The Use of 4-Hetaryliden- and 4-Aryliden-5(4*H*)-oxazolones as Dienophiles. Appropriate Reagents for the Synthesis of Cyclic Analogues of Natural Amino Acids

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This report describes the behavior of 4-hetaryliden- and 4-aryliden-5(4*H*)-oxazolones as dienophiles in the Diels-Alder reaction with several dienes. The application of this reaction to the synthesis of different conformationally constrained cyclic analogues of natural amino acids of pharmacological interest is also described.

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The importance of 2-oxazolin-5-ones or 5(4*H*)-oxazolones as versatile reagents in organic chemistry is well known . It may be attributed to the fact that they have been used to prepare other important heterocyclic compounds [1] and they are versatile reagents for the synthesis of α-keto and arylacetic acids, peptides and α-amino acids [2]. In particular, the chemistry of unsaturated 5(4*H*)-oxazolones has been well investigated and, in spite of the importance and well known reactivity of the exocyclic double bond [3], only very recently has it been reported that this double bond can act as a dienophile in the Diels-Alder reaction. In this area, we have previously reported the behavior of 2-phenyl-4-benzyliden-5(4*H*)-oxazolone as a dienophile in the Diels-Alder cycloaddition with different dienes such as cyclopentadiene [4,5], 2,3-dimethyl-1,3-butadiene, 1,3-butadiene [6] or Danishefsky's diene [7]. In this context, and as a part of our research project on the synthesis of α-amino acids, we have exploited the reactivity of this dienophile to prepare a variety of conformationally constrained cyclic amino acid analogues of phenylalanine in a racemic form [5,6,7].

Encouraged by the undoubted interest in conformationally constrained α-amino acids and the excellent behavior of 2-phenyl-4-benzyliden-5(4*H*)-oxazolone towards several dienes, we have decided to extend our study to the 2-phenyl-4-aryliden(or hetaryliden)-5(4*H*)-oxazolones. The aim behind this study is to explore their behavior as dienophiles in the Diels-Alder reaction, and the potential versatility of this reaction in the synthesis of different cyclic analogues of natural amino acids of pharmacological interest.

In order to establish a general overall view of the behavior in the Diels-Alder reaction, we have investigated the reactivity of several 2-phenyl-4-aryliden-5(4*H*)-oxazolones **1a-h** bearing one or two electron-withdrawing or non-withdrawing substituents, in *ortho-*, *meta-* or *para*-positions of

Scheme 1

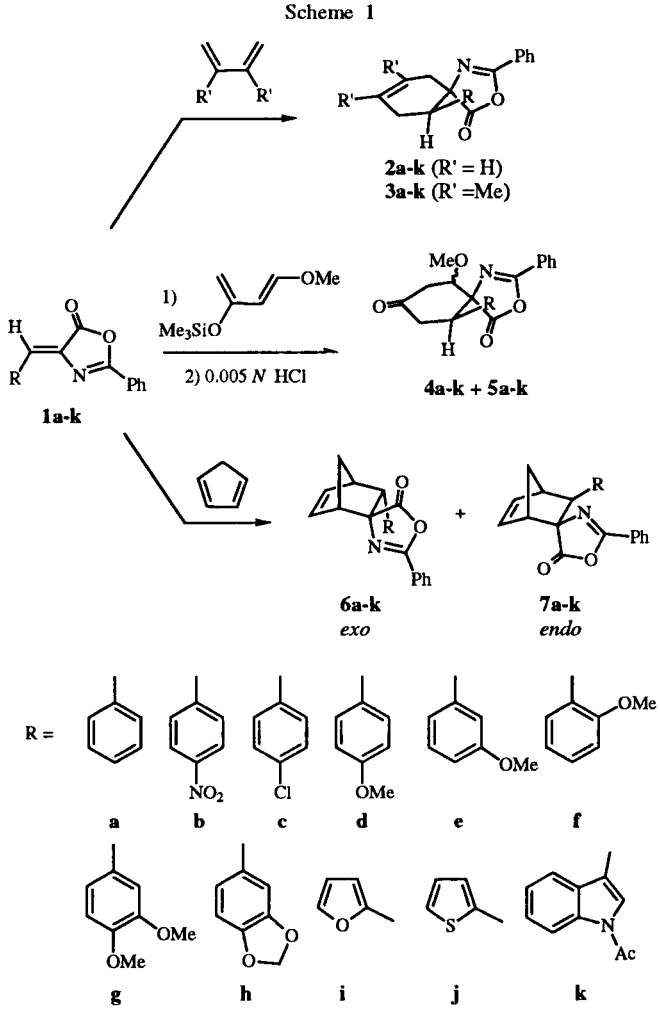


Table 1
Diels-Alder Reactions of 4-Hetaryliden- and Aryliden-5(4*H*)-oxazolones

Compound	Diene [a] (equivalents)	Lewis Acid (equivalents)	time (hours)	T (°C)	Yield (%)	*Endo*/*Exo*
1a	Cyclopentadiene (3)	$AlCl_3$ (0.50)	2	-25	95	0.87
1a	2,3-Dimethyl-1,3-butadiene(3)	$AlCl_2Et$ (0.75)	48	-30	100	–
1a	Butadiene (11)	$AlCl_2Et$ (0.75)	72	0	64	–
1a	Danishefsky's diene (2) [b]	–	48	100	93	0.82
1b	Cyclopentadiene (3)	$AlCl_3$ (0.75)	15	-25	100	0.87
1b	2,3-Dimethyl-1,3-butadiene (6)	$AlCl_3$ (0.75)	48	-25	67	–
1c	Cyclopentadiene (3)	$AlCl_3$ (0.75)	15	-25	100	0.83
1c	2,3-Dimethyl-1,3-butadiene (6)	$AlCl_2Et$ (0.75)	48	-25	75	–
1c	Butadiene (10)	$AlCl_2Et$ (0.75)	48	0	60	–
1d	Cyclopentadiene (3)	$AlCl_2Et$ (0.75)	48	-40	50	0.76
1d	2,3-Dimethyl-1,3-butadiene (6)	$AlCl_2Et$ (0.75)	48	-25	50	–
1e	Cyclopentadiene (3)	$AlCl_3$ (0.75)	24	0	100	0.71
1e	2,3-Dimethyl-1,3-butadiene (6)	$AlCl_3$ (0.75)	48	0	69	–
1f	Cyclopentadiene (3)	$AlCl_3$ (0.75)	1	0	100	0.85
1f	2,3-Dimethyl-1,3-butadiene (6)	$AlCl_3$ (0.75)	5	0	100	–
1f	Butadiene (10)	$AlCl_2Et$ (0.75)	48	0	57	–
1f	Danishefsky's diene (2)	–	48	100	100	1.34
1g	Cyclopentadiene (3)	$AlCl_2Et$ (0.75)	48	-40	50	0.77
1g	2,3-Dimethyl-1,3-butadiene (6)	$AlCl_2Et$ (0.75)	48	-25	50	–
1g	Butadiene (10)	$AlCl_2Et$ (0.75)	336	0	8	–
1g	Danishefsky's diene (2)	–	48	100	100	0.82
1h	Cyclopentadiene (3)	$AlCl_2Et$ (0.75)	48	-25	81	0.82
1i	Cyclopentadiene (5)	$AlCl_2Et$ (1.10)	5	-45	70	0.83
1i	2,3-Dimethyl-1,3-butadiene (5)	$AlCl_3$ (1.10)	12	0	60	–
1j	Cyclopentadiene (5)	$AlCl_2Et$ (1.10)	72	25	71	0.85
1j	2,3-Dimethyl-1,3-butadiene (3)	$AlCl_2Et$ (1.10)	48	0	73	–
1k	Cyclopentadiene (3)	$AlCl_2Et$ (1.10)	21	0	43	0.77
1k	2,3-Dimethyl-1,3-butadiene (3)	$AlCl_2Et$ (1.10)	24	25	25	–

[a] Dichloromethane was used as solvent.
[b] With Danishefsky's diene the reactions were carried out without a catalyst, and toluene was used as the solvent.

the aromatic ring. The reactivity of 2-phenyl-4-hetaryliden-5(4*H*)-oxazolones **1i-k** has been also studied.

The 5(4*H*)-oxazolones **1a-k** were synthesized by the Erlenmeyer-Plöchl method, starting from the corresponding aldehyde and hippuric acid [8]. The Diels-Alder cycloaddition reactions of these dienophiles with cyclopentadiene, 2,3-dimethyl-1,3-butadiene or 1,3-butadiene were performed in an inert atmosphere in the presence of a Lewis acid using dichloromethane as the solvent. However, with Danishefsky's diene, toluene was used as the solvent in the absence of a Lewis acid (Scheme 1). The results of the reactions are summarized in Table 1.

Based on our previous investigation, the Diels-Alder reaction of 2-phenyl-4-benzyliden-5(4*H*)-oxazolone **1a** was, with the exception of the reaction with Danishefsky's diene, carried out using aluminiun derivatives (aluminium chloride and ethylaluminium dichloride) as Lewis acids. The ratio of Lewis acid to dienophile was 0.75/1 or 1.1/1 when aluminium catalysts were used. Lesser quantities of Lewis acid decrease the reaction rate and larger quantities cause considerable isomerization of (*Z*)-oxazolones to the corresponding (*E*)-oxazolones, even when the reaction is carried out at low temperatures, and also increase polymerization of the diene. The relative excess of the diene used with respect to the dienophile depends on the dienes reactivity and its propensity for polymerization.

The reaction temperature selected corresponds to a balance between the increased reaction rate observed when working at temperatures near to 0-25° and the aim of avoiding the isomerization reaction by working at low temperatures. Thus, in the case of oxazolones **1d**, **1g** and **1i** isomerization was observed even at -25°. This observation obliged us to work at -40°, leading to a decrease in the reaction yield. In general, it can be seen from Table 1 that the reactivity of 2-phenyl-4-aryliden-5(4*H*)-oxazolones **1b-h** is lesser than that of 2-phenyl-4-benzyliden-5(4*H*)-oxazolone **1a**. Only in the case of oxazolone **1f** is the behavior similar to that of oxazolone **1a**. The most important feature is that when activating substituents are present in the *para*-position of the ring, isomerization constitutes a significant problem.

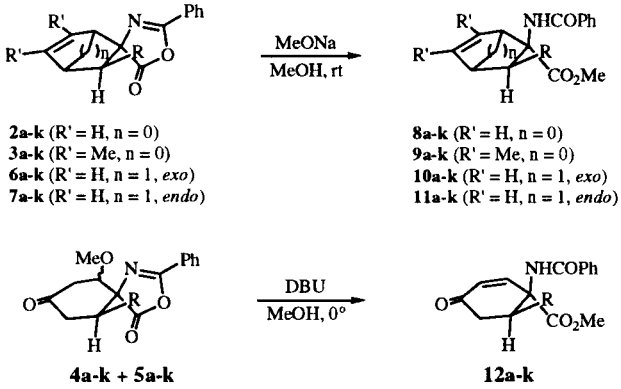
Several 2-phenyl-4-hetaryliden-5(4*H*)-oxazolones were investigated (2-furyl, 2-thienyl, *N*-methyl-2-pyrrolyl and *N*-acetyl-3-indolyl), but only with the 2-furyl, 2-thienyl and *N*-acetyl-3-indolyl derivatives was a reaction

observed and their reactivity was lower than that of 2-phenyl-4-aryliden-5(4*H*)-oxazolones **1a-h**. The problem is the same as that described in the case discussed above; isomerization is caused by the coordination of the Lewis acid to the oxygen of the carbonyl group. Because of this, we attempted to carry out the Diels-Alder reactions in the absence of a Lewis acid. However, no reaction occurred even in polar solvents or organic-aqueous mixtures of solvents at moderate or high temperatures, which is a method described by several authors as greatly increasing the Diels-Alder reaction rate [9].

The *endo/exo* ratio observed in the reactions with cyclopentadiene was similar to that obtained with 5(4*H*)-oxazolone **1a** and thus it appears that the *endo/exo* ratio does not depend on the nature of the substituent.

The reactions were monitored by tlc and the results of the conversion and *endo/exo* ratio were established by ^{1}H nmr spectroscopy of the crude mixture [10]. In order to characterize the corresponding cycloadducts, the crude mixture of each Diels-Alder cycloaddition reaction was purified by column chromatography (silica gel). In the cases of the reactions with cyclopentadiene we also attempted to separate *endo* and *exo* adducts. However, in all cases the spiroxazolone adducts were retained on the column, probably due to the action of the silica gel opening the heterocycle ring. Only a few milligrams of spiroxazolone adducts were obtained for characterization by ^{1}H nmr and ^{13}C nmr spectroscopy. In some cases, insufficient amounts were obtained for characterization and the mixture of adducts was, in each case, treated with sodium methoxide in methanol in order to obtain the corresponding methyl *N*-benzoylamino ester derivatives **8a-k**, **9a-k**, **10a-k** and **11a-k**. This procedure was followed when 1,3-butadiene, 2,3-dimethyl-1,3-butadiene or cyclopentadiene were used. The same situation occurred with Danishefsky's diene but, in this case, the mixture of cycloadducts **4a-k** and **5a-k** were treated with 1,8-diazabicyclo[5.4.0]undec-7-ene in methanol at 0° to produce the corresponding methyl α,β-unsaturated *N*-benzoylamino ester derivatives **12a-k** (Scheme 2).

Scheme 2



2a-k (R' = H, n = 0)
3a-k (R' = Me, n = 0)
6a-k (R' = H, n = 1, *exo*)
7a-k (R' = H, n = 1, *endo*)

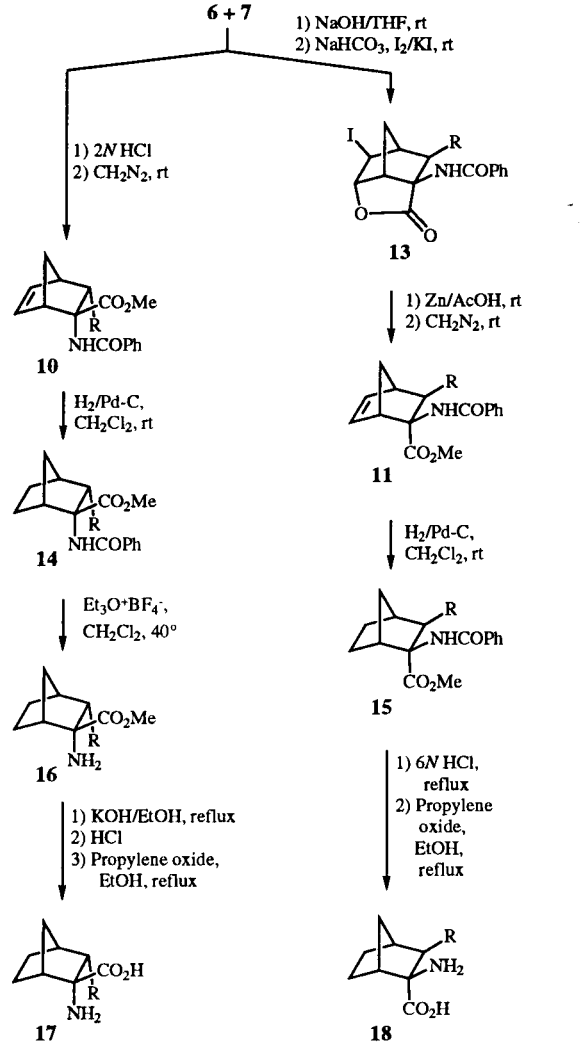
8a-k (R' = H, n = 0)
9a-k (R' = Me, n = 0)
10a-k (R' = H, n = 1, *exo*)
11a-k (R' = H, n = 1, *endo*)

4a-k + 5a-k

12a-k

In order to demonstrate the validity of this synthetic procedure to obtain cyclic analogues of natural amino acids we decided to synthesize some conformationally constrained cyclic analogues of α-amino acids with pharmacological interest, such as dopa and triptophan. In this way, the mixture of spiroxazolone adducts **6k** and **7k** was stereospecifically hydrolyzed by treatment with a 5% aqueous solution of sodium hydroxide in tetrahydrofuran at room temperature to afford the *exo*- and *endo*-*N*-benzoyl-α-amino acids, which were separated by a typical iodolactonization procedure (Scheme 3).

Scheme 3



Methyl ester **10k** was prepared by quantitative esterification of *endo*-*N*-benzoyl-α-amino acid with diazomethane. On the other hand, methyl ester **11k** was obtained by treatment of the iodolactone **13k** with zinc-acetic acid and further esterification with diazomethane.

Both compounds **10k** and **11k** were hydrogenated using 10% palladium on carbon as a catalyst to give the corre-

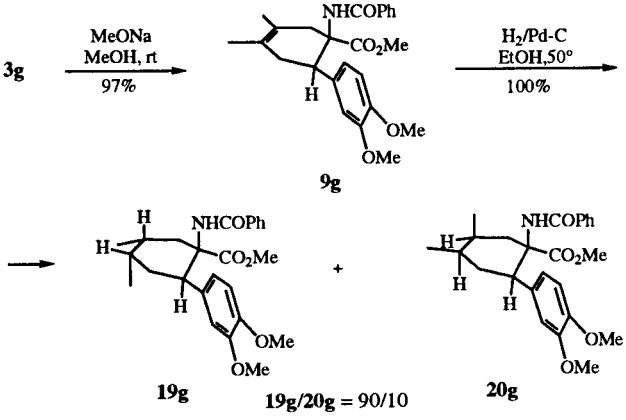
sponding saturated compounds **14k** and **15k**. Unluckily, the hydrolysis of the benzamido group in these compounds did not take place either in an acid medium (6 *N* hydrochloric acid under reflux) or using another hydrolysis procedure based on the imidate formation by addition of Meerwein's reagent (triethyloxonium tetrafluoroborate) [11].

We then attempted the synthesis of new cyclic methyl 3-hydroxytyrosine analogues, taking into account that, to the best of our knowledge, only the synthesis and pharmacological activity of 1-amino-2-(3',4'-dihydroxyphenyl)-cyclohexane-1-carboxylic acid obtained through the Bucherer-Bergs synthesis, presumably as a mixture of stereoisomers, has been previously reported [12].

Unfortunately, 1,3-butadiene is less reactive than cyclopentadiene [13], so all attempts to react oxazolone **1g** with 1,3-butadiene were unsuccessful, and we were unable to prepare the corresponding 1-amino-2-(3',4'-dimethoxyphenyl) cyclohexane-1-carboxylic acid. Indeed, only an 8% yield of conversion was observed, even after 14 days at 0°, when oxazolone **1g**, 1,3-butadiene and ethylaluminium dichloride were used in a ratio of 1:10:0.75.

By exploiting the higher reactivity of 2,3-dimethyl-1,3-butadiene in comparison with 1,3-butadiene [13], the spiroxazolone adduct **3g** was transformed, by the action of sodium methoxide, into the corresponding *N*-benzoyl methyl ester **9g**. Compound **9g** was hydrogenated using 10% palladium on carbon at 50° in ethanol to give a mixture of isomers **19g** and **20g** in a ratio of 90/10 as determined by ^{1}H nmr (Scheme 4).

Scheme 4



The geometry of these compounds was established by consideration of their nmr spectral data, taking particular account of the multiplicity of protons H_{6a} and H_{3a} and the values of their coupling constants. Proton H_{6a} , in the major compound, shows a doublet of doublets collapsed into a triplet system due to strong couplings with protons H_{6e} and H_{5a} ($J_{6a\text{-}6e} = J_{6a\text{-}5a} = 13.7$ Hz) corresponding to the geminal coupling constant and to the axial-axial coupling constant, respectively. Proton H_{3a} shows a doublet of doublet of doublets collapsed into a triplet of doublets system. The large couplings observed in the triplet ($J_{3a\text{-}3e} = J_{3a\text{-}2a} = 13.7$ Hz) show that proton H_{3a} has an axial neighbor (H_{2a}) as well as a geminal partner (H_{3e}).

These results can only be explained if the major product has the structure **19g**. The remarkable stereochemical control in the hydrogenation could be due to the presence of the benzamido group, which is capable of coordinating to the catalyst surface in such a way that it forces the addition of hydrogen to its own side of the molecule [14]. This mixture of hydrogenated products could not be separated by either silica gel column chromatography or by hydrolysis under any conditions (Scheme 4).

On the other hand, we have synthesized two new conformationally constrained cyclic *O*-methyl 3-hydroxytyrosine analogues, **17g** and **18g**, starting from the spiroxazolone adducts **6g** and **7g** by a similar procedure to that described above for the analogues of tryptophan (Scheme 3). In this case, the benzamide group in compound **15g** was hydrolyzed in 6 *N* hydrochloric acid under reflux without difficulty and the free α-amino acid **18g** was obtained by heating a mixture of the hydrochloride salt in ethanol under reflux with an excess of propylene oxide. Nevertheless, hydrolysis of the amide group in compound **14g** occurred in very low yield under the same conditions and once again we used Meerwein's reagent [11]. After hydrolysis with 10% aqueous acetic acid, the work-up yielded the α-amino methyl ester **16g**, which was saponified with 10% potassium hydroxide-ethanol under reflux for 6 hours. The isolation of the free α-amino acid **17g** was achieved using the procedure described above for α-amino acid **18g**.

In summary, 2-phenyl-4-aryliden-5(4*H*)-oxazolones and 2-phenyl-4-hetaryliden-5(4*H*)-oxazolones behave as dienophiles in the Diels-Alder reaction and their reactivity depends on the nature of the subtituents on the aromatic ring. This dependency means that their use as appropriate reagents in the synthesis of cyclic analogues of natural amino acids is not a general procedure. However, in a number of cases the dienophile behavior can be of great utility, although it is necessary to undertake a careful study in each particular case.

EXPERIMENTAL

Solvents were purified according to standard procedures. Analytical tlc was performed using Polychrom SI F_{254} plates. ^{1}H and ^{13}C nmr spectra were recorded on a Bruker ARX-300 spectrometer. The ^{1}H and ^{13}C nmr spectra were recorded in deuteriochloroform with tetramethylsilane as the internal standard and in deuterium oxide-trifluoroacetic acid with tetramethylsilane as the external standard using a coaxial microtube (chemical shifts are reported in ppm on the δ scale, coupling

constants in Hz). Melting points were determined on a Büchi SMP-20 melting point apparatus and are uncorrected. Microanalyses were carried out on a Perkin-Elmer 240-C analyzer and were in good agreement with the calculated values.

General Procedure for the Diels-Alder Reaction of 5(4*H*)-Oxazolones **1a-k** with Cyclopentadiene, 2,3-Dimethyl-1,3-butadiene or 1,3-Butadiene, **2a-k**, **3a-k**, **6a-k** and **7a-k**.

All of these reactions were carried out under an inert atmosphere.

Method A with Aluminium Chloride.

Oxazolone **1a-k** (1 mmole) and the corresponding quantity of the aluminium chloride (see Table 1) were dissolved in dichloromethane (10 ml) at the temperature indicated in Table 1. After stirring for 1 hour, a solution of the corresponding quantity of the diene (see Table 1) in dry dichloromethane (5 ml), at the same temperature, was added dropwise and the mixture was stirred for an additional time reported in Table 1 at the corresponding temperature. The reaction was quenched by the addition of solid sodium carbonate decahydrate, the precipitate was filtered and the solvent was evaporated *in vacuo*. The residue was purified by silica gel column chromatography to afford the cycloadducts **2a-k**, **3a-k**, **6a-k** and **7a-k**.

Method B with Ethylaluminium Dichloride.

A solution of 1 *M* aluminium catalyst in hexane (0.75 ml) was added to a solution of oxazolone **1a-k** (1 mmole) in dry dichloromethane (10 ml) under an inert atmosphere. After 1 hour stirring at the temperature indicated in Table 1, a solution of the corresponding quantity of the diene (see Table 1) in dry dichloromethane (5 ml), at the same temperature, was added dropwise and the mixture was stirred for an additional time reported in Table 1 at the corresponding temperature. The reaction was quenched by the addition of solid sodium carbonate decahydrate, the precipitate was filtered off and the solvent was evaporated *in vacuo*. The residue was purified by silica gel column chromatography to afford the cycloadducts **2a-k**, **3a-k**, **6a-k** and **7a-k**.

cis-6-(4'-Chlorophenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**2c**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1c** with 1,3-butadiene, by silica gel column chromatography (toluene), gave 171 mg (51%) of compound **2c**, as an oil; ^{1}H nmr: δ 2.19-2.42 (m, 2H, H_{5a}, H_{5e}), 2.70-2.94 (m, 2H, H_{2a}, H_{2e}), 3.34 (dd, 1H, J_{6a-5a} = 12.0, J_{6a-5e} = 5.4, H_{6a}), 5.76-5.85 (m, 1H, H_3), 5.94-6.03 (m, 1H, H_4), 7.04-7.18 (m, 4H, Arom), 7.38-7.58 (m, 3H, Arom), 7.84-7.92 (m, 2H, Arom); ^{13}C nmr: δ 28.8, 35.5, 45.5 (C_2, C_5, C_6), 72.1 (C_1), 122.1, 125.6, 126.8, 127.9, 128.4, 128.7, 130.0, 132.7, 133.5, 137.0 (C_3, C_4, Arom), 160.8 (C=N), 179.8 (COO).

Anal. Calcd. for $C_{20}H_{16}NO_2Cl$: C, 71.11; H, 4.77; N, 4.15; Cl, 10.50. Found C, 70.89; H, 4.83; N, 4.20; Cl, 10.58.

cis-6-(2'-Methoxyphenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**2f**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1f** with 1,3-butadiene, by silica gel column chromatography (toluene), gave 216 mg (65%) of compound **2f**, as an oil; ^{1}H nmr: δ 2.18-2.32 (m, 2H, H_{5a}, H_{5e}), 2.62-2.80 (m, 1H, H_{2a}), 2.87-2.99 (m, 1H, H_{2e}), 3.80 (s, 3H, OCH_3), 4.20 (dd, 1H, J_{6a-5a} = 12.3, J_{6a-5e} = 5.4, H_{6a}), 5.77-5.85 (m, 1H, H_3), 5.96-6.04 (m, 1H, H_4), 6.56-6.65 (m, 1H, Arom), 6.78-6.85 (m, 1H, Arom), 7.03-7.18 (m, 2H, Arom), 7.38-7.57 (m, 3H, Arom), 7.89-7.94 (m, 2H, Arom); ^{13}C nmr: δ 29.4, 35.6, 35.9 (C_2, C_5, C_6), 55.7 (OCH_3), 72.1 (C_1), 111.1, 120.0, 126.0, 127.5, 127.6, 127.9, 128.2, 128.3, 128.6, 132.4, 137.4, 157.0 (C_3, C_4, Arom), 160.5 (C=N), 179.7 (COO).

Anal. Calcd. for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found C, 75.79; H, 5.83; N, 4.10.

cis-6-(3',4'-Dimethoxyphenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**2g**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1g** with 1,3-butadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave 29 mg (8%) of compound **2g**, as an oil; ^{1}H nmr: δ 2.80-3.10 (m, 4H, H_{2a}, H_{2e}, H_{5a}, H_{5e}), 3.66 (s, 3H, OCH_3), 3.82-3.88(m, 4H, OCH_3, H_{6a}), 6.80-7.92 (m, 10H, H_3, H_4, Arom); ^{13}C nmr: δ 29.6, 31.5, 31.8 (C_2, C_5, C_6), 55.5, 55.7 (2OCH_3), 61.7 (C_1), 110.7, 112.0, 124.0, 126.6, 126.9, 127.3, 128.7, 128.8, 132.0, 132.1, 148.5, 149.8 (C_3, C_4, Arom), 165.5 (C=N), 179.8 (COO).

Anal. Calcd. for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found C, 72.79; H, 5.73; N, 3.90.

cis-3,4-Dimethyl-6-(4'-nitrophenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3b**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1b** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (toluene), gave 210 mg (53%) of compound **3b**, as an oil; ^{1}H nmr: δ 1.72 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.14-2.22 (m, 2H, H_{2e}, H_{5e}), 2.85-2.90 (m, 2H, H_{5a}, H_{2a}), 3.46 (dd, 1H, J_{6a-5a} = 12.3, J_{6a-5e} = 4.9, H_{6a}), 7.32-7.60 (m, 5H, Arom), 7.85-8.10 (m, 4H, Arom); ^{13}C nmr: δ 18.4 (CH_3), 18.9 (CH_3), 34.6, 41.2, 46.2 (C_2, C_5, C_6), 72.7 (C_1), 121.2, 123.3, 123.9, 125.3, 127.9, 128.7, 129.6, 132.7, 132.9, 146.3 (C_3, C_4, Arom), 160.9 (C=N), 179.4 (COO).

Anal. Calcd. for $C_{22}H_{20}N_2O_4$: C, 70.21; H, 5.36; N, 7.44. Found C, 70.09; H, 5.43; N, 7.53.

cis-3,4-Dimethyl-6-(4'-chlorophenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3c**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1c** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (hexane-toluene 1:3), gave 110 mg (31%) of compound **3c**, as an oil; ^{1}H nmr: δ 1.70 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 2.04-2.18 (m, 2H, H_{2e}, H_{5e}), 2.72-2.90 (m, 2H, H_{2a}, H_{5a}), 3.32 (dd, 1H, J_{6a-5a} = 12.2, J_{6a-5e} = 5.1, H_{6a}), 7.08-7.12 (m, 4H, Arom), 7.38-7.56 (m, 3H, Arom), 7.86-7.92 (m, 2H, Arom); ^{13}C nmr: δ 18.4 (CH_3), 19.0 (CH_3), 35.0, 41.2, 46.3 (C_2, C_5, C_6), 73.0 (C_1), 121.0, 125.7, 127.9, 128.4, 129.0, 130.0, 132.6, 133.3, 133.5, 137.1, (C_3, C_4, Arom), 160.6 (C=N), 179.9 (COO).

Anal. Calcd. for $C_{22}H_{20}NO_2Cl$: C, 72.23; H, 5.51; N, 3.83; Cl, 9.69. Found: C, 72.14; H, 5.89; N, 3.71; Cl, 9.75.

cis-3,4-Dimethyl-6-(4'-methoxyphenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3d**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1d** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave 105 mg (30%) of compound **3d**, as an oil; ^{1}H nmr: δ 1.70 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 2.05-2.20 (m, 2H, H_{2e}, H_{5e}), 2.75-2.90 (m, 2H, H_{2a}, H_{5a}), 3.30 (dd, 1H, J_{6a-5a} = 12.3, J_{6a-5e} = 5.2, H_{6a}), 3.67 (s, 3H,

OCH_3), 6.62-6.70 (m, 2H, Arom), 7.06-7.12 (m, 2H, Arom), 7.38-7.56 (m, 3H, Arom), 7.86-7.92 (m, 2H, Arom); ^{13}C nmr: δ 18.4 (CH_3), 19.0 (CH_3), 35.2, 41.0, 46.2 (C_2, C_5, C_6), 55.0 (OCH_3), 73.4 (C_1), 113.4, 120.9, 126.0, 127.9, 128.3, 128.6, 129.6, 130.5, 132.4, 158.7 (C_3, C_4, Arom), 160.4 (C=N), 180.2 (COO).

Anal. Calcd. for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88. Found: C, 76.38; H, 6.43; N, 3.86.

cis-3,4-Dimethyl-6-(3'-methoxyphenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3e**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1e** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave 180 mg (50%) of compound **3e**, as an oil; ^1H nmr: δ 1.71 (s, 3H, CH_3), 1.76 (s, 3H, CH_3), 2.05-2.22 (m, 2H, H_{2e}, H_{5e}), 2.76-2.92 (m, 2H, H_{2a}, H_{5a}), 3.31 (dd, 1H, $J_{6a\text{-}5a}$ = 12.2, $J_{6a\text{-}5e}$ = 5.2, H_{6a}), 3.53 (s, 3H, OCH_3), 6.64-6.78 (m, 3H, Arom), 7.00-7.06 (m, 1H, Arom), 7.36-7.56 (m, 3H, Arom), 7.86-7.94 (m, 2H, Arom); ^{13}C nmr: δ 17.4 (CH_3), 18.2 (CH_3), 34.1, 40.2, 46.1 (C_2, C_5, C_6), 52.7 (OCH_3), 72.2 (C_1), 112.5, 112.7, 119.9, 120.1, 125.0, 126.9, 127.3, 127.7, 128.2, 131.5, 139.2, 158.2 (C_3, C_4, Arom), 159.5 (C=N), 179.0 (COO).

Anal. Calcd. for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88. Found: C, 76.40; H, 6.39; N, 3.87.

cis-3,4-Dimethyl-6-(2'-methoxyphenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3f**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1f** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave 255 mg (70%) of compound **3f**, as an oil; ^1H nmr: δ 1.71 (s, 3H, CH_3), 1.76 (s, 3H, CH_3), 2.02-2.16 (m, 2H, H_{2e}, H_{5e}), 2.70-2.82 (m, 1H, H_{5a}), 2.93 (d, 1H, $J_{2a\text{-}2e}$ = 16.8, H_{2a}), 3.79 (s, 3H, OCH_3), 4.21 (dd, 1H, $J_{6a\text{-}5a}$ = 12.3, $J_{6a\text{-}5e}$ = 5.1, H_{6a}), 6.56-6.64 (m, 1H, Arom), 6.76-6.84 (m, 1H, Arom), 7.02-7.10 (m, 1H, Arom), 7.16-7.20 (m, 1H, Arom), 7.36-7.54 (m, 3H, Arom), 7.88-7.96 (m, 2H, Arom); ^{13}C nmr: δ 18.3 (CH_3), 18.9 (CH_3), 35.4, 36.5, 41.4 (C_2, C_5, C_6), 55.5 (OCH_3), 72.7 (C_1), 110.8, 119.7, 120.8, 126.0, 126.2, 127.3, 127.7, 128.0, 128.2, 128.4, 132.2, 156.8 (C_3, C_4, Arom.), 160.2 (C=N), 179.6 (COO).

Anal. Calcd. for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88. Found: C, 76.50; H, 6.44; N, 3.90.

cis-3,4-Dimethyl-6-(3',4'-dimethoxyphenyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3g**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1g** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave 100 mg (30%) of compound **3g**, as an oil; ^1H nmr: δ 1.71 (s, 3H, CH_3), 1.76 (s, 3H, CH_3), 2.04-2.20 (m, 2H, H_{2e}, H_{5e}), 2.72-2.92 (m, 2H, H_{2a}, H_{5a}), 3.29 (dd, 1H, $J_{6a\text{-}5a}$ = 18.0, $J_{6a\text{-}5e}$ = 6.0, H_{6a}), 3.49 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 6.60-6.74 (m, 3H, Arom), 7.36-7.54 (m, 3H, Arom), 7.86-7.94 (m, 2H, Arom); ^{13}C nmr: δ 18.4 (CH_3), 19.0 (CH_3), 35.4, 41.0, 46.7 (C_2, C_5, C_6), 55.3, 55.6 ($2OCH_3$), 73.8 (C_1), 110.6, 111.0, 120.9, 121.3, 125.9, 127.9, 128.0, 128.6, 131.1, 132.5, 148.1, 148.2 (C_3, C_4, Arom), 160.5 (C=N), 180.1 (COO).

Anal. Calcd. for $C_{24}H_{25}NO_4$: C, 73.64; H, 6.44; N, 3.58. Found: C, 73.59; H, 6.41; N, 3.59.

cis-3,4-Dimethyl-6-(2'-furyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3i**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1i** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave 100 mg (40%) of compound **3i**, as an oil; ^1H nmr: δ 1.68 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 2.06 (d, 1H, $J_{2e\text{-}2a}$ = 17.4, H_{2e}), 2.23 (dd, 1H, $J_{5e\text{-}5a}$ = 16.8, $J_{5e\text{-}6a}$ = 5.3, H_{5e}), 2.72-2.85 (m, 2H, H_{5a}, H_{2a}), 3.50 (dd, 1H, $J_{6a\text{-}5a}$ = 17.3, $J_{6a\text{-}5e}$ = 5.3, H_{6a}), 6.00 (d, 1H, $J_{3'\text{-}4'}$ = 3.1, $H_{3'}$), 6.12 (dd, 1H, $J_{4'\text{-}3'}$ = 3.1, $J_{4'\text{-}5'}$ = 1.8, $H_{4'}$), 7.17 (dd, 1H, $J_{5'\text{-}4'}$ = 1.8, $J_{5'\text{-}3'}$ = 0.7, $H_{5'}$), 7.37-7.50 (m, 3H, Arom), 7.88-7.91 (m, 2H, Arom); ^{13}C nmr: δ 18.4 (CH_3), 18.9 (CH_3), 33.0, 40.4, 40.6 (C_2, C_5, C_6), 71.8 (C_1), 106.7, 110.0 ($C_{3'}$, $C_{4'}$), 121.0, 125.1 (C_4, C_3), 126.0, 127.7, 128.0, 128.5, 132.4, 141.6 ($C_{2'}$, $C_{5'}$, Arom), 106.6 (C=N), 180.2 (COO).

Anal. Calcd. for $C_{20}H_{19}NO_3$: C, 74.76; H, 5.91; N, 4.36. Found: C, 74.96; H, 6.02; N, 4.32.

cis-3,4-Dimethyl-6-(2'-thienyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3j**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1j** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave 20 mg (6%) of compound **3j**, as an oil; ^1H nmr: δ 1.69 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 2.10 (d, 1H, $J_{2e\text{-}2a}$ = 19.5, H_{2e}), 2.26 (dd, 1H, $J_{5e\text{-}5a}$ = 16.5, $J_{5e\text{-}6a}$ = 5.2, H_{5e}), 2.72-2.88 (m, 2H, H_{2a}, H_{5a}), 3.72 (dd, 1H, $J_{6a\text{-}5a}$ = 12.5, $J_{6a\text{-}5e}$ = 5.2, H_{6a}), 6.50 (d, 1H, $J_{3'\text{-}4'}$ = 3.1, $H_{3'}$), 6.80 (dd, 1H, $J_{4'\text{-}5'}$ = 5.0, $J_{4'\text{-}3'}$ = 3.1, $H_{4'}$), 7.02 (d, 1H, $J_{5'\text{-}4'}$ = 5.0, $H_{5'}$), 7.40-7.96 (m, 5H, Arom); ^{13}C nmr: δ 18.4 (CH_3), 18.9 (CH_3), 37.2, 40.8, 42.5 (C_2, C_5, C_6), 73.15 (C_1), 121.1, 124.7, 125.9, 126.0, 126.4, 128.2, 128.6, 128.7, 129.0, 132.5, (C_3, C_4, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$, Arom), 158.4 (C=N), 175.5 (COO).

Anal. Calcd. for $C_{20}H_{19}NO_2S$: C, 71.19; H, 5.68; N, 4.15; S, 9.51. Found: C, 71.31; H, 5.73; N, 4.09; S, 9.63.

cis-3,4-Dimethyl-6-(*N*-acetyl-3'-indolyl)cyclohex-1-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-3-ene (**3k**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1k** with 2,3-dimethyl-1,3-butadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave 187 mg (45%) of compound **3k**, as an oil; ^1H nmr: δ 1.74 (s, 3H, CH_3), 1.76 (s, 3H, CH_3), 2.16 (s, 3H, $COCH_3$), 2.19-2.36 (m, 2H, H_{2e}, H_{5e}), 2.78 (dd, 1H, $J_{5a\text{-}5e}$ = 16.0, $J_{5a\text{-}6a}$ = 12.0, H_{5a}), 2.93 (d, 1H, $J_{2a\text{-}2e}$ = 17.1, H_{2a}), 3.68 (dd, 1H, $J_{6a\text{-}5a}$ = 12.0, $J_{6a\text{-}5e}$ = 5.1, H_{6a}), 7.1-8.30 (m, 10H, Arom); ^{13}C nmr: δ 18.4 (CH_3), 18.9 (CH_3), 23.4 ($COCH_3$), 36.1, 37.6, 40.4 (C_2, C_5, C_6), 72.3 (C_1), 116.3, 119.4, 120.4, 121.3, 123.1, 123.4, 125.4, 125.7, 125.8, 127.8, 128.7, 129.5, 132.7, 135.3 (Arom, C_3, C_4), 161.0 (C=N), 168.2 ($COCH_3$), 179.9 (COO).

Anal. Calcd. for $C_{26}H_{24}N_2O_3$: C, 75.70; H, 5.87; N, 6.79. Found: C, 75.78; H, 5.94; N, 6.73.

cis-endo-3-(4'-Nitrophenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**6b**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1b** with cyclopentadiene, by silica gel column chromatography (toluene), gave 111.6 mg (31%) of compound **6b**, as an oil; ^1H nmr: δ 1.67 (d, 1H, $J_{7s\text{-}7a}$ =9.3, H_{7s}), 2.40 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 3.20 (broad s, 1H, H_4), 3.31 (broad s, 1H, H_1), 3.91 (d, 1H, $J_{3x\text{-}4}$ = 2.7, H_{3x}), 6.48-6.56 (m, 2H, H_5, H_6), 7.36-7.54 (m, 5H, Arom), 7.78-7.84 (m, 2H, Arom), 8.00-8.06 (m, 2H, Arom); ^{13}C nmr: δ 46.9, 49.9, 55.7, 57.7 (C_1, C_3, C_4, C_7), 76.6 (C_2), 122.6, 127.6, 127.7, 128.6, 128.7, 130.8, 132.7, 136.4, 137.3, 146.1 (Arom, C_5, C_6), 160.0 (C=N), 181.4 (COO).

Anal. Calcd. for $C_{21}H_{16}N_2O_4$: C, 69.99; H, 4.48; N, 7.77. Found: C, 69.90; H, 4.50; N, 7.75.

cis-exo-3-(4'-Nitrophenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**7b**).

Despite this compound being easily separated from its isomer **6b**, compound **7b** could not be separated from a side-product, so it was only possible to obtain the ^{1}H nmr spectrum of this mixture; ^{1}H nmr: δ 1.97 (dd, 1H, $J_{7s\text{-}7a}$ = 9.0, $J_{7s\text{-}3n}$ = 1.0, H_{7s}), 2.73 (d, 1H, $J_{7a\text{-}7s}$ = 9.0, H_{7a}), 3.03 (broad s, 1H, H_4), 3.30 (d, 1H, $J_{3n\text{-}4}$ = 1.0, H_{3n}), 4.19 (broad s, 1H, H_1), 6.38 (dd, 1H, $J_{6\text{-}5}$ = 5.5, $J_{6\text{-}1}$ = 2.9, H_6), 6.73 (dd, 1H, $J_{5\text{-}6}$ = 5.3, $J_{5\text{-}4}$ = 3.2, H_5), 7.30-8.10 (m, 9H, Arom).

cis-endo-3-(4'-Chlorophenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**6c**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1c** with cyclopentadiene, by silica gel column chromatography (toluene), gave 115 mg (33%) of compound **6c**, as an oil; ^{1}H nmr: δ 1.64 (d, 1H, $J_{7s\text{-}7a}$ = 9.1, H_{7s}), 2.37 (d, 1H, $J_{7a\text{-}7s}$ = 9.2, H_{7a}), 3.16 (broad s, 1H, H_4), 3.25 (broad s, 1H, H_1), 3.81 (d, 1H, $J_{3x\text{-}4}$ = 3.1, H_{3x}), 6.46-6.54 (m, 2H, H_5, H_6), 7.12-7.54 (m, 7H, Arom), 7.28-7.84 (m, 2H, Arom); ^{13}C nmr: δ 46.9, 49.7, 55.5, 57.5 (C_1, C_3, C_4, C_7), 76.5 (C_2), 127.7, 127.8, 128.6, 129.0, 131.2, 132.4, 133.5, 136.7, 136.8, 153.8 (Arom, C_5, C_6), 159.6 (C=N), 182.0 (COO).

Anal. Calcd. for $C_{21}H_{16}NO_2Cl$: C, 72.10; H, 4.61; N, 4.00; Cl, 10.13. Found: C, 72.09; H, 4.69; N, 4.10; Cl, 10.20.

cis-exo-3-(4'-Chlorophenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**7c**).

Despite this compound being easily separated from its isomer **6c**, compound **7c** could not be separated from a side-product, so it was only possible to obtain the ^{1}H nmr spectrum of this mixture; ^{1}H nmr: δ 1.78 (d, 1H, $J_{7s\text{-}7a}$ = 11.0, H_{7s}), 1.88 (d, 1H, $J_{7a\text{-}7s}$ = 11.0, H_{7a}), 3.25 (broad s, 1H, H_4), 3.30 (broad s, 1H, H_{3n}), 4.04 (broad s, 1H, H_1), 6.05-6.10 (m, 1H, H_6), 6.64-6.70 (m, 1H, H_5), 7.10-7.84 (m, 9H, Arom).

cis-endo-3-(4'-Methoxyphenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**6d**).

This compound could not be separated from compound **7d**, but due to the different integration of their signals in the ^{1}H nmr spectrum, the following assignment was established; ^{1}H nmr: δ 1.75 (d, 1H, $J_{7s\text{-}7a}$ = 9.3, H_{7s}), 1.90 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 3.25 (broad s, 1H, H_4), 3.80 (s, 3H, OCH_3), 4.00 (broad s, 1H, H_1), 4.55 (d, 1H, $J_{3x\text{-}4}$ = 2.1, H_{3x}), 6.64-6.70 (m, 2H, H_5, H_6), 6.85-7.00 (m, 4H, Arom), 7.20-7.40 (m, 5H, Arom).

cis-exo-3-(4'-Methoxyphenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**7d**).

The assignment of **7d** was established from the mixture of compounds **6d** and **7d**; ^{1}H nmr: δ 1.60 (d, 1H, $J_{7s\text{-}7a}$ = 9.3, H_{7s}), 2.35 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 3.15 (broad s, 1H, H_4), 3.25 (broad s, 1H, H_1), 3.70 (s, 3H, OCH_3), 4.00 (m, 1H, H_{3n}), 6.40-6.46 (m, 1H, H_6), 6.50-6.58 (m, 1H, H_5), 6.64-6.70 (m, 2H, Arom), 7.10-7.18 (m, 2H, Arom), 7.20-7.40 (m, 3H, Arom), 7.78-7.82 (m, 2H, Arom).

cis-endo-3-(3'-Methoxyphenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**6e**).

This compound could not be separated from compound **7e**, but due to the different integration of their signals in the ^{1}H nmr spectrum, the following assignment was established; ^{1}H nmr: δ 1.65 (d, 1H, $J_{7s\text{-}7a}$ = 9.3, H_{7s}), 1.85 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 3.22 (broad s, 1H, H_4), 3.70 (s, 3H, OCH_3), 3.96 (broad s, 1H, H_1), 4.43 (d, 1H, $J_{3x\text{-}4}$ = 2.7, H_{3x}), 5.98 (dd, 1H, $J_{6\text{-}5}$ = 5.7, $J_{6\text{-}1}$ = 3.6, H_6), 6.60 (dd, 1H, $J_{5\text{-}6}$ = 5.4, $J_{5\text{-}4}$ = 2.4, H_5), 6.78-6.96 (m, 3H, Arom), 7.12-7.38 (m, 6H, Arom).

cis-exo-3-(3'-Methoxyphenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**7e**).

The assignment of **7e** was established from the mixture of compounds **6e** and **7e**; ^{1}H nmr: δ 1.77 (dd, 1H, $J_{7s\text{-}7a}$ = 9.3, $J_{7s\text{-}3n}$ = 1.2, H_{7s}), 1.95 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 3.09 (broad s, 1H, H_4), 3.72 (s, 3H, OCH_3), 3.90-3.98 (m, 2H, H_1, H_{3n}), 6.10-6.16 (m, 1H, H_6), 6.50 (dd, 1H, $J_{5\text{-}6}$ = 5.7, $J_{5\text{-}4}$ = 3.3, H_5), 6.80-6.90 (m, 3H, Arom), 7.12-7.38 (m, 6H, Arom).

cis-endo-3-(2'-Methoxyphenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**6f**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1f** with cyclopentadiene, by silica gel column chromatography (hexane-toluene 1:3), gave 86 mg (25%) of compound **6f**, as an oil; ^{1}H nmr: δ 1.74 (d, 1H, $J_{7s\text{-}7a}$ = 9.3, H_{7s}), 2.38 (d, 1H, $J_{7a\text{-}7s}$ = 9.0, H_{7a}), 3.07 (broad s, 1H, H_4), 3.44 (m, 4H, OCH_3, H_1), 3.79 (d, 1H, $J_{3x\text{-}4}$ = 2.1, H_{3x}), 6.28 (dd, 1H, $J_{6\text{-}5}$ = 5.4, $J_{6\text{-}1}$ = 3.0, H_6), 6.50-6.58 (m, 1H, Arom), 6.84-6.92 (m, 2H, H_5, Arom), 7.08-7.26 (m, 2H, Arom), 7.30-7.50 (m, 3H, Arom), 7.73-7.80 (m, 2H, Arom); ^{13}C nmr: δ 45.4, 47.2, 53.7, 54.2, 54.3 (C_1, C_3, C_4, C_7, OCH_3), 76.2 (C_2), 108.6, 120.3, 126.4, 127.0, 127.6, 127.9, 128.0, 128.4, 132.0, 135.4, 136.8, 157.0 (Arom, C_5, C_6), 160.0 (C=N), 182.7 (COO).

Anal. Calcd. for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.40; H, 5.64; N, 4.04.

cis-exo-3-(2'-Methoxyphenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**7f**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1f** with cyclopentadiene, by silica gel column chromatography (hexane-toluene 1:3), gave 87 mg (25%) of compound **7f**, as an oil; ^{1}H nmr: δ 1.70 (dd, 1H, $J_{7s\text{-}7a}$ = 8.7, $J_{7s\text{-}3n}$ = 1.8, H_{7s}), 2.55 (d, 1H, $J_{7a\text{-}7s}$ = 8.7, H_{7a}), 3.20 (broad s, 1H, H_4), 3.30 (d, 1H, $J_{3n\text{-}7s}$ = 1.8, H_{3n}), 3.42 (s, 3H, OCH_3), 3.47 (broad s, 1H, H_1), 6.37 (dd, 1H, $J_{6\text{-}5}$ = 5.1, $J_{6\text{-}1}$ = 2.7, H_6), 6.52-6.58 (m, 1H, Arom), 6.55 (dd, 1H, $J_{5\text{-}6}$ = 5.4, $J_{5\text{-}4}$ = 3.0, H_5), 6.92-7.00 (m, 1H, Arom), 7.10-7.18 (m, 1H, Arom), 7.26-7.36 (m, 3H, Arom), 7.40-7.46 (m, 1H, Arom), 7.60-7.68 (m, 2H, Arom); ^{13}C nmr: δ 45.2, 48.0, 52.7, 54.2, 54.7 (C_1, C_3, C_4, C_7, OCH_3), 74.8 (C_2), 108.5, 120.3, 125.8, 126.5, 127.3, 127.4, 128.5, 128.6, 131.9, 132.9, 141.1, 157.0 (Arom, C_5, C_6), 158.9 (C=N), 182.3 (COO).

Anal. Calcd. for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.27; H, 5.68; N, 4.01.

cis-endo-3-(3',4'-Methylenedioxyphenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**6h**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1h** with cyclopentadiene, by silica gel column chromatography (toluene), gave 160 mg (44%) of compound **6h**, as a white solid, mp 191-193°; ^{1}H nmr: δ 2.35-2.38 (m, 2H, H_{7a}, H_{7s}), 3.16 (broad s, 1H, H_4), 3.25 (broad s, 1H, H_1), 3.80 (d, 1H, $J_{3x\text{-}4}$ = 3.0, H_{3x}), 5.88 (s, 2H, OCH_2O), 6.49 (dd, 1H, $J_{6\text{-}5}$ = 5.5, $J_{6\text{-}1}$ = 3.0, H_6), 6.57 (dd, 1H, $J_{5\text{-}6}$ = 5.5, $J_{5\text{-}4}$ = 2.7, H_5), 6.63-6.64 (m, 1H, Arom), 6.84-6.85 (m, 1H, Arom), 7.26 (broad s, 1H, Arom), 7.39-7.44 (m, 2H, Arom), 7.48-7.54 (m, 1H, Arom),

7.85-7.88 (m, 2H, Arom); ^{13}C nmr: δ 46.9, 50.0, 55.5, 58.0 (C_1, C_3, C_4, C_7), 77.5 (C_2), 100.8 (OCH_2O), 107.4, 110.2, 123.2, 126.1, 127.8, 128.6, 132.0, 132.4, 136.6, 137.0, 146.2, 146.9 (Arom, C_5, C_6), 159.3 (C=N), 182.3 (COO).

Anal. Calcd. for $C_{22}H_{17}NO_4$: C, 73.50; H, 4.77; N, 3.90. Found: C, 73.59; H, 4.80; N, 3.86.

cis-exo-3-(3',4'-Methylenedioxyphenyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**7h**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1h** with cyclopentadiene, by silica gel column chromatography (toluene), gave 131 mg (36%) of compound **7h**, as a white solid, mp 190-192°; ^{1}H nmr: δ 1.87-1.94 (m, 1H, H_{7s}), 2.70-2.77 (m, 1H, H_{7a}), 2.99 (broad s, 1H, H_4), 3.16 (broad s, 1H, H_{3n}), 3.23 (broad s, 1H, H_1), 5.86-5.91 (m, 2H, OCH_2O), 6.33-6.36 (m, 1H, H_6), 6.55-6.75 (m, 4H, H_5, Arom), 7.36-7.51 (m, 3H, Arom), 7.74-7.77 (m, 2H, Arom); ^{13}C nmr: δ 48.8, 49.0, 54.7, 58.9 (C_1, C_3, C_4, C_7), 75.5 (C_2), 100.8 (OCH_2O), 107.9, 108.4, 121.6, 126.1, 127.7, 128.6, 132.3, 132.6, 132.7, 142.4, 146.0, 147.4 (Arom, C_5, C_6), 158.7 (C=N), 180.8 (COO).

Anal. Calcd. for $C_{22}H_{17}NO_4$: C, 73.50; H, 4.77; N, 3.90. Found: C, 73.64; H, 4.69; N, 3.88.

cis-endo-3-(2'-Furyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**6i**).

This compound could not be separated from compound **7i**, but due to the different integration of their signals in the ^{1}H nmr spectrum, the following assignment was established; ^{1}H nmr: δ 1.65 (d, 1H, $J_{7s\text{-}7a}$ = 9.0, H_{7s}), 2.35 (d, 1H, $J_{7a\text{-}7s}$ = 9.0, H_{7a}), 3.13 (broad s, 1H, H_4), 3.37 (broad s, 1H, H_1), 3.88 (broad s, 1H, H_{3x}), 6.05 (d, 1H, $J_{3'\text{-}4'}$ = 3.1, $H_{3'}$), 6.17 (dd, 1H, $J_{4'\text{-}3'}$ = 3.1, $J_{4'\text{-}5'}$ = 1.8, $H_{4'}$), 6.41 (dd, 1H, $J_{6\text{-}5}$ = 5.5, $J_{6\text{-}1}$ = 3.0, H_6), 6.59 (dd, 1H, $J_{5\text{-}6}$ = 5.5, $J_{5\text{-}4}$ = 2.9, H_5), 7.17-7.19 (m, 1H, $H_{5'}$), 7.36-8.15 (m, 5H, Arom).

cis-exo-3-(2'-Furyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**7i**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1h** with cyclopentadiene, by silica gel column chromatography (toluene), gave 131 mg (36%) of compound **7i**, as an oil; ^{1}H nmr: δ 1.72 (d, 1H, $J_{7s\text{-}7a}$ = 9.0, H_{7s}), 2.68 (d, 1H, $J_{7a\text{-}7s}$ = 9.0, H_{7a}), 3.00 (broad s, 1H, H_4), 3.20 (s, 1H, H_{3n}), 3.28 (broad s, 1H, H_1), 6.17-6.20 (m, 1H, $H_{3'}$), 6.29-6.31 (m, 1H, $H_{4'}$), 6.36 (dd, 1H, $J_{6\text{-}5}$ = 5.5, $J_{6\text{-}1}$ = 2.7, H_6), 6.63 (dd, 1H, $J_{5\text{-}6}$ = 5.5, $J_{5\text{-}4}$ = 3.3, H_5), 7.24-7.26 (m, 1H, $H_{5'}$), 7.42-7.54 (m, 3H, Arom), 7.99-8.01 (m, 2H, Arom); ^{13}C nmr: δ 46.0, 46.1, 51.6, 54.3 (C_3, C_7, C_4, C_1), 76.8 (C_2), 107.1, 110.1 ($C_{3'}$, $C_{4'}$), 127.8, 127.9, 128.6, 128.7 (Arom, $C_{2'}$), 132.5, 135.7, 139.0, 141.8 (Arom, C_5, C_6, $C_{5'}$), 160.7 (C=N), 178.4 (COO).

Anal. Calcd. for $C_{19}H_{15}NO_3$: C, 74.75; H, 4.91; N, 4.59. Found: C, 74.92; H, 4.98; N, 4.50.

cis-endo-3-(*N*-acetyl-3'-indolyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**6k**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1k** with cyclopentadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave an analytical sample of compound **6k**, as an oil; ^{1}H nmr: δ 1.67 (d, 1H, $J_{7s\text{-}7a}$ = 9.3, H_{7s}), 2.48 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 2.57 (s, 3H, $COCH_3$), 3.20 (broad s, 1H, H_4), 3.37 (broad s, 1H, H_1), 4.06 (d, 1H, $J_{3x\text{-}4}$ = 3, H_{3x}), 6.40 (dd, 1H, $J_{6\text{-}5}$ = 5.4, $J_{6\text{-}1}$ = 3.0, H_6), 6.49 (dd, 1H, $J_{5\text{-}6}$ = 5.4, $J_{5\text{-}4}$ = 3.0, H_5), 7.19-8.34 (m, 10H, Arom); ^{13}C nmr: δ 23.9, 46.0, 48.2, 48.2, 55.5 (C_1, C_3, C_4, C_7,$COCH_3$), 76.5 (C_2), 116.4, 118.1, 119.6, 123.4, 124.1, 125.1, 125.9, 127.5, 128.6, 130.8, 132.5, 134.9, 136.5, 137.2 (Arom, C_5, C_6), 160.0 (C=N), 168.3 ($COCH_3$), 181.9 (COO).

Anal. Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.75; H, 5.05; N, 7.07. Found: C, 75.91; H, 5.13; N, 6.98.

cis-exo-3-(*N*-Acetyl-3'-indolyl)bicyclo[2.2.1]hept-2-spiro-{4"[2"-phenyl-5"(4"*H*)-oxazolon]}-5-ene (**7k**).

Purification of the residue from the Diels-Alder reaction of oxazolone **1k** with cyclopentadiene, by silica gel column chromatography (hexane-ethyl acetate 7:3), gave an anlytical sample of compound **7k**, as an oil; ^{1}H nmr: δ 1.88 (dd, 1H, $J_{7s\text{-}7a}$ = 8.7, $J_{7s\text{-}3n}$ = 1.2, H_{7s}), 2.60-2.64 (m, 4H, $COCH_3$, H_{7a}), 3.01 (broad s, 1H, H_4), 3.27 (broad s, 1H, H_1), 3.38 (broad s, 1H, H_{3n}), 6.34 (dd, 1H, $J_{6\text{-}5}$ = 5.4, $J_{6\text{-}1}$ = 3.0, H_6), 6.73 (dd, 1H, $J_{5\text{-}6}$ = 5.4, $J_{5\text{-}4}$ = 3.0, H_5), 7.06-8.29 (m, 10H, Arom); ^{13}C nmr: δ 24.0, 48.3, 49.3, 49.5, 55.9 (C_1, C_3, C_4, C_7, $COCH_3$), 74.5 (C_2), 116.4, 117.8, 121.3, 122.3, 123.5, 125.5, 125.8, 127.4, 127.8, 128.5, 132.2, 132.3, 135.0, 141.4 (Arom, C_5, C_6), 159.5 (C=N), 168.4 ($COCH_3$), 180.5 (COO).

Anal. Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.75; H, 5.05; N, 7.07. Found: C, 75.89; H, 5.11; N, 7.01.

General Procedure for the Diels-Alder Reaction of 5(4*H*)-Oxazolones **1a,f,g** with Danishefsky's Diene and Treatment of Cycloadducts **4a,f,g** and **5a,f,g** with diazabicyclo[5.4.0]undec-7-ene **12a,f,g**.

Danishefsky's diene (244 mg, 2.00 mmoles) was added to a solution of 5(4*H*)-oxazolone **1a,f,g** (1.00 mmole) in dry toluene (30 ml). After stirring and heating under reflux for the time reported in Table 1, the solvent was evaporated *in vacuo* and a mixture of a solution of 0.005 *N* hydrochloric acid and tetrahydrofuran (1:4) (20 ml) was added to the residue. The reaction mixture was stirred for 7 hours, the solvent was removed and the mixture was diluted with dichloromethane (30 ml). The organic solution was washed with brine (2 x 20 ml) and 5% aqueous sodium hydrogencarbonate solution (2 x 20 ml), dried over anhydrous magnesium sulfate and filtered. Evaporation of the solvent gave a residue that was dissolved in methanol (40 ml) and diazabicyclo[5.4.0]undec-7-ene (126 mg, 0.84 mmole) was added. The reaction mixture was stirred for 3 days at 0° and, after evaporation of the solvent, the residue was purified by silica gel column chromatography to afford enones **12a,f,g**.

Methyl *cis*-1-Benzamido-6-(2'-methoxyphenyl)-4-oxo-2-cyclohexen-1-carboxylate (**12f**).

Compound **12f**, an oil, was purified by silica gel column chromatography (hexane-ethyl acetate 1:1) to yield 270 mg (66% from **1f**); ^{1}H nmr: δ 2.65 (dd, 1H, $J_{5e\text{-}5a}$ = 17.1, $J_{5e\text{-}6a}$ = 3.9, H_{5e}), 3.54-3.64 (m, 4H, H_{5a}, OCH_3), 3.93 (s, 3H, $COOCH_3$), 4.00-4.12 (m, 1H, H_{6a}), 6.19 (d, 1H, $J_{2\text{-}3}$ = 10.2, H_2), 6.96-7.10 (m, 3H, Arom, CONH, H_3), 7.26-7.53 (m, 5H, Arom), 7.64-7.71 (m, 3H, Arom); ^{13}C nmr: δ 38.6, 52.7, 55.9, 55.9, 62.1 (C_5, C_1, C_6, OCH_3, $COOCH_3$), 111.9, 121.7, 125.3, 126.9, 128.4, 128.5, 129.8, 130.5, 131.8, 133.8, 148.0, 157.0 (C_2, C_3, Arom), 167.9 (CONH), 171.5 ($COOCH_3$), 198.0 (CO).

Anal. Calcd. for $C_{22}H_{21}NO_5$: C, 69.65; H, 5.58; N, 3.69. Found: C, 69.54; H, 5.49; N, 3.78.

Methyl *cis*-1-Benzamido-6-(3',4'-dimethoxyphenyl)-4-oxo-2-cyclohexen-1-carboxylate (**12g**).

Compound **12g**, an oil, was purified by silica gel column chromatography (hexane-ethyl acetate 1:1) to yield 260 mg (66%

from **1g**); ^{1}H nmr: δ 2.77 (dd, 1H, $J_{5e\text{-}5a}$ = 16.7, $J_{5e\text{-}6a}$ = 4.6, H_{5e}), 3.17 (dd, 1H, $J_{5a\text{-}5e}$ = 16.7, $J_{5a\text{-}6a}$ = 10.6, H_{5a}), 3.76 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.87 (s, 3H, $COOCH_3$), 3.96 (dd, 1H, $J_{6a\text{-}5a}$ = 10.6, $J_{6a\text{-}5e}$ = 4.6, H_{6a}), 6.29 (d, 1H, $J_{2\text{-}3}$ = 10.6, H_2), 6.61-6.79 (m, 3H, Arom, CONH), 6.85 (d, 1H, $J_{3\text{-}2}$ = 10.6, H_3), 7.26-7.61 (m, 6H, Arom); ^{13}C nmr: δ 39.7, 47.1 (C_5, C_6), 53.3, 55.7, 55.8 (2OCH_3, $COOCH_3$), 61.6 (C_1), 111.1, 111.3, 119.9, 126.8, 128.7, 129.4, 129.7, 132.1, 133.3, 145.7, 149.1, 149.3 (C_2, C_3, Arom), 167.5 (CONH), 171.6 (*C*$OOCH_3$), 197.5 (CO).

Anal. Calcd. for $C_{23}H_{23}NO_6$: C, 67.47; H, 5.66; N, 3.42. Found: C, 67.35; H, 5.59; N, 3.48.

General Procedure for the Reaction of Spirooxazolone Adducts with Sodium Methoxide **8a,c**, **9a,g,j,k**, **10a,i,j** and **11a,i,j**.

To a solution of the corresponding spirooxazolone adduct (0.50 mmole) in dry methanol (15 ml) was added sodium methoxide (81 mg, 1.5 mmoles) and the mixture was stirred at room temperature for 4 hours. The precipitate was filtered off and the solution was evaporated under reduced pressure and purified by filtration through a short column of silica gel, eluting with dichloromethane, to quantitatively give the required methyl ester derivatives **8a,c**, **9a,g,j,k**, **10a,i,j** and **11a,i,j**.

Methyl *cis*-1-Benzamido-6-(4'-chlorophenyl)-3-cyclohexen-1-carboxylate (**8c**).

Compound **8c** was obtained as an oil; ^{1}H nmr: δ 2.19-2.42 (m, 2H), 2.75-2.85 (m, 1H), 2.92-3.02 (m, 1H) 3.60-3.75 (m, 4H, H_{6a}, $COOCH_3$), 5.73-5.83 (m, 1H, H_3), 5.83-5.92 (m, 1H, H_4), 5.99 (broad s, 1H, CONH), 7.20-7.59 (m, 9H, Arom); ^{13}C nmr: δ 29.4, 31.0, 42.7, 52.5 (C_2, C_5, C_6, $COOCH_3$), 60.2 (C_1), 123.9, 126.0, 126.8, 128.5, 128.6, 129.7, 131.8, 133.4, 134.0, 139.9 (C_3, C_4, Arom), 166.9 (CONH), 172.5 (*C*$OOCH_3$).

Anal. Calcd. for $C_{21}H_{20}ClNO_3$: C, 68.20; H, 5.45; N, 3.79. Found: C, 68.13; H, 5.56; N, 3.77.

Methyl *cis*-1-Benzamido-3,4-dimethyl-6-(3',4'-dimethoxy)-phenyl-3-cyclohexen-1-carboxylate (**9g**).

Compound **9g** was obtained as an oil; ^{1}H nmr: δ 1.69 (m, 6H, 2CH_3), 2.30-2.40 (m, 2H, H_{2e}, H_{5e}), 2.50-2.60 (m, 1H, H_{5a}), 2.90 (d, 1H, $J_{2a\text{-}2e}$ = 17.0, H_{2a}), 3.42-3.48 (m, 1H, H_{6a}), 3.60 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 3.80 (s, 3H, $COOCH_3$), 6.80-6.90 (m, 4H, Arom, CONH), 7.30-7.48 (m, 3H, Arom), 7.54-7.60 (m, 2H, Arom); ^{13}C nmr: δ 18.6 (CH_3), 18.7 (CH_3), 35.5, 36.7, 44.0 (C_2, C_5, C_6), 52.4, 55.6, 55.8 (2OCH_3, $COOCH_3$), 60.8 (C_1), 111.2, 111.6, 120.1, 123.5, 123.7, 126.8, 128.5, 131.6, 133.6, 134.2, 148.4, 149.0 (C_3, C_4, Arom), 166.5 (CONH), 173.0 (*C*$OOCH_3$).

Anal. Calcd. for $C_{25}H_{29}NO_5$: C, 70.90; H, 6.90; N, 3.31. Found: C, 71.03; H, 6.86; N, 3.37.

Methyl *cis*-1-Benzamido-3,4-dimethyl-6-(2'-thienyl)-3-cyclohexen-1-carboxylate (**9j**).

Compound **9j** was obtained as an oil; ^{1}H nmr: δ 1.66 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 2.23 (dd, 1H, $J_{5e\text{-}5a}$ = 16.2, $J_{5e\text{-}6a}$ = 5.0, H_{5e}), 2.44-2.55 (m, 2H, H_{5a}, H_{2e}), 3.12 (d, 1H, $J_{2a\text{-}2e}$ = 18.0, H_{2a}), 3.67 (s, 3H, $COOCH_3$), 3.82 (dd, 1H, $J_{6a\text{-}5a}$ = 5.8, $J_{6a\text{-}5e}$ = 5.0, H_{6a}), 6.41 (broad s, 1H, CONH), 6.97-6.99 (m, 2H, $H_{3'}$, $H_{4'}$), 7.21-7.23 (m, 1H, $H_{5'}$), 7.33-7.50 (m, 3H, Arom), 7.59-7.63 (m, 2H, Arom); ^{13}C nmr: δ 18.6, 18.8 (2CH_3), 36.2, 37.0, 41.4 (C_2, C_5, C_6), 52.6 ($COOCH_3$), 60.7 (C_1), 122.1, 124.5, 125.6, 126.4, 126.5, 126.9, 128.5, 131.6, 134.0, 142.9 (Arom, C_3, C_4), 166.5 (CONH), 172.8 (*C*$OOCH_3$).

Anal. Calcd. for $C_{21}H_{23}NO_3S$: C, 68.27; H, 6.27; N, 3.79; S, 8.69. Found: C, 68.40; H, 6.36; N, 3.70; S, 8.72.

Methyl *cis*-1-Benzamido-3,4-dimethyl-6-(3'-indolyl)-3-cyclohexen-1-carboxylate (**9k**).

Compound **9k** was deacetylated in the reaction conditions and obtained as an oil; ^{1}H nmr: δ 1.70 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 2.27-2.33 (m, 2H, H_{5e}, H_{2e}), 2.50 (dd, 1H, $J_{5a\text{-}5e}$ = 16.0, $J_{5a\text{-}6a}$ = 5.2, H_{5a}), 3.19 (d, 1H, $J_{2a\text{-}2e}$ = 17.0, H_{2a}), 3.63 (s, 3H, $COOCH_3$), 3.87 (dd, 1H, $J_{6a\text{-}5a}$ = 5.2, $J_{6a\text{-}5e}$ = 4.7, H_{6a}), 6.56 (broad s, 1H, CONH), 7.17-7.80 (m, 10H, Arom), 8.32 (broad s, 1H, NH); ^{13}C nmr: δ 18.7, 18.8 (2CH_3), 35.9, 36.0, 36.4 (C_2, C_5, C_6), 52.53 ($COOCH_3$), 61.3 (C_1), 111.6 115.0, 118.2, 120.1, 122.0, 122.6, 122.6, 124.3, 126.9, 127.7, 128.2, 131.3, 133.7, 135.5 (Arom, C_3, C_4), 166.4 (CONH), 173.3 (*C*$OOCH_3$).

Anal. Calcd. for $C_{25}H_{26}N_2O_3$: C, 74.60; H, 6.51; N, 6.96. Found: C, 74.77; H, 6.65; N, 6.87.

Methyl *endo*-2-Benzamido-*endo*-3-(2'-furyl)bicyclo[2.2.1]hept-5-ene-*exo*-2-carboxylate (**10i**).

Compound **10i** was obtained as an oil; ^{1}H nmr: δ 1.71 (d, 1H, $J_{7s\text{-}7a}$ = 9.3, H_{7s}), 2.01 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 3.14 (broad s, 1H, H_4), 3.76 (s, 3H, $COOCH_3$), 3.86 (d, 1H, $J_{3x\text{-}4}$ = 2.7, H_{3x}), 3.90 (broad s, 1H, H_1), 6.17 (dd, 1H, $J_{6\text{-}5}$ = 5.5, $J_{6\text{-}1}$ = 2.7, H_6), 6.19-6.20 (m, 1H, CONH), 6.23 (d, 1H, $J_{3'\text{-}4'}$ = 3.0, $H_{3'}$), 6.36 (dd, 1H, $J_{4'\text{-}3'}$ = 3.0, $J_{4'\text{-}5'}$ = 1.8, $H_{4'}$), 6.52 (dd, 1H, $J_{5\text{-}6}$ = 5.5, $J_{5\text{-}4}$ = 3.0, H_5), 7.28-7.44 (m, 6H, $H_{5'}$, Arom); ^{13}C nmr: δ 46.9, 48.7, 49.8, 50.3, 52.7 (C_1, C_3, C_4, C_7, $COOCH_3$), 66.5 (C_2), 109.3, 110.6 ($C_{3'}$, $C_{4'}$), 126.7, 126.9, 128.4 (Arom), 131.5, 133.8, 135.6, 138.2, 142.5 (Arom, $C_{2'}$, $C_{5'}$, C_5, C_6), 166.3 (CONH), 173.8 (*C*$OOCH_3$).

Anal. Calcd. for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.45; H, 5.72; N, 4.10.

Methyl *exo*-2-Benzamido-*exo*-3-(2'-furyl)bicyclo[2.2.1]hept-5-ene-*endo*-2-carboxylate (**11i**).

Compound **11i** was obtained as an oil; ^{1}H nmr: δ 1.76 (dd, 1H, $J_{7s\text{-}7a}$ = 9.3, $J_{7s\text{-}3n}$ = 1.5, H_{7s}), 2.19 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 3.03 (broad s, 1H, H_4), 3.46-3.48 (m, 2H, H_1, H_{3n}), 3.69 (s, 3H, $COOCH_3$), 6.29-6.31 (m, 2H, $H_{3'}$, $H_{4'}$), 6.36-6.38 (m, 3H, H_5, H_6, CONH), 7.29-7.34 (m, 2H, Arom), 7.40-7.44 (m, 4H, $H_{5'}$, Arom); ^{13}C nmr: δ 47.0, 47.2, 48.2, 50.5, 52.3 ($COOCH_3$, C_1, C_3, C_4, C_7), 67.2 (C_2), 109.2, 110.7 ($C_{3'}$, $C_{4'}$), 126.6, 126.7, 128.4 (Arom), 131.4, 133.9, 136.4, 138.3, 142.4 (Arom, $C_{2'}$, $C_{5'}$, C_5, C_6), 166.2 (CONH), 172.3 (*C*$OOCH_3$).

Anal. Calcd. for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.32; H, 5.81; N, 4.06.

Methyl *endo*-2-Benzamido-*endo*-3-(2'-thienyl)bicyclo[2.2.1]-hept-5-ene-*exo*-2-carboxylate (**10j**).

Compound **10j** was obtained as an oil; ^{1}H nmr: δ 1.78 (d, 1H, $J_{7s\text{-}7a}$ = 9.0, H_{7s}), 2.06 (d, 1H, $J_{7a\text{-}7s}$ = 9.0, H_{7a}), 3.21 (broad s, 1H, H_4), 3.78 (s, 3H, $COOCH_3$), 4.00 (broad s, 1H, H_1), 4.03 (d, 1H, $J_{3x\text{-}4}$ = 3.0, H_{3x}), 6.11 (broad s, 1H, CONH), 6.22 (dd, 1H, $J_{6\text{-}5}$ = 5.7, $J_{6\text{-}1}$ = 2.7, H_6), 6.60 (dd, 1H, $J_{5\text{-}6}$ = 5.7, $J_{5\text{-}4}$ = 2.7, H_5), 7.00-7.40 (m, 8H, $H_{3'}$, $H_{4'}$, $H_{5'}$, Arom); ^{13}C nmr: δ 48.2, 49.3, 50.3, 51.9, 52.6 (C_1, C_3, C_4, C_7, $COOCH_3$), 68.0 (C_2), 125.5, 126.6, 126.8, 127.4, 128.3, 128.4, 128.4, 131.5, 137.2, 137.6 (Arom, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$, C_5, C_6), 166.2 (CONH), 174.1 (*C*$OOCH_3$).

Anal. Calcd. for $C_{20}H_{19}NO_3S$: C, 67.97; H, 5.42; N, 3.96; S, 9.06. Found C, 68.19; H, 5.56; N, 3.91; S, 9.17.

Methyl *exo*-2-Benzamido-*exo*-3-(2'-thienyl)bicyclo[2.2.1]hept-5-ene-*endo*-2-carboxylate (**11j**).

Compound **11j** was obtained as an oil; ^{1}H nmr: δ 1.90-1.97 (m, 1H, H_{7s}), 2.73 (d, 1H, J_{7a-7s} = 10.0, H_{7a}), 3.00 (d, 1H, J_{3n-7s} = 2.3, H_{3n}), 3.03 (broad s, 1H, H_4), 3.24 (s, 3H, $COOCH_3$), 4.00 (broad s, 1H, H_1), 6.19 (dd, 1H, J_{6-5} = 5.5, J_{6-1} = 3.0, H_6), 6.43 (broad s, 1H, CONH), 6.50 (dd, 1H, J_{5-6} = 5.5, J_{5-4} = 3.0, H_5), 6.90-7.80 (m, 8H, $H_{3'}$, $H_{4'}$, $H_{5'}$, Arom); ^{13}C nmr: δ 48.3, 49.6, 49.6, 51.8, 55.5 (C_1, C_3, C_4, C_7, $COOCH_3$), 70.7 (C_2), 124.1, 125.7, 126.4, 127.0, 127.1, 128.6, 131.8, 135.5, 137.0, 139.5 (C_5, C_6, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$, Arom), 167.3 (CONH), 171.7 ($COOCH_3$).

Anal. Calcd. for $C_{20}H_{19}NO_3S$: C, 67.97; H, 5.42; N, 3.96. Found: C, 68.08; H, 5.50; N, 3.89.

General Procedure for the Preparation of the Iodolactones **13g** and **13k**.

To a solution of the crude mixture of **6g,7g** and **6k,7k** (from 8 mmoles of oxazolones **1g,k**) in tetrahydrofuran (80 ml) was added a 5% aqueous sodium hydroxide solution (60 ml). The mixture was stirred for 2 hours at room temperature (in the case of mixture **6k,7k** deacetylation was observed). After evaporation of the solvent, the residue was taken up in methanol (10 ml) and a 5% aqueous sodium hydrogen carbonate solution (75 ml) was added. The mixture was treated with an excess of a stock solution of iodine [prepared from iodine (5 g) and potassium iodide (10 g) in water (30 ml)] and allowed to stand for 1 hour. The precipitate was collected by filtration, washed with a mixture of methanol and cold 10% aqueous sodium thiosulfate (1:1) (15 ml) and dried to afford iodolactones **13g,k** which were purified by column chromatography.

exo-2-Benzamido-*exo*-5-iodo-*exo*-3-(3',4'-dimethoxyphenyl)-*endo*-6-hydroxybicyclo[2.2.1]heptane-*endo*-2-carboxylic Acid Lactone (**13g**).

Iodolactone **13g,** an oil, was purified by silica gel column chromatography (hexane-ethyl acetate 1:1) to yield 502 mg (30% from **1g**); ^{1}H nmr: δ 2.41 (d, 1H, J_{7s-7a} = 12.0, H_{7s}), 2.60 (dd, 1H, J_{7a-7s} = 12.0, J_{7a-5n} = 1.2, H_{7a}), 3.06 (broad s, 1H, H_4), 3.36 (broad s, 1H, H_1), 3.83 (dd, 1H, J_{5n-4} = 5.1, J_{5n-7a} = 1.2, H_{5n}), 3.87 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.06 (d, 1H, J_{3n-7s} = 2.4, H_{3n}), 5.29 (d, 1H, J_{6x-1} = 5.4, H_{6x}), 5.80 (s, 1H, CONH), 6.72-6.76 (m, 1H, Arom), 6.82-6.96 (m, 2H, Arom), 7.24-7.40 (m, 5H, Arom); ^{13}C nmr: δ 29.7, 35.8, 47.3, 51.0, 55.1, 56.0, 56.2 (C_1, C_3, C_2, C_4, C_7, $2OCH_3$), 62.2, 86.2 (C_5, C_6), 111.7, 111.8, 120.8, 126.2, 126.6, 128.6, 132.0, 132.8 149.3, 149.7 (Arom), 165.9 (CONH), 175.1 (COO).

Anal. Calcd. for $C_{23}H_{22}NO_5I$: C, 53.17; H, 4.27; N, 2.70; I, 24.45. Found: C, 53.05; H, 4.19; N, 2.78; I, 24.49.

exo-2-Benzamido-*exo*-5-iodo-*exo*-3-(3'-indolyl)-*endo*-6-hydroxybicyclo [2.2.1]heptane-*endo*-2-carboxylic Acid Lactone (**13k**).

Iodolactone **13k,** an oil, was purified by silica gel column chromatography (hexane-ethyl acetate 1:1) to yield 1.00 g (33% from **1g**); ^{1}H nmr: δ 2.37 (d, 1H, J_{7s-7a} = 12.0, H_{7s}), 2.42 (d, 1H, J_{7a-7s} = 12.0, H_{7a}), 3.08 (broad s, 1H, H_4), 3.61 (d, 1H, J_{5n-4} = 4.8, H_{5n}), 3.81 (s, 1H, H_{3n}), 4.47 (broad s, 1H, H_1), 5.38 (d, 1H, J_{6x-1} = 5.1, H_{6x}), 6.15 (broad s, 1H, CONH), 6.80-7.57 (m, 10H, Arom), 11.5 (broad s, 1H, NH); ^{13}C nmr: δ 30.6 (C_5), 35.0 (C_7), 46.9 (C_3), 48.3 (C_4), 50.8 (C_1), 61.1 (C_2), 85.7 (C_6), 107.7, 112.1, 118.4, 119.7, 122.2, 124.3, 126.1, 126.9, 128.4, 131.8, 132.9, 136.0 (Arom), 164.8 (CONH), 175.2 (COO).

Anal. Calcd. for $C_{23}H_{19}N_2O_3I$: C, 55.44; H, 3.84; N, 5.62; I, 25.47. Found: C, 55.53; H, 3.76; N, 5.51; I, 25.29.

General Procedure for the Preparation of Compounds **10g** and **10k**.

Compounds **10g,k** were prepared from the filtrate obtained in the preparation of iodolactones **13g,k**. The filtrate was acidified with concentrated hydrochloric acid and extracted with diethyl ether (3 x 30 ml). The organic layer was washed successively with a 10% aqueous sodium thiosulfate solution (2 x 15 ml), water (2 x 25 ml), and dried over anhydrous sodium sulfate. After evaporating the sovent, the residue was dissolved in diethyl ether (50 ml) and esterified with an excess of diazomethane in diethyl ether during 30 minutes. The solvent was removed under vacuum and the required compound was purified by column chromatography.

Methyl *endo*-2-Benzamido-*endo*-3-(3',4'-dimethoxyphenyl)bicyclo[2.2.1]hept-5-ene-*exo*-2-carboxylate (**10g**).

Compound **10g,** an oil, was purified by silica gel column chromatography (hexane-ethyl acetate 1:1) to yield 505 mg (40% from **1g**); ^{1}H nmr: δ 1.77 (d, 1H, J_{7s-7a} = 9.3, H_{7s}), 2.07 (d, 1H, J_{7a-7s} = 9.3, H_{7a}), 3.20 (broad s, 1H, H_4), 3.70 (d, 1H, J_{3x-4} = 2.9, H_{3x}), 3.78 (s, 3H, $COOCH_3$), 3.82 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.00 (broad s, 1H, H_1), 5.97 (broad s, 1H, CONH), 6.11 (dd, 1H, J_{6-5} = 5.6, J_{6-1} = 3.2, H_6), 6.55 (dd, 1H, J_{5-6} = 5.6, J_{5-4} = 2.7, H_5), 6.80-6.98 (m, 3H, Arom), 7.21-7.42 (m, 5H, Arom); ^{13}C nmr: δ 46.6, 49.4, 50.4, 52.5 (C_1, C_3, C_4, C_7), 55.7, 55.8, 56.1 ($2OCH_3$, $COOCH_3$), 65.4 (C_2), 111.1, 112.8, 121.3, 126.5, 128.4, 129.5, 131.5, 133.5, 136.6, 137.0, 148.4, 148.9 (Arom, C_5, C_6), 166.0 (CONH), 174.7 ($COOCH_3$).

Anal. Calcd. for $C_{24}H_{25}NO_5$: C, 70.73; H, 6.19; N, 3.44. Found: C, 70.81; H, 6.23; N, 3.50.

Methyl *endo*-2-Benzamido-*endo*-3-(3'-indolyl)bicyclo[2.2.1]-hept-5-ene-*exo*-2-carboxylate (**10k**).

Compound **10k,** an oil, was purified by silica gel column chromatography (hexane-ethyl acetate 1:1) to yield 503 mg (21% from **1k**); ^{1}H nmr: δ 1.78 (d, 1H, J_{7s-7a} = 9.3, H_{7s}), 2.26 (d, 1H, J_{7a-7s} = 9.3, H_{7a}), 3.21 (broad s, 1H, H_4), 3.78 (s, 3H, $COOCH_3$), 4.02 (d, 1H, J_{3x-4} = 3.0, H_{3x}), 4.13 (broad s, 1H, H_1), 6.22 (dd, 1H, J_{6-5} = 5.4, J_{6-1} = 3.0, H_6), 6.29 (broad s, 1H, CONH), 6.56 (dd, 1H, J_{5-6} = 5.4, J_{5-4} = 2.7, H_5), 7.11-7.63 (m, 10H, Arom), 8.33 (broad s, 1H, NH); ^{13}C nmr: δ 47.9, 48.3, 49.4, 50.8, 52.3 (C_1, C_3, C_4, C_7, $COOCH_3$), 64.8 (C_2), 111.2, 117.8, 119.6, 120.2, 122.9, 123.0, 126.7, 127.8, 128.3, 131.2, 134.0, 136.1, 137.3, 137.5 (Arom, C_5, C_6), 166.2 (CONH), 175.1 ($COOCH_3$).

Anal. Calcd. for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.72; H, 5.88; N, 7.19.

General Procedure for the Preparation of Compounds **11g** and **11k**.

Zinc dust (4 g) was slowly added to a stirred solution of iodolactones **13g,k** (0.6 mmole) in glacial acetic acid (35 ml). After 6 hours, the mixture was filtered and the solid was washed with diethyl ether (2 x 20 ml). The combined mother liquors and filtrate were evaporated to afford a residue, which was taken up in dichloromethane (50 ml) and extracted with 5% aqueous sodium hydrogen carbonate solution (2 x 30 ml). After acidifying with concentrated hydrochloric acid, the aqueous solution was extracted with dichloromethane (3 x 25 ml), dried over anhydrous magnesium sulfate and treated with a slight excess of a solution of

diazomethane in diethyl ether during 30 minutes. Evaporation of the solvent afforded the required compound in good yield.

Methyl *exo*-2-Benzamido-*exo*-3-(3',4'-dimethoxyphenyl)bicyclo[2.2.1]hept-5-ene-*endo*-2-carboxylate (**11g**).

Evaporation of the solvent gave 180 mg (73%) of compound **11g** as an oil; ^{1}H nmr: δ 1.79 (dd, 1H, $J_{7s\text{-}7a}$ = 9.0, $J_{7s\text{-}3n}$ = 1.7, H_{7s}), 1.98 (d, 1H, $J_{7a\text{-}7s}$ = 9.3, H_{7a}), 3.07 (broad s, 1H, H_4), 3.22 (dd, 1H, $J_{3n\text{-}7s}$ = 1.5, $J_{3n\text{-}4}$ = 1.5, H_{3n}), 3.65 (broad s, 1H, H_1), 3.73 (s, 3H, $COOCH_3$), 3.87 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 6.09 (broad s, 1H, CONH), 6.38 (dd, 1H, $J_{6\text{-}5}$ = 5.7, $J_{6\text{-}1}$ = 3.3, H_6), 6.53 (dd, 1H, $J_{5\text{-}6}$ = 5.7, $J_{5\text{-}4}$ = 3.0, H_5), 6.92-7.02 (m, 3H, Arom), 7.20-7.30 (m, 4H, Arom), 7.35-7.40 (m, 1H, Arom); ^{13}C nmr: δ 46.3, 46.9, 49.5, 52.2 (C_1, C_3, C_4, C_7), 54.4, 55.9, 56.1 ($2OCH_3$, $COOCH_3$), 66.3 (C_2), 111.3, 113.2, 120.3, 126.5, 128.4, 130.5, 131.5, 133.8, 137.9, 138.0, 148.6, 149.2 (Arom, C_5, C_6), 165.8 (CONH), 173.4 ($COOCH_3$).

Anal. Calcd. for $C_{24}H_{25}NO_5$: C, 70.73; H, 6.19; N, 3.44. Found: C, 70.84; H, 6.26; N, 3.53.

Methyl *exo*-2-Benzamido-*exo*-3-(3'-indolyl)bicyclo[2.2.1]hept-5-ene-*endo*-2-carboxylate (**11k**).

Evaporation of the solvent gave 650 mg (90%) of compound **11k** as an oil; ^{1}H nmr: δ 1.80 (dd, 1H, $J_{7s\text{-}7a}$ = 9.0, $J_{7s\text{-}3n}$ = 1.7, H_{7s}), 2.06 (d, 1H, $J_{7a\text{-}7s}$ = 9.0, H_{7a}), 3.06 (broad s, 1H, H_4), 3.47 (d, 1H, $J_{3n\text{-}7s}$ = 1.7, H_{3n}), 3.72 (s, 3H, $COOCH_3$), 3.76 (broad s, 1H, H_1), 6.37 (dd, 1H, $J_{6\text{-}5}$ = 5.4, $J_{6\text{-}1}$ = 3.0, H_6), 6.60 (dd, 1H, $J_{5\text{-}6}$ = 5.4, $J_{5\text{-}4}$ = 3.0, H_5), 6.61 (broad s, 1H, CONH), 7.09-7.72 (m, 10H, Arom), 8.82 (broad s, 1H, NH); ^{13}C nmr: δ 47.2, 47.8, 48.4, 49.7, 51.9 (C_1, C_3, C_4, C_7, $COOCH_3$), 65.6 (C_2), 111.3, 113.7, 120.0, 120.2, 122.8, 122.9, 126.5, 127.5, 128.3, 131.2, 134.1, 136.3, 137.2, 137.7 (Arom, C_5, C_6), 166.0 (CONH), 173.6 ($COOCH_3$).

Anal. Calcd. for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.68; H, 5.81; N, 7.21.

General Procedure for the Preparation of Compounds **14g,k** and **15g,k** by Hydrogenation.

A solution of the corresponding unsaturated compound (0.30 mmole) in dry dichloromethane (15 ml) was hydrogenated at atmospheric pressure during 4 hours with a 10% palladium-carbon catalyst (50 mg). Removal of the catalyst and the solvent gave the required compound.

Methyl *endo*-2-Benzamido-*endo*-3-(3',4'-dimethoxyphenyl)bicyclo[2.2.1]heptane-*exo*-2-carboxylate (**14g**).

Compound **14g** was obtained quantitatively as an oil; ^{1}H nmr: δ 1.16-1.22 (m, 2H, H_{5n}, H_{6n}), 1.60-1.70 (m, 3H, H_{5x}, H_{6x}, H_{7s}), 2.12 (d, 1H, $J_{7a\text{-}7s}$ = 10.2, H_{7a}), 2.72 (broad s, 1H, H_4), 3.37 (d, 1H, $J_{3x\text{-}4}$ = 2.0, H_{3x}), 2.84 (broad s, 1H, H_1), 3.90-3.96 (m, 9H, $2OCH_3$, $COOCH_3$), 6.44 (broad s, 1H, CONH), 6.86-7.02 (m, 2H, Arom), 7.16-7.20 (m, 1H, Arom), 7.28-7.50 (m, 5H, Arom); ^{13}C nmr: δ 22.1, 24.7 (C_5, C_6), 38.6, 38.9, 45.6, 52.5, 53.8, 55.8, 55.9 (C_1, C_3, C_4, C_7, $2OCH_3$, $COOCH_3$), 63.7 (C_2), 111.2, 112.8, 121.9, 126.7, 128.0, 128.6, 131.6, 133.5, 148.0, 149.0 (Arom), 166.6 (CONH), 174.8 ($COOCH_3$).

Anal. Calcd. for $C_{24}H_{27}NO_5$: C, 70.38; H, 6.65; N, 3.42. Found: C, 70.31; H, 6.54; N, 3.51.

Methyl *exo*-2-Benzamido-*exo*-3-(3',4'-dimethoxyphenyl)bicyclo[2.2.1]heptane-*endo*-2-carboxylate (**15g**).

Compound **15g** was obtained quantitatively as an oil; ^{1}H nmr: δ 1.40-1.75 (m, 5H, H_{5n}, H_{5x}, H_{6n}, H_{6x}, H_{7s}), 2.70 (d, 1H, $J_{7a\text{-}7s}$ = 10.0, H_{7a}), 2.60 (broad s, 1H, H_4); 2.84 (broad s, 1H, H_1), 3.70-3.85 (m, 10H, $2OCH_3$, $COOCH_3$, H_{3n}), 5.80 (broad s, 1H, CONH), 6.70-6.90 (m, 3H, Arom), 7.14-7.38 (m, 5H, Arom); ^{13}C nmr: δ 23.7, 29.4 (C_5, C_6), 38.0, 42.5, 45.8, 52.3, 54.9, 55.9, 55.9 (C_1, C_3, C_4, C_7, $2OCH_3$, $COOCH_3$), 69.9 (C_2), 110.7, 113.7, 119.9, 126.4, 128.3, 131.2, 132.0, 134.4, 147.8, 148.3 (Arom), 165.9 (CONH), 172.6 ($COOCH_3$).

Anal. Calcd. for $C_{24}H_{27}NO_5$: C, 70.38; H, 6.65; N, 3.42. Found: C, 70.28; H, 6.52; N, 3.44.

Methyl *endo*-2-Benzamido-*endo*-3-(3'-indolyl)bicyclo[2.2.1]-heptane-*exo*-2-carboxylate (**14k**).

Compound **14k** was obtained quantitatively as an oil; ^{1}H nmr: δ 1.30-1.55 (m, 5H, H_{5n}, H_{5x}, H_{6n}, H_{6x}, H_{7s}), 2.12 (d, 1H, $J_{7a\text{-}7s}$ = 9.9, H_{7a}), 2.48 (broad s, 1H, H_4), 3.30 (broad s, 1H, H_1), 3.57 (s, 3H, $COOCH_3$), 3.59 (broad s, 1H, H_{3x}), 6.60 (broad s, 1H, CONH), 6.92-7.42 (m, 10H, Arom), 10.17 (broad s, 1H, NH); ^{13}C nmr: δ 22.7, 23.8 (C_5, C_6), 38.9, 40.7, 45.1, 47.7, 51.7 (C_1, C_3, C_4, C_7, $COOCH_3$), 62.6 (C_2), 109.3, 111.2, 118.9, 119.0, 121.8, 123.4, 126.3, 127.3, 128.0, 131.0, 133.5, 135.8 (Arom), 166.5 (CONH), 174.5 ($COOCH_3$).

Anal. Calcd. for $C_{24}H_{24}N_2O_3$: C, 74.21; H, 6.23; N, 7.21. Found: C, 74.40; H, 6.28; N; 7.11.

Methyl *exo*-2-Benzamido-*exo*-3-(3'-indolyl)bicyclo[2.2.1]heptane-*endo*-2-carboxylate (**15k**).

Compound **15k** was obtained quantitatively as an oil; ^{1}H nmr: δ 1.51-1.68 (m, 4H, H_{5n}, H_{5x}, H_{6n}, H_{6x}), 2.03 (dd, 1H, $J_{7s\text{-}7a}$ = 10.3, $J_{7s\text{-}3n}$ = 0.9, H_{7s}), 2.12 (d, 1H, $J_{7a\text{-}7s}$ = 10.3, H_{7a}), 2.60 (broad s, 1H, H_4), 3.34 (s, 1H, H_1), 3.74 (s, 3H, $COOCH_3$), 3.90 (d, 1H, $J_{3n\text{-}7s}$ = 0.9, H_{3n}), 6.09 (broad s, 1H, CONH), 7.00-7.67 (m, 10H, Arom), 8.41 (broad s, 1H, NH); ^{13}C nmr: δ 23.6, 30.0 (C_5, C_6), 38.1, 43.6, 44.9, 48.8, 52.2 (C_1, C_3, C_4, C_7, $COOCH_3$), 68.6 (C_2), 111.1, 114.1, 119.8, 119.9, 122.3, 122.5, 126.4, 127.4, 128.1, 130.9, 134.6, 136.0 (Arom), 165.7 (CONH), 173.2 ($COOCH_3$).

Anal. Calcd. for $C_{24}H_{24}N_2O_3$: C, 74.21; H, 6.23; N, 7.21. Found: C, 74.33; H, 6.32; N, 7.14.

Methyl *endo*-2-Amino-*endo*-3-(3',4'-dimethoxyphenyl)bicyclo[2.2.1]heptane-*exo*-2-carboxylate (**16g**).

A solution of 1 *M* triethyloxonium tetrafluoroborate in dichloromethane (7 ml) was added to a stirred solution of the saturated benzamide derivative **14g** (204 mg, 0.5 mmole) in dry dichloromethane (7 ml) and kept under an inert atmosphere for 5 days at 40°. The reaction mixture was concentrated and then stirred overnight with a mixture of tetrahydrofuran and 10% aqueous acetic acid (1:1). Dilution with diethyl ether (30 ml) and extraction with 5% aqueous hydrochloric acid (2 x 10 ml) gave an aqueous fraction which was made basic to *p*H 8 by the addition of 10% aqueous sodium hydroxide. The aqueous layer was extracted with dichloromethane (3 x 20 ml) and the combined organic extracts were dried over anhydrous magnesium sulfate and then concentrated to give 50 mg (41%) of the amino derivative **16g** as an oil; ^{1}H nmr: δ 1.30-1.58 (m, 3H), 1.70-2.00 (m, 5H), 2.54-2.68 (m, 2H, H_1, H_4), 3.50 (d, 1H, $J_{3x\text{-}4}$ = 2.1, H_{3x}), 3.76 (s, 3H, $COOCH_3$), 3.83 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 6.75-6.90 (m, 3H, Arom); ^{13}C nmr: δ 21.6, 23.0 (C_5, C_6), 38.5, 40.7, 47.1, 52.0, 52.1, 52.4, 55.8 (C_1, C_3, C_4, C_7, $2OCH_3$, $COOCH_3$), 63.2 (C_2), 111.0, 113.2, 121.8, 130.6, 147.4, 148.5 (Arom), 178.2 ($COOCH_3$).

Anal. Calcd. for $C_{17}H_{23}NO_4$: C, 66.85; H, 7.60; N, 4.59. Found: C, 66.73; H, 7.51; N, 4.54.

endo-2-Amino-*endo*-3-(3',4'-dimethoxyphenyl)bicyclo-[2.2.1]heptane-*exo*-2-carboxylic Acid (**17g**).

Methyl ester derivative **16g** (61 mg, 0.2 mmole) was heated under reflux with a 10% ethanolic potassium hydroxide (10 ml) for 6 hours. The solvent was removed under reduced pressure, the residue was acidified with 6 *N* aqueous hydrochloric acid (10 ml) and the solvent was evaporated. The amino acid hydrochloride was dissolved in ethanol (6 ml) and propylene oxide (2 ml) was added. The mixture was heated under reflux for 1 hour and the precipitate was filtered off to give 22 mg (47%) of the required amino acid **17g** as a white solid; ^{1}H nmr (deuterium oxide-trifluoroacetic acid): δ 1.43-1.53 (m, 1H, H_{7s}), 1.70-2.13 (m, 4H, H_{5x}, H_{6x}, H_{5n}, H_{6n}), 2.23-2.38 (m, 1H, H_{7a}), 2.93 (broad s, 2H, H_4, H_1), 3.83 (m, 1H, H_{3x}), 3.93 (m, 6H, $2OCH_3$), 6.40-7.13 (m, 3H, Arom).

Anal. Calcd. for $C_{16}H_{21}NO_4$: C, 65.95; H, 7.27; N, 4.81. Found: C, 65.83; H, 7.35; N, 4.74.

exo-2-Amino-*exo*-3-(3',4'-dimethoxyphenyl)bicyclo[2.2.1]heptane-*endo*-2-carboxylic Acid (**18g**).

Methyl *N*-benzoyl-α-amino ester **15g** (204 mg, 0.5 mmole) was dissolved in 6 *N* aqueous hydrochloric acid (35 ml) and heated under reflux for 24 hours. The solvent was removed under reduced pressure. The residue of amino acid hydrochloride was dissolved in ethanol (6 ml) and propylene oxide (2 ml) was added. The mixture was heated under reflux for 1 hour and the precipitate was filtered off to give 60 mg (40%) of the required amino acid **18g** as a white solid; ^{1}H nmr (deuterium oxide-trifluoroacetic acid): δ 1.55-1.65 (m, 1H, H_{7s}), 1.70-1.90 (m, 4H, H_{5x}, H_{6x}, H_{5n}, H_{6n}), 2.29 (d, 1H, $J_{7a\text{-}7s}$ = 11.4, H_{7a}), 2.79 (m, 2H, H_4, H_1), 3.93 (m, 1H, H_{3n}), 3.94 (m, 6H, $2OCH_3$), 6.85-7.10 (m, 3H, Arom).

Anal. Calcd. for $C_{16}H_{21}NO_4$: C, 65.95; H, 7.27; N, 4.81. Found: C, 65.81; H, 7.38; N, 4.71.

Methyl 1-Benzamido-*c*-4,*c*-5-dimethyl-*t*-2-(3',4'-dimethoxy)-phenyl-*r*-1-cyclohexanecarboxylate (**19g**).

A solution of the unsaturated methyl *N*-benzoyl-α-amino ester **9g** (210 mg, 0.49 mmole) in dry ethanol (30 ml) was hydrogenated at 50° with 10% palladium-carbon catalyst (50 mg) during 2 weeks. Removal of the catalyst and the solvent quantitatively gave a mixture of the saturated compounds **19g** and **20g** in a ratio of 90:10. Only an analytical sample of compound **19g** could be separated by silica gel column chromatography (hexane-ethyl acetate 4:1); ^{1}H nmr: δ 0.88-1.05 (m, 8H, $2CH_3$, H_{4e}, H_{5a}), 1.58-1.69 (m, 1H, H_{3e}), 2.06 ('t', 1H, $J_{6a\text{-}6e} \sim J_{6a\text{-}5a}$ = 13.5, H_{6a}), 2.35 ('t'd, 1H, $J_{3a\text{-}3e} \sim J_{3a\text{-}2a}$ = 13.8, $J_{3a\text{-}4e}$ = 4.4, H_{3a}), 2.95 (dd, 1H, $J_{6e\text{-}6a}$ = 13.5, $J_{6e\text{-}5a}$ = 2.4, H_{6e}), 3.36 (dd, 1H, $J_{2a\text{-}3a}$ = 13.7, $J_{2a\text{-}3e}$ = 3.1, H_{2a}), 3.52 (s, 3H, $COOCH_3$), 3.83 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 6.17 (broad s, 1H, NH), 6.60-6.86 (m, 3H, Arom), 7.34-7.68 (m, 5H, Arom); ^{13}C nmr: δ 11.7 (CH_3), 19.0 (CH_3), 29.0 (C_3), 32.2 (C_4), 32.4 (C_6), 34.4 (C_5), 42.7 (C_2), 52.1 ($COOCH_3$), 55.8 ($2OCH_3$), 65.0 (C_1), 111.3, 111.3, 119.0, 126.8, 128.6, 131.5, 132.2, 135.5, 148.6, 149.1 (Arom), 168.0 (CONH), 173.6 ($COOCH_3$).

Anal. Calcd. for $C_{25}H_{31}NO_5$: C, 70.57; H, 7.34; N, 3.29. Found: C, 70.68; H, 7.21; N, 3.29.

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[10] The ratio of the *endo* and *exo* adducts **4/5** was determined by the integration of the corresponding protons of products **4** and **5** in the ^{1}H-nmr spectrum of the crude mixture; **4f** (*endo*): 4.30 (dd, 1H, $J_{2e\text{-}3a}$ = 14.4, $J_{2e\text{-}3e}$ = 4.2, H_{2e}); **5f** (*exo*): 4.69 (dd, 1H, $J_{2a\text{-}3a}$ = 12.0, $J_{2a\text{-}3e}$ = 5.0, H_{2a}); **4g** (*endo*): 2.80-2.90 (m, 1H, H_{3e}); **5g** (*exo*): 2.50-2.58 (m, 1H, H_{5e}). For *endo/exo* ratio of cycloadducts **6** and **7**, see Experimental.

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