angles between the planes of the pyrrolidinone and piperidinone rings are 16.3°, 16.0°, and 17.6° for **9i**, **9i′**, and **13a**, respectively. In all compounds, the substituent at C1 is in an equatorial position, whereas the substituents at the C3 (for **9i** and **9i′**) and C4 are in axial positions.

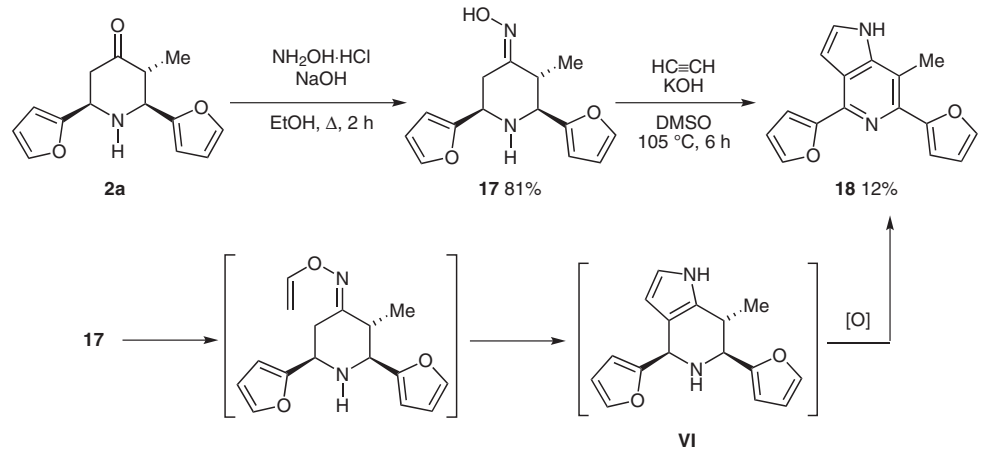
As stated above, according to the X-ray data (Figures 1–3), the substituents in positions 3 and 4 occupy unfavorable axial positions in the piperidine ring of the adducts **9** and **11**. We suppose that the steric hindrance is responsible for the relatively low yield (~50%) of the adducts from the cycloaddition of maleic anhydride and acryloyl chloride with 2,6-difuryl-3,5-diphenylpiperidinone **2f**. The adducts **9f** and **11f** seem to require bulky substituents in the *N*-acyl intermediates **IV** and **V** (Scheme 4) to occupy axial positions in transition states.

The reaction between piperidinols **6a**,**b** and maleic anhydride proceeds via the acylation of the nitrogen atom only, the axial 4-hydroxy group does not participate in the reaction (Scheme 8). Similarly to the preceding cases, the acylations of nitrogen result in spontaneous *exo*-[4+2] cycloaddition to give hydroxy acids **15a**,**b** in high yield and stereoselectivity. The reaction of the amino alcohol **6a** with acryloyl chloride yields adduct **14** in moderate yield. Methyl ester **16** was obtained after boiling the 8,10a-epoxypyrido[2,1-*a*]isoindole carboxylic acid **15a** in methanol.

The configuration of the adducts **14**–**16** were determined by ^{1}H and ^{13}C NMR spectroscopy based on analogy to the adducts **9** and **11**.



Scheme 8



Scheme 9

To our astonishment, the reaction of piperidinol **5** with maleic anhydride under the same conditions gave a mixture of at least four *exo*-adducts from the cycloaddition in ~80% total yield. All attempts to isolate individual isomers from this mixture were unsuccessful. The same situation was observed for the reaction of piperidinol **5** and acryloyl chloride. Two major products were detected in the reaction mixture, the structures of which were not established. The behavior of amino alcohol **5** under the conditions of the cycloaddition reaction is unclear.

In the last part of our investigation we attempted to obtain previously unknown furylpyrrolo[3,2-*c*]pyridines based on piperidinone **2a** by the Trofimov reaction.[17] However, treatment of the oxime **17** with gaseous acetylene in presence of super base (KOH/DMSO) unexpectedly afforded the aromatic pyrrolopyridine **18** in low yield (Scheme 9). Obviously, the reaction mechanism is similar to the Trofimov mechanism, but the initial diaryl-substituted 4,5,6,7-tetrahydro-1*H*-pyrrolo[3,2-*c*]pyridine **VI** is unstable under the reaction conditions and gives pyrrolo[3,2-*c*]pyridine **18** after the dehydrogenation in presence of dimethyl sulfoxide and atmospheric oxygen.

Herein we reported an efficient two-stage method for the synthesis of octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindoles and their 7-carboxylic acids based on the IMDAF reaction between 2-furylpiperidines and anhydrides of α,β-unsaturated carboxylic acids. The reaction proceeds as an *exo*-[4+2] cycloaddition with high regio- and stereoselectivity giving the target compounds in good yields.

All reagents were purchased from Acros Chemical Co. All solvents were used without further purification. Melting points were determined using a SMP10 and are uncorrected. IR spectra were obtained in KBr pellets for solids or in thin film for oils using an IR-Fourier spectrophotometer Infralum FT-801. NMR spectra ^{1}H (400 or 600 MHz) and ^{13}C (100.6 or 150.9 MHz) were recorded for solns in $CDCl_3$ or DMSO-d_6 at 30 °C and traces of $CHCl_3$ (^{1}H NMR δ = 7.26 and ^{13}C NMR δ = 76.90) or DMSO-d_5 (^{1}H NMR δ = 2.49 and ^{13}C NMR δ =39.43) were used as the internal standard. Mass spectra were measured either on Thermo Focus DSQ II (EI, 70 eV, ion source temperature was 200 °C, gas chromatographic inlet with Varian FactorFour VF-5ms column) or on Thermo Trace DSQ (EI, 70 eV, ion source temperature was 200 °C, direct inlet probe). The purity of the obtained substances and composition of the reaction mixtures were controlled by TLC Sorbfile plates. The separation of the final products was carried out by column chromatography on

alumina (activated, neutral, 50–200 mm) or by the fractional crystallization.

X-ray Crystal Structure Determination of the Cycloadducts 9i, 9i′, and 13a (Figures 1–3)

Compound **9i***:* ($C_{22}H_{21}NO_4$, M = 375.41), monoclinic, space group $P2_1/c$, at T = 100 K: a = 13.9081(6), b = 10.9800(5), c = 13.6640(6) Å, β = 118.0570(10)°, V = 1841.42(14) Å^3, Z = 4, d_{calcd} = 1.354 g/cm^3, $F(000)$ = 792, μ = 0.093 mm^{-1}. 27584 total reflections (6675 unique reflections, R_{int} = 0.032) were measured on a Bruker SMART APEX II CCD diffractometer [λ(MoKα) radiation, graphite monochromator, ω and φ scan mode, $2\theta_{max}$ = 65°]. The structure was determined by direct methods and refined by full-matrix least squares technique with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H) = 1.5U_{eq}(C) for the CH_3 groups and U_{iso}(H) = 1.2U_{eq}(C) for the other groups]. The final divergence factors were R_1 = 0.042 for 5612 independent reflections with $I > 2\sigma(I)$ and wR_2 = 0.116 for all independent reflections, S = 1.006. All calculations were carried out using the SHELXTL program.[18,19]

Compound **9i′***:* ($C_{22}H_{21}NO_4$, M = 375.41), monoclinic, space group Pc, at T = 120 K: a = 15.807(3), b = 9.8372(18), c = 23.727(4) Å, β = 90.299(3)°, V = 3689.5(12) Å^3, Z = 8, d_{calcd} = 1.352 g/cm^3, $F(000)$ = 1584, μ = 0.093 mm^{-1}. 27376 total reflections (6337 unique reflections, R_{int} = 0.036) were measured on a Bruker SMART 1000 CCD diffractometer [λ(MoKα) radiation, graphite monochromator, ω and φ scan mode, $2\theta_{max}$ = 50°]. The structure was determined by direct methods and refined by full-matrix least squares technique with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H) = 1.5U_{eq}(C) for the CH_3 groups and U_{iso}(H) = 1.2U_{eq}(C) for the other groups]. The final divergence factors were $R1$ = 0.104 for 5744 independent reflections with $I > 2\sigma(I)$ and $wR2$ = 0.229 for all independent reflections, S = 1.007. All calculations were carried out using the SHELXTL program.[18,19]

Compound **13a***:* ($C_{19}H_{19}NO_6$, M = 357.35), monoclinic, space group Cc, at T = 293 K: a = 9.839(2), b = 18.078(4), c = 10.664(2) Å, β = 113.86(3)°, V = 1734.7(6) Å^3, Z = 4, d_{calcd} = 1.368 g/cm^3, $F(000)$ = 752, μ = 0.103 mm^{-1}. 2229 total reflections (2202 unique reflections, R_{int} = 0.021) were measured on an Enraf-Nonius CAD-4 four-circle automated diffractometer [λ(MoKα) radiation, graphite monochromator, ω scan mode, $2\theta_{max}$ = 56°]. The structure was determined by direct methods and refined by full-matrix least squares technique with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H) = 1.5U_{eq}(C) for the CH_3 groups and U_{iso}(H) = 1.2U_{eq}(C) for the other groups]. The final divergence factors were $R1$ = 0.043 for 1748 independent reflections with $I > 2\sigma(I)$ and $wR2$ = 0.123 for all independent reflections, S = 1.000. All calculations were carried out using the SHELXTL program.[18,19]

Piperidinones 2a–l; Typical Procedure

A soln of furfural or 5-methylfurfural (~25 mL, 0.3 mol) and NH_4OAc (23 g, 0.3 mol) in EtOH (150 mL) was added to a soln of **1a**–**j** (0.15 mol) in EtOH (50 mL). The resulting clear mixture was allowed to react at r.t. for 3 d. The brown mixture obtained was then diluted with Et_2O (400 mL) and washed with H_2O (3 × 200 mL). The organic layer was separated, dried ($MgSO_4$), filtered, evaporated, and purified by column chromatography (alumina, hexane) to give **2a**,**b**,**f**–**j**,**l** as white prisms in good to moderate yields. Piperidinone **2k** was isolated as bright-yellow needles. In case of poor crystallizing piperidinones **2c**,**d**,**e**, column chromatography was not used. After evaporation of Et_2O, the residue (viscous brown oil) was transformed into its oxalate by the following method: to the residue, dissolved in anhyd Et_2O (250–350 mL), sat. anhyd oxalic acid in Et_2O (70–150 mL) was added until pale-brown residue formation was complete. The residue was filtered off, washed with acetone (100 mL), and then boiled in acetone (200 mL). The remaining residue was filtered off and dried in air to give piperidinone oxalates of **2c**,**d**,**e**. For further transformations the oxalates were dissolved in H_2O and 10% NH_4OH soln was added until pH 9–10. The thus obtained free base was extracted with Et_2O. The organic layers were separated, dried ($MgSO_4$), filtered, and evaporated to give pale-yellow viscous oils that occasionally crystallized when left to stand.

(2*S**,3*R**,6*R**)-2,6-Di-2-furyl-3-methylpiperidin-4-one (2a)

Yield: 34%; mp 63–64 °C (Lit.[11b] 40 °C).

IR: 3317 (NH), 1706 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, $J_{3,Me}$ = 6.5 Hz, 3 H, 3-CH_3), 2.35 (br s, 1 H, NH), 2.71 (dd, $J_{5B,6}$ = 3.0 Hz, $^2J_{5,5}$ = 13.6 Hz, 1 H, H5$_B$), 2.84 (dq, $J_{3,2}$ = 10.7 Hz, $J_{3,Me}$ = 6.5 Hz, 1 H, H3), 2.85 (dd, $J_{5A,6}$ = 12.1 Hz, $^2J_{5,5}$ = 13.6 Hz, 1 H, H5$_A$), 3.80 (d, $J_{2,3}$ = 10.7 Hz, 1 H, H2), 4.17 (dd, $J_{6,5A}$ = 12.1 Hz, $J_{6,5B}$ = 3.0 Hz, 1 H, H6), 6.21 (br d, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ*), 6.29 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ), 6.32 (m, 2 H, Hβ′, Hβ′*), 7.36 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα), 7.39 (dd, $J_{\beta',\alpha}$ = 0.6 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα*).

MS (EI, 70 eV): *m*/*z* (%) = 245 (28) [M]$^+$, 175 (3), 174 (10), 150 (2), 146 (2), 136 (5), 123 (14), 122 (31), 108 (10), 95 (30), 94 (100), 93 (97), 79 (31), 66 (40), 65 (35), 56 (23), 40 (12).

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.48; H, 6.20; N, 5.89.

(2*S**,3*R**,6*R**)-3-Ethyl-2,6-di-2-furylpiperidin-4-one (2b)

Yield: 33%; mp 45–47 °C (Lit.[11b] 47 °C).

IR: 3316 (NH), 1707 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, $J_{CH2,Me}$ = 7.0 Hz, 3 H, CH_3), 1.28 (m, 1 H, CH_AH$_B$CH$_3$), 1.60 (m, 1 H, CH$_A$$H_BCH_3$), 2.31 (br s, 1 H, NH), 2.70 (dd, $J_{5B,6}$ = 2.5 Hz, $^2J_{5,5}$ = 13.0 Hz, 1 H, H5$_B$), 2.73 (m, 1 H, H3), 2.84 (dd, $^2J_{5,5}$ = $J_{5A,6}$ = 13.0 Hz, 1 H, H5$_A$), 3.91 (d, $J_{2,3}$ = 10.9 Hz, 1 H, H2), 4.15 (dd, $J_{6,5B}$ = 2.5 Hz, $J_{6,5A}$ = 13.0 Hz, 1 H, H6), 6.21 (br d, $J_{\beta',\beta}$ = 3.1 Hz, 1 H, Hβ′), 6.31 (m, 3 H, Hβ, Hβ*, Hβ′*), 7.35 (br d, $J_{\alpha,\beta}$ = 1.6 Hz, 1 H, Hα), 7.39 (br d, $J_{\alpha,\beta}$ = 1.6 Hz, 1 H, Hα*).

MS (EI, 70 eV): *m*/*z* (%) = 259 (15) [M]$^+$, 174 (10), 149 (3), 137 (9), 122 (21), 107 (6), 96 (14), 94 (100), 77 (8), 65 (10), 55 (14), 39 (27).

Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.39; H, 6.55; N, 5.45.

(2*S**,3*R**,6*R**)-2,6-Di-2-furyl-3-propylpiperidin-4-one (2c)

Yield: 28%; mp (oxalate) 154 °C.

IR: 3316 (NH), 1713 cm^{-1} (C=O).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.75 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 1.02 (m, 2 H, CH_2CH_3), 1.27 (m, 1 H, CH$_A$$H_B$$CH_2CH_3$), 1.63 (m, 1 H, C$H_AH_B$$CH_2CH_3$), 2.27 (br s, 1 H, NH), 2.67 (dd, $J_{5B,6}$ = 3.0 Hz, $^2J_{5,5}$ = 13.4 Hz, 1 H, H5$_B$), 2.72 (ddd, $J_{3,2}$ = 10.5 Hz, $J_{3,CH2A}$ = 7.6 Hz, $J_{3,CH2B}$ = 2.0 Hz, 1 H, H3), 2.80 (dd, $J_{5A,6}$ = 12.1 Hz, $^2J_{5,5}$ = 13.4 Hz, 1 H, H5$_A$), 3.85 (d, $J_{3,2}$ = 10.5 Hz, 1 H, H2), 4.12 (dd, $J_{5B,6}$ = 3.0 Hz, $J_{5A,6}$ = 12.1 Hz, 1 H, H6), 6.17 (br d, $J_{\beta,\beta'}$ = 3.2 Hz, 1 H, Hβ′), 6.24 (br d, $J_{\beta,\beta'}$ = 3.2 Hz, 1 H, Hβ′), 6.27 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta,\beta'}$ = 3.2 Hz, 1 H, Hβ), 6.29 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta,\beta'}$ = 3.2 Hz, 1 H, Hβ), 7.31 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\alpha,\beta'}$ = 0.6 Hz, 1 H, Hα), 7.35 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\alpha,\beta'}$ = 0.6 Hz, 1 H, Hα).

MS (EI, 70 eV): *m*/*z* (%) = 273 (14) [M]$^+$, 244 (3), 188 (2), 174 (5), 151 (4), 122 (11), 96 (19), 94 (100), 77 (13), 66 (18), 55 (51).

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.29; H, 7.33; N, 5.19.

(2*S,3*R**,6*R**)-2,6-Di-2-furyl-3-isopropylpiperidin-4-one (2d)**
Yield: 31%; mp 54–55 °C.

IR: 3288 (NH), 1703 cm^{-1} (C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.74 [d, $J_{CH,Me}$ = 7.3 Hz, 3 H, $CH(CH_3)_A(CH_3)_B$], 1.02 [d, $J_{CH,Me}$ = 6.7 Hz, 3 H, $CH(CH_3)_A(CH_3)_B$], 1.93 [m, 1 H, $CH(CH_3)_2$], 2.25 (br s, 1 H, NH), 2.67 (dd, $J_{5B,6}$ = 2.7 Hz, $^2J_{5,5}$ = 14.1 Hz, 1 H, $H5_B$), 2.77 (dd, $J_{3,2}$ = 11.4 Hz, $J_{3,CH(Me)2}$ = 6.5 Hz, 1 H, H3), 2.79 (dd, $J_{5A,6}$ = 11.2 Hz, $^2J_{5,5}$ = 14.1 Hz, 1 H, $H5_A$), 4.14 (d, $J_{2,3}$ = 11.4 Hz, 1 H, H2), 4.17 (dd, $J_{6,5A}$ = 11.2 Hz, $J_{6,5B}$ = 2.7 Hz, 1 H, H6), 6.32–6.19 (m, 4 H, Hβ, Hβ′, Hβ*, Hβ′*), 7.34 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\alpha,\beta'}$ = 0.8 Hz, 1 H, Hα), 7.38 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\alpha,\beta'}$ = 0.8 Hz, 1 H, Hα*).

MS (EI, 70 eV): *m*/*z* (%) = 273 (21) $[M]^+$, 258 (8), 188 (8), 174 (11), 151 (7), 122 (11), 121 (11), 96 (18), 95 (11), 94 (100), 88 (5), 69 (22), 65 (5).

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.17; H, 7.24; N, 5.09.

(2*S,3*R**,6*R**)-3-Allyl-2,6-di-2-furylpiperidin-4-one (2e)**
Yield: 28%; mp (oxalate) 138 °C.

IR: 3294 (NH), 1712 cm^{-1} (C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 2.14–2.27 (m, 2 H, $CH_2CH=CH_2$), 2.72 (dd, $J_{5B,6}$ = 2.4 Hz, $^2J_{5,5}$ = 13.7 Hz, 1 H, $H5_B$), 2.84 (dd, $J_{5A,6}$ = 12.0 Hz, $^2J_{5,5}$ = 13.7 Hz, 1 H, $H5_A$), 2.89 (m, 1 H, H3), 3.96 (d, $J_{2,3}$ = 10.9 Hz, 1 H, H2), 4.16 (dd, $J_{6,5B}$ = 2.4 Hz, $J_{6,5A}$ = 12.0 Hz, 1 H, H6), 4.85 (br d, $J_{2',3'trans}$ = 17.2 Hz, 1 H, $CH_2CH=CH_{trans}H_{cis}$), 4.91 (br d, $J_{2',3'cis}$ = 10.5 Hz, 1 H, $CH_2CH=CH_{trans}H_{cis}$), 5.67 (ddt, $J_{2',1'}$ = 7.2 Hz, $J_{2',3'cis}$ = 10.5 Hz, $J_{2',3'trans}$ = 17.2 Hz, 1 H, $CH=CH_2$), 6.20 (br d, $J_{\beta',\beta}$ = 3.0 Hz, 1 H, Hβ′), 6.28–6.32 (m, 3 H, Hβ, Hβ*, Hβ′*), 7.34 (br d, $J_{\alpha,\beta}$ = 1.6 Hz, 1 H, Hα), 7.38 (br d, $J_{\alpha,\beta}$ = 1.6 Hz, 1 H, Hα*).

MS (EI, 70 eV): *m*/*z* (%) = 271 (7) $[M]^+$, 228 (1), 105 (5), 94 (100), 65 (25), 53 (14), 39 (44).

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.65; H, 6.40; N, 5.11.

(2*R,3*S**,5*R**,6*S**)-2,6-Di-2-furyl-3,5-diphenylpiperidin-4-one (2f)**
Yield: 62%; mp 149–151 °C.

IR: 3283 (NH), 1693 cm^{-1} (C=O).

^1H NMR (600 MHz, $CDCl_3$): δ = 2.63 (br s, 1 H, NH), 4.23 (d, $J_{2,3(5,6)}$ = 11.0 Hz, 2 H, H3, H5), 4.54 (d, $J_{2,3(5,6)}$ = 11.0 Hz, 2 H, H2, H6), 5.93 (br d, $J_{\alpha,\beta}$ = 3.3 Hz, 2 H, Hβ′), 6.09 (dd, $J_{\alpha,\beta}$ = 3.3 Hz, $J_{\alpha,\beta}$ = 1.6 Hz, 2 H, Hβ), 7.03 (dd, $J_{ortho,para}$ = 1.0 Hz, $J_{meta,ortho}$ = 7.7 Hz, 4 H, H_{ortho} Ph), 7.13 (dt, $J_{meta,para}$ = 7.7 Hz, $J_{ortho,para}$ = 1.0 Hz, 2 H, H_{para} Ph), 7.19 (br t, $J_{meta,para}$ = $J_{meta,ortho}$ = 7.7 Hz, 4 H, H_{meta}), 7.25 (dd, $J_{\beta',\alpha}$ = 0.7 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 2 H, Hα).

MS (EI, 70 eV): *m*/*z* (%) = 383 (7) $[M]^+$, 366 (8), 335 (3), 207 (9), 185 (28), 174 (88), 179 (100), 141 (93), 118 (26), 115 (79), 91 (47), 90 (76), 77 (20), 65 (18).

Anal. Calcd for $C_{25}H_{21}NO_3$: C, 78.31; H, 5.52; N, 3.65. Found: C, 78.21; H, 5.78; N, 3.75.

(2*R,3*S**,5*R**,6*S**)-2,6-Di-2-furyl-3,5-dimethylpiperidin-4-one (2g)**
Yield: 66%; mp 73.5–74.5 °C (Lit.[11b] 57 °C).

IR: 3315 (NH), 1705 cm^{-1} (C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.91 (d, $J_{Me,3(Me,5)}$ = 6.6 Hz, 6 H, 3-CH_3, 5-CH_3), 2.27 (br s, 1 H, NH), 2.95 (dq, $J_{2,3(5,6)}$ = 10.8 Hz, $J_{Me,3(Me,5)}$ = 6.6 Hz, 2 H, H3, H5), 3.76 (d, $J_{2,3(5,6)}$ = 10.8 Hz, 2 H, H2, H6), 6.27 (dd, $J_{\alpha,\beta'}$ = 0.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 2 H, Hβ′), 6.31 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 2 H, Hβ), 7.38 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 2 H, Hα).

MS (EI, 70 eV): *m*/*z* (%) = 259 (13) $[M]^+$, 174 (14), 146 (3), 136 (29), 123 (23), 108 (100), 96 (16), 80 (16), 79 (54), 77 (27), 55 (14), 53 (15), 39 (42).

Anal. Calcd for $C_{17}H_{15}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.30; H, 6.51; N, 5.61.

Diethyl 2,2′-[(2*R,3*S**,5*R**,6*S**)-2,6-Di-2-furyl-4-oxopiperidine-3,5-diyl]diacetate (2h)**
Yield: 30%; mp 62 °C.

IR: 3313 (NH), 1715 (C=O), 1726 cm^{-1} (CO_2Et).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.19 (t, $J_{CH2,Me}$ = 7.0 Hz, 6 H, CH_2CH_3), 2.20 (dd, ^2J = 17.2 Hz, $J_{CH2A,3(5)}$ = 3.8 Hz, 2 H, $CH_AH_BCO_2Et$), 2.56 (dd, ^2J = 17.2 Hz, $J_{CH2B,3}$ = 7.6 Hz, 2 H, $CH_AH_BCO_2Et$), 3.39 (ddd, $J_{2,3(5,6)}$ = 11.0 Hz, $J_{CH2A,3}$ = 3.8 Hz, $J_{CH2B,3}$ = 7.6 Hz, 2 H, H3, H5), 4.01 (q, $J_{CH2,Me}$ = 7.0 Hz, 4 H, CH_2CH_3), 4.03 (d, $J_{2,3(5,6)}$ = 11.0 Hz, 2 H, H2, H6), 6.28 (m, 4 H, Hβ, Hβ′), 7.37 (dd, $J_{\beta',\alpha}$ = 0.6 Hz, $J_{\alpha,\beta}$ = 1.6 Hz, 2 H, Hα).

MS (EI, 70 eV): *m*/*z* (%) = 403 (39) $[M]^+$, 386 (4), 358 (44), 316 (27), 298 (6), 274 (10), 270 (12), 228 (17), 208 (50), 195 (47), 175 (26), 174 (27), 146 (9), 122 (60), 107 (41), 96 (15), 79 (11), 55 (21), 44 (100).

Anal. Calcd for $C_{21}H_{25}NO_7$: C, 62.52; H, 6.25; N, 3.47. Found: C, 62.45, H, 6.25; N, 3.49.

(2*R,3*S**,5*R**,6*S**)-2,6-Di-2-furyl-5-methyl-3-phenylpiperidin-4-one (2i)**
Yield: 56%; mp 129 °C.

IR: 3326 (NH), 1726 cm^{-1} (C=O).

^1H NMR (600 MHz, $CDCl_3$): δ = 1.00 (d, $J_{5,Me}$ = 6.5 Hz, 3 H, 5-CH_3), 2.49 (br s, 1 H, NH), 3.10 (ddq, $J_{5,\beta'}$ = 0.9 Hz, $J_{5,Me}$ = 6.5 Hz, $J_{5,6}$ = 10.9 Hz, 1 H, H5), 4.00 (d, $J_{5,6}$ = 10.9 Hz, 1 H, H6), 4.16 (d, $J_{2,3}$ = 11.1 Hz, 1 H, H3), 4.40 (d, $J_{2,3}$ = 11.1 Hz, 1 H, H2), 5.93 (dd, $J_{\alpha,\beta'}$ = 0.7 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ′), 6.11 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ), 6.36 (dd, $J_{\alpha,\beta'}$ = 0.7 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ′*), 6.38 (dd, $J_{\alpha,\beta}$ = 1.9 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ*), 7.05 (dd, $J_{meta,ortho}$ = 7.2 Hz, $J_{para,ortho}$ = 0.8 Hz, 2 H, H_{ortho}), 7.21 (m, 1 H, H_{para}), 7.26 (m, 2 H, H_{meta}), 7.26 (dd, $J_{\beta',\alpha}$ = 0.7 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα), 7.44 (dd, $J_{\beta',\alpha}$ = 0.7 Hz, $J_{\alpha,\beta}$ = 1.9 Hz, 1 H, Hα*).

MS (EI, 70 eV): *m*/*z* (%) = 321 (13) $[M]^+$, 240 (3), 226 (2), 202 (6), 198 (3), 185 (38), 174 (41), 170 (14), 161 (5), 141 (6), 136 (5), 122 (6), 118 (24), 108 (100), 96 (10), 79 (9).

Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.61; H, 5.51; N, 4.35.

(2*R,3*S**,5*R**,6*S**)-3-Ethyl-2,6-di-2-furyl-5-phenylpiperidin-4-one (2j)**
Yield: 31%; mp 116–117 °C.

IR: 3329 (NH), 1713 cm^{-1} (C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, $J_{CH2,Me}$ = 7.5 Hz, 3 H, CH_2CH_3), 1.25 (ddq, $J_{CH2,Me}$ = 7.5 Hz, $J_{CH2A,3}$ = 3.2 Hz, $^2J_{CH2}$ = 15.1 Hz, 1 H, $CH_AH_BCH_3$), 1.68 (m, 1 H, $CH_AH_BCH_3$), 2.42 (br s, 1 H, NH), 2.92 (ddd, $J_{CH2A,3}$ = 3.2 Hz, $J_{2,3}$ = 10.9 Hz, $J_{CH2B,3}$ = 7.5 Hz, 1 H, H3), 4.05 (d, $J_{2,3}$ = 10.9 Hz, 1 H, H2), 4.11 (br d, $J_{6,5}$ = 10.8 Hz, 1 H, H6), 4.33 (d, $J_{6,5}$ = 10.8 Hz, 1 H, H5), 5.87 (dd, $J_{\alpha,\beta'}$ = 0.8 Hz, $J_{\beta',\beta}$ = 3.3 Hz, 1 H, Hβ′), 6.06 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.3 Hz, 1 H, Hβ), 6.31 (dd, $J_{\alpha,\beta'}$ = 0.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ′*), 6.34 (dd, $J_{\alpha,\beta}$ = 1.6 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ*), 7.02 (dd, $J_{meta,ortho}$ = 7.3 Hz, $J_{para,ortho}$ = 1.0 Hz, 2 H, H_{ortho}), 7.24–7.15 (m, 3 H, H_{para}, H_{meta}), 7.23

(dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα), 7.40 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα*).

MS (EI, 70 eV): *m/z* (%) = 335 (12) $[M]^+$, 240 (3), 216 (4), 198 (2), 185 (40), 174 (44), 170 (20), 150 (7), 141 (12), 123 (6), 122 (100), 118 (16), 107 (15), 96 (9), 91 (7), 81 (6), 79 (6).

Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 75.35; H, 6.37; N, 3.99.

(2*S,3*R**,6*R**)-3-Methyl-2,6-bis(5-methyl-2-furyl)piperidin-4-one (2k)**

Yield: 27%; mp 70–72 °C.

IR: 3306 (NH), 1712 cm^{-1} (C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, $J_{3,Me}$ = 6.5 Hz, 3 H, 3-CH_3), 2.25 (br s, 3 H, furyl-CH_3), 2.27 (br s, 3 H, furyl-CH_3*), 2.28 (br s, 1 H, NH), 2.69 (dd, $J_{5B,6}$ = 2.6 Hz, $J_{5B,5A}$ = 13.7 Hz, 1 H, $H5_B$), 2.83 (dq, $J_{3,2}$ = 10.7 Hz, $J_{3,Me}$ = 6.5 Hz, 1 H, H3), 2.82 (dd, $J_{5A,6}$ = 12.1 Hz, $J_{5A,5B}$ = 13.7 Hz, 1 H, $H5_A$), 3.70 (d, $J_{2,3}$ = 10.7 Hz, 1 H, H2), 4.08 (dd, $J_{6,5B}$ = 2.6 Hz, $J_{6,5A}$ = 12.1 Hz, 1 H, H6), 5.89 (m, 2 H, Hβ, Hβ*), 6.07 (br d, $J_{\beta',\beta}$ = 2.9 Hz, 1 H, Hβ′), 6.14 (br d, $J_{\beta',\beta}$ = 2.9 Hz, 1 H, Hβ′*).

MS (EI, 70 eV): *m/z* (%) = 256 (14), $[M]^+$, 214 (10), 213 (5), 171 (8), 107 (9), 91 (25), 77 (47), 53 (22, 43 (100).

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.19; H, 6.87; N, 5.09.

(2*R,3*S**,5*R**,6*S**)-3,5-Dimethyl-2,6-bis(5-methyl-2-furyl)piperidin-4-one (2l)**

Yield: 41%; mp 85–86 °C.

IR: 3282 (NH), 1704 cm^{-1} (C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, $J_{Me,3(Me,5)}$ = 6.5 Hz, 6 H, 3-CH_3, 5-CH_3), 2.27 (d, $J_{Me,\beta'}$ = 0.6 Hz, 6 H, furyl-CH_3, furyl-CH_3*), 2.75 (br s, 1 H, NH), 2.90 (dq, $J_{3,2(5,6)}$ = 10.8 Hz, $J_{Me,3(Me,5)}$ = 6.5 Hz, 2 H, H3, H5), 3.66 (d, $J_{3,2(5,6)}$ = 10.8 Hz, 2 H, H2, H6), 5.88 (dq, $J_{Me,\beta'}$ = 0.6 Hz, $J_{\beta',\beta}$ = 3.0 Hz, 2 H, Hβ′, Hβ′*), 6.12 (br d, $J_{\beta',\beta}$ = 3.0 Hz, 2 H, Hβ, Hβ*).

MS (EI, 70 eV): *m/z* (%) = 287 (35) $[M]^+$, 244 (5), 202 (20), 150 (40), 137 (13), 122 (100), 110 (20), 101 (8), 79 (7), 77 (6), 43 (7).

Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found: C, 70.98; H, 7.50; N, 4.75.

(2*R,3*S**,5*R**,6*S**)-1-Acetyl-2,6-di-2-furyl-3,5-dimethylpiperidin-4-one (3)**

A mixture of **2g** (3.8 g, 1.5 mmol) in toluene (20 mL) and Ac_2O (7.5 mL, 7.5 mmol) was refluxed at 110 °C for 2 h. Then the mixture was cooled, poured into H_2O (150 mL), and aq 25% NH_3 soln was added until pH 9–10. The organic products were extracted with EtOAc (3 × 70 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to give crude **3**. Further crystallization (hexane–EtOAc) gave **3** as large white crystals; yield: 76%; mp 70–76 °C.

IR: (KBr): 1646 (NAc), 1711 cm^{-1} (C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, $J_{Me,3(Me,5)}$ = 7.0 Hz, 6 H, 3-CH_3, 5-CH_3), 2.19 (br s, 3 H, NAc), 3.26 (dq, $J_{Me,3(Me,5)}$ = 7.0 Hz, $J_{2,3(6,5)}$ = 6.5 Hz, 2 H, H3, H5), ~5.3 (very br s, 2 H, H2, H6), 6.09 (br s, 2 H, Hβ′, Hβ′*), 6.29 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 2 H, Hβ, Hβ*), 7.26 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 2 H, Hα, Hα*).

MS (EI, 70 eV): *m/z* (%) = 301 (8) $[M]^+$, 258 (1), 242 (100), 220 (3), 165 (52), 150 (24), 123 (42), 108 (38), 79 (18), 77 (10), 43 (12).

Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.78; H, 6.25; N, 4.56.

(2*R,3*R**,5*R**,6*S**)-2,6-Di-2-furyl-3,5-dimethylpiperidine (4)**

A mixture of **2g** (8.0 g, 30.9 mmol), ethylene glycol (90 mL), and hydrazine hydrate (7.8 mL, 0.15 mol) was boiled for 3 h (TLC monitoring). The mixture was cooled and powdered KOH (10.4 g, 0.18 mmol) was added. Then the mixture was refluxed for ~3 h. When the evolution of gas had ceased, the mixture was cooled, poured into H_2O (350 mL), and extracted with EtOAc (5 × 70 mL). The combined organic extracts were washed with H_2O (2 × 80 mL), dried ($MgSO_4$), and concentrated. The residue, viscous brown oil, was purified by column chromatography (alumina, hexane–EtOAc, 15:1). The first fraction crystallized on standing to give crude **4** as a yellow solid. Further crystallization (hexane with charcoal) gave **4** as big transparent crystals; yield: 3.9 g (50%); mp 72–73 °C.

IR: 3307 cm^{-1} (NH).

^1H NMR ($CDCl_3$, 400 MHz): δ = 0.75 (d, $J_{5,Me}$ = 6.8 Hz, 3 H, 5-CH_3), 0.94 (d, $J_{3,Me}$ = 6.8 Hz, 3 H, 3-CH_3), 1.53 [br dt, $J_{5(e),4(a)}$ = 4.6 Hz, $^2J_{4,4}$ = $J_{3(a),4(a)}$ = 13.1, Hz, 1 H, H4(a)], 1.79 [ddd, $J_{3(a),4(e)}$ = 2.6 Hz, $J_{5(e),4(e)}$ = 3.8 Hz, $^2J_{4,4}$ = 13.1 Hz, 1 H, H4(e)], 1.82 (br s, 1 H, NH), 2.05 [dddq, $J_{3(a),4(e)}$ = 2.6 Hz, $J_{3,Me}$ = 6.8 Hz, $J_{3(a),2(a)}$ = 10.5 Hz, $J_{3(a),4(a)}$ = 13.1 Hz, 1 H, H3(a)], 2.20 (dddq, $J_{5(e),6(a)}$ = 2.7 Hz, $J_{5(e),4(e)}$ = 3.8 Hz, $J_{5(e),4(a)}$ = 4.6 Hz, $J_{5,Me}$ = 6.8 Hz, 1 H, H5(e)], 3.44 [d, $J_{2(a),3(a)}$ = 10.5 Hz, 1 H, H2(a)], 4.07 [d, $J_{6(a),5(e)}$ = 2.7 Hz, 1 H, H6(a)], 6.12 (br dd, $J_{\alpha,\beta'}$ = 0.7 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ′*), 6.23 (dd, $J_{\alpha,\beta'}$ = 0.6 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ′), 6.29 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ), 6.31 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ*), 7.30 (br dd, $J_{\beta',\alpha}$ = 0.7 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα*), 7.35 (dd, $J_{\beta',\alpha}$ = 0.6 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.1 and 18.9 (3-CH_3, 5-CH_3), 32.2 and 29.7 (C_3, C_5), 40.8 (C_4), 59.0 and 62.8 (C_2, C_6), 104.8 and 106.5 ($C_{\beta'}$, $C_{\beta'*}$), 110.0 (2C, C_β, $C_{\beta*}$), 141.5 and 140.9 (C_α, $C_{\alpha*}$), 156.7 and 156.4 (furyl-C_q, furyl-C_{q*}).

MS (EI, 70 eV): *m/z* (%) = 245 (39) $[M]^+$, 230 (2), 216 (9), 202 (3), 175 (11), 146 (10), 137 (21), 136 (21), 124 (39), 122 (13), 108 (54), 96 (21), 95 (43), 94 (63), 81 (55), 79 (57), 77 (32), 68 (19), 55 (100).

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.16; N, 5.92; H, 7.39.

(2*R,3*S**,4*S**,5*R**,6*S**)-2,6-Di-2-furyl-3,5-dimethylpiperidin-4-ol (5)**

$NaBH_4$ (0.76 g, 0.019 mmol) was added to a soln of **2g** (5.0 g, 0.019 mmol) in MeOH (70 mL). The mixture was refluxed with vigorously stirring for 1 h. Then the resultant mixture was cooled, poured into H_2O (250 mL), and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. Further crystallization of the solid residue (hexane–EtOAc) gave the **5** as white crystals; yield: 54%; mp 113–114 °C.

IR: 3317 (br, OH), 3310 cm^{-1} (NH).

^1H NMR (600 MHz, $CDCl_3$): δ = 0.86 (d, $J_{Me,3(Me,5)}$ = 6.9 Hz, 6 H, 3-CH_3, 5-CH_3), 1.59 and 1.83 (br s, 1 H + 1 H, OH, NH), 2.14 (ddq, $J_{3,4(4,5)}$ = 2.5 Hz, $J_{Me,3(Me,5)}$ = 6.9 Hz, $J_{2,3(5,6)}$ = 10.7 Hz, 2 H, H3, H5), 3.87 (br t, $J_{3,4(4,5)}$ = 2.5 Hz, 1 H, H4), 4.02 (d, $J_{2,3(5,6)}$ = 10.7 Hz, 2 H, H2, H6), 6.23 (dd, $J_{\alpha,\beta'}$ = 0.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 2 H, Hβ′), 6.30 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 2 H, Hβ), 7.35 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 2 H, Hα).

MS (EI, 70 eV): *m/z* (%) = 261 (21) $[M]^+$, 232 (3), 214 (1), 202 (2), 175 (8), 174 (12), 160 (10), 152 (12), 146 (6), 136 (11), 124 (10), 108 (36), 96 (100), 94 (27), 81 (35), 79 (45), 77 (24), 57 (23), 41 (55).

Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 69.13; H, 7.51; N, 5.47.

Piperidinols 6a,b; General Procedure

A soln of **2g** (6.0 g, 23 mmol) in anhyd Et_2O (70 mL) was added dropwise at reflux to a stirred soln of MeMgI [prepared from MeI

(4.7 mL, 75 mmol) and Mg turnings (2.3 g, 94 mmol) in anhyd Et_2O (100 mL)] (for **6a**) or to a soln of PhLi [prepared from PhBr (12 mL, 0.115 mol) and Li wire (1.6 g, 0.23 mol) in anhyd Et_2O (150 mL)] (for **6b**). After the addition of **2g**, the mixture was stirred at reflux for 1–2 h. Then the cooled mixture was poured into sat. aq NH_4Cl soln (100 mL) under ice cooling. The mixture was extracted with Et_2O (3 × 100 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Further crystallization of the solid products (hexane–EtOAc) gave **6a**,**b** as white needles.

(2*R,3*S**,4*S**,5*R**,6*S**)-2,6-Di-2-furyl-3,4,5-trimethylpiperidin-4-ol (6a)**
Yield: 72%; mp 88–90 °C.

IR: 3310–3956 (br, OH), 2983 cm^{-1} (NH).

^1H NMR (600 MHz, $CDCl_3$): δ = 0.80 (d, $J_{Me,3(Me,5)}$ = 6.8 Hz, 6 H, 3-CH_3, 5-CH_3), 1.31 (s, 3 H, 4-CH_3), 1.96 (br s, 2 H, NH, OH), 1.98 (dq, $J_{Me,3(Me,5)}$ = 6.8 Hz, $J_{2,3(5,6)}$ = 10.7 Hz, 2 H, H3, H5), 3.96 (d, $J_{2,3(5,6)}$ = 10.7 Hz, 2 H, H2, H6), 6.23 (dd, $J_{\alpha,\beta'}$ = 0.8 Hz, $J_{\beta',\beta}$ = 3.1 Hz, 2 H, Hβ′), 6.29 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.1 Hz, 2 H, Hβ), 7.34 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 2 H, Hα).

^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 11.1 (3-CH_3, 5-CH_3), 25.4 (4-CH_3), 44.2 (C_3, C_5), 56.6 (C_2, C_6), 72.8 (C_4), 107.1 and 109.9 (C_β, $C_{\beta'}$), 141.5 (C_α), 156.0 (furyl-C_q).

MS (EI, 70 eV): *m*/*z* (%) = 275 (20) $[M]^+$, 258 (1), 176 (5), 175 (5), 174 (13), 166 (7), 160 (40), 146 (4), 136 (11), 108 (30), 96 (100), 79 (27), 43 (66), 39 (31).

Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.44; N, 7.69. Found: C, 69.61; H, 7.48; N, 7.72.

(2*R,3*S**,4*S**,5*R**,6*S**)-2,6-Di-2-furyl-3,5-dimethyl-4-phenylpiperidin-4-ol (6b)**
Yield: 29%; mp 80–83 °C.

IR: 3599 (OH), 2973 cm^{-1} (NH).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.44 (d, $J_{Me,3(Me,5)}$ = 6.8 Hz, 6 H, 3-CH_3, 5-CH_3), 1.92 (br s, 1 H, NH or OH), 2.46 (dq, $J_{Me,3(Me,5)}$ = 6.8 Hz, $J_{2,3(5,6)}$ = 10.6 Hz, 2 H, H3, H5), 4.15 (d, $J_{2,3(5,6)}$ = 10.6 Hz, 2 H, H2, H6), 6.24 (dd, $J_{\alpha,\beta'}$ = 0.6 Hz, $J_{\beta',\beta}$ = 3.1 Hz, 2 H, Hβ′), 6.28 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.1 Hz, 2 H, Hβ), 7.24 (br t, $J_{ortho,para}$ = 7.3 Hz, 1 H, H_{para} Ph), 7.34 (dd, $J_{\beta',\alpha}$ = 0.6 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 2 H, Hα), 7.38–7.36 (m, 4 H, H_{ortho}, H_{meta} Ph).

MS (EI, 70 eV): *m*/*z* (%) = 337 (10) $[M]^+$, 319 (1), 304 (2), 228 (5), 202 (3), 177 (5), 160 (100), 136 (18), 108 (21), 105 (40), 96 (98), 77 (18), 44 (7).

Anal. Calcd for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.52; H, 6.97; N, 4.19.

(2*R,3*R**,6*S**)-2,6-Di-2-furyl-3,4,5-trimethyl-1,2,5,6-tetrahydropyridine (7)**
A mixture of **6a** (2.5 g, 9.73 mmol), anhyd *p*-TsOH (1.0 g, 5.8 mmol) and anhyd oxalic acid (8.76 g, 0.10 mol) was heated at 160–165 °C for 30 min. Then the mixture was cooled, dissolved in H_2O (150 mL), neutralized with aq 25% NH_3 soln, and extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with 10% aq NH_3 soln (2 × 70 mL), dried ($MgSO_4$), and concentrated. The residue, a deep-brown oil, was purified by column chromatography (alumina, hexane, then Et_2O) to give **7** as pale-yellow viscous oil; yield: 40%; R_f = 0.72 (hexane–EtOAc, 1:2).

IR: 3546 (NH), 1633 cm^{-1} (C=C).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.97 (d, $J_{Me,5}$ = 6.8 Hz, 3 H, 5-CH_3), 1.41 (d, $^4J_{5,Me}$ = 1.0 Hz, 3 H, 4-CH_3), 1.70 (d, $^4J_{2,Me}$ = 1.0 Hz, 3 H, 3-CH_3), 1.95 (dq, $J_{Me,5}$ = 6.8 Hz, $J_{5,6}$ = 9.5 Hz, 1 H, H5), 2.58 (br t, 1 H, NH), 3.65 (d, $J_{5,6}$ = 9.5 Hz, 1 H, H6), 4.56 (br s, 1 H, H2), 6.16 (dd, $J_{\alpha,\beta'}$ = 0.7 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ′*), 6.20 (br d, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ′), 6.25 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ), 6.27 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ*), 7.29 (dd, $J_{\beta',\alpha}$ = 0.7 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα*), 7.31 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα).

MS (EI, 70 eV): *m*/*z* (%) = 257 (6) $[M]^+$, 242 (7), 176 (5), 162 (100), 147 (64), 133 (11), 119 (26), 91 (10).

Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.99; H, 7.61; N, 5.40.

2,6-Di-2-furyl-3,4,5-trimethylpyridine (8)
Sulfur powder (1.2 g, 36.3 mmol) was added to a soln of **6a** (1.0 g, 3.70 mmol) in DMF (25 mL). The resultant mixture was refluxed for 8 h (TLC monitoring). Then the mixture was cooled, poured into H_2O (250 mL), and extracted with EtOAc (4 × 80 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and purified by column chromatography (alumina, EtOAc–hexane, 1:10) to give **8** as yellow needles; yield: 0.68 g (74%); mp 120 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 3 H, 4-CH_3), 2.47 (s, 6 H, 3-CH_3, 5-CH_3), 6.51 (dd, $J_{\alpha,\beta}$ = 1.7 Hz, $J_{\beta',\beta}$ = 3.3 Hz, 2 H, Hβ), 6.83 (dd, $J_{\alpha,\beta'}$ = 0.8 Hz, $J_{\beta',\beta}$ = 3.3 Hz, 2 H, Hβ′), 7.55 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.7 Hz, 2 H, Hα).

MS (EI, 70 eV): *m*/*z* (%) = 253 (100) $[M]^+$, 224 (40), 198 (25), 181 (20), 167 (3), 127 (4), 115 (9), 91 (5), 77 (7).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.80; H, 6.08; N, 5.69.

Adducts 9a–h,k,l, 9i,j, 9i′,j′, and 10; Typical Procedure
A mixture of **2a–l** or **4** (10 mmol) in benzene (25 mL), acryloyl chloride (1.3 mL, 15 mmol), and Et_3N (2.5 mL, 20 mmol) was refluxed for 6 h (TLC monitoring). The mixture was then poured into H_2O (100 mL) and aq 5% HCl soln was added until pH ~6 and it was extracted with EtOAc (3 × 80 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give crude products. Further crystallization (hexane–EtOAc) gave **9a–h**,**k**,**l** and mixtures of regioisomers **9i/9i′** and **9j/9j′** as white needles. The mixtures of regioisomers **9i/9i′** and **9j/9j′** were separated using column chromatography (alumina, hexane–EtOAc, 5:1) or fractional crystallization (hexane–EtOAc). For adducts **9i** and **9i′** monocrystals were obtained by the slow crystallization (Et_2O–heptane–EtOAc).

(1*R,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-4-(2-Furyl)-1-methyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9a)**
Yield: 67%; mp 146 °C.

IR: 1729 (C=O), 1696 cm^{-1} (N–C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.14 (d, $J_{1,1\text{-}CH3}$ = 7.0 Hz, 3 H, 1-CH_3), 1.62 (dd, $J_{7endo,6a}$ = 8.8 Hz, $J_{7endo,7exo}$ = 11.9 Hz, 1 H, $H7_{endo}$), 2.21 (ddd, $J_{7exo,6a}$ = 3.5 Hz, $J_{7exo,8}$ = 4.5 Hz, $J_{7exo,7endo}$ = 11.9 Hz, 1 H, $H7_{exo}$), 2.54 (dd, $J_{6a,7exo}$ = 3.5 Hz, $J_{6a,7endo}$ = 8.8 Hz, 1 H, H6a), 2.90 (dd, $J_{3A,4}$ = 5.7 Hz, $^2J_{3,3}$ = 17.0 Hz, 1 H, $H3_A$), 2.93 (dd, $J_{3B,4}$ = 2.6 Hz, $^2J_{3,3}$ = 17.0 Hz, 1 H, $H3_B$), 2.97 (dq, $J_{1,10b}$ = 12.0 Hz, $J_{1,1\text{-}CH3}$ = 7.0 Hz, 1 H, H1), 4.34 (d, $J_{10b,1}$ = 12.0 Hz, 1 H, H10b), 5.11 (dd, $J_{8,9}$ = 0.8 Hz, $J_{8,7exo}$ = 4.5 Hz, 1 H, H8), 5.34 (dd, $J_{4,3B}$ = 2.6 Hz, $J_{4,3A}$ = 5.7 Hz, 1 H, H4), 6.22 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.24 (dd, $J_{3',5'}$ = 0.7 Hz, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 6.38 (br s, 2 H, H10, H9), 7.25 (dd, $J_{5',3'}$ = 0.7 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 208.1 (C_2), 173.6 (C_6), 152.4 (d, $C_{2'}$), 142.2 ($C_{5'}$), 136.8 and 132.9 (C_9, C_{10}), 110.4 and 107.5 ($C_{3'}$, $C_{4'}$), 90.6 (C_{10a}), 78.8 (C_8), 59.3 (C_{6a}), 47.9, 46.2, 44.5 (C_1, C_4, C_{10b}), 41.8 (C_3), 28.4 (C_7), 10.2 (1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 299 (10) $[M]^+$, 271 (3), 228 (11), 200 (2), 190 (8), 177 (8), 162 (23), 148 (11), 135 (23), 121 (12), 108 (43), 94 (74), 79 (36), 66 (54), 65 (50), 55 (100), 39 (78).

Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.72; N, 4.68. Found: C, 68.32; H, 5.62; N, 4.58.

(1*R,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-1-Ethyl-4-(2-furyl)-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9b)**
Yield: 63%; mp 169 °C.

IR: 1725 (C=O), 1691 cm^{-1} (N–C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, $J_{CH2,Me}$ = 7.5 Hz, 3 H, CH_2CH_3), 1.58 (m, $J_{CH2,Me}$ = 7.5 Hz, $^2J_{CH2}$ = 14.4 Hz, $J_{1,CH2A}$ = 5.6 Hz, $J_{1,CH2B}$ = 3.9 Hz, 2 H, CH_2CH_3), 1.62 (dd, $J_{7endo,6a}$ = 8.9 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, H7$_{endo}$), 2.21 (ddd, $J_{7exo,6a}$ = 3.8 Hz, $J_{7exo,8}$ = 4.5 Hz, $J_{7exo,7endo}$ = 11.8 Hz, 1 H, H7$_{exo}$), 2.55 (dd, $J_{6a,7exo}$ = 3.8 Hz, $J_{6a,7endo}$ = 8.9 Hz, 1 H, H6a), 2.90 (dd, $J_{3B,4}$ = 2.1 Hz, $^2J_{3,3}$ = 16.9 Hz, 1 H, H3$_B$), 2.98 (dd, $J_{3A,4}$ = 6.1 Hz, $^2J_{3,3}$ = 16.9 Hz, 1 H, H3$_A$), 2.89 (ddd, $J_{1,10b}$ = 12.1 Hz, $J_{1,CH2A}$ = 5.6 Hz, $J_{1,CH2B}$ = 3.9 Hz, 1 H, H1), 4.60 (d, $J_{10b,1}$ = 12.1 Hz, 1 H, H10b), 5.12 (br d, $J_{8,7exo}$ = 4.5 Hz, 1 H, H8), 5.33 (dd, $J_{4,3B}$ = 2.1 Hz, $J_{4,3A}$ = 6.1 Hz, 1 H, H4), 6.23 (s, 2 H, H3′, H4′), 6.41 (br s, 2 H, H9, H10), 7.26 (s, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.9 (C_2), 173.6 (C_6), 152.5 ($C_{2'}$), 142.2 ($C_{5'}$), 136.9 and 132.6 (C_9, C_{10}), 110.3 and 107.4 ($C_{3'}$, $C_{4'}$), 90.5 (C_{10a}), 78.7 (C_8), 56.4 (C_{6a}), 49.7, 48.0, 46.3 (C_{10b}, C_1, C_4), 43.0 (C_3), 28.4 (C_7), 18.3 (CH_2CH_3), 10.3 (CH_2CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 313 (7) $[M]^+$, 284 (2), 242 (11), 190 (3), 174 (5), 163 (10), 162 (16), 148 (7), 135 (10), 122 (32), 107 (18), 94 (63), 77 (20), 66 (40), 65 (34), 55 (100), 39 (55).

Anal. Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.89; H, 6.23; N, 4.56.

(1*R,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-4-(2-Furyl)-1-propyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9c)**
Yield: 45%; mp 183 °C.

IR: 1718 (C=O), 1692 cm^{-1} (N–C=O).

^1H NMR (600 MHz, $CDCl_3$): δ = 0.86 (t, $J_{CH2,Me}$ = 7.3 Hz, 3 H, CH_2CH_3), 1.26 (m, 1 H, $CH_AH_BCH_3$), 1.42 (m, 1 H, $CH_AH_BCH_3$), 1.53 (m, 1 H, $CH_AH_BCH_2CH_3$), 1.59 (dd, $J_{7endo,6a}$ = 8.7 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, H7$_{endo}$), 1.73 (m, 1 H, $CH_AH_BCH_2CH_3$), 2.19 (ddd, $J_{7exo,6a}$ = 3.2 Hz, $J_{7exo,8}$ = 4.4 Hz, $J_{7exo,7endo}$ = 11.8 Hz, 1 H, H7$_{exo}$), 2.53 (dd, $J_{6a,7exo}$ = 3.2 Hz, $J_{6a,7endo}$ = 8.7 Hz, 1 H, H6a), 2.87 (m, 1 H, H1), 2.89 (dd, $J_{3B,4}$ = 6.0 Hz, $^2J_{3,3}$ = 16.7 Hz, 1 H, H3$_B$), 2.96 (dd, $J_{3A,4}$ = 2.0 Hz, $^2J_{3,3}$ = 16.7 Hz, 1 H, H3$_A$), 4.54 (d, $J_{10b,1}$ = 12.1 Hz, 1 H, H10b), 5.10 (d, $J_{8,7exo}$ = 4.4 Hz, 1 H, H8), 5.31 (dd, $J_{4,3A}$ = 2.0 Hz, $J_{4,3B}$ = 6.0 Hz, 1 H, H4), 6.21 (s, 2 H, H3′, H4′), 6.38 (br s, 2 H, H9, H10), 7.24 (s, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.9 (C_2), 173.6 (C_6), 152.5 ($C_{2'}$), 142.2 ($C_{5'}$), 136.9 and 132.6 (C_9, C_{10}), 110.3 and 107.4 ($C_{3'}$, $C_{4'}$), 90.5 (C_{10a}), 78.7 (C_8), 57.1 (C_{6a}), 49.0, 48.0, 46.3 (C_{10b}, C_1, C_4), 42.7 (C_3), 28.4 and 27.6 (C_7, $CH_2CH_2CH_3$), 19.5 ($CH_2CH_2CH_3$), 14.4 ($CH_2CH_2CH_3$).

MS (EI, 70 eV): *m*/*z* (%) = 327 (10) $[M]^+$, 299 (1), 256 (11), 190 (2), 176 (3), 163 (13), 148 (7), 136 (16), 107 (19), 94 (61), 77 (18), 66 (36), 55 (100).

Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.81; H, 6.67; N, 4.38.

(1*R,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-4-(2-Furyl)-1-isopropyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9d)**
Yield: 55%; mp 226 °C.

IR: 1720 (C=O), 1689 cm^{-1} (N–C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.98 [d, $J_{CH,Me(A)}$ = 7.0 Hz, 3 H, $CH(CH_3)_A(CH_3)_B$], 1.19 [d, $J_{CH,Me(B)}$ = 7.0 Hz, 3 H, $CH(CH_3)_A(CH_3)_B$], 1.61 (dd, $J_{7endo,6a}$ = 9.0 Hz, $J_{7endo,7exo}$ = 11.6 Hz, 1 H, H7$_{endo}$), 2.05 [m, 1 H, $CH(CH_3)_2$], 2.20 (dt, $J_{7exo,6a}$ = $J_{7exo,8}$ = 3.5 Hz, $J_{7exo,7endo}$ = 11.6 Hz, 1 H, H7$_{exo}$), 2.53 (dd, $J_{6a,7exo}$ = 3.5 Hz, $J_{6a,7endo}$ = 9.0 Hz, 1 H, H6a), 2.81 (dd, $J_{1,1'}$ = 1.9 Hz, $J_{1,10b}$ = 11.9 Hz, 1 H, H1), 2.86 (dd, $J_{3A,4}$ = 2.4 Hz, $^2J_{3,3}$ = 16.0 Hz, 1 H, H3$_A$), 2.92 (dd, $J_{3B,4}$ = 5.7 Hz, $^2J_{3,3}$ = 16.0 Hz, 1 H, H3$_B$), 4.64 (d, $J_{10b,1}$ = 11.9 Hz, 1 H, H10b), 5.11 (dd, $J_{8,7exo}$ = 3.5 Hz, $J_{8,9}$ = 1.3 Hz, 1 H, H8), 5.29 (dd, $J_{4,3A}$ = 2.4 Hz, $J_{4,3B}$ = 5.7 Hz, 1 H, H4), 6.20–6.22 (m, 2 H, H3′, H4′), 6.36 (dd, $J_{9,8}$ = 1.3 Hz, $J_{9,10}$ = 5.7 Hz, 1 H, H9), 6.40 (d, $J_{9,10}$ = 5.7 Hz, 1 H, H10), 7.26 (br s, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.9 (C_2), 173.8 (C_6), 152.9 ($C_{2'}$), 142.5 ($C_{5'}$), 136.7 (C_9), 133.3 (C_{10}), 110.6 ($C_{4'}$), 107.5 ($C_{3'}$), 90.7 (C_{10a}), 79.0 (C_8), 57.1 (C_{10b}), 54.1 (C_1), 48.4 (C_{6a}), 46.8 (C_4), 44.4 (C_3), 28.7 (C_7), 27.3 [$CH(CH_3)_2$], 22.4 and 17.3 [$CH(CH_3)_2$].

MS (EI, 70 eV): *m*/*z* (%) = 327 (63) $[M]^+$, 284 (32), 272 (4), 256 (69), 207 (10), 190 (48), 174 (7), 163 (38), 162 (40), 148 (11), 136 (100), 121 (79), 94 (80), 69 (10), 55 (37).

Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.66; H, 6.78; N, 4.23.

(1*R,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-1-Allyl-4-(2-furyl)-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9e)**
Yield: 45%; mp 106 °C.

IR: 1693 (N–C=O), 1719 cm^{-1} (C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.61 (dd, $J_{7endo,6a}$ = 9.0 Hz, $J_{7endo,7exo}$ = 11.4 Hz, 1 H, H7$_{endo}$), 2.18 (ddd, $J_{7exo,6a}$ = 3.0 Hz, $J_{7exo,8}$ = 4.5 Hz, $J_{7exo,7endo}$ = 11.4 Hz, 1 H, H7$_{exo}$), 2.24 (m, 1 H, $CH_AH_BCH{=}CH_2$), 2.53 (dd, $J_{6a,7exo}$ = 3.0 Hz, $J_{6a,7endo}$ = 9.0 Hz, 1 H, H6a), 2.84 (dd, $J_{3A,4}$ = 6.2 Hz, $^2J_{3,3}$ = 16.3 Hz, 1 H, H3$_A$), 2.87 (m, 1 H, H1), 2.97 (dd, $J_{3B,4}$ = 1.5 Hz, $^2J_{3,3}$ = 16.3 Hz, 1 H, H3$_B$), 3.99 (m, 1 H, $CH_AH_BCH{=}CH_2$), 4.59 (d, $J_{10b,1}$ = 12.0 Hz, 1 H, H10b), 5.09–5.13 (m, 2 H, $CH{=}CH_2$), 5.13 (br d, $J_{8,7exo}$ = 4.5 Hz, 1 H, H8), 5.32 (br d, $J_{4,3B}$ = 1.5 Hz, $J_{4,3A}$ = 6.2 Hz, 1 H, H4), 5.69 (ddt, $J_{2',1'}$ = 5.4 Hz, $J_{2',3'cis}$ = 9.4 Hz, $J_{2',3'trans}$ = 16.8 Hz, 1 H, $CH{=}CH_2$), 6.22 (br s, 2 H, H3′, H4′), 6.39 (dd, $J_{10,9}$ = 6.0 Hz, $J_{8,9}$ = 1.3 Hz, 1 H, H9), 6.40 (d, $J_{9,10}$ = 6.0 Hz, 1 H, H10), 7.25 (br s, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.1 (C_2), 173.5 (C_6), 152.4 ($C_{2'}$), 142.2 ($C_{5'}$), 136.6, 133.9, 132.8 (C_9, C_{10}, $CH_2CH{=}CH_2$), 118.5 ($CH_2CH{=}CH_2$), 110.3 and 107.4 ($C_{3'}$, $C_{4'}$), 90.5 (C_{10a}), 78.6 (C_8), 56.2 (C_{6a}), 48.6, 47.9, 46.3 (C_1, C_4, C_{10b}), 43.0 (C_3), 29.7 ($CH_2CH{=}CH_2$), 28.3 (C_7).

MS (EI, 70 eV): *m*/*z* (%) = 325 (3) $[M]^+$, 283 (3), 270 (1), 254 (5), 213 (1), 190 (3), 174 (3), 162 (7), 148 (3), 134 (13), 121 (24), 107 (7), 94 (58), 81 (15), 77 (17), 66 (44), 55 (100), 39 (55).

Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.24; H, 5.98; N, 4.32.

(1*R,3*S**,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-4-(2-Furyl)-1,3-diphenyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9f)**
Yield: 45%; mp 116 °C.

IR: 1699 cm^{-1} (br, N–C=O, C=O).

^1H NMR (600 MHz, $CDCl_3$): δ = 1.54 (dd, $J_{7,6a}$ = 8.8 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, H7$_{endo}$), 2.21 (ddd, $J_{7exo,6a}$ = 3.4 Hz, $J_{8,7exo}$ = 4.5 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, H7$_{exo}$), 2.45 (dd, $J_{7endo,6a}$ = 8.8 Hz, $J_{6a,7exo}$ = 3.4 Hz, 1 H, H6a), 4.18 (d, $J_{10b,1}$ = 12.2 Hz, 1 H, H10b), 4.40 (br s, 1 H, H3), 4.45 (d, $J_{10b,1}$ = 12.2 Hz, 1 H, H1), 5.05 (dd, $J_{8,9}$ = 1.6 Hz, $J_{8,7}$ = 4.5 Hz, 1 H, H8), 5.35 (d, $J_{9,10}$ = 5.8 Hz, 1 H, H10), 5.93 (br s, 1 H, H4), 6.00 (dd, $J_{8,9}$ = 1.6 Hz, $J_{9,10}$ = 5.8 Hz, 1 H, H9), 6.29 (dd, $J_{3',4'}$ = 3.2 Hz, $J_{5',4'}$ = 1.8 Hz,

1 H, H4′), 6.45 (br dd, $J_{3',4'}$ = 3.2 Hz, $J_{5',3'}$ = 0.7 Hz, 1 H, H3′), 6.75 (dd, $J_{ortho,para}$ = 0.9 Hz, $J_{ortho,meta}$ = 7.5 Hz, 2 H, H_{ortho} Ph), 7.13–7.18 (m, 3 H, H_{Ph}), 7.33 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{3',5'}$ = 0.7 Hz, 1 H, H5′), 7.41 (br t, $J_{para,meta}$ = 7.5 Hz, 1 H, H_{para} Ph), 7.48 (br t, J = 7.5 Hz, 2 H, H_{Ph}), 7.53 (br d, J = 7.5 Hz, 2 H, H_{Ph}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 205.2 (C_2), 174.1 (C_6), 151.9 ($C_{2'}$), 142.6 ($C_{5'}$), 135.3 and 132.1 (C_9, C_{10}), 129. 6 and 129.5 (4 C, $C_{ortho\text{-}Ph}$), 128.4 and 127.1 (4 C, $C_{meta\text{-}Ph}$), 128.2 and 127.6 (2 C, $C_{para\text{-}Ph}$), 110.4 and 107.8 ($C_{3'}$, $C_{4'}$), 90.5 (C_{10a}), 78.6 (C_8), 56.4, 49.7, 48.0, 46.3, 43.0 (C_{10b}, C_1, C_3, C_4, C_{6a}), 28.4 (C_7).

MS (EI, 70 eV): *m*/*z* (%) = 437 (44) [M]$^+$, 409 (7), 366 (16), 240 (11), 239 (29), 238 (7), 224 (14), 198 (10), 197 (19), 184 (10), 174 (12), 171 (28), 170 (100), 169 (49), 157 (13), 147 (19), 142 (61), 128 (10), 115 (23), 91 (11), 90 (12), 81 (12), 59 (16), 58 (11), 55 (39).

Anal. Calcd for $C_{28}H_{23}NO_4$: C, 76.87; N, 3.20; H, 5.30. Found: C, 76.96; N, 3.23; H, 5.31.

(1*R,3*S**,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-4-(2-Furyl)-1,3-dimethyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9g)**
Yield: 82%; mp 116 °C.

IR: 1692 cm^{-1} (br, C=O, N–C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13 (d, $J_{3,3\text{-}CH3}$ = 6.7 Hz, 3 H, 3-CH_3), 1.36 (d, $J_{1,1\text{-}CH3}$ = 7.6 Hz, 3 H, 1-CH_3), 1.63 (dd, $J_{7endo,6a}$ = 8.9 Hz, $J_{7endo,7exo}$ = 11.7 Hz, 1 H, H7$_{endo}$), 2.24 (ddd, $J_{7exo,6a}$ = 3.8 Hz, $J_{7exo,8}$ = 4.3 Hz, $J_{7exo,7endo}$ = 11.7 Hz, 1 H, H7$_{exo}$), 2.55 (dd, $J_{6a,7exo}$ = 3.8 Hz, $J_{6a,7endo}$ = 8.9 Hz, 1 H, H6a), 2.93–3.09 (m, 2 H, H3, H1), 4.28 (d, $J_{10b,1}$ = 12.2 Hz, 1 H, H10b), 5.03 (br s, 1 H, H4), 5.14 (d, $J_{8,7exo}$ = 4.3 Hz, 1 H, H8), 6.22 (br d, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.26 (br d, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 6.39 (br s, 2 H, H10, H9), 7.25 (dd, $J_{5',3'}$ = 0.6 Hz, $J_{5',4'}$ = 1.6 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 210.3 (C_2), 174.3 (C_6), 152.4 ($C_{2'}$), 141.9 ($C_{5'}$), 136.6 and 132.8 (C_9, C_{10}), 110.2 and 107.3 ($C_{3'}$, $C_{4'}$), 90.9 (C_{10a}), 78.7 (C_8), 59.0 (C_{6a}), 52.6, 47.8, 46.3, 43.8 (C_{10b}, C_1, C_3, C_4), 28.4 (C_7), 17.3 and 10.1 (1-CH_3, 3-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 313 (9) [M]$^+$, 298 (3), 285 (1), 242 (11), 214 (2), 177 (8), 162 (46), 148 (9), 135 (8), 122 (10), 108 (65), 94 (16), 79 (67), 66 (31), 55 (100), 39 (37).

Anal. Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 69.34; H, 6.25; N, 4.51.

Diethyl 2,2′-(1*R,3*S**,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-2,2′-[4-(2-Furyl)-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-1,3-diyl]diacetate (9h)**
Yield: 86%; mp 132–133 °C.

IR: 1694 (N–C=O), 1730 cm^{-1} (C=O, CO_2Et).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, $J_{CH2,Me}$ = 7.4 Hz, 3 H, A-CH_2CH_3), 1.27 (t, $J_{CH2,Me}$ = 7.4 Hz, 3 H, B-CH_2CH_3), 1.61 (dd, $J_{7endo,6a}$ = 8.9 Hz, $J_{7endo,7exo}$ = 12.0 Hz, 1 H, H7$_{endo}$), 2.23 (ddd, $J_{7exo,6a}$ = 3.5 Hz, $J_{7exo,8}$ = 4.6 Hz, $J_{7exo,7endo}$ = 12.0 Hz, 1 H, H7$_{exo}$), 2.47 (dd, $^2J_{CH2}$ = 17.7 Hz, $J_{1,CH2A}$ = 5.4 Hz, 1 H, 1-CH_AH$_B$$CO_2$Et), 2.53 (dd, $J_{6a,7exo}$ = 3.5 Hz, $J_{6a,7endo}$ = 8.9 Hz, 1 H, H6a), 2.70 (dd, $^2J_{CH2}$ = 16.8 Hz, $J_{3,CH2A}$ = 8.7 Hz, 1 H, 3-CH_AH$_B$$CO_2$Et), 2.77 (dd, $^2J_{CH2}$ = 16.8 Hz, $J_{3,CH2B}$ = 4.7 Hz, 1 H, 3-CH$_A$$H_B$$CO_2$Et), 2.95 (dd, $^2J_{CH2}$ = 17.7 Hz, $J_{1,CH2B}$ = 4.0 Hz, 1 H, 1-CH$_A$$H_B$$CO_2$Et), 3.23 (ddd, $J_{1,CH2B}$ = 4.0 Hz, $J_{1,CH2A}$ = 5.4 Hz, $J_{10b,1}$ = 12.0 Hz, 1 H, H1), 3.51 (ddd, $J_{3,CH2B}$ = 4.7 Hz, $J_{3,CH2A}$ = 8.7 Hz, $J_{3,4}$ = 2.8 Hz, 1 H, H3), 4.12 (q, $J_{CH2,Me}$ = 7.4 Hz, 2 H, $CO_2CH_2CH_3$), 4.21–4.12 (m, 2 H, $CO_2CH_2CH_3$), 4.90 (d, $J_{10b,1}$ = 12.0 Hz, 1 H, H10b), 5.12 (dd, $J_{8,9}$ = 1.3 Hz, $J_{8,7exo}$ = 4.7 Hz, 1 H, H8), 5.14 (br d, $J_{4,3}$ = 2.8 Hz, 1 H, H4), 6.24 (dd, $J_{4',5'}$ = 1.9 Hz, $J_{4',3'}$ = 3.3 Hz, 1 H, H4′), 6.29 (dd, $J_{3',5'}$ = 0.8 Hz, $J_{3',4'}$ = 3.3 Hz, 1 H, H3′), 6.30 (d, $J_{10,9}$ = 6.0 Hz, 1 H, H10), 6.41 (dd, $J_{9,8}$ = 1.7 Hz, $J_{10,9}$ = 6.0 Hz, 1 H, H9), 7.31 (br d, $J_{5',4'}$ = 1.9 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.3 (C_2), 174.0 (C_6), 171.4 and 170.5 (CO_2Et), 151.5 ($C_{2'}$), 142.4 ($C_{5'}$), 137.7 and 132.3 (C_9, C_{10}), 110.3 and 108.3 ($C_{3'}$, $C_{4'}$), 90.3 (C_{10a}), 78.9 (C_8), 61.2 and 60.9 ($CO_2CH_2CH_3$), 56.4 (C_4), 51.0, 48.4, 48.0, 45.8 (C_1, C_3, C_{6a}, C_{10b}), 34.7 and 29.5 (CH_2CO_2Et), 28.4 (C_7), 14.19 and 14.18 ($CO_2CH_2CH_3$).

MS (EI, 70 eV): *m*/*z* (%) = 457 (15) [M]$^+$, 412 (11), 386 (23), 371 (25), 370 (100), 356 (12), 352 (17), 344 (20), 340 (11), 324 (20), 316 (15), 312 (37), 296 (10), 282 (11), 270 (40), 266 (15), 228 (17), 194 (60), 190 (34), 180 (23), 179 (15), 174 (13), 162 (18), 149 (25), 148 (17), 122 (31), 107 (61), 96 (20), 95 (15), 81 (12), 79 (14), 65 (11), 55 (66), 43 (38).

Anal. Calcd for $C_{24}H_{27}NO_8$: C, 63.01; H, 5.95; N, 3.06. Found: C, 62.73; H, 5.72; N, 3.15.

(1*R,3*S**,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-4-(2-Furyl)-3-methyl-1-phenyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9i) and (1*S**,3*R**,4*S**,6a*S**,8*R**,10a*R**,10b*R**)-4-(2-Furyl)-1-methyl-3-phenyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9i′)**
Total yield of isomers mixture: 77%; ratio **9i/9i′** (isolated mixture) 1:4 (^{1}H NMR).

Compound 9i
Yield: 11%; mp 161–163 °C (hexane–EtOAc).

IR: 1703 cm^{-1} (br, N–C=O, C=O).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.59 (dd, $J_{7endo,6a}$ = 8.8 Hz, $J_{7endo,7exo}$ = 11.9 Hz, 1 H, H7$_{endo}$), 1.61 (d, $J_{3,3\text{-}CH3}$ = 7.7 Hz, 3 H, 3-CH_3), 2.24 (ddd, $J_{7exo,6a}$ = 3.4 Hz, $J_{7exo,8}$ = 4.6 Hz, $J_{7exo,7endo}$ = 11.9 Hz, 1 H, H7$_{exo}$), 2.52 (dd, $J_{6a,7exo}$ = 3.4 Hz, $J_{6a,7endo}$ = 8.8 Hz, 1 H, H6a), 3.26 (dq, $J_{3,4}$ = 2.0 Hz, $J_{3,3\text{-}CH3}$ = 7.7 Hz, 1 H, H3), 4.17 (d, $J_{10b,1}$ = 12.3 Hz, 1 H, H10b), 4.82 (d, $J_{10b,1}$ = 12.3 Hz, 1 H, H1), 5.11 (dd, $J_{8,9}$ = 1.7 Hz, $J_{8,7exo}$ = 4.6 Hz, 1 H, H8), 5.19 (d, $J_{4,3}$ = 2.0 Hz, 1 H, H4), 5.52 (d, $J_{9,10}$ = 5.8 Hz, 1 H, H10), 6.08 (dd, $J_{9,10}$ = 5.8 Hz, $J_{9,8}$ = 1.7 Hz, 1 H, H9), 6.31 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.3 Hz, 1 H, H4′), 6.42 (dd, $J_{3',5'}$ = 0.9 Hz, $J_{3',4'}$ = 3.3 Hz, 1 H, H3′), 7.12–7.14 (m, 2 H, H_{ortho} Ph), 7.30–7.35 (m, 3 H, H_{para}, H_{meta} Ph), 7.34 (dd, $J_{5',3'}$ = 0.9 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 209.0 (C_2), 174.7 (C_6), 152.4 (d, $C_{2'}$), 142.3 ($C_{5'}$), 135.4 and 132.2 (C_9, C_{10}), 134.2 ($C_{ipso\text{-}Ph}$), 130.0 (2 C, $C_{meta\text{-}Ph}$), 128.6 (2 C, $C_{ortho\text{-}Ph}$), 127.8 ($C_{para\text{-}Ph}$), 110.4 and 107.5 ($C_{3'}$, $C_{4'}$), 90.9 (C_{10a}), 78.8 (C_8), 59.5, 55.7, 52.7, 47.9, 47.4 (C_1, C_3, C_4, C_{6a}, C_{10b}), 28.6 (C_7), 17.2 (3-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 375 (88) [M]$^+$, 360 (2), 347 (6), 320 (4), 304 (38), 239 (29), 238 (11), 177 (12), 174 (25), 171 (13), 170 (84), 169 (12), 162 (21), 148 (29), 141 (24), 135 (11), 118 (31), 115 (12), 109 (10), 108 (100), 79 (12), 55 (37).

Anal. Calcd for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73. Found: C, 73.30; H, 5.53; N, 3.77.

Compound 9i′
Yield: 27%; mp 187–188 °C.

IR: 1702 cm^{-1} (N–C=O, C=O).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.11 (dd, $^4J_{4,1\text{-}CH3}$ = 0.3 Hz, $J_{1,1\text{-}CH3}$ = 7.0 Hz, 3 H, 1-CH_3), 1.64 (dd, $J_{7endo,6a}$ = 8.7 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, H7$_{endo}$), 2.27 (ddd, $J_{7exo,6a}$ = 3.7 Hz, $J_{7exo,8}$ = 4.6 Hz, $J_{7exo,7endo}$ = 11.8 Hz, 1 H, H7$_{exo}$), 2.54 (dd, $J_{6a,7exo}$ = 3.7 Hz, $J_{6a,7endo}$ = 8.7 Hz, 1 H, H6a), 3.04 (dq, $J_{1,10b}$ = 12.1 Hz, $J_{1,1\text{-}CH3}$ = 7.0 Hz, 1 H, H1), 4.07 ($J_{10b,1}$ = 12.1 Hz, 1 H, H10b), 4.28 (d, $J_{4,3}$ = 0.8 Hz, 1 H, H3), 5.14 (dd, $J_{8,9}$ = 1.4 Hz, $J_{8,7exo}$ = 4.5

Hz, 1 H, H8), 5.84 (d, $J_{3,4}$ = 0.8 Hz, 1 H, H4), 6.27 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.28 (dd, $J_{9,10}$ = 6.0 Hz, 1 H, H10), 6.33 (br d, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 6.38 (dd, $J_{8,9}$ = 1.4 Hz, $J_{9,10}$ = 6.0 Hz, 1 H, H9), 7.31 (dd, $J_{5',3'}$ = 0.8 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 7.35 (m, 1 H, H_{para} Ph), 7.39–7.43 (m, 4 H, H_{ortho}, H_{meta} Ph).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.4 (C_2), 174.0 (C_6), 152.0 (d, $C_{2'}$), 142.5 ($C_{5'}$), 136.9 and 132.7 (C_9, C_{10}), 134.4 ($C_{ipso\text{-}Ph}$), 129.4 (2 C, $C_{meta\text{-}Ph}$), 126.8 (2 C, $C_{ortho\text{-}Ph}$), 127.9 ($C_{para\text{-}Ph}$), 110.4 and 107.8 ($C_{3'}$, $C_{4'}$), 90.7 (C_{10a}), 78.8 (C_8), 58.3 and 55.9 (C_1, C_4), 49.4, 47.9, 44.3 (C_3, C_{6a}, C_{10b}), 28.5 (C_7), 11.5 (1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 375 (19) $[M]^+$, 347 (5), 304 (4), 294 (2), 239 (6), 177 (5), 174 (16), 170 (62), 169 (30), 148 (24), 141 (83), 135 (19), 118 (38), 115 (57), 108 (100), 90 (53), 79 (76), 77 (51), 66 (62).

Anal. Calcd for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73. Found: C, 73.51; H, 5.58; N, 3.70.

(1*R,3*S**,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-3-Ethyl-4-(2-furyl)-1-phenyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9j) and (1*S**,3*R**,4*S**,6a*S**,8*R**,10a*R**,10b*R**)-1-Ethyl-4-(2-furyl)-3-phenyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9j′)**

Total yield of isomers mixture: 78%; ratio **9j/9j′** (isolated mixture) 1:1.3 (^{1}H NMR).

Compound 9j

Yield: 35%; mp 161–163 °C.

IR: 1693 cm^{-1} (br, C=O, N–C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (d, $J_{3,3\text{-}CH3}$ = 7.4 Hz, 3 H, 3-CH_2CH_3), 1.57 (dd, $J_{7endo,6a}$ = 8.8 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, $H7_{endo}$), 1.90–2.10 (m, 2 H, 3-CH_2CH_3), 2.22 (ddd, $J_{7exo,6a}$ = 3.3 Hz, $J_{7exo,8}$ = 4.4 Hz, $J_{7exo,7endo}$ = 11.8 Hz, 1 H, $H7_{exo}$), 2.50 (dd, $J_{6a,7exo}$ = 3.3 Hz, $J_{6a,7endo}$ = 8.8 Hz, 1 H, H6a), 2.97 (m, 1 H, H3), 4.12 (d, $J_{10b,1}$ = 12.4 Hz, 1 H, H10b), 4.82 (d, $J_{10b,1}$ = 12.4 Hz, 1 H, H1), 5.09 (dd, $J_{8,9}$ = 1.3 Hz, $J_{8,7exo}$ = 4.4 Hz, 1 H, H8), 5.19 (br d, $J_{4,3}$ = 1.0 Hz, 1 H, H4), 5.50 (d, $J_{9,10}$ = 5.8 Hz, 1 H, H10), 6.07 (dd, $J_{9,10}$ = 5.8 Hz, $J_{9,8}$ = 1.3 Hz, 1 H, H9), 6.28 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.40 (br d, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 7.08–7.11 (m, 2 H, H_{ortho} Ph), 7.27–7.32 (m, 4 H, H_{para}, H_{meta} Ph, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 208.4 (C_2), 174.7 (C_6), 152.6 (d, $C_{2'}$), 142.3 ($C_{5'}$), 135.4 and 132.2 (C_9, C_{10}), 134.5 ($C_{ipso\text{-}Ph}$), 130.0 (2 C, $C_{meta\text{-}Ph}$), 128.6 (2 C, $C_{ortho\text{-}Ph}$), 127.8 ($C_{para\text{-}Ph}$), 110.4 and 107.4 ($C_{3'}$, $C_{4'}$), 91.0 (C_{10a}), 78.8 (C_8), 59.2 (C_4), 55.5, 54.8, 50.2, 47.9 (C_1, C_3, C_{6a}, C_{10b}), 28.6 (C_7), 24.7 (3-CH_2CH_3), 12.3 (3-CH_2CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 389 (74) $[M]^+$, 360 (9), 318 (15), 298 (3), 266 (4), 244 (6), 239 (18), 224 (9), 191 (6), 174 (14), 170 (100), 169 (23), 148 (23), 141 (31), 122 (64), 107 (16), 91 (15), 77 (11), 55 (43).

Anal. Calcd for $C_{24}H_{23}NO_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 73.93; H, 6.15; N, 3.71.

Compound 9j′

Yield: 31%.

IR: 1693 (N–C=O), 1718 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.63 (d, $J_{1,1\text{-}CH3}$ = 7.5 Hz, 3 H, 1-CH_2CH_3), 1.46 (m, 1 H, 1-$CH_AH_BCH_3$), 1.62 (dd, $J_{7endo,6a}$ = 8.9 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, $H7_{endo}$), 1.90 (m, 1 H, 1-$CH_AH_BCH_3$), 2.23 (dt, $J_{7exo,6a}$ = $J_{7exo,8}$ = 4.0 Hz, $J_{7exo,7endo}$ = 11.8 Hz, 1 H, $H7_{exo}$), 2.53 (dd, $J_{6a,7exo}$ = 4.0 Hz, $J_{6a,7endo}$ = 8.9 Hz, 1 H, H6a), 3.01 (br dt, $J_{1,CH2}$ ~ 3.8 Hz, $J_{1,10b}$ = 11.4 Hz, 1 H, H1), 4.25 (d, $J_{3,4}$ = 0.5 Hz, 1 H, H3), 4.27 (d, $J_{10b,1}$ = 11.4 Hz, 1 H, H10b), 5.12 (dd, $J_{8,9}$ = 1.1 Hz, $J_{8,7exo}$ = 4.0 Hz, 1 H, H8), 5.81 (br d, $J_{4,3}$ = 0.5 Hz, 1 H, H4), 6.26 (dd, $J_{4',5'}$ = 1.5 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 7.27 (d, $J_{9,10}$ = 5.8 Hz, 1 H, H10), 6.32 (br d, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 6.37 (dd, $J_{9,10}$ = 5.8 Hz, $J_{9,8}$ = 1.1 Hz, 1 H, H9), 7.42 (br d, $J_{5',4'}$ = 1.5 Hz, 1 H, H5′), 7.30–7.44 (m, 5 H, H_{Ph}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 206.6 (C_2), 174.0 (C_6), 154.0 (d, $C_{2'}$), 142.5 ($C_{5'}$), 136.9 and 132.5 (C_9, C_{10}), 133.3 ($C_{ipso\text{-}Ph}$), 129.3 (2 C, $C_{meta\text{-}Ph}$), 126.9 (2 C, $C_{ortho\text{-}Ph}$), 127.9 ($C_{para\text{-}Ph}$), 110.4 and 107.8 ($C_{3'}$, $C_{4'}$), 90.6 (C_{10a}), 78.7 (C_8), 56.2, 55.2, 49.7, 48.9, 48.0 (C_1, C_3, C_4, C_{6a}, C_{10b}), 28.5 (C_7), 18.4 (1-CH_2CH_3), 9.9 (1-CH_2CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 389 (86) $[M]^+$, 360 (9), 318 (30), 298 (16), 266 (4), 244 (25), 239 (59), 238 (29), 224 (7), 211 (19), 191 (3), 174 (31), 170 (75), 169 (30), 149 (18), 148 (66), 141 (59), 122 (100), 118 (24), 115 (30), 107 (32), 91 (21), 77 (14), 55 (50).

Anal. Calcd for $C_{24}H_{23}NO_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 73.83; H, 6.17; N, 3.51.

(1*R,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-1,8-Dimethyl-4-(5-methyl-2-furyl)-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9k)**

Yield: 57%; mp 206–207 °C.

IR: 1701 cm^{-1} (br, C=O, N–C=O).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.16 (d, $J_{1,1\text{-}CH3}$ = 6.8 Hz, 3 H, 1-CH_3), 1.69 (s, 3 H, 8-CH_3), 1.73 (dd, $J_{7endo,6a}$ = 8.7 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, $H7_{endo}$), 1.99 (dd, $J_{7exo,6a}$ = 3.5 Hz, $J_{7exo,7endo}$ = 11.8 Hz, 1 H, $H7_{exo}$), 2.21 (br s, 3 H, 5-CH_3′), 2.67 (dd, $J_{6a,7exo}$ = 3.5 Hz, $J_{6a,7endo}$ = 8.7 Hz, 1 H, H6a), 2.93 (dd, $^2J_{3,3}$ = 17.1 Hz, $J_{3B,4}$ = 6.2 Hz, 1 H, $H3_B$), 2.95 (dq, $J_{1,1\text{-}CH3}$ = 6.8 Hz, $J_{10b,1}$ = 12.0 Hz, 1 H, H1), 3.02 (dd, $^2J_{3,3}$ = 17.1 Hz, $J_{3A,4}$ = 2.0 Hz, 1 H, $H3_A$), 4.28 (d, $J_{10b,1}$ = 12.0 Hz, 1 H, H10b), 5.32 (br dd, $J_{3B,4}$ = 6.2 Hz, $J_{3A,4}$ = 2.0 Hz, 1 H, H4), 5.83 (dq, $^4J_{5'\text{-}CH3,4'}$ = 0.7 Hz, $J_{3',4'}$ = 3.0 Hz, 1 H, H4′), 6.12 (br d, $J_{4',3'}$ = 3.0 Hz, 1 H, H3′), 6.24 (d, $J_{10,9}$ = 5.7 Hz, 1 H, H10), 6.39 (br d, $J_{10,9}$ = 5.7 Hz, 1 H, H9).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 208.4 (C_2), 173.8 (C_6), 151.8 and 150.6 ($C_{2'}$, $C_{5'}$), 140.1 and 133.4 (C_9, C_{10}), 107.9 and 106.3 ($C_{3'}$, $C_{4'}$), 90.4 (C_{10a}), 87.1 (C_8), 59.6 (C_{6a}), 51.2 (C_4), 46.3 and 44.5 (C_1, C_{10b}), 42.1 (C_3), 34.6 (C_7), 18.9 (5-CH_3′), 13.5 and 10.2 (1-CH_3, 8-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 327 (80) $[M]^+$, 310 (2), 284 (30), 256 (66), 232 (6), 190 (9), 177 (26), 176 (52), 149 (38), 122 (100), 108 (58), 79 (18), 77 (15), 55 (32).

Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.61; H, 6.57; N, 4.38.

(1*R,3*S**,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-1,3,8-Trimethyl-4-(5-methyl-2-furyl)-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-dione (9l)**

Yield: 87%; mp 195 °C.

IR: 1714 (C=O), 1685 cm^{-1} (N–C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (d, $J_{1,1\text{-}CH3}$ = 6.7 Hz, 3 H, 1-CH_3), 1.36 (d, $J_{3,3\text{-}CH3}$ = 7.8 Hz, 3 H, 3-CH_3), 1.67 (s, 3 H, 8-CH_3), 1.71 (dd, $J_{7endo,6a}$ = 8.7, $J_{7endo,7exo}$ = 11.9 Hz, 1 H, $H7_{endo}$), 1.97 (dd, $J_{7exo,6a}$ = 3.5, $J_{7exo,7endo}$ = 11.9 Hz, 1 H, $H7_{exo}$), 2.17 (br s, 3 H, 5-CH_3′), 2.65 (dd, $J_{6a,7exo}$ = 3.5, $J_{6a,7endo}$ = 8.7 Hz, 1 H, H6a), 2.94 (dq, $J_{1,1\text{-}CH3}$ = 6.7 Hz, $J_{1,10b}$ = 12.2 Hz, 1 H, H1), 3.05 (dq, $J_{3,3\text{-}CH3}$ = 7.8 Hz, $J_{3,4}$ = 12.2 Hz, 1 H, H3), 4.21 (d, $J_{10b,1}$ = 12.2 Hz, 1 H, H10b), 4.98 (br d, $J_{4,3}$ = 2.1 Hz, 1 H, H4), 5.78 (dq, $J_{4',3'}$ = 3.0 Hz, $J_{4',Me}$ = 1.0 Hz, 1 H, H4′), 6.11 (br d, $J_{3',4'}$ = 3.0 Hz, 1 H, H3′), 6.22 (d, $J_{9,10}$ = 5.6 Hz, 1 H, H10), 6.37 (d, $J_{9,10}$ = 5.6 Hz, 1 H, H9).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 210.9 (C_2), 174.6 (C_6), 151.8 and 150.7 ($C_{2'}$, $C_{5'}$), 140.0 and 133.4 (C_9, C_{10}), 107.8 and 106.2 ($C_{3'}$, $C_{4'}$), 90.8 (C_{10a}), 87.1 (C_8), 59.2 (C_4), 52.7, 51.2, 46.7, 43.9 (C_1, C_3, C_{6a}, C_{10b}), 34.74 (C_7), 18.9 and 17.7 (8-CH_3, 5-CH_3′), 13.5 and 10.3 (1-CH_3, 3-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 341 (76) $[M]^+$, 326 (4), 298 (6), 270 (62), 246 (8), 191 (24), 176 (100), 149 (25), 122 (77), 77 (13), 55 (22).

Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.58; H, 6.88; N, 4.19.

(1*S,3*S**,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-4-(2-Furyl)-1,3-dimethyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindol-6(8*H*)-one (10)**

Maize yellow rhombuses; yield: 0.6 g (70%); mp 131–132 °C.

IR: 1680 cm^{-1} (C=C, N–C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.97 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.01 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.32 [m, 1 H, H2(e)], 1.53 (dd, $J_{7endo,6a}$ = 8.9 Hz, $J_{7,7}$ = 11.8 Hz, 1 H, $H7_{endo}$), 1.56 [ddd, $^2J_{2,2}$ = 13.8, ^3J = 9.6 Hz, ^3J = 12.0 Hz, 1 H, H2(a)], 2.13 (ddd, $J_{6a,7exo}$ = 3.6 Hz, $J_{7,7}$ = 11.8 Hz, $J_{8,7exo}$ = 4.6 Hz, 1 H, $H7_{exo}$), 2.32 (m, 1 H, H3), 2.43 (dd, $J_{6aendo,7endo}$ = 8.9 Hz, $J_{6aendo,7exo}$ = 3.6 Hz, 1 H, $H6a_{endo}$), 2.46 (m, 1 H, H1), 3.94 (d, $J_{10b,1}$ = 11.8 Hz, 1 H, H10b), 4.86 (br d, $J_{3,4}$ = 4.4 Hz, 1 H, H4), 5.06 (d, $J_{8,9}$ = 1.7 Hz, $J_{8,7exo}$ = 4.6 Hz, 1 H, H8), 6.24 (dd, $J_{3',5'}$ = 0.8 Hz, $J_{4',3'}$ = 3.3 Hz, 1 H, H3′), 6.27 (dd, $J_{5',4'}$ = 1.8 Hz, $J_{3',4'}$ = 3.3 Hz, 1 H, H4′), 6.34 (dd, $J_{8,9}$ = 1.7 Hz, $J_{9,10}$ = 5.8 Hz, 1 H, H9), 6.40 (d, $J_{9,10}$ = 5.8 Hz, 1 H, H10), 7.31 (dd, $J_{5',3'}$ = 0.8 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.1 (C_6), 152.6 ($C_{2'}$), 141.4 ($C_{5'}$), 135.9 and 133.8 (C_9, C_{10}), 109.9 and 107.9 ($C_{3'}$, $C_{4'}$), 90.9 (C_{10a}), 78.4 (C_8), 59.4, 52.6 and 47.6 (C_4, C_{6a}, C_{10b}), 34.5 (C_2), 31.2 and 27.4 (C_3, C_1), 27.8 (C_7), 18.4 and 17.6 (1-CH_3, 3-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 299 (36) $[M]^+$, 271 (1), 231 (2), 229 (4), 228 (21), 213 (7), 177 (9), 162 (12), 147 (2), 136 (3), 122 (8), 121 (9), 108 (8), 91 (7), 81 (13), 79 (15), 77 (12), 65 (10), 55 (100).

Anal. Calcd for $C_{18}H_{21}NO_3$: C, 77.22; H, 7.07; N, 4.68. Found: C, 76.94; H, 4.50; N, 4.75.

8,10a-Epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acids 11a–h,k,l, 11i,j, and 11i′,j′; Typical Procedure

A soln of **2a–l** (21.0 mmol) and maleic anhydride (2.06 g, 21.0 mmol) in toluene (30 mL) was refluxed for 6–8 h. The mixture was then cooled and formation of white, yellow, or brown solids was observed. The crystals were filtered off and washed first with toluene (2 × 30 mL), then with acetone (2 × 20 mL) to give **11a–h**,**k**,**l** and regioisomeric mixtures **11i/11i′** and **11j/11j′** as white or pale-brown powders. In some cases (for example, in case of acids **11c–e**), adducts were isolated as viscous oils on the flask walls. In such cases, after cooling, toluene was poured off, and the remained oil was triturated with Et_2O. The obtained crystals were filtered off, washed with acetone, and dried in air. The mixture of regioisomers **11i/11i′** and **11j/11j′** was not separated additionally because of the poor solubility of the obtained compounds in common organic solvents. After the fraction crystallization (EtOH–DMF) the major isomers **11i′** and **11j′** only were isolated. Mp, IR, EI-MS, ^1H and ^{13}C NMR, and element analysis data are described for the major regioisomers **11i′** and **11j′**.

(1*R,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-1-Methyl-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11a)**

Yield: 84%; mp 219–220.5 °C.

IR: 3505 (br, OH), 1726 (CO_2H, C=O), 1667 cm^{-1} (N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.99 (d, $J_{1,1\text{-}CH3}$ = 6.9 Hz, 3 H, 1-CH_3), 2.49 (dq, $J_{1,10b}$ = 11.7 Hz, $J_{1,1\text{-}CH3}$ = 6.9 Hz, 1 H, H1), 2.56 (d, $J_{7endo,6a}$ = 9.3 Hz, 1 H, H6a), 2.75 (dd, $J_{3B,4}$ = 1.7 Hz, $^2J_{3,3}$ = 16.6 Hz, 1 H, $H3_B$), 2.97 (d, $J_{6a,7endo}$ = 9.3 Hz, 1 H, $H7_{endo}$), 3.29 (dd, $J_{3A,4}$ = 6.2 Hz, $^2J_{3,3}$ = 16.6 Hz, 1 H, $H3_A$), 4.62 (d, $J_{10b,1}$ = 11.7 Hz, 1 H, H10b), 5.11 (d, $J_{8,9}$ = 1.4 Hz, 1 H, H8), 5.19 (dd, $J_{4,3B}$ = 1.7 Hz, $J_{4,3A}$ = 6.2 Hz, 1 H, H4), 6.27 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.0 Hz, 1 H, H4′), 6.34 (br d, $J_{3',4'}$ = 3.0 Hz, 1 H, H3′), 6.46 (dd, $J_{8,9}$ = 1.4 Hz, $J_{9,10}$ = 5.7 Hz, 1 H, H9), 6.60 (d, $J_{9,10}$ = 5.7 Hz, 1 H, H10), 7.51 (dd, $J_{5',3'}$ = 0.7 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.32 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 208.9 (C_2), 173.6 (C_6), 170.4 (CO_2H), 153.5 ($C_{2'}$), 142.9 ($C_{5'}$), 136.9 (C_9), 135.8 (C_{10}), 110.8 ($C_{4'}$), 107.6 ($C_{3'}$), 90.3 (C_{10a}), 81.4 (C_8), 57.4 (C_{10b}), 51.2 (C_7), 46.4, 45.1, 44.5 (C_1, C_4, C_{6a}), 42.4 (C_3), 10.4 (1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 343 (21) $[M]^+$, 325 (2), 298 (1), 262 (2), 244 (30), 229 (11), 228 (88), 202 (12), 189 (19), 176 (38), 162 (100), 161 (23), 135 (33), 122 (34), 108 (56), 94 (66), 77 (14), 66 (21), 65 (24), 55 (9).

Anal. Calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08. Found: C, 63.05; H, 5.13; N, 3.90.

(1*R,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-1-Ethyl-4-(2-furyl)-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11b)**

Yield: 82%; mp 226 °C.

IR: 3407 (OH), 1737 (CO_2H), 1717 (C=O), 1654 cm^{-1} (N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.84 (t, $J_{CH2,Me}$ = 7.3 Hz, 3 H, CH_2CH_3), 1.44 (m, 1 H, $CH_AH_BCH_3$), 1.69 (m, 1 H, $CH_AH_BCH_3$), 2.48 (m, 1 H, H1), 2.56 (d, $J_{7endo,6a}$ = 9.3 Hz, 1 H, H6a), 2.75 (dd, $J_{3B,4}$ = 1.0 Hz, $^2J_{3,3}$ = 16.1 Hz, 1 H, $H3_B$), 2.95 (d, $J_{6a,7endo}$ = 9.3 Hz, 1 H, $H7_{endo}$), 3.27 (dd, $J_{3A,4}$ = 6.1 Hz, $^2J_{3,3}$ = 16.1 Hz, 1 H, $H3_A$), 4.83 (d, $J_{10b,1}$ = 11.9 Hz, 1 H, H10b), 5.12 (d, $J_{8,9}$ = 1.0 Hz, 1 H, H8), 5.17 (dd, $J_{4,3B}$ = 1.0 Hz, $J_{4,3A}$ = 6.1 Hz, 1 H, H4), 6.27 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.32 (br d, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 6.46 (dd, $J_{8,9}$ = 1.0 Hz, $J_{9,10}$ = 5.6 Hz, 1 H, H9), 6.65 (d, $J_{9,10}$ = 5.6 Hz, 1 H, H10), 7.51 (br d, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.33 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 209.0 (C_2), 173.5 (C_6), 170.4 (CO_2H), 153.5 ($C_{2'}$), 142.9 ($C_{5'}$), 137.0 (C_9), 135.6 (C_{10}), 110.8 ($C_{4'}$), 107.5 ($C_{3'}$), 90.2 (C_{10a}), 81.4 (C_8), 55.0 (C_{10b}), 51.3 (C_7), 49.9, 46.5, 45.1 (C_1, C_4, C_{6a}), 43.4 (C_3), 18.6 (CH_2CH_3), 10.9 (CH_2CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 357 (20) $[M]^+$, 339 (2), 276 (3), 258 (26), 242 (98), 235 (9), 207 (10), 190 (24), 189 (24), 176 (17), 162 (100), 161 (22), 136 (19), 122 (94), 121 (31), 107 (28), 99 (15), 79 (19), 66 (20), 65 (26), 55 (12).

Anal. Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.91; H, 5.14; N, 3.84.

(1*R,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-2,6-dioxo-1-propyl-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11c)**

Yield: 67%; mp 203–204 °C.

IR: 3497 (OH), 1721 (CO_2H), 1736 (C=O), 1655 cm^{-1} (N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.75 (t, $J_{CH2,Me}$ = 6.7 Hz, 3 H, CH_2CH_3), 1.15 (m, 1 H, $CH_AH_BCH_2CH_3$), 1.42 (m, 2 H, $CH_2CH_2CH_3$), 1.55 (m, 1 H, $CH_AH_BCH_2CH_3$), 2.48 (m, 1 H, H1), 2.54 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H6a), 2.72 (dd, $J_{3B,4}$ = 1.0 Hz, $^2J_{3,3}$ = 16.3 Hz, 1 H, $H3_B$), 2.92 (d, $J_{6a,7endo}$ = 9.2 Hz, 1 H, $H7_{endo}$), 3.24 (dd, $J_{3A,4}$ = 5.0 Hz, $^2J_{3,3}$ = 16.3 Hz, 1 H, $H3_A$), 4.77 (d, $J_{10b,1}$ = 11.9 Hz, 1 H, H10b), 5.10 (d, $J_{8,9}$ = 1.5 Hz, 1 H, H8), 5.15 (dd, $J_{4,3B}$ = 1.0 Hz, $J_{4,3A}$ = 5.0 Hz, 1 H, H4), 6.25 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.30 (br d, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 6.44 (dd, $J_{8,9}$ = 1.5 Hz, $J_{9,10}$ = 5.5 Hz, 1 H, H9), 6.61 (d, $J_{9,10}$ = 5.5 Hz, 1 H, H10), 7.48 (br d, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.23 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 209.1 (C_2), 173.5 (C_6), 170.3 (CO_2H), 153.5 ($C_{2'}$), 142.9 ($C_{5'}$), 136.9 (C_9), 135.6 (C_{10}), 110.8 ($C_{4'}$), 107.5 ($C_{3'}$), 90.2 (C_{10a}), 81.4 (C_8), 55.5 (C_{10b}), 51.3 (C_7),

49.0, 46.5, 45.1 (C_1, C_4, C_{6a}), 43.2 (C_3), 27.9 ($CH_2CH_2CH_3$), 19.6 ($CH_2CH_2CH_3$), 14.8 ($CH_2CH_2CH_3$).

MS (EI, 70 eV): *m*/*z* (%) = 371 (19) $[M]^+$, 353 (2), 329 (2), 290 (3), 272 (24), 256 (92), 235 (7), 228 (5), 207 (23), 204 (18), 189 (28), 174 (11), 163 (29), 162 (100), 161 (33), 150 (12), 136 (60), 122 (42), 121 (33), 107 (33), 94 (82), 79 (16), 65 (23), 55 (18).

Anal. Calcd for $C_{20}H_{21}NO_6$: C, 64.68; H, 5.70; N, 3.77. Found: C, 64.41; H, 5.78; N, 3.93.

(1*R,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-1-isopropyl-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11d)**
Yield: 40%; mp 204–206 °C.

IR: 3510 (br, OH), 1741 (CO_2H), 1701 (C=O), 1671 cm^{-1} (N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.90 [d, $J_{CH,Me(A)}$ = 6.0 Hz, 3 H, $CH(CH_3)_A(CH_3)_B$], 1.04 [d, $J_{CH,Me(B)}$ = 6.7 Hz, 3 H, $CH(CH_3)_A(CH_3)_B$], 1.91 [m, 1 H, $CH(CH_3)_2$], 2.47 (dd, $J_{CH,CHMe2}$ = 6.5 Hz, $J_{1,10b}$ = 12.0 Hz, 1 H, H1), 2.57 (d, $J_{7endo,6a}$ = 9.4 Hz, 1 H, H6a), 2.67 (dd, $J_{3B,4}$ = 1.8 Hz, $^2J_{3,3}$ = 15.4 Hz, 1 H, $H3_B$), 2.92 (d, $J_{7endo,6a}$ = 9.4 Hz, 1 H, H7$_{endo}$), 3.28 (dd, $J_{3A,4}$ = 5.7 Hz, $^2J_{3,3}$ = 15.4 Hz, 1 H, $H3_A$), 4.91 (d, $J_{10b,1}$ = 12.0 Hz, 1 H, H10b), 5.13 (d, $J_{8,9}$ = 1.5 Hz, 1 H, H8), 5.13 (dd, $J_{4,3B}$ = 1.8 Hz, $J_{4,3A}$ = 5.7 Hz, 1 H, H4), 6.28 (br s, 2 H, H3′, H4′), 6.44 (dd, $J_{8,9}$ = 1.5 Hz, $J_{9,10}$ = 5.3 Hz, 1 H, H9), 6.66 (d, $J_{9,10}$ = 5.3 Hz, 1 H, H10), 7.51 (br d, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.32 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 209.1 (C_2), 173.5 (C_6), 170.4 (CO_2H), 153.4 ($C_{2'}$), 142.9 ($C_{5'}$), 136.9 and 135.6 (C_9, C_{10}), 110.8 ($C_{4'}$), 107.3 ($C_{3'}$), 90.0 (C_{10a}), 81.4 (C_8), 55.3 (C_{10b}), 51.3 (C_7), 54.1, 46.8, 45.0 (C_1, C_4, C_{6a}), 44.5 (C_3), 27.0 [$CH(CH_3)_2$], 22.7 and 17.2 [$CH(CH_3)_2$].

MS (EI, 70 eV): *m*/*z* (%) = 371 (22) $[M]^+$, 343 (1), 329 (1), 328 (4), 290 (2), 272 (24), 257 (11), 256 (90), 249 (10), 234 (10), 216 (12), 207 (11), 189 (20), 174 (8), 163 (24), 162 (100), 150 (21), 136 (98), 121 (90), 107 (9), 99 (17), 94 (78), 65 (34), 55 (12).

Anal. Calcd for $C_{20}H_{21}NO_6$: C, 64.68; H, 5.70; N, 3.77. Found: C, 64.50; H, 5.78; N, 3.92.

(1*R,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-1-Allyl-4-(2-furyl)-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11e)**
Yield: 70%; mp 202 °C.

IR: 3129 (OH), 1731 (CO_2H), 1654 cm^{-1} (N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 2.13 (m, 1 H, H1), 2.56 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H6a), 2.49–2.61 (m, 2 H, $CH_2CH{=}CH_2$), 2.77 (dd, $J_{3B,4}$ = 1.0 Hz, $^2J_{3,3}$ = 16.0 Hz, 1 H, $H3_B$), 2.97 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H7$_{endo}$), 3.25 (dd, $J_{3A,4}$ = 6.1 Hz, $^2J_{3,3}$ = 16.3 Hz, 1 H, $H3_A$), 4.77 (d, $J_{10b,1}$ = 11.8 Hz, 1 H, H10b), 4.99–5.03 (m, 2 H, $CH_2CH{=}CH_2$), 5.13 (d, $J_{8,9}$ = 1.0 Hz, 1 H, H8), 5.16 (dd, $J_{4,3B}$ = 1.0 Hz, $J_{4,3A}$ = 6.1 Hz, 1 H, H4), 5.73 (m, 1 H, $CH_2CH{=}CH_2$), 6.27 (br d, $J_{4',3'}$ = 3.2 Hz, 1 H, H3′), 6.32 (br d, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.47 (dd, $J_{8,9}$ = 1.0 Hz, $J_{9,10}$ = 5.5 Hz, 1 H, H9), 6.66 (d, $J_{9,10}$ = 5.5 Hz, 1 H, H10), 7.51 (br d, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.34 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 208.2 (C_2), 173.5 (C_6), 170.4 (CO_2H), 153.4 ($C_{2'}$), 142.9 ($C_{5'}$), 136.9 and 135.6 (C_9, C_{10}), 134.8 ($CH_2CH{=}CH_2$), 118.4 ($CH_2CH{=}CH_2$), 110.8 ($C_{4'}$), 107.5 ($C_{3'}$), 90.1 (C_{10a}), 81.4 (C_8), 55.1 (C_{10b}), 51.3 (C_7), 59.0, 46.5, 45.0 (C_1, C_4, C_{6a}), 43.4 (C_3), 29.9 ($CH_2CH{=}CH_2$).

MS (EI, 70 eV): *m*/*z* (%) = 369 (19) $[M]^+$, 351 (2), 328 (4), 327 (7), 270 (32), 256 (9), 254 (74), 235 (7), 228 (20), 213 (22), 202 (11), 189 (22), 162 (100), 148 (29), 134 (40), 122 (34), 121 (76), 105 (17), 99 (19), 94 (84), 91 (21), 81 (18), 66 (25), 65 (34), 55 (20).

Anal. Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.18; N, 3.79. Found: C, 64.72; H, 5.37; N, 3.89.

(1*R,3*S**,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-2,6-dioxo-1,3-diphenyl-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11f)**
Yield: 55%; mp >220 °C (dec).

IR: 3389 (br, OH), 1724 (CO_2H, C=O), 1700 cm^{-1} (N–C=O).

^1H NMR (600 MHz, DMSO-d_6): δ = 2.50 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H6a), 2.79 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H7$_{endo}$), 4.40 (d, $J_{1,10b}$ = 10.8 Hz, 1 H, H10b), 4.47 (d, $J_{3,4}$ = 6.6 Hz, 1 H, H3), 5.02 (d, $J_{1,10b}$ = 10.8 Hz, 1 H, H1), 5.10 (d, $J_{8,9}$ = 1.7 Hz, 1 H, H8), 5.58 (d, $J_{4,3}$ = 6.6 Hz, 1 H, H4), 5.70 (d, $J_{9,10}$ = 5.7 Hz, 1 H, H10), 6.11 (dd, $J_{5',3'}$ = 0.6 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H3′), 6.17 (dd, $J_{8,9}$ = 1.7 Hz, $J_{9,10}$ = 5.7 Hz, 1 H, H9), 6.40 (dd, $J_{5',4'}$ = 1.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.77 (dd, *J* = 1.6 Hz, *J* = 7.8 Hz, 2 H, H_{Ph}), 7.12–7.18, 7.37–7.29 (m, 7 H, H_{Ph}), 7.23 (t, *J* = 7.7 Hz, 1 H, H_{Ph}), 7.86 (br d, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.24 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 203.1 (C_2), 172.6 (CO_2H), 168.6 (C_6), 150.5 ($C_{2'}$), 143.3 ($C_{5'}$), 135.3 and 134.9 (C_9, C_{10}), 134.5 and 134.1 ($C_{ipso\text{-}Ph}$), 130.15, 130.04, 128.0, 127.4 ($C_{meta\text{-}Ph}$, $C_{ortho\text{-}Ph}$), 127.22 and 127.10 ($C_{para\text{-}Ph}$), 110.7 and 109.8 ($C_{3'}$, $C_{4'}$), 89.6 (C_{10a}), 80.8 (C_8), 59.8, 56.8, 55.2, 51.9 (C_1, C_3, C_4, C_{6a}), 49.7 (C_7), 44.9 (C_{10b}).

MS (EI, 70 eV): *m*/*z* (%) = 481 (24) $[M]^+$, 437 (21), 382 (12), 367 (21), 366 (57), 301 (5), 289 (7), 288 (8), 283 (32), 265 (13), 239 (10), 238 (27), 198 (22), 197 (45), 174 (24), 171 (35), 170 (100), 169 (67), 142 (13), 141 (45), 118 (10), 115 (32), 96 (13), 95 (14), 81 (20), 55 (22), 43 (28).

Anal. Calcd for $C_{29}H_{23}NO_6$: C, 72.34; H, 4.81; N, 2.91. Found: C, 72.24; H, 4.91; N, 2.81.

(1*R,3*S**,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-1,3-dimethyl-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11g)**
Yield: 86%; mp 236–237.5 °C.

IR: 3232 (br, OH), 1731 (CO_2H), 1713 (C=O), 1678 cm^{-1} (N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.98 (d, $J_{1,1\text{-}CH3}$ = 6.7 Hz, 3 H, 1-CH_3), 1.31 (d, $J_{3,3\text{-}CH3}$ = 8.1 Hz, 3 H, 3-CH_3), 2.57 (d, $J_{7endo,6a}$ = 9.4 Hz, 1 H, H6a), 2.63 (dq, $J_{1,10b}$ = 12.1 Hz, $J_{1,1\text{-}CH3}$ = 6.7 Hz, 1 H, H1), 2.95 (dq, $J_{3,4}$ = 2.0 Hz, $J_{3,3\text{-}CH3}$ = 8.1 Hz, 1 H, H3), 3.00 (d, $J_{6a,7endo}$ = 9.4 Hz, 1 H, H7$_{endo}$), 4.58 (d, $J_{10b,1}$ = 12.1 Hz, 1 H, H10b), 4.94 (d, $J_{3,4}$ = 2.0 Hz, 1 H, H4), 5.13 (d, $J_{8,9}$ = 1.3 Hz, 1 H, H8), 6.28 (dd, $J_{4',5'}$ = 2.0 Hz, $J_{4',3'}$ = 3.4 Hz, 1 H, H4′), 6.44 (br d, $J_{3',4'}$ = 3.4 Hz, 1 H, H3′), 6.46 (dd, $J_{8,9}$ = 2.0 Hz, $J_{9,10}$ = 6.0 Hz, 1 H, H9), 6.59 (d, $J_{9,10}$ = 6.0 Hz, 1 H, H10), 7.51 (dd, $J_{5',3'}$ = 0.7 Hz, $J_{5',4'}$ = 2.0 Hz, 1 H, H5′), 12.31 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 210.9 (C_2), 173.6 (C_6), 171.2 (CO_2H), 153.2 ($C_{2'}$), 142.8 ($C_{5'}$), 136.8 and 135.7 (C_9, C_{10}), 110.8 ($C_{4'}$), 108.0 ($C_{3'}$), 90.7 (C_{10a}), 81.5 (C_8), 57.0 (C_{10b}), 52.4, 51.1, 46.9, 45.3, 43.9 (C_1, C_3, C_4, C_{6a}, C_7), 17.1 (3-CH_3), 10.4 (1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 357 (14) $[M]^+$, 339 (1), 313 (1), 276 (8), 258 (18), 242 (60), 221 (10), 203 (22), 176 (100), 162 (13), 148 (10), 135 (17), 122 (26), 108 (42), 79 (29), 77 (18), 65 (9), 55 (6).

Anal. Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.48; H, 5.28; N, 3.81.

(1*R,3*S**,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-1,3-Bis(2-ethoxy-2-oxoethyl)-4-(2-furyl)-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11h)**
Yield: 80%; mp 218 °C.

IR: 3406 (br, OH), 1711 cm^{-1} (CO_2, C=O).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.15 (t, $J_{CH2,Me}$ = 7.0 Hz, 3 H, CH_2CH_3), 1.20 (t, $J_{CH2,Me}$ = 7.0 Hz, 3 H, CH_2CH_3), 2.37 (dd, $^2J_{CH2}$ = 17.0 Hz, $J_{1,CH2A}$ = 6.7 Hz, 1 H, 1-$CH_AH_BCO_2Et$), 2.57 (d, $J_{6a,7endo}$ = 9.2 Hz, 1 H, H6a), 2.54–2.68 (m, 2 H, 3-CH_2CO_2Et), 2.85 (dd, $^2J_{CH2}$ = 17.0 Hz, $J_{1,CH2B}$ = 8.8 Hz, 1 H, 1-$CH_AH_BCO_2Et$), 2.99 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H7$_{endo}$), 3.03 (m, 1 H, H1), 3.30 (m, 1 H, H3), 4.03 (q, $J_{CH2,Me}$ = 7.0 Hz, 2 H, $CO_2CH_2CH_3$), 4.11 (q, $J_{CH2,Me}$ = 7.0 Hz, 2 H, $CO_2CH_2CH_3$), 4.82 (d, $J_{10b,1}$ = 12.3 Hz, 1 H, H10b), 5.00 (br d, $J_{4,3}$ = 1.5 Hz, 1 H, H4), 5.13 (br s, 1 H, H8), 6.31 (dd, $J_{4',5'}$ = 1.9 Hz, $J_{4',3'}$ = 3.3 Hz, 1 H, H4′), 6.45 (dd, $J_{3',5'}$ = 0.8 Hz, $J_{3',4'}$ = 3.3 Hz, 1 H, H3′), 6.49 (br s, 2 H, H9, H10), 7.31 (br d, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.33 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 207.8 (C_2), 173.5 (C_6), 171.04, 170.99, 170.97 (CO_2Et, CO_2H), 152.2 ($C_{2'}$), 143.2 ($C_{5'}$), 137.1 and 135.1 (C_9, C_{10}), 110.9 and 108.7 ($C_{3'}$, $C_{4'}$), 90.1 (C_{10a}), 81.6 (C_8), 61.1 and 60.8 ($CO_2CH_2CH_3$), 54.9 (C_4), 51.2, 50.8, 48.5, 45.9, 45.1 (C_1, C_3, C_{6a}, C_7, C_{10b}), 34.6 and 29.9 (CH_2CO_2Et), 14.50 and 14.46 ($CO_2CH_2CH_3$).

MS (EI, 70 eV): *m*/*z* (%) = 501 (11) [M]$^+$, 456 (8), 414 (12), 402 (7), 388 (13), 386 (56), 356 (11), 340 (44), 313 (16), 312 (100), 270 (26), 266 (31), 247 (47), 238 (40), 228 (40), 202 (20), 194 (74), 174 (59), 148 (29), 122 (64), 107 (88), 91 (35), 79 (50), 77 (43), 65 (19), 55 (37).

Anal. Calcd for $C_{25}H_{27}NO_{10}$: C, 59.88; H, 5.43; N, 2.79. Found: C, 59.49; H, 5.48; N, 2.98.

(1*R,3*S**,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-3-methyl-2,6-dioxo-1-phenyl-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11i) and (1*S**,3*R**,4*S**,6a*S**,7*R**,8*S**,10a*R**,10b*R**)-4-(2-Furyl)-1-methyl-2,6-dioxo-3-phenyl-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11i′)**

Total yield of isomers mixture: 68%; ratio **11i/11i′** (isolated mixture) 1:4 (^{1}H NMR). After crystallization (EtOH–DMF) individual isomer **11i′** was isolated as a white powder.

Compound 11i′

Yield: 42%; mp 144–145 °C.

IR: 3540 (br, OH), 1714 (CO_2H, C=O), 1652 cm^{-1} (N–C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, $J_{1,1\text{-}CH3}$ = 6.3 Hz, 3 H, 1-CH_3), 2.82 and 2.85 (2 d, $J_{7endo,6a}$ = 9.1 Hz, 1 H + 1 H, H7$_{endo}$, H6a), 3.22 (dq, $J_{1,10b}$ = 10.4 Hz, $J_{1,1\text{-}CH3}$ = 6.3 Hz, 1 H, H1), 4.22 (d, $J_{4,3}$ = 6.4 Hz, 1 H, H3), 4.50 ($J_{10b,1}$ = 10.4 Hz, 1 H, H10b), 5.38 (s, 1 H, H8), 5.74 (d, $J_{3,4}$ = 6.4 Hz, 1 H, H4), 6.00 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.25 (br d, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 6.52 (s, 2 H, H9, H10), 6.80 (m, 2 H, H_{ortho} Ph), 7.17–7.26 (m, 3 H, H_{para}, H_{meta} Ph), 7.43 (br d, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.8 (C_2), 173.5 (C_6), 169.9 (CO_2H), 150.0 (d, $C_{2'}$), 142.7 ($C_{5'}$), 137.1 and 135.3 (C_9, C_{10}), 133.2 ($C_{ipso\text{-}Ph}$), 130.2 (2 C, $C_{meta\text{-}Ph}$), 127.9 (2 C, $C_{ortho\text{-}Ph}$), 127.6 ($C_{para\text{-}Ph}$), 110.76 and 110.73 ($C_{3'}$, $C_{4'}$), 90.1 (C_{10a}), 81.7 (C_8), 61.4 and 57.4 (C_1, C_4), 52.9, 50.7, 45.7, 43.9 (C_3, C_{6a}, C_7, C_{10b}), 10.4 (1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 419 (4) [M]$^+$, 387 (1), 376 (3), 338 (3), 320 (10), 318 (9), 305 (13), 304 (35), 283 (10), 265 (10), 238 (53), 221 (21), 203 (14), 197 (25), 184 (19), 176 (49), 170 (97), 141 (94), 118 (87), 108 (100), 96 (57), 90 (45), 80 (63), 78 (73), 65 (25), 55 (57).

Anal. Calcd for $C_{24}H_{21}NO_6$: C, 68.73; H, 5.05; N, 3.34. Found: C, 68.44; H, 4.85; N, 3.17.

(1*R,3*S**,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-3-Ethyl-4-(2-furyl)-2,6-dioxo-1-phenyl-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11j) and (1*S**,3*R**,4*S**,6a*S**,7*R**,8*S**,10a*R**,10b*R**)-1-Ethyl-4-(2-furyl)-2,6-dioxo-3-phenyl-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11j′)**

Total yield of isomers mixture: 72%; ratio **11j/11j′** (isolated mixture) 1:6 (^{1}H NMR). After crystallization (EtOH–DMF) individual isomer **11j′** was isolated as a white powder.

Compound 11j′

Yield: 52%; mp 208–209 °C.

IR: 3224 (OH), 1745 (CO_2H), 1710 (C=O), 1689 cm^{-1} (N–C=O).

^{1}H NMR (600 MHz, DMSO-d_6): δ = 0.97 (t, $J_{CH2,Me}$ = 7.3 Hz, 3 H, CH_2CH_3), 1.57 (ddq, $J_{CH2A,Me}$ = 7.3 Hz, $J_{1,CH2A}$ = 2.3 Hz, $^2J_{CH2}$ = 12.7 Hz, 1 H, $CH_AH_BCH_3$), 1.71 (ddq, $^2J_{CH2}$ = 12.7 Hz, $J_{CH2B,Me}$ = 7.3 Hz, $J_{1,CH2B}$ = 8.2 Hz, 1 H, $CH_AH_BCH_3$), 2.56 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H6a), 2.84 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H7$_{endo}$), 3.02 (ddd, $J_{1,10b}$ = 11.0 Hz, $J_{1,CH2B}$ = 8.2 Hz, $J_{1,CH2A}$ = 2.3 Hz, 1 H, H1), 4.33 (d, $J_{4,3}$ = 6.7 Hz, 1 H, H3), 4.64 ($J_{10b,1}$ = 11.0 Hz, 1 H, H10b), 5.14 (d, $J_{8,9}$ = 1.6 Hz, 1 H, H8), 5.50 (d, $J_{3,4}$ = 6.7 Hz, 1 H, H4), 6.03 (br d, $J_{4',3'}$ = 3.2 Hz, 1 H, H3′), 6.36 (dd, $J_{5',4'}$ = 1.8 Hz, $J_{3',4'}$ = 3.2 Hz, 1 H, H3′), 6.47 (dd, $J_{8,9}$ = 1.6 Hz, $J_{9,10}$ = 5.5 Hz, 1 H, H9), 6.66 (d, $J_{9,10}$ = 5.5 Hz, 1 H, H10), 6.76 (br d, $J_{ortho,meta}$ = 6.9 Hz, 2 H, H_{ortho} Ph), 7.17–7.20 (m, 3 H, H_{para}, H_{meta} Ph), 7.70 (dd, $J_{5',3'}$ = 0.6 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.23 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 205.4 (C_2), 173.1 (CO_2H), 169.0 (C_6), 151.0 (d, $C_{2'}$), 143.5 ($C_{5'}$), 136.9 (C_9), 136.1 (C_{10}), 134.6 ($C_{ipso\text{-}Ph}$), 130.6 (2 C, $C_{meta\text{-}Ph}$), 127.9 (2 C, $C_{ortho\text{-}Ph}$), 127.6 ($C_{para\text{-}Ph}$), 111.1 ($C_{3'}$), 110.1 ($C_{4'}$), 90.1 (C_{10a}), 81.3 (C_8), 58.4 (C_4), 57.3 (C_1), 52.5 (C_{10b}), 50.3 (C_{6a}), 50.0 (C_3), 45.3 (C_7), 18.1 (CH_2CH_3), 11.9 (CH_2CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 433 (49) [M]$^+$, 415 (4), 404 (4), 389 (19), 372 (9), 352 (22), 334 (36), 318 (100), 283 (41), 265 (25), 263 (27), 235 (54), 232 (55), 184 (15), 170 (57), 169 (20), 148 (10), 141 (29), 122 (63), 118 (34), 107 (31), 96 (20), 80 (25), 78 (21), 55 (19).

Anal. Calcd for $C_{25}H_{23}NO_6$: C, 69.27; H, 5.35; N, 3.23. Found: C, 68.93; H, 5.15; N, 3.40.

(1*R,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-1,8-Dimethyl-4-(5-methyl-2-furyl)-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11k)**

Yield: 87%; mp 198–200 °C.

IR: 3179 (OH), 1747 (CO_2H), 1719 (C=O), 1666 cm^{-1} (N–C=O).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.99 (d, $J_{1,1\text{-}CH3}$ = 6.9 Hz, 3 H, 1-CH_3), 1.59 (s, 3 H, 8-CH_3), 2.17 (s, 3 H, 5-CH_3′), 2.46 (dq, $J_{1,10b}$ = 11.7 Hz, $J_{1,1\text{-}CH3}$ = 6.9 Hz, 1 H, H1), 2.58 (d, $J_{6a,7endo}$ = 9.1 Hz, 1 H, H6a), 2.72 (dd, $^2J_{3,3}$ = 16.5 Hz, $J_{3B,4}$ = 1.8 Hz, 1 H, H3$_B$), 2.98 (d, $J_{7endo,6a}$ = 9.1 Hz, 1 H, H7$_{endo}$), 3.26 (dd, $^2J_{3,3}$ = 16.5 Hz, $J_{3A,4}$ = 6.3 Hz, 1 H, H3$_A$), 4.55 (d, $J_{10b,1}$ = 11.7 Hz, 1 H, H10b), 5.11 (br dd, $J_{3B,4}$ = 1.8 Hz, $J_{3A,4}$ = 6.3 Hz, 1 H, H4), 5.88 (dq, $^4J_{5'\text{-}CH3,3'}$ = 0.7 Hz, $J_{3',4'}$ = 3.0 Hz, 1 H, H4′), 6.29 (d, $J_{10,9}$ = 5.4 Hz, 1 H, H9), 6.34 (br d, $J_{4',3'}$ = 3.0 Hz, 1 H, H3′), 6.62 (d, $J_{10,9}$ = 5.4 Hz, 1 H, H10), 12.30 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 209.2 (C_2), 172.3 and 170.5 (CO_2H, C_6), 151.7 and 151.2 ($C_{2'}$ and $C_{5'}$), 139.9 and 137.0 (C_9, C_{10}), 108.2 and 106.8 ($C_{3'}$, $C_{4'}$), 89.5 and 88.9 (C_8, C_{10a}), 57.8 (C_{6a}), 54.7 (C_4), 48.3, 44.7, 46.5 (C_1, C_7, C_{10b}), 42.5 (C_3), 16.3 (5-CH_3′), 13.7 (8-CH_3), 10.6 (1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 371 (8) [M]$^+$, 276 (3), 272 (4), 257 (11), 256 (100), 228 (7), 203 (6), 190 (40), 176 (68), 149 (20), 136 (34), 122 (52), 108 (46), 107 (29), 79 (12), 77 (10), 65 (4), 53 (5).

Anal. Calcd for $C_{20}H_{21}NO_6$: C, 64.68; H, 5.70; N, 3.77. Found: C, 64.78; H, 5.61; N, 3.93.

(1*R,3*S**,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-1,3,8-Trimethyl-4-(5-methyl-2-furyl)-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (11l)**
Yield: 84%; mp 220 °C.

IR: 3535, 3196 (br OH), 1751 (CO_2H), 1723 (C=O), 1669 cm^{-1} (N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.96 (d, $J_{1,1\text{-}CH3}$ = 6.7 Hz, 3 H, 1-CH_3), 1.27 (d, $J_{3,3\text{-}CH3}$ = 7.5 Hz, 3 H, 3-CH_3), 1.58 (s, 3 H, 8-CH_3), 2.15 (br d, $J_{4',Me}$ = 0.5 Hz, 3 H, 5-CH_3'), 2.56 (d, $J_{7endo,6a}$ = 8.9 Hz, 1 H, H7$_{endo}$), 2.61 (dq, $J_{1,1\text{-}CH3}$ = 6.7 Hz, $J_{1,10b}$ = 12.4 Hz, 1 H, H1), 2.89 (dq, $J_{3,3\text{-}CH3}$ = 7.5 Hz, $J_{3,4}$ = 2.0 Hz, 1 H, H3), 2.98 (d, $J_{6a,7endo}$ = 8.9 Hz, 1 H, H6a), 4.48 (d, $J_{10b,1}$ = 12.4 Hz, 1 H, H10b), 4.81 (br d, $J_{4,3}$ = 2.0 Hz, 1 H, H4), 5.86 (dq, $J_{4',3'}$ = 2.7 Hz, $J_{4',Me}$ = 0.5 Hz, 1 H, H4′), 6.26 (d, $J_{9,10}$ = 5.6 Hz, 1 H, H9), 6.39 (d, $J_{3',4'}$ = 2.7 Hz, 1 H, H3′), 6.59 (d, $J_{9,10}$ = 5.6 Hz, 1 H, H10), 12.24 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 211.1 (C_2), 172.2 and 171.1 (C_6, CO_2H), 151.4 and 151.1 ($C_{2'}$, $C_{5'}$), 139.9 and 136.8 (C_9, C_{10}), 108.6 and 106.8 ($C_{3'}$, $C_{4'}$), 90.0 and 88.9 (C_{10a}, C_8), 57.4, 54.5, 52.6, 48.4, 47.1, 44.1 (C_1, C_3, C_4, C_{6a}, C_7, C_{10b}), 17.1 (3-CH_3), 16.3 (5-CH_3'), 13.7 (8-CH_3), 10.5 (1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 385 (10) $[M]^+$, 324 (2), 290 (13), 271 (11), 270 (98), 242 (5), 235 (5), 217 (12), 202 (5), 190 (100), 176 (17), 149 (19), 136 (32), 122 (60), 107 (20), 95 (11), 79 (15), 77 (11), 43 (12).

Anal. Calcd for $C_{21}H_{23}NO_6$: C, 65.44; H, 6.02; N, 3.63. Found: C, 65.33; H, 6.12; N, 3.74.

(1*S,3*S**,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-1,3-dimethyl-6-oxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (12)**
A mixture of **4** (2.7 g, 11.0 mmol) and maleic anhydride (1.12 g, 11.4 mmol) in toluene (20 mL) was refluxed for 4 h. The mixture was then cooled and formation of yellow species was observed. The crystals were filtered off, washed first with toluene (25 mL), then with acetone (2 × 15 mL) to give **12** as white needles; yield: 2.26 g (58%); mp 202–204 °C.

IR: 3472, 3195 (br, OH), 1750 (CO_2H), 1665 cm^{-1} (br, C=O, N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.90 (d, $J_{1,1\text{-}CH3}$ = 6.7 Hz, 3 H, 1-CH_3), 0.96 (d, $J_{3,3\text{-}CH3}$ = 6.7 Hz, 3 H, 3-CH_3), 1.26 (m, 2 H, H2), 2.22 and 2.33 (two m, 1 H + 1 H, H1, H3), 2.46 (d, $J_{7endo,6a}$ = 9.3 Hz, 1 H, H6a), 2.79 (d, $J_{6a,7endo}$ = 9.3 Hz, 1 H, H7$_{endo}$), 4.06 (d, $J_{10b,1}$ = 11.7 Hz, 1 H, H10b), 4.67 (br d, $J_{3,4}$ = 4.1 Hz, 1 H, H4), 5.04 (d, $J_{8,9}$ = 1.2 Hz, 1 H, H8), 6.25 (dd, $J_{3',5'}$ = 0.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H3′), 6.29 (dd, $J_{5',4'}$ = 1.8 Hz, $J_{3',4'}$ = 3.2 Hz, 1 H, H4′), 6.40 (dd, $J_{8,9}$ = 1.2 Hz, $J_{9,10}$ = 5.7 Hz, 1 H, H9), 6.58 (d, $J_{9,10}$ = 5.7 Hz, 1 H, H10), 7.48 (dd, $J_{5',3'}$ = 0.8 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 12.12 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 173.4 and 169.9 (CO_2H, C_6), 153.7 ($C_{2'}$), 142.1 ($C_{5'}$), 136.6 and 136.3 (C_9, C_{10}), 110.6 ($C_{4'}$), 108.2 ($C_{3'}$), 90.8 (C_{10a}), 81.1 (C_8), 57.9 (C_4), 52.8 and 51.2 (C_{6a}, C_7), 44.9 (C_{10b}), 34.6 (C_2), 31.3 (C_3), 27.6 (C_1), 18.6 and 18.3 (1-CH_3, 3-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 245 (5) $[M - 98]^+$, 244 (40), 228 (30), 213 (10), 202 (7), 188 (3), 176 (19), 162 (22), 147 (11), 136 (35), 122 (56), 121 (100), 108 (65), 99 (26), 91 (36), 81 (70), 79 (65), 77 (61), 65 (37), 55 (41), 39 (70).

Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.28; H, 6.35; N, 4.25.

Esters 13a,b; Typical Procedure
The acid **11a** (3.6 g, 10.5 mmol) was added to MeOH or EtOH (130 mL) and H_2SO_4 (0.5 mL) was added to the mixture. The resulting mixture was refluxed for 12 h (TLC monitoring). The mixture was then cooled, poured into H_2O (400 mL), and extracted with CH_2Cl_2 (5 × 80 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and purified by column chromatography (alumina, CH_2Cl_2) to give a brown oil that crystallized. The crystals of esters **13a**,**b** were washed (Et_2O) to give bright brown rhombuses of **13a**,**b**.

Methyl (1*R,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-1-methyl-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylate (13a)**
Yield: 70%; mp 205–207 °C.

IR: 1734 (CO_2Me), 1716 (C=O), 1680 cm^{-1} (N–C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.07 (d, $J_{1,1\text{-}CH3}$ = 6.9 Hz, 3 H, 1-CH_3), 2.73 (d, $J_{7endo,6a}$ = 9.1 Hz, 1 H, H6a), 2.86 (dq, $J_{1,10b}$ = 12.0 Hz, $J_{1,1\text{-}CH3}$ = 6.9 Hz, 1 H, H1), 2.87 (d, $J_{6a,7endo}$ = 9.1 Hz, 1 H, H7$_{endo}$), 2.90 (dd, $J_{3B,4}$ = 6.2 Hz, $^2J_{3,3}$ = 17.2 Hz, 1 H, $H3_B$), 3.03 (dd, $J_{3A,4}$ = 2.1 Hz, $^2J_{3,3}$ = 17.2 Hz, 1 H, $H3_A$), 3.62 (s, 3 H, CO_2Me), 4.31 (d, $J_{10b,1}$ = 12.0 Hz, 1 H, H10b), 5.19 (d, $J_{8,9}$ = 1.7 Hz, 1 H, H8), 5.28 (br dd, $J_{3A,4}$ = 2.1 Hz, $J_{4,3B}$ = 6.2 Hz, 1 H, H4), 6.21 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{4',3'}$ = 3.3 Hz, 1 H, H4′), 6.46 (d, $J_{9,10}$ = 5.8 Hz, 1 H, H10), 6.38 (ddd, $J_{3',4'}$ = 3.3 Hz, $J_{3',5'}$ = 0.8, $^4J_{3',4}$ = 1.2 Hz, 1 H, H3′), 6.41 (dd, $J_{8,9}$ = 1.7 Hz, $J_{9,10}$ = 5.8 Hz, 1 H, H9), 7.22 (ddd, $J_{5',3'}$ = 0.8 Hz, $J_{5',4'}$ = 1.8, ^5J = 0.7 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.4 (s, C_2), 171.7 (s, CO_2Me), 169.9 (s, C_6), 151.6 (s, $C_{2'}$), 142.0 (d, *J* = 203.0 Hz, $C_{5'}$), 136.3 (d, *J* = 177.5 Hz, C_9), 134.7 (d, *J* = 178.0 Hz, C_{10}), 110.3 (d, *J* = 175.5 Hz, $C_{4'}$), 107.41 (d, *J* = 178.0 Hz, $C_{3'}$), 89.9 (s, C_{10a}), 80.9 (d, *J* = 168.5 Hz, C_8), 58.2 (d, *J* = 140.0 Hz, C_{10b}), 51.9 (q, *J* = 147.3 Hz, CO_2Me), 51.2 (d, *J* = 141.5 Hz, C_7), 46.1 (d, *J* = 146.5 Hz, C_4), 45.1 (d, *J* = 141.7 Hz, C_{6a}), 44.2 (d, *J* = 129.5 Hz, C_1), 41.3 (dd, *J* = 125.5, 138.0 Hz, C_3), 9.7 (q, *J* = 129.2 Hz, 1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 357 (26) $[M]^+$, 249 (4), 244 (71), 229 (14), 228 (100), 221 (7), 203 (7), 184 (24), 176 (61), 175 (10), 174 (7), 162 (92), 161 (14), 136 (10), 135 (37), 124 (16), 122 (62), 121 (46), 114 (11), 113 (45), 108 (52), 94 (64), 84 (12), 79 (12), 65 (10), 59 (10).

Anal. Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.51; H, 5.39; N, 3.80.

Ethyl (1*R,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-1-methyl-2,6-dioxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylate (13b)**
Yield: 75%; mp 251–252 °C.

IR: 1724 (br, C=O, CO_2Et), 1678 cm^{-1} (br, N–C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.12 (d, $J_{1,1\text{-}CH3}$ = 6.9 Hz, 3 H, 1-CH_3), 1.25 (t, $J_{CH2,CH3}$ = 7.1 Hz, 3 H, OCH_2CH_3), 2.78 (d, $J_{7endo,6a}$ = 9.1 Hz, 1 H, H6a), 2.95 (dq, $J_{1,10b}$ = 12.0 Hz, $J_{1,1\text{-}CH3}$ = 6.9 Hz, 1 H, H1), 2.95 (d, $J_{6a,7endo}$ = 9.1 Hz, 1 H, H7$_{endo}$), 2.94 (dd, $J_{3B,4}$ = 5.7 Hz, $^2J_{3,3}$ = 17.2 Hz, 1 H, $H3_B$), 3.12 (dd, $J_{3A,4}$ = 1.8 Hz, $^2J_{3,3}$ = 17.2 Hz, 1 H, $H3_A$), 4.18 (m, 2 H, OCH_2CH_3), 4.33 (d, $J_{10b,1}$ = 12.0 Hz, 1 H, H10b), 5.26 (d, $J_{8,9}$ = 1.5 Hz, 1 H, H8), 5.35 (dd, $J_{3A,4}$ = 1.8 Hz, $J_{4,3B}$ = 5.7 Hz, 1 H, H4), 6.26 (dd, $J_{4',5'}$ = 1.7 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H4′), 6.46 (dd, $J_{3',4'}$ = 3.2 Hz, $J_{3',5'}$ = 0.8 Hz, 1 H, H3′), 6.47 (dd, $J_{8,9}$ = 1.5 Hz, $J_{9,10}$ = 5.7 Hz, 1 H, H9), 6.50 (d, $J_{9,10}$ = 5.7 Hz, 1 H, H10), 7.26 (dd, $J_{5',3'}$ = 0.8 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 207.6 (C_2), 171.5 (CO_2Et), 170.1 (C_6), 151.8 ($C_{2'}$), 142.2 ($C_{5'}$), 136.7 (C_9), 134.9 (C_{10}), 110.6 ($C_{4'}$), 107.9 ($C_{3'}$), 90.1 (C_{10a}), 81.3 (C_8), 61.3 (OCH_2CH_3), 58.6

(C_{10b}), 51.4 (C_4), 46.4, 45.5, 44.5 (C_1, C_{6a}, C_7), 41.6 (C_3), 14.1 (OCH_2CH_3), 10.0 (1-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 351 (1) $[M]^+$, 244 (21) $[M - 127]^+$, 228 (23), 189 (9), 176 (13), 162 (100), 135 (42), 122 (42), 121 (40), 108 (67), 99 (56), 94 (72), 79 (26), 65 (47), 55 (17), 39 (48).

Anal. Calcd for $C_{20}H_{21}NO_6$: C, 64.68; H, 5.70; N, 3.77. Found: C, 65.07; H, 6.01; N, 3.50.

(1*R,2*S**,3*S**,4*R**,6a*R**,8*S**,10a*S**,10b*S**)-4-(2-Furyl)-2-hydroxy-1,2,3-trimethyl-1,3,4,6a,7,10b-hexahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-2,6(8*H*)-one (14)**

A mixture of **6a** (1.6 g, 5.1 mmol) in benzene (40 mL), acryloyl chloride (0.62 mL, 7.6 mmol), and Et_3N (1.4 mL, 10.2 mmol) was refluxed for 6 h (TLC monitoring). The resulting mixture was poured into H_2O (100 mL), washed with aq 5% HCl soln (50 mL), and extracted with EtOAc (5 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give the crude adduct. Further crystallization (hexane–EtOAc) gave **14** as white rhombuses; yield: 0.68 g (40%); mp 237–238 °C.

IR: 3414 (OH), 1682 cm^{-1} (N–C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.74 and 1.06 (2 d, $J_{Me,1(3)}$ = 6.7 Hz, 3 H + 3 H, 3-CH_3, 1-CH_3), 1.26 (s, 3 H, 2-CH_3), 1.48 (dd, $J_{7endo,6a}$ = 8.9 Hz, $J_{7endo,7exo}$ = 11.8 Hz, 1 H, H7$_{endo}$), 1.92 and 1.99 (2 dq, $J_{Me,1(3)}$ = 6.7 Hz, $J_{1,10b(3,4)}$ = 11.0 Hz, 1 H + 1 H, H1, H3), 2.11 (ddd, $J_{7exo,6a}$ = 3.8 Hz, $J_{7exo,8}$ = 4.3 Hz, $J_{7exo,7endo}$ = 11.8 Hz, 1 H, H7$_{exo}$), 2.28 (ddd, $J_{6a,7exo}$ = 3.8 Hz, $J_{6a,7endo}$ = 8.9, $^5J_{6a,4}$ = 0.9 Hz, 1 H, H6a), 4.02 (d, $J_{10b,1}$ = 11.0 Hz, 1 H, H10b), 4.26 (dd, $J_{3,4}$ = 11.0, $^5J_{6a,4}$ = 0.9 Hz, 1 H, H4), 5.04 (dd, $J_{8,7exo}$ = 4.3 Hz, $J_{8,9}$ = 1.7 Hz, 1 H, H8), 6.21 (dd, $J_{4',3'}$ = 3.2 Hz, $J_{3',5'}$ = 0.8 Hz, 1 H, H3′), 6.30 (dd, $J_{8,9}$ = 1.7 Hz, $J_{9,10}$ = 5.7 Hz, 1 H, H9), 6.33 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{3',4'}$ = 3.2 Hz, 1 H, H4′), 6.40 (d, $J_{9,10}$ = 5.7 Hz, 1 H, H10), 7.42 (dd, $J_{5',3'}$ = 0.8 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 172.8 (C_6), 151.8 ($C_{2'}$), 141.5 ($C_{5'}$), 135.2 and 135.0 (C_9, C_{10}), 110.1 and 108.9 ($C_{3'}$, $C_{4'}$), 89.9 (C_{10a}), 78.5 (C_8), 72.0 (C_2), 59.2 (C_4), 54.0 (C_{10b}), 48.0, 43.5, 40.1 (C_1, C_3, C_{6a}), 28.7 (C_7), 24.7 (CH_3-2), 10.7 and 10.0 (1-CH_3, 3-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 329 (98) $[M]^+$, 311 (19), 296 (26), 258 (17), 242 (30), 207 (14), 178 (70), 166 (44), 162 (17), 124 (100), 108 (50), 96 (16), 81 (22), 79 (24), 55 (28).

Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.39; H, 6.84; N, 4.29.

Pyrido[2,1-*a*]isoindole-7-carboxylic Acids 15a,b; Typical Procedure

A mixture of **6a** or **6b** (~3 g, 11.0 mmol) and maleic anhydride 1.19 g (12.1 mmol) in toluene (30 mL) was boiled for 4–8 h. At the end of the reaction formation of bright yellow crystals was observed. The crystals were filtered, washed first with benzene (2 × 20 mL), then with acetone (2 × 15 mL), and dried in the open air to give **15a**,**b** as white powders.

(1*R,2*S**,3S*,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-2-hydroxy-1,2,3-trimethyl-6-oxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (15a)**

Yield: 96%; mp 220–225 °C.

IR: 3469 (OH), 1747 (CO_2H), 1680 cm^{-1} (br, N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.57 (d, $J_{Me,3}$ = 6.6 Hz, 3 H, 3-CH_3), 0.91 (d, $J_{Me,1}$ = 6.6 Hz, 3 H, 1-CH_3), 1.10 (s, 3 H, 2-CH_3), 1.72 (dq, $J_{Me,3}$ = 6.6 Hz, $J_{3,4}$ = 10.6 Hz, 1 H, H3), 2.38 (d, $J_{7endo,6a}$ = 9.2 Hz, 1 H, H6a), 2.50 (dq, $J_{Me,1}$ = 6.6 Hz, $J_{1,10b}$ = 11.1 Hz, 1 H, H1), 2.62 (br d, $J_{6a,7endo}$ = 9.2 Hz, 1 H, H7$_{endo}$), 3.97 (d, $J_{10b,1}$ = 11.1 Hz, 1 H, H10b), 4.11 (d, $J_{3,4}$ = 10.6 Hz, 1 H, H4), 4.49 (s, 1 H, OH), 4.95 (d, $J_{8,9}$ = 1.6 Hz, 1 H, H8), 6.13 (br d, $J_{4',3'}$ = 3.2 Hz, 1 H, H3′), 6.26 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{3',4'}$ = 3.2 Hz, 1 H, H4′), 6.34 (dd, $J_{8,9}$ = 1.6 Hz, $J_{9,10}$ = 5.6 Hz, 1 H, H9), 6.56 (d, $J_{9,10}$ = 5.6 Hz, 1 H, H10), 7.45 (dd, $J_{5',3'}$ = 0.6 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 173.5 (CO_2H), 169.6 (C_6), 153.0 ($C_{2'}$), 141.7 ($C_{5'}$), 137.5 and 135.4 (C_{10}, C_9), 110.3 and 108.6 ($C_{4'}$, $C_{3'}$), 89.9 (C_{10a}), 81.0 (C_8), 70.6 (C_2), 58.1 (C_4), 53.9, 50.9, 45.1, 44.4, 40.6 (C_1, C_3, C_{6a}, C_7, C_{10b}), 24.4 (2-CH_3), 11.3 and 10.3 (1-CH_3, 3-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 373 (16) $[M]^+$, 275 (30), 274 (19), 258 (15), 222 (17), 206 (4), 176 (14), 174 (13), 166 (36), 160 (46), 151 (5), 136 (11), 124 (52), 108 (45), 96 (100), 81 (37), 79 (30), 72 (9), 55 (18), 43 (76).

Anal. Calcd for $C_{20}H_{23}NO_6$: C, 64.33; H, 6.21; N, 3.75. Found: C, 64.15; H, 6.31; N, 3.70.

(1*R,2*S**,3S*,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-(2-Furyl)-2-hydroxy-1,3-dimethyl-6-oxo-2-phenyl-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylic Acid (15b)**

Yield: 88%; mp 176–180 °C.

IR: 3179 (br, OH), 1750 (CO_2H), 1673 cm^{-1} (N–C=O).

^1H NMR (400 MHz, DMSO-d_6): δ = 0.18 (d, $J_{Me,3}$ = 6.7 Hz, 3 H, 3-CH_3), 0.54 (d, $J_{Me,1}$ = 6.7 Hz, 3 H, 1-CH_3), 2.22 (m, 2 H, H1, H3), 2.42 (dd, $J_{7endo,6a}$ = 9.2, $^5J_{6a,4}$ = 0.8 Hz, 1 H, H6a), 2.70 (d, $J_{6a,7endo}$ = 9.2 Hz, 1 H, H7$_{endo}$), 4.19 (d, $J_{10b,1}$ = 11.0 Hz, 1 H, H10b), 4.33 (dd, $J_{3,4}$ = 11.0, $^5J_{6a,4}$ = 0.8 Hz, 1 H, H4), 4.98 (d, $J_{8,9}$ = 1.5 Hz, 1 H, H8), 5.06 (s, 1 H, OH), 6.19 (dd, $J_{5',3'}$ = 0.8 Hz, $J_{4',3'}$ = 3.2 Hz, 1 H, H3′), 6.27 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{3',4'}$ = 3.2 Hz, 1 H, H4′), 6.35 (dd, $J_{8,9}$ = 1.5 Hz, $J_{9,10}$ = 5.7 Hz, 1 H, H9), 6.53 (d, $J_{9,10}$ = 5.7 Hz, 1 H, H10), 7.20 (br t, 1 H, H_{Ph}), 7.32–7.41 (m, 4 H, H_{Ph}), 7.46 (dd, $J_{5',3'}$ = 0.8 Hz, $J_{5',4'}$ = 1.8 Hz, 1 H, H5′), 11.09 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ = 173.5 (CO_2H), 169.7 (C_6), 152.3 ($C_{2'}$), 145.8 ($C_{ipso\text{-}Ph}$), 141.9 ($C_{5'}$), 137.1 and 135.8 (C_{10}, C_9), 128.5 (2 C, C_{Ph}), 126.8 ($C_{para\text{-}Ph}$), 125.7 (2 C, C_{Ph}), 110.3 and 108.7 ($C_{4'}$, $C_{3'}$), 89.7 (C_{10a}), 81.1 (C_8), 77.2 (C_2), 58.7 (C_4), 54.2, 50.9, 45.2, 45.0, 41.3 (C_1, C_3, C_{6a}, C_7, C_{10b}), 11.5 and 10.8 (1-CH_3, 3-CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 435 (12) $[M]^+$, 391 (1), 362 (3), 336 (9), 327 (11), 320 (7), 228 (62), 222 (44), 202 (12), 176 (18), 160 (26), 108 (28), 105 (100), 96 (27), 81 (17), 79 (25), 77 (30), 65 (7).

Anal. Calcd for $C_{25}H_{25}NO_6$: C, 68.95; H, 5.79; N, 3.22. Found: C, 68.98; H, 5.89; N, 3.46.

Methyl (1*R,2*S**,3*S**,4*R**,6a*R**,7*S**,8*R**,10a*S**,10b*S**)-4-Furan-2-yl-2-hydroxy-1,2,3-trimethyl-6-oxo-1,3,4,6,6a,7,8,10b-octahydro-2*H*-8,10a-epoxypyrido[2,1-*a*]isoindole-7-carboxylate (16)**

Acid **15a** (3.3 g, 8.5 mmol) added to MeOH (120 mL) and several drops of H_2SO_4 were added. The resulting mixture was refluxed for 12 h (TLC monitoring). The soln was then cooled, poured into H_2O (250 mL), and extracted with CH_2Cl_2 (5 × 80 mL). The organic layers were combined, dried ($MgSO_4$), concentrated, and purified by column chromatography (alumina, CH_2Cl_2) to give **16** as bright brown crystals; yield: 2.97 g (90%); mp 206–208 °C.

IR: 3442 (br, OH), 1711 (CO_2Me), 1682 cm^{-1} (N–C=O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.74 (d, $J_{Me,3}$ = 6.7 Hz, 3 H, 3-CH_3), 1.03 (d, $J_{Me,1}$ = 6.7 Hz, 3 H, 1-CH_3), 1.21 (s, 3 H, 2-CH_3), 1.97 (dq, $J_{Me,3}$ = 6.7 Hz, $J_{3,4}$ = 10.5 Hz, 1 H, H3), 2.05 (dq, $J_{Me,1}$ = 6.7 Hz, $J_{1,10b}$ = 11.1 Hz, 1 H, H1), 2.56 (d, $J_{7endo,6a}$ = 9.1 Hz, 1 H, H6a), 2.64 (d, $J_{6a,7endo}$ = 9.1 Hz, 1 H, H7$_{endo}$), 3.60 (s, 3 H, CO_2Me), 4.00 (d, $J_{10b,1}$ = 11.1 Hz, 1 H, H10b), 4.21 (d, $J_{3,4}$ = 10.5 Hz, 1 H, H4), 5.13 (d, $J_{8,9}$ = 1.7 Hz, 1 H, H8), 6.15 (br d, $J_{3',4'}$ = 3.6 Hz, 1 H, H3′), 6.26 (dd, $J_{4',5'}$ = 1.9 Hz, $J_{4',3'}$ = 3.6 Hz, 1 H, H4′), 6.33 (dd, $J_{8,9}$ = 1.7 Hz,

$J_{9,10}$ = 5.7 Hz, 1 H, H9), 6.50 (d, $J_{9,10}$ = 5.7 Hz, 1 H, H10), 7.30 (br d, $J_{5',4'}$ = 1.9 Hz, 1 H, H5′).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 172.1 (CO_2CH_3), 169.6 (C_6), 152.2 ($C_{2'}$), 141.1 ($C_{5'}$), 136.9 (C_9), 135.0 (C_{10}), 110.1 ($C_{4'}$), 108.1 ($C_{3'}$), 89.8 (C_{10a}), 81.0 (C_8), 71.8 (C_2), 58.3 (C_4), 53.9 (C_{10b}), 52.1 (CO_2CH_3), 51.3 (C_{6a}), 45.4 (C_7), 43.8 (C_3), 39.8 (C_1), 24.8 (2-CH_3), 11.0 (3-CH_3), 9.9 (1-CH_3).

MS (EI, 70 eV): *m/z* (%) = 387 (25) $[M]^+$, 369 (3), 356 (1), 274 (45), 258 (14), 256 (13), 236 (20), 202 (7), 176 (17), 166 (35), 124 (60), 113 (47), 108 (36), 96 (21), 81 (32), 79 (37), 65 (18), 59 (21), 43 (100).

Anal. Calcd for $C_{21}H_{25}NO_6$: C, 65.10; H, 6.50; N, 3.62. Found: C, 64.82; H, 6.65; N, 3.72.

(2*S,3*R**,6*R**)(4*E*)-2,6-Di-2-furyl-3-methylpiperidin-4-one Oxime (17)**

A soln of **2a** (5.0 g, 0.02 mol), NH_2OH·HCl (1.35 g, 0.04 mol), and NaOH (1.6 g, 0.04 mol) in EtOH (70 mL) was refluxed for 2 h. The resulting mixture was poured into H_2O (250 mL) and extracted with EtOAc (3 × 70 mL). The combined organic extracts were dried ($MgSO_4$), concentrated, and purified by the crystallization (hexane–EtOAc) to give **18** as white crystals; yield: 4.2 g (81%); mp 182–183 °C (Lit.[11b] 112 °C).

IR: 3260 (br), 3155, 2978 (NH, OH), 1667 cm^{-1} (C=N).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (d, $J_{3,Me}$ = 6.5 Hz, 3 H, 3-CH_3), 2.15 [dd, $J_{5(a),6}$ = 12.4 Hz, $^2J_{5,5}$ = 13.8 Hz, 1 H, H5(a)], 2.20 (br s, 1 H, NH), 2.69 (dq, $J_{3,2}$ = 10.5 Hz, $J_{3,Me}$ = 6.5 Hz, 1 H, H3), 3.98 (d, $J_{2,3}$ = 10.5 Hz, 1 H, H2), 3.74 [dd, $J_{5(e),6}$ = 3.0 Hz, $^2J_{5,5}$ = 13.8 Hz, 1 H, H5(e)], 3.95 (dd, $J_{6,5(e)}$ = 3.0 Hz, $J_{6,5(a)}$ = 12.4 Hz, 1 H, H6), 6.22 (br d, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ*), 6.28 (dd, $J_{\alpha,\beta}$ = 1.8 Hz, $J_{\beta',\beta}$ = 3.2 Hz, 1 H, Hβ), 6.32–6.29 (m, 2 H, Hβ′, Hβ′*), 7.33 (dd, $J_{\beta',\alpha}$ = 0.8 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα), 7.36 (dd, $J_{\beta',\alpha}$ = 0.6 Hz, $J_{\alpha,\beta}$ = 1.8 Hz, 1 H, Hα*), 7.67 (s, 1 H, OH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 159.0 (C_4), 155.2 and 154.4 (C_{α}, $C_{\alpha*}$), 142.0 and 141.9 (C_{ipso}, C_{ipso*}), 110.2 (2 C, $C_{\beta'}$, $C_{\beta'*}$), 107.5 and 105.6 (C_{β}, $C_{\beta*}$), 61.5 (C_2), 53.6 (C_6), 41.5 (C_3), 29.6 (C_5), 12.0 (3-CH_3).

MS (EI, 70 eV): *m/z* (%) = 260 (60) $[M]^+$, 243 (33), 231 (3), 175 (17), 174 (27), 148 (12), 120 (7), 97 (22), 96 (100), 94 (40), 68 (28), 65 (11).

Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.51; H, 6.31; N, 10.86.

4,6-Di-2-furyl-7-methyl-1*H*-pyrrolo[3,2-*c*]pyridine (18)

Powdered KOH (0.89 g, 0.016 mol) was added to a soln of **17** (4.2 g, 0.016 mol) in DMSO (100 mL). The resulting mixture was heated up to 95 °C and treated with acetylene gas for 5 h. The mixture was the poured into H_2O (350 mL) and extracted with Et_2O (6 × 80 mL). The combined organic layers were dried (Na_2SO_4), concentrated, and purified by column chromatography (alumina, hexane) to give **18** as brown needles; yield: 0.52 g (12%); mp 94–96 °C.

IR: 3494 cm^{-1} (NH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, 7-CH_3), 6.50 (dd, $J_{\alpha,\beta}$ = 1.6 Hz, $J_{\beta,\beta'}$ = 3.3 Hz, 1 H, Hβ), 6.64 (dd, $J_{\alpha,\beta}$ = 1.6 Hz, $J_{\beta,\beta'}$ = 3.3 Hz, 1 H, Hβ), 6.77 (br d, $J_{\beta,\beta'}$ = 3.3 Hz, 1 H, Hβ′), 6.91 (br d, $J_{\beta,\beta'}$ = 3.3 Hz, 1 H, Hβ′), 7.44 (br d, $J_{2,3}$ = 3.1 Hz, 1 H, H2), 7.46 (br d, $J_{\beta,\alpha}$ = 1.6 Hz, 1 H, Hα), 7.52 (s, 1 H, NH), 7.69 (br d, $J_{\beta,\alpha}$ = 1.6 Hz, 1 H, Hα), 7.46 (br d, $J_{2,3}$ = 3.1 Hz, 1 H, H3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 153.9 and 148.8 (C_{ipso}, C_{ipso*}), 144.2 and 142.1 (C_{α}, $C_{\alpha*}$), 131.4 and 131.2 (C_4, C_6), 118.5 (C_2), 114.7 (C_3), 112.2, 112.1, 111.9 (C_7, $C_{\beta'}$, $C_{\beta'*}$), 111.4 and 110.7 (C_{3a}, C_{7a}), 106.6 and 103.8 (C_{β}, $C_{\beta*}$), 10.4 (7-CH_3).

MS (EI, 70 eV): *m/z* (%) = 264 (100) $[M]^+$, 263 (58), 235 (4), 170 (13), 141 (7), 115 (10), 89 (5), 63 (4).

Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.29; N, H, 4.69; 10.97.

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(19) Crystallographic data for **9i**, **9i′**, and **13a** have been deposited with the Cambridge Crystallographic Data Centre, CCDC 719969 – CCDC 719971. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk].