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SYNTHESIS AND CYCLOADDITION REACTIONS OF NEW CAPTODATIVE OLEFINS *N*-SUBSTITUTED 5-ALKYLIDENE-1,3-OXAZOLIDINE-2,4-DIONES

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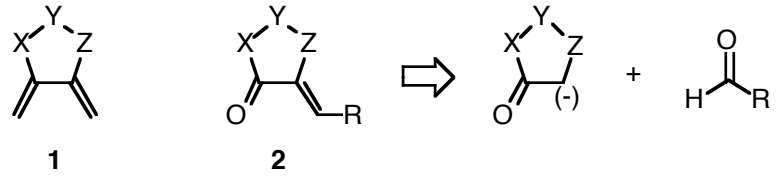
Abstract **-** An efficient and straightforward synthesis of the new captodative olefins *N*-substituted 5-alkylidene-1,3-oxazolidine-2,4-diones (**8**-**10**) is described, by a chemoselective oxidative cleavage of the novel *exo*-2-oxazolidinone dienes (**3**, **4**, and **7**), respectively. A study of the reactivity and selectivity of olefins (**8**-**10**), was carried out in Diels-Alder cycloadditions to cyclic and unsymmetric acyclic olefins. In all reactions, the corresponding adducts were obtained in high stereo- and regioselectivity. These results have been rationalized in terms of FMO theory by *ab initio* calculations. 1,3-Dipolar additions of nitrones to olefin (**8a**) were also highly regioselective, yielding only the C-5 substituted adducts.

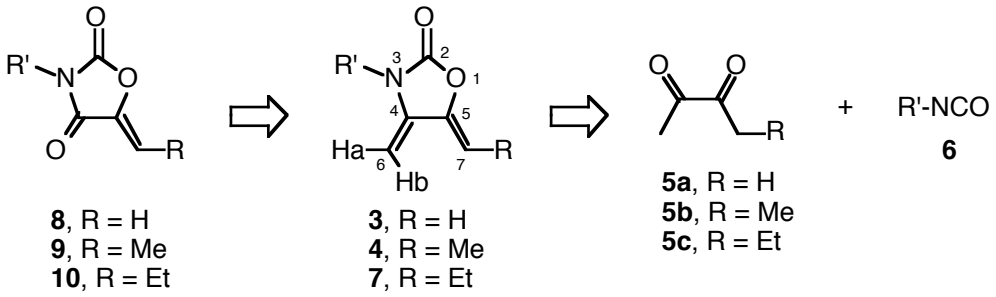
In the last decade, an intense effort has been displayed in the synthesis and study of reactivity of outer-ring *o*-xylylenes.[1] In particular, *exo*-heterocyclic dienes (**1**) have been prepared looking for new heteroatom combinations, and by original and more efficient synthetic methods.[2] An interesting class of compounds related to these dienes, which would be considered as heterodienes,[3] are the *exo*-heterocyclic enones (**2**).[4] Their significant biological activity,[5] natural occurrence,[6] and attractive structure as potential chiral synthons,[7] have prompted the development of new and more versatile synthetic strategies. Among them, the aldol-type condensation of the heterocyclic carbonylic species with the corresponding aldehyde has been widely used for the preparation of these molecules (Scheme 1).[8] The exocyclic enone moiety may be expected to behave not only as a Michael acceptor,[9] but also as a captodative olefin[10] in Diels-Alder[11] and 1,3-dipolar[12] additions.

Recently, we described a highly convergent method to prepare the novel *N*-substituted *exo*-2-oxazolidinone dienes (**3**) and (**4**).[13,14] This strategy involved the concept of a tandem interaction between two species bearing both, potential nucleophilic and electrophilic centers,[15] by using α-diketones (**5**) and isocyanates (**6**) (Scheme 2). These dienes proved to be very reactive, regio- and stereoselective in Diels-Alder cycloadditions.[14] A synthetic application of some of the corresponding adducts resulted in a new method for the preparation of the carbazole skeleton.[16]



Scheme 1

In order to devise an efficient and versatile synthetic methodology for the preparation of *exo*-heterocyclic enones (**8**-**10**), dienes (**3**, **4**, and **7**) might be suitable substrates, inasmuch as the enamide-like C-4 methylene could be transformed into a carbonyl group by an efficient oxidizing agent (Scheme 2).[17]



Scheme 2

Herein, we describe the preparation of the new *N*-substituted 5-alkylidene-1,3-oxazolidine-2,4-diones (**8**-**9**) by selective C-4 methylene cleavage of dienes (**3**) and (**4**). The behavior of these compounds as captodative olefins in Diels-Alder and 1,3-dipolar cycloadditions, with cyclic and unsymmetric non-cyclic dienes, and nitrones, respectively, is also reported. In order to synthesize diones (**10**), it has been necessary to prepare the novel (5*Z*)-4-methylene-5-propenylene-2-oxazolidinones (**7**). We disclose MO calculations as well, which rationalize the regioselectivity observed in the [4+2] addition processes.

RESULTS AND DISCUSSION

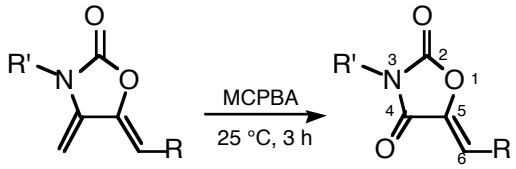
Diones (**8**-**10**) were readily available by oxidation of dienes (**3**, **4**, and **7**) with *m*-chloroperbenzoic acid (MCPBA) in methylene chloride at room temperature for 3 h (Table 1). The conversion was almost complete, since the analysis (^{1}H NMR and MS spectrometries) of the crude reaction mixtures did not reveal any further product. The modest yields of compounds (**8**-**10**) are mainly due to their decomposition under column chromatography with silica gel. The latter had to be impregnated with methanol in order to minimize decomposition of the dione. The chemoselectivity was confirmed by ^{1}H NMR spectra, because the methyl or ethyl groups remained in the double bond.

Dienes (**7a**) and (**7b**) were prepared in fair yields, following the general procedure for the preparation of dienes (**4**), by using 2,3-hexanedione (**5c**) as the starting α-diketone. As in the case of dienes (**3**) and (**4**), the^{1}H NMR spectral analysis of the crude mixtures of dienes (**7**) did not give evidence of the presence of any other isomer.

This selective oxidation reflects a high difference in reactivity among the exocyclic double bonds of the dienes. This is probably due to the higher polarizability of the nitrogen lone pair, as seems to be the case for Diels-Alder additions,[14] and for Michael conjugate additions.[18]

In general, olefins are readily epoxidized with MCPBA, and the mechanism seems to be concerted and stereospecific.[19] However, the oxidative cleavage of the olefin by this reagent is not common,[20] unless the double bond is strongly activated by electron-donor groups, and the peracid is used in excess, to give the corresponding carbonyl products.[21] As many other oxidizing methods, the cleavage may give rise either to the aldehyde or to the acid.[22] In the case of the enamidic double bond of dienes (**3**, **4**, and **7**), the reaction would lead to the carbonylic compounds (**8**-**10**), and, on the other side, to the oxidized formyl fragment.[23]

Table 1. Reaction Conditions and Yields in the Preparation of Oxazolidindiones (8-10).[a]



3, R = H
4, R = Me
7, R = Et

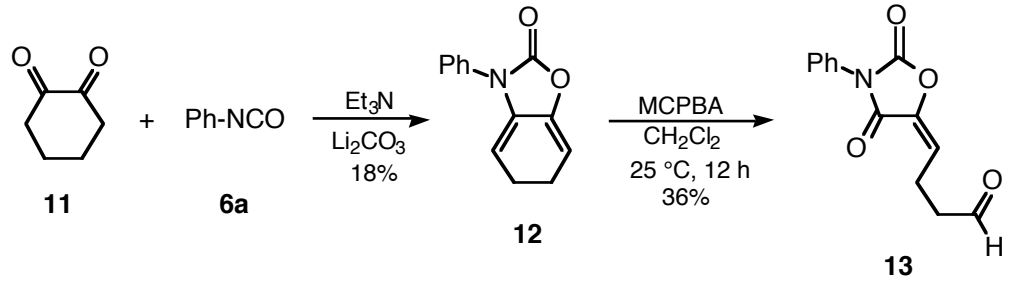
8, R = H
9, R = Me
10, R = Et

Diene	R'	Dione	mp (°C)	Yield (%)[b]
3a	Ph	**8a**	108-109	25
3b	*p*-ClC_6H_4	**8b**	131-132	53
3c	*p*-MeC_6H_4	**8c**	90-91	41
4a	Ph	**9a**	112-113	58
4b	*p*-ClC_6H_4	**9b**	122-123	69
7a	Ph	**10a**	105-106	69
7b	*p*-ClC_6H_4	**10b**	113-114	76

[a] CH_2Cl_2 as the solvent, with MCPBA (1.5 mol eq).
[b] After column chromatography and recrystallization.

Since the formyl fragment was not unambiguously detected, neither as formaldehyde nor formic acid, we decided to carry out the same experiment with a cyclic diene, in order to isolate both oxidized fragments of the olefin. Diene (**12**) was prepared in low yield (18%) by the tandem condensation of 1,2-cyclohexanedione (**11**) with phenyl isocyanate (**6a**) in the presence of triethylamine and lithium carbonate (25 °C, 12 h) (Scheme 3). Treatment of **12** with MCPBA provided aldehyde (**13**) in 36% yield. Neither the acid nor other isomeric products were detected in the crude reaction mixture.

Oxazolidine-2,4-diones (**8**-**10**) were evaluated in terms of reactivity and selectivity towards cyclic and unsymmetrical acyclic dienes in Diels-Alder reactions. Thus, diones (**8a**) and (**8b**) reacted with a large excess of isoprene (**14**) under thermal (190 °C) conditions (Table 2), to give mixtures of regioisomers (**15a**/**16a**) and (**15b**/**16b**), respectively, in comparable ratios (Scheme 4).



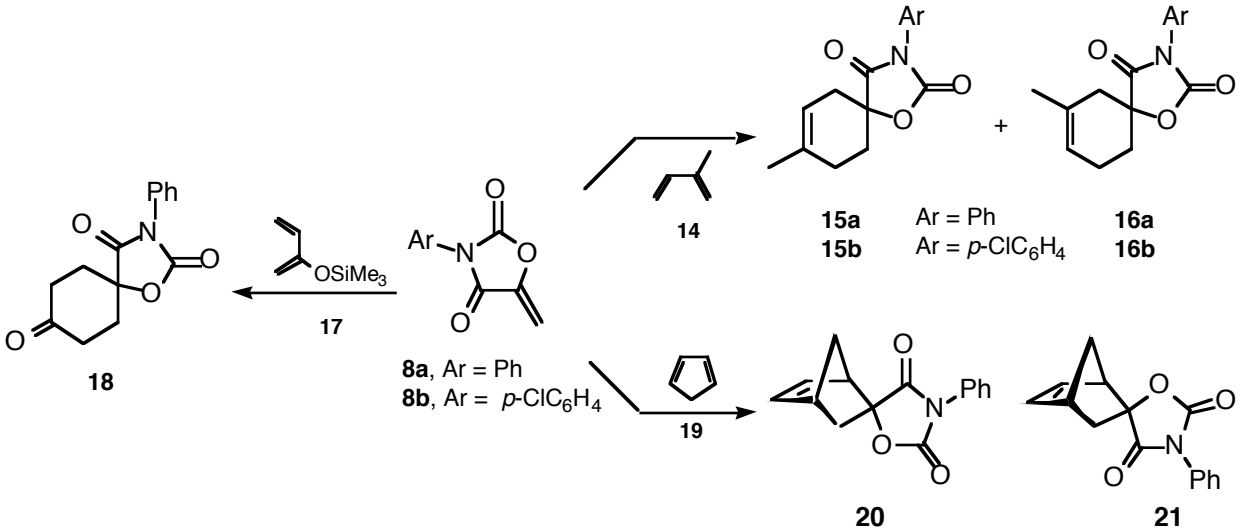
Scheme 3

Similar results were obtained under sonication for both olefins (Entries 3 and 4), giving the major *para* (1,4-) isomer (**15**), but olefin (**8b**) was slightly less selective. In contrast, substituted olefins (**9a**) and (**10a**) were not reactive enough toward the addition of **14** neither under these conditions nor under Lewis acid catalysis. Likely, the presence of the alkyl group deactivates the double bond, as we have observed with several β-substituted captodative olefins.[24]

Table 2. Diels-Alder Cycloadditions of Olefins (8a) and (8b) with Dienes (14, 17, and 19).[a]

Entry	Olefin	Diene[b]	Solvent	*T* (°C)	*t* (h)	Products (ratio)[c]	Yield (%)[d]
1	**8a**	**14**	xylene	190	198	**15a**/**16a** (75:25)	89
2	**8b**	**14**	xylene	190	216	**15b**/**16b** (77:23)	93
3[e]	**8a**	**14**	---	65	168	**15a**/**16a** (80:20)	96
4[e]	**8b**	**14**	---	65	216	**15b**/**16b** (75:25)	97
5	**8a**	**17**	xylene	160	120	**18**	53
6[e]	**8a**	**19**	---	65	72	**20**/**21** (100:0)	73

[a] All under N_2 atmosphere, and in the presence of 1-2% hydroquinone. [b] 20 Mol equiv with diene (**14**) under thermal, and 38 mol equiv with diene (**14**) under sonication; 2 mol equiv with diene (**17**), and 19 mol equiv with diene (**19**). [c] Calculated by ^{1}H NMR from the crude reaction mixtures. [d] Corresponding to the isomeric mixture after column chromatography and recrystallization. [e] Reactions carried out without solvent, in a sonicated water-bath.



Scheme 4

An increase in regioselectivity was observed when the 2-substituted diene (**17**), which is bearing a stronger electron-donor group, was used; hence the *para* adduct was exclusively obtained, and isolated as its hydrolyzed product (**18**) (Scheme 4). The hydrolysis took place under column chromatography with silica gel. Olefin (**8a**) underwent a highly stereoselective addition towards cyclopentadiene (**19**) by means of sonication to give the bicyclic *exo*-adduct (**20**) in good yield; no *endo*-adduct (**21**) was detected.

The structures of the major isomers (**15a**, **15b**, and **20**) were characterized by spectroscopy, and the crystal structure of **15a** was determined by X-Ray diffraction (Figure 1).[25] Adducts (**15a**) and (**20**) were also hydrolyzed (NaOH, EtOH, 25 °C, 2 h) to their corresponding α-hydroxy *N*-benzamides (**22**) and (**23**) with the goal of facilitating their characterization. The *exo* configuration of compound (**20**) and its derivative (**23**) was assigned in agreement with ^{1}H NMR spectroscopic arguments. Thus, the spectra of both compounds exhibit the vicinal proton *syn* to the amide carbonyl group, H-3x, shifted down-field with respect to proton H-3n. This deshielding effect produced by the carbonyl group upon the *syn* H-3 proton is characteristic of the skeleton of norbornene derivatives.[26] This stereochemistry was also supported by low-resolution X-Ray diffraction data of a monocrystal of benzamide (**23**).[27] For the spiro ketone (**18**), its symmetrical structure was easily recognized in the ^{1}H and ^{13}C NMR spectra.

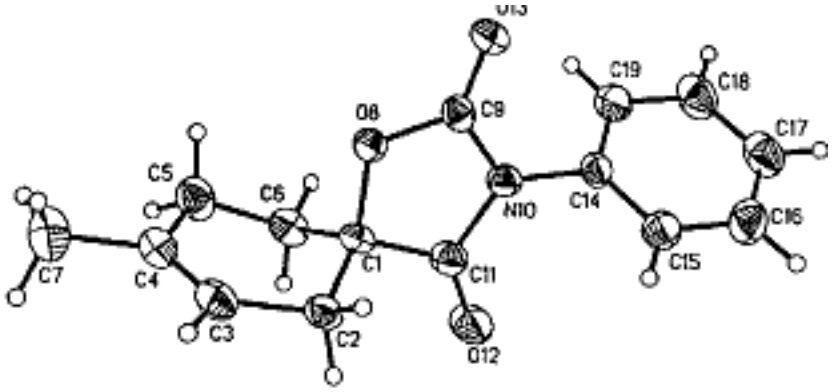
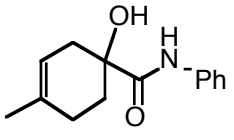


Figure 1. ORTEP Structure of **15a**.



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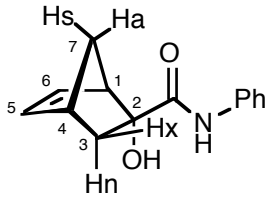
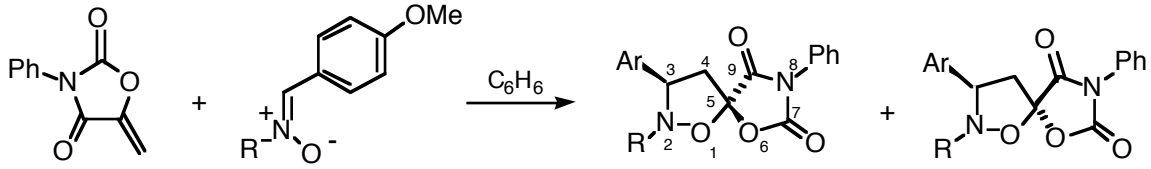


23

We also examined the outcome of 1,3-dipolar cycloadditions of olefin (**8a**) with nitrones (**24a**) and (**24b**), in order to test their regio- and stereoselectivities.[12] Thus, **8a** undergoes a smooth cycloaddition to **24a** (2.0 mol equiv) on gentle heating (C_6H_6, 60 ° C) for 12 h to give a mixture of the *endo*/*exo* stereoisomers

(**25a**/**26a**) in 72:28 ratio (68%) (Scheme 5). Interestingly, a single regioisomer was detected in the crude reaction mixture, and assigned to the C-5 substituted isoxazolidine. This is in agreement with additions of other captodative olefins to the same nitrone.[28] The same regiochemistry was obtained in carrying the reaction (C_6H_6, 80 °C, 24 h) with the *N*-benzylnitrone (**24b**), however, the stereoisomeric ratio **25b**/**26b** (57:43) (80%) was lower than that of **24a**. The greater motion of the benzyl group of **24b**, in comparison with that of the phenyl group of **24a**, may be at the origin of this decrease in selectivity. The relative configuration of major stereoisomers (**25**) was attributed in accordance with the *endo* preference displayed by captodative olefins in the addition to nitrones (**24**).[29] ^{1}H NMR spectra of adducts (**25**) and (**26**) appear to support this attribution, considering the unambiguously established structure of many analogous adducts.[29] Thus, for **25**, the geminal coupling constant for protons H-4 is larger than that of **26**; besides, the vicinal coupling constants of these protons with H-3 are generally smaller for the *endo* adducts (**25**), than those of the *exo* adducts (**26**). This behavior is due to differences among these stereiosomers in ring and torsion angles between the H-3 and H-4 protons, arising from the preferential conformation assumed by the isoxazolidine rings when they have an oxygenated function attached to the anomeric carbon C-5;[29,30] i.e. the oxygen of the carbamate function takes the pseudo-axial position, leaving the amide carbonyl group in a pseudo-equatorial orientation.



8a **24a**, R = Ph; **24b**, R = Bn **25a**, R = Ph; **25b**, R = Bn **26a**, R = Ph; **26b**, R = Bn

Ar = *p*-OMeC_6H_4

Scheme 5

We have been able to explain satisfactorily the regioselectivity of Diels-Alder cycloadditions of captodative olefins, **27** among them, by FMO theory.[31] Therefore, this model should be useful as well to correlate the energies and coefficients of the frontier molecular orbitals of olefins (**8**-**10**) with those of diene (**14**).[10] Frontier orbitals of olefins (**8**-**10**) were obtained from *ab initio* RHF calculations. Geometries were fully optimized at the AM1 semiempirical method,[32] and employed as the starting point for optimization using the 3-21G and 6-31G* basis sets.[33] The orbital energies derived from these calculations are summarized in Table 3, and compared to those previously calculated for olefin (**27**).[10] It appears that the *normal electron demand* interaction,[34] HOMO-diene/LUMO-dienophile, is largely preferred [3.12 eV (3-21G); 3.66 eV (6-31G*)] for all the interactions between olefins (**8**-**10**). The energies for the LUMO of olefins (**9**) and (**10**) are higher than those of β-unsubstituted olefins (**8**), at both 3-21G and 6-31G* levels. Consequently, olefins (**8**) should be more reactive and selective in [4+2] cycloadditions with diene (**14**). Indeed, olefins (**9**) and (**10**) did not react with this diene under thermal and catalytic conditions.

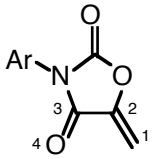
Table 3. ***Ab initio*** **RHF/3-21G, and 6-31G* Frontier Molecular Orbital Energies of Olefins (8a-8c, 9a-9b, 10a-10b, and 27), and Diene (14).**

		3-21G	6-31G*			3-21G	6-31G*
Compound	FMO	*E* (eV)	*E* (eV)	Compound	FMO	*E* (eV)	*E* (eV)
8a	HOMO[a]	-10.9570	-10.7127	**10a**	HOMO[a]	-10.4375	-10.2365
8a	LUMO	1.8553	2.2564	**10a**	LUMO	2.0810	2.4724
8b	HOMO[a]	-11.1518	-10.8770	**10b**	HOMO[a]	-10.6188	-10.3924
8b	LUMO	1.6360	2.0613	**10b**	LUMO	1.8708	2.2791
8c	HOMO[a]	-10.9153	-10.6718	**27**[b]	HOMO	-11.0460	-11.0123
8c	LUMO	1.9034	2.3064	**27**[b]	LUMO	2.2417	2.4588
9a	HOMO[a]	-10.4977	-10.2762	**14**[c]	HOMO	-8.7107	-8.6193
9a	LUMO	2.0749	2.4782	**14**[c]	LUMO	3.5451	3.5337
9b	HOMO[a]	-10.6833	-10.4348				
9b	LUMO	1.8607	2.2810				

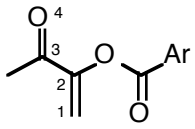
[a] These values are for the 2NHOMO, since the HOMO does not have any p_z contribution on the diene π system. [b] Of the most stable nonplanar *s-trans* conformation; see ref. 10. [c] See ref. 10.

Oxazolidine-2,4-diones (**8a**) and (**8b**) proved to be as regioselective as the captodative olefin (**27**) (*para*/*meta*, (1,4-/1,3-) isomers, 75:25) when the addition was carried out with isoprene (**14**). This behavior is foreseen from the point of view of coefficients, because the difference between coefficents C_1 and C_2 are also similar (Table 4). However, they were less reactive, since olefin (**27**) adds to **14** at 130 °C for 35 h. This does not agree with FMO theory, inasmuch as the LUMOs of captodative olefins (**8a**-**8c**) are more stable than the LUMO of olefin (**27**) (Table 3), thereby they should be more reactive. This unexpected reactivity seems to be due to an interplay of electronic and steric effects, associated with their distinct structural features, rather than only to an FMO factor.

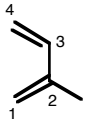
Table 4. ***Ab initio*** **RHF/6-31G* Coefficients (C_i) of the Frontier Molecular Orbitals for Diones (8a-8b), Olefin (27), and Diene (14).**[a]**



8a, Ar = Ph
8b, Ar = *p*-ClC_6H_4



27, Ar = *p*-$NO_2C_6H_4$



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	HOMO					LUMO				
Compound	C_1	C_2	C_3	C_4	ΔC_i[b]	C_1	C_2	C_3	C_4	ΔC_i[b]
8a[c]	0.356	0.337	-0.004	-0.156	0.019	0.295	-0.226	-0.298	0.243	0.069
8b[c]	0.356	0.339	-0.004	-0.156	0.017	0.291	-0.219	-0.298	0.242	0.072
27[d]	-0.359	-0.356	0.024	0.168	0.003	0.294	-0.239	-0.289	0.280	0.055
14[d]	0.375	0.252	-0.218	-0.286	0.089	0.259	-0.224	-0.231	0.279	-0.020

[a] These are the values of the $2p_z$ coefficients, the relative $2p_z$' contributions and their ΔC_i are analogous.
[b] Carbon 1 - carbon 4 for the diene and carbon 1 - carbon 2 for the olefins. [c] These values are for the 2NHOMO, the HOMO does not have any p_z contribution. [d] See ref. 10.

It is noteworthy that the substitution on the *N*-aryl ring modifies the energy of the LUMOs of these molecules, suggesting a long-range electronic effect upon the orbital energies of the exocyclic π system. Thus, the methyl group in the *N*-phenyl ring destabilises the FMOs in **8c**, in comparison with the unsubstituted enone (**8a**). On the other hand, the chlorine atom affects the energy of LUMO by stabilizing it. This is probably due to the inductive effect of the substituent. However, in accord with the experimental results, these effects would be negligible. A similar observation was done in the cycloaddition of dienes (**3**) and (**4**) with several dienophiles.[14] This was explained by the fact that the aryl ring molecular π orbitals cannot overlap efficiently with the nitrogen lone-pair, because they are almost orthogonal, as shown by X-Ray diffraction of these dienes.[14]

The regioselectivity found for captodative olefins (**8a**) and (**8b**) agrees with recent reports describing Diels-Alder additions of analogous olefins.[11a] Interestingly, the *exo* stereoselectivity shown by **8a** appears to be common for this kind of exocyclic captodative olefins, as displayed by some other olefins with cyclopentadiene (**19**), though, to a lesser extent.[11a-11c] In addition, *exo*/*endo* ratio seems to be kinetically controlled.[11b] The high preference for the *exo* adducts in cycloadditions of **19** with exocyclic captodative olefins (**8**) is in sharp contrast with that observed for the acyclic counterparts,[11c] such as **27**. In this case, addition to **19** is not stereoselective under similar reaction conditions.[26]

Recently, we have shown that FMO theory was unable to predict the regiochemistry between captodative olefins like **27** and dipoles such as nitrile oxides,[35] and nitrones.[29] A successful theoretical approach has been found in the DFT-HSAB model, which is based on the estimation of the local-global hardnesses in both π-systems.[29b] The orientation seems to be controlled by a hard-hard interaction between the unsubstituted terminus of the olefin and the carbon atom center in the dipoles. The hardness of the olefin is mainly induced by the electron-donor group. Consequently, the regioselectivity observed for dipolarophile (**8a**) and nitrones (**24a**) and (**24b**) would be rationalized following the same arguments.

In summary, dienes (**3**, **4**, and **7**) showed a high chemoselectivity when they were treated with MCPBA. Thus, the enamide-like moiety of the exocyclic diene suffered selective oxidative fission to yield the new *N*-substituted 5-alkylidene-1,3-oxazolidine-2,4-diones (**8**-**10**). Highly reactive and selective Diels-Alder and 1,3-dipolar cycloadditions were undergone by these exocyclic captodative olefins with diverse dienes and nitrones. These results were consistent with the behavior of analogous captodative olefins. The regioselectivity of the Diels-Alder additions of alefins (**8**) with diene (**14**) was rationalized by FMO theory, suggesting that their control can be ascribed to the electronic interactions involved during the process.

EXPERIMENTAL

General. Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. NMR spectra were recorded at 270, 300, and 400 MHz for ^{1}H, and at 67.9, 75.4, and 100.0 MHz for ^{13}C, on a JEOL GSX-270 (270 MHz), Varian Gemini-300 (300 MHz), and JEOL-400 (400 MHz) instruments, using TMS as internal standard. MS spectra (EI) were obtained at 70 eV on a Hewlett-

Packard 5971A spectrometer. X-Ray analyses were collected on a P-4 Siemens diffractometer, using Mo Kα radiation (graphite crystal monochromator, λ = 0.71073 Å). Microanalyses were performed by M-H-W Laboratories (Phoenix, AZ). Analytical TLC was carried out using E. Merck silica gel 60 F_{254} coated 0.25 plates, visualizing by long- and short-wavelength UV lamp. All air moisture sensitive reactions were carried out under nitrogen using oven-dried glassware. Dioxane, and xylene were freshly distilled from sodium, and methylene chloride from calcium hydride, prior to use. Li_2CO_3 was dried overnight at 120 °C before using. Triethylamine was freshly distilled from NaOH. All other reagents were used without further purification.

General Procedure for the Preparation of *N*-Substituted (5*Z*)-4-Methylene-5-propylidene-2-oxazolidinones (7a and 7b). To a stirred solution of triethylamine (0.71 g, 7.0 mmol) in dry dioxane (2 mL) containing dry Li_2CO_3 (0.31 g, 4.2 mmol), under an N_2 atmosphere, and at rt, a solution of 2,3-hexanedione (**5c**) (0.40 g, 3.5 mmol) in dry dioxane (1 mL) was slowly added. After stirring for 30 min at the same temperature, a solution of the isocyanate (**6**) (5.2 mmol) in dry dioxane (2 mL) was added dropwise, and the mixture was stirred for 12 h at rt. The solution was filtered and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel impregnated with triethylamine (10%) in hexane (hexane/EtOAc, 9:1) to give dienes (**7a-7b**).

(5*Z*)-4-Methylene-*N*-phenyl-5-propylidene-2-oxazolidinone (7a). Using the general procedure with 0.62 g (5.2 mmol) of phenyl isocyanate (**6a**) gave 0.30 g (40%) of **7a** as colorless crystals (CH_2Cl_2/hexane, 7:3): R_f 0.55 (hexane/EtOAc, 9:1); mp 55-56 °C; IR (KBr) 1773, 1691, 1620, 1495, 1397, 1288, 1206, 1031 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.10 (t, *J* = 7.5 Hz, 3H, H-9), 2.33 (dt, *J* = 7.7, 7.5 Hz, 1H, H-8), 4.19 (d, *J* = 2.9 Hz, 1H, H-6a), 4.59 (d, *J* = 2.9 Hz, 1H, H-6b), 5.38 (t, *J* = 7.7 Hz, 1H, H-7), 7.30-7.54 (m, 5H, PhH); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.7 (C-9), 18.6 (C-8), 81.8 (C-6), 106.0 (C-7), 127.0 (C-11), 128.6 (C-13), 129.7 (C-12), 133.2 (C-10), 139.2 (C-4), 142.0 (C-5), 151.8 (C-2); MS (70 eV) 215 (M^+, 4), 170 (2), 156 (2), 118 (59), 104 (8), 91 (11), 77 (96), 55 (63), 51 (100). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.73; H, 6.22; N, 6.48.

(5*Z*)-*N*-(*p*-Chlorophenyl)-4-methylene-5-propylidene-2-oxazolidinone (7b). Using the general procedure with 0.79 g (5.2 mmol) of *p*-chlorophenyl isocyanate (**6b**) gave 0.52 g (60%) of **7b** as colorless crystals (CH_2Cl_2/hexane, 7:3): R_f 0.59 (hexane/EtOAc, 9:1); mp 64-65 °C; IR (KBr) 1778, 1686, 1637, 1495, 1402, 1299, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.09 (t, *J* = 7.5 Hz, 3H, H-9), 2.35 (dt, *J* = 7.7, 7.5 Hz, 1H, H-8), 4.20 (d, *J* = 3.1 Hz, 1H, H-6a), 4.62 (d, *J* = 3.1 Hz, 1H, H-6b), 5.40 (t, *J* = 7.7 Hz, 1H, H-7), 7.27-7.35 (m, 2H, ArH), 7.45-7.52 (m, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.6 (C-9), 18.5 (C-8), 81.8 (C-6), 106.4 (C-7), 128.3 (C-11), 129.9 (C-12), 131.7 (C-10), 134.4 (C-13), 138.8 (C-4), 141.8 (C-5), 152.4 (C-2); MS (70 eV) 249 (M^+, 8), 204 (6), 152 (76), 138 (10), 125 (14), 111 (84), 90 (20), 75 (100), 63 (30), 55 (40). Anal. Calcd for $C_{13}H_{12}NO_2Cl$: C, 62.53; H, 4.84; N, 5.61. Found: C, 62.70; H, 4.97; N, 5.61.

General Procedure for the Preparation of *N*-Substituted 5-Alkylidene-1,3-oxazolidine-2,4-diones. 5-Methylene-*N*-phenyl-1,3-oxazolidine-2,4-dione (8a). To a stirred solution of 0.831 g (4.82 mmol) of MCPBA (77% max.) in dry CH_2Cl_2 (3 mL), under an N_2 atmosphere, 0.60 g (3.2 mmol) of **3a** in dry CH_2Cl_2 (6 mL) was added dropwise through a cannula at rt. The mixture was stirred at the same

temperature for 3 h, diluted with CH_2Cl_2 (20 mL), and washed with a saturated solution of $NaHCO_3$ (3 x 10 mL), and with cold water until neutral. The organic layer was dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by column chromatography on silica gel impregnated with dry MeOH (15 g, hexane/CH_2Cl_2, 9:1) to give 0.152 g (25%) of **8a** as colorless crystals. R_f 0.25 (hexane/EtOAc, 8:2); mp 108-109 °C; IR (KBr) 1845, 1753, 1681, 1406, 1277 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.46 (d, J = 3.4 Hz, 1H, H-6), 5.75 (d, J = 3.4 Hz, 1H, H-6), 7.42-7.56 (m, 5H, PhH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 99.4 (C-6), 125.5, 129.3, 129.6, 130.5, 145.2, 150.8 (C-2), 160.1 (C-4); MS (70 eV) m/z 189 (M^+, 60), 119 (100), 91 (31), 77 (5), 64 (14). Anal. Calcd for $C_{10}H_7NO_3$: C, 63.49; H, 3.73; N, 7.40. Found: C, 63.21; H, 4.00; N, 7.19.

***N*-(*p*-Chlorophenyl)-5-methylene-1,3-oxazolidine-2,4-dione (8b).** The same procedure as for **8a** was used, with 0.709 g (3.20 mmol) of **3b** to give 0.379 g (53%) of **8b** as colorless crystals (hexane/EtOAc, 9:1): R_f 0.48 (hexane/EtOAc, 8:2); mp 131-132 °C; IR (KBr) 1810, 1743, 1680, 1496, 1400 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.47 (d, J = 3.5 Hz, 1H, H-6), 5.75 (d, J = 3.5 Hz, 1H, H-6), 7.42-7.52 (m, 4H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 99.5 (C-6), 126.4, 128.9, 129.6, 135.0, 144.8, 150.2 (C-2), 159.6 (C-4); MS (70 eV) m/z 225 (M^++2, 22), 223 (M^+, 65), 153 (100), 125 (29), 90 (25). Anal. Calcd for $C_{10}H_6NO_3Cl$: C, 53.71; H, 2.70; N, 6.26. Found: C, 53.51; H, 2.76; N, 6.39.

5-Methylene-*N*-(*p*-tolyl)-1,3-oxazolidine-2,4-dione (8c). The same procedure as for **8a** was used, with 0.643 g (3.20 mmol) of **3c** to give 0.266 g (41%) of **8c** as colorless crystals (hexane/CH_2Cl_2, 9:1): R_f 0.46 (hexane/EtOAc, 8:2); mp 90-91 °C; IR (KBr) 1839, 1819, 1739, 1680, 1411 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, 3H, MeAr), 5.44 (d, J = 3.4 Hz, 1H, H-6), 5.73 (d, J = 3.4 Hz, 1H, H-6), 7.27-7.35 (m, 4H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 21.2 (CH_3Ar), 98.9 (C-6), 125.2, 127.7, 130.0, 139.4, 145.2, 150.7 (C-2), 160.1 (C-4); MS (70 eV) m/z 203 (M^+, 79), 188 (1), 158 (1), 134 (9), 133 (100), 104 (28), 91 (13), 77 (17). Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.11; H, 4.62; N, 7.06.

(5*Z*)-5-Ethylidene-*N*-phenyl-1,3-oxazolidine-2,4-dione (9a). The same procedure as for **8a** was used, with 0.643 g (3.20 mmol) of **4a** to give 0.376 g (58%) of **9a** as colorless crystals (hexane/EtOAc, 9:1): R_f 0.41 (hexane/EtOAc, 8:2); mp 112-113 °C; IR (KBr) 1813, 1746, 1693, 1499, 1399 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.00 (d, J = 7.4 Hz, 3H, CH_3CH=), 6.23 (q, J = 7.4 Hz, 1H, H-6), 7.41-7.58 (m, 5H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 11.2 (CH_3CH=), 113.8 (C-6), 125.4, 128.9, 129.4, 130.6, 140.3, 151.0 (C-2), 159.9 (C-4); MS (70 eV) m/z 203 (M^+, 66), 119 (100), 91 (29), 56 (82). Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.05; H, 4.55; N, 6.60.

(5*Z*)-*N*-(*p*-Chlorophenyl)-5-ethylidene-1,3-oxazolidine-2,4-dione (9b). The same procedure as for **8a** was used, with 0.753 g (3.40 mmol) of **4b** to give 0.523 g (69%) of **9b** as colorless crystals (hexane/EtOAc, 9:1): R_f 0.42 (hexane/EtOAc, 8:2); mp 122-123 °C; IR (KBr) 1822, 1745, 1692, 1500, 1409, 1313 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.99 (d, J = 7.4 Hz, 3H, MeCH=), 6.23 (q, J = 7.4 Hz, 1H, H-6), 7.42-7.50 (m, 4H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 11.2 (CH_3CH=), 114.2 (C-6), 126.4, 129.1, 129.5, 134.6, 140.1, 150.5 (C-2), 159.6 (C-4); MS (70 eV) m/z 239 (M^++2, 17), 237 (M^+, 51), 155 (29), 153 (87), 127 (7), 125 (21), 90 (20). Anal. Calcd for $C_{11}H_8NO_3Cl$: C, 55.60; H, 3.93; N, 5.89. Found: C, 55.84; H, 3.55; N, 5.78.

(5*Z*)-*N*-Phenyl-5-propylidene-1,3-oxazolidine-2,4-dione (10a). The same procedure as for **8a** was used, with 0.688 g (3.20 mmol) of **7a** to give 0.479 g (69%) of **10a** as a colorless crystalline powder (hexane/EtOAc, 8:2): R_f 0.53 (hexane/EtOAc, 8:2); mp 105-106 °C; IR (KBr) 1814, 1739, 1689, 1500, 1404 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (t, J = 7.6 Hz, 3H, CH_3), 2.37-2.50 (m, 2H, CH_2CH=), 6.19 (t, J = 7.9 Hz, 1H, H-6), 7.42-7.56 (m, 5H, PhH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.8 (CH_3), 19.3 (CH_2), 120.0 (C-6), 125.4, 128.9, 129.4, 130.6, 139.0, 151.0 (C-2), 160.2 (C-4). Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.04; N, 6.45. Found: C, 66.24; H, 5.24; N, 6.36.

(5*Z*)-*N*-(*p*-Chlorophenyl)-5-propylidene-1,3-oxazolidine-2,4-dione (10b). The same procedure as for (**8a**) was used, with 0.789 g (3.2 mmol) of **7b** to give 0.611 g (76%) of **10b** as a white powder (hexane/EtOAc, 8:2): R_f 0.38 (hexane/EtOAc, 8:2); mp 113-114 °C; IR (KBr) 1832, 1745, 1697, 1500, 1418 cm^{-1}; ^1H RMN (300 MHz, $CDCl_3$) δ 1.17 (t, J = 7.6 Hz, 3H, CH_3), 2.37-2.50 (m, 2H, CH_2CH=), 6.19 (t, J = 7.9 Hz, 1H, H-6), 7.45-7.56 (m, 4H, ArH); ^{13}C RMN (75.4 MHz, $CDCl_3$) δ 12.8 (CH_3), 19.3 (CH_2), 120.5 (C-6), 126.5, 129.2, 129.5, 134.7, 138.8, 150.6 (C-2), 159.8 (C-4); MS (70 eV) m/z 253 (M^++2, 16), 251 (M^+, 46), 223 (2), 179 (1), 153 (66), 127 (5), 125 (16), 90 (18), 70 (91), 55 (100). Anal. Calcd for $C_{12}H_{10}NO_3Cl$: C, 57.27; H, 4.00; N, 5.56. Found: C, 57.23; H, 4.06; N, 5.37.

***N*-Phenyl-5,6-dihydrobenzoxazol-2-one (12).** Using the general procedure of preparation of dienes **7**, with 0.39 g (3.5 mmol) of **11**, and 0.62 g of phenyl isocyanate (**6a**) gave 0.13 g (18%) of **12** as colorless crystals (CH_2Cl_2/hexane, 1:1); R_f 0.55 (hexane/EtOAc, 7:3); mp 81-82 °C; IR (KBr) 1779, 1655, 1493, 1408, 1193, 1123 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.33-2.51 (m, 4H, H-5, H-6), 4.94-4.98 (m, 1H, H-4), 5.25-5.29 (m, 1H, H-7), 7.32-7.50 (m, 5H, PhH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 21.2 (C-5), 21.3 (C-6), 95.3 (C-4), 96.8 (C-7), 125.2 (C-9), 127.8 (C-11), 129.4 (C-10), 131.9 (C-3a), 133.6 (C-8), 142.7 (C-7a), 155.8 (C-2); MS (70 eV) 213 (M^+, 9), 157 (3), 130 (4), 119 (78), 93 (100), 78 (11). Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.22; H, 5.20; N, 6.57. Found: C, 73.09; H, 5.16; N, 6.65.

(5*E*)-5-(4-Oxobutylidene)-3-phenyl-1,3-oxazolidine-2,4-dione (13). The same procedure as for **8a** was used, with 0.44 g (2.55 mmol) of MCPBA (77% max.), and 0.18 g (0.84 mmol) of **12** in dry CH_2Cl_2 (2 mL). The mixture was stirred at rt for 12 h, and the purification by column chromatography on silica gel (6 g, hexane/EtOAc, 99:1) yielded 0.074 g (36%) of **13** as a white powder. R_f 0.25 (hexane/EtOAc, 7:3); mp 81-82 。C; IR (KBr) 1802, 1730, 1679, 1405, 1185 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.72 (t, J = 7.0 Hz, 2H, CH_2CHO), 3.00-3.05 (dt, J = 8.4, 7.0 Hz, 2H, CH_2C=), 6.15 (t, J = 8.4 Hz, 1H, H-6), 7.42-7.50 (m, 5H, PhH), 9.79 (s, 1H, CHO); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 18.0 (CH_2C=), 42.6 (CH_2CHO), 120.8 (*C*H=), 125.4, 128.9, 129.2, 130.3, 139.0 (C-5), 150.4 (C-2), 160.0 (C-4), 200.0 (CHO); MS (70 eV) m/z 245 (M^+, 60), 216 (32), 190 (10), 126 (25), 119 (100), 91 (43), 70 (62). Anal. Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.61; H, 4.45; N, 5.60.

General Procedure for the Preparation of Adducts (15/16). 8-Methyl-3-phenyl-1-oxa-3-azaspiro[4.5]dec-7-ene-2,4-dione (15a). 7-Methyl-3-phenyl-1-oxa-3-azaspiro[4.5]dec-7-ene-2,4-dione (16a). Method A. A mixture of 0.05 g (0.26 mmol) of **8a**, 0.34 g (5.0 mmol) of **14**, and hydroquinone (3 mg) in dry xylene (1 mL), was placed in a threaded ACE glass pressure tube with a sealed Teflon screw cap, under an N_2 atmosphere, and in the dark. The mixture was stirred and heated to 190 °C for 198 h. The

solvent was removed under vacuum, and the residue was purified by column chromatography on silica gel (8 g, hexane/EtOAc, 99:1) to give 0.06 g (89%) of a mixture of **15a**/**16a** (75:25). This mixture was recrystallized (hexane/CH_2Cl_2, 2:1) to give **15a** as a white crystalline powder.

Method B. In a threaded ACE glass pressure tube with a sealed Teflon screw cap, under an N_2 atmosphere, and in the dark, a mixture of 0.05 g (0.26 mmol) of **8a**, 0.68 g (0.01 mol) of **14**, and hydroquinone (3 mg), was placed in a sonicated water bath, controlling the temperature at 65 °C for 168 h. The excess of **14** was removed under vacuum, and the residue was purified by column chromatography on silica gel (10 g, hexane/EtOAc, 99:1) to give 0.065 g (96%) of a mixture of **15a**/**16a** (80:20). This mixture was recrystallized (hexane/CH_2Cl_2, 2:1) to give **15a** as a white crystalline powder: R_f 0.65 (hexane/EtOAc, 8:2); mp 119-121 °C; IR (KBr) 1817, 1750, 1500, 1415 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.75 (s, 3H, MeC=), 2.01-2.23 (m, 3H), 2.27-2.47 (m, 2H), 2.70-2.84 (m, 1H), 5.37 (br s, 1H, CH=), 7.32-7.52 (m, 5H, PhH); signals attributed to isomer **16a**: 5.57 (br s, CH=); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 23.1 (*C*H_3C=), 25.5 (CH_2), 28.7 (CH_2), 32.3 (CH_2), 83.3 (C-5), 115.0 (CH=), 125.4, 128.6, 129.1, 130.9, 133.7 (CH_3*C*H=), 153.4 (C-2), 174.5 (C-4). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.89; H, 6.02; N, 5.55.

3-(*p*-Chlorophenyl)-8-methyl-1-oxa-3-azaspiro[4.5]dec-7-ene-2,4-dione (15b). 3-(*p*-Chlorophenyl)-7-methyl-1-oxa-3-azaspiro[4.5]dec-7-ene-2,4-dione (16b). Method A. The same procedure as for **15a** was used, with 0.05 g (0.22 mmol) of **8b** and 0.34 g (5.0 mmol) of **14**. The reaction was carried out at 190 °C for 216 h. Column chromatography on silica gel (8 g, hexane/EtOAc, 99:1) yielded 0.061 g (93%) of a mixture of **15b**/**16b** (77:23). This mixture was recrystallized (hexane/CH_2Cl_2, 2:1), to give **15b** as a colorless crystalline powder. **Method B.** The same procedure as for **15a** was used, with 0.05 g (0.22 mmol) of **8b** and 0.34 g (5.0 mmol) of **14**. The reaction was carried out at 65 °C for 216 h. Column chromatography on silica gel (8 g, hexane) yielded 0.063 g (96%) of a mixture of **15b**/**16b** (75:25). This mixture was recrystallized (hexane/CH_2Cl_2, 2:1) to give **15b** as a colorless crystalline powder: R_f 0.70 (hexane/EtOAc, 8:2); mp 140-141 °C; IR (KBr) 1816, 1753, 1498, 1415 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.78 (s, 3H, MeC=), 2.02-2.25 (m, 3H), 2.26-2.45 (m, 2H), 2.67-2.83 (m, 1H), 5.39 (br s, 1H, CH=), 7.35-7.53 (m, 4H, ArH); signals attributed to isomer **16b**: 5.58 (br s, CH=); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 24.1 (*C*H_3C=), 26.8 (CH_2), 30.0 (CH_2), 33.8 (CH_2), 84.5 (C-5), 116.0 (CH=), 127.8, 129.8, 130.6, 133.8, 134.8, 154.2 (C-2), 174.8 (C-4); signals attributed to isomer **16b**: 22.0, 29.3, 37.6, 85.0; MS (70 eV) m/z 293 (M^++2, 12), 291 (M^+, 35), 246 (86), 232 (19), 153 (46), 119 (32), 94 (91), 79 (100). Anal. Calcd for $C_{15}H_{14}NO_3Cl$: C, 61.97; H, 4.85; N, 4.82. Found: C, 61.77; H, 5.13; N, 4.76.

3-Phenyl-1-oxa-3-azaspiro[4.5]decane-2,4,8-trione (18). The same procedure as for **15a** (Method A) was used, with 0.05 g (0.26 mmol) of **8a** and 0.074 g (0.52 mmol) of **17**. The reaction was carried out at 160 °C for 120 h. Column chromatography on silica gel (6 g, hexane) yielded 0.036 g (53%) of **18** as a white crystalline powder: R_f 0.36 (hexane/EtOAc, 8:2); mp 221-223 °C; IR (KBr) 1821, 1739, 1719, 1498, 1418, 1193 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.28-2.40 (m, 2H), 2.42-2.53 (m, 2H), 2.57-2.66 (m, 2H), 2.67-2.82 (m, 2H), 7.40-7.56 (m, 5H, PhH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.3 ($2CH_2$), 36.0 ($2CH_2$), 82.9 (C-5), 125.4, 129.2, 129.4, 130.6, 153.0 (C-2), 173.2 (C-4), 206.4 (C-8); MS (70 eV) m/z 259 (M^+, 37), 214

(75), 187 (33), 130 (60), 119 (100), 112 (40), 91 (48). Anal. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.76; H, 5.16; N, 5.34.

(1*R,2*R**,4*R**)-4-Phenylspiro[bicyclo[2.2.1]hept-5-ene-2,2'-oxazolidine]-3',5'-dione (20).** In a threaded ACE glass pressure tube with a sealed Teflon screw cap, under an N_2 atmosphere, and in the dark, a mixture of 0.15 g (0.79 mmol) of **8a**, 1.0 g (0.015 mol) of **19**, and hydroquinone (3 mg), was placed in a sonicated water bath, controlling the temperature at 65 °C for 72 h. The excess of **19** was removed under vacuum, and the residue was purified by column chromatography on silica gel (15 g, hexane/EtOAc, 99:1) to give 0.148 g (73%) of **20** as a white powder: R_f 0.52 (hexane/EtOAc, 8:2); mp 156-157 °C; IR (KBr) 1816, 1741, 1415, 1164 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.53-1.72 (m, 2H, H-7s, H-3n), 2.18 (br d, *J* = 8.9 Hz, 1H, H-7a), 2.42 (dd, *J* = 12.4, 3.5 Hz, 1H, H-3x), 3.09 (br s, 1H, H-4), 3.22 (br s, 1H, H-1), 6.21 (dd, *J* = 5.5, 3.0 Hz, 1H, H-6), 6.56 (dd,*J* = 5.5, 3.0 Hz, 1H, H-5), 7.36-7.51 (m, 5H, PhH); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 40.3 (C-3), 42.4 (C-4), 48.0 (C-7), 52.0 (C-1), 91.0 (C-2), 125.6, 128.8, 129.3, 131.2, 132.9 (C-6), 141.0 (C-5), 153.8 (C-5'), 175.5 (C-3'); MS (70 eV) m/z 255 (M^+, 4), 190 (10), 119 (15), 91 (15), 77 (10), 66 (100). Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.68; H, 5.00; N, 5.51.

1- Hydroxy-4-methylcyclohex-3-ene-1-carboxylic acid *N*-phenylamide (22). A solution of 0.23 g (0.89 mmol) of **15a** in dry EtOH (2 mL), under an N_2 atmosphere and at rt, was treated with a solution of 0.18 g (4.5 mmol) of NaOH in dry EtOH (0.5 mL). After being stirred for 2 h at rt, and the solvent was removed under vacuum. The residue was dissolved in CH_2Cl_2 (20 mL), and the mixture was washed with aqueous 5% HCl (3 x 20 mL), with saturated solution of $NaHCO_3$ (3 x 20 mL), and with cold water until neutral. The organic layer was dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by column chromatography on silica gel (10 g, hexane/EtOAc, 99:1) to give 0.07 g (34%) of **22** as a white crystalline powder: R_f 0.59 (hexane/EtOAc, 7:3); mp 189-191 °C; IR (KBr) 3301, 1649, 1601, 1555, 1443, 1099 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$/DMSO) δ 1.57 (br s, 3H, CH_3C=), 1.59-1.67 (m, 1H), 1.65-1.88 (m, 1H), 1.89-2.00 (m, 2H), 2.00-2.17 (m, 1H), 2.53-2.68 (m, 1H), 4.65 (s, 1H, -OH), 5.20 (br s, 1H, H-3), 6.89-6.96 (m, 1H, PhH), 7.12-7.19 (m, 2H, PhH), 7.42-7.48 (m, 2H, PhH), 8.92 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$/DMSO) δ 23.5 (CH_3), 26.0 (CH_2), 30.7 (CH_2), 35.1 (CH_2), 73.1 (C-1), 117.4 (C-3), 119.4, 123.8, 128.8, 133.0, 137.9, 175.2 (CON); MS (70 eV) m/z 231 (M^+, 3), 212 (17), 121 (47), 93 (100), 77 (44). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.94; H, 7.21; N, 5.94.

(1*R,2*R**,4*R**)-2-Hydroxybicyclo[2.2.1]hept-5-ene-2-carboxylic acid *N*-phenylamide (23).** The same procedure as for **22** was used, with 0.14 g (0.55 mmol) of **20** and 0.18 g (4.5 mmol) of NaOH. The purification by column chromatography on silica gel yielded 0.044 g (35%) of **23** as a white powder: R_f 0.57 (hexane/EtOAc, 7:3); mp 149-150 °C; IR (KBr) 3359, 3306, 1656, 1599, 1540, 1441 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.15 (dd, *J* = 12.0, 3.7 Hz, 1H, H-7s), 1.56-1.62 (m, 1H, H-3n), 2.19 (br s, 1H, OH), 2.33 (br d, *J* = 8.8 Hz, 1H, H-3x), 2.64 (dd, *J* = 12.0, 3.7 Hz, H-7a), 3.02 (br s, 1H, H-4), 3.07 (br s, 1H, H-1), 6.25 (dd, *J* = 5.5, 3.0 Hz, 1H, H-6), 6.64 (dd, *J* = 5.5, 3.0 Hz, 1H, H-5), 7.07-7.14 (m, 1H, PhH), 7.29-7.37 (m, 2H, PhH), 7.56-7.62 (m, 2H, PhH), 8.80 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.9 (C-4), 43.4 (C-7), 49.8 (C-3), 53.7 (C-1), 82.5 (C-2), 119.7, 124.1, 129.0, 133.0 (C-6), 137.9, 143.5 (C-5),

173.6 (CON); MS (70 eV) m/z 229 (M^+, 1), 201 (2), 163 (4), 118 (15), 93 (100), 77 (38). Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.50; H, 6.57; N, 6.20.

(3*R,5*R**)-3-(*p*-Anisyl)-2,8-diphenyl-1,6-dioxa-2,8-diazaspiro[4.4]nonane-7,9-dione (25a). (3*S**,5*R**)-3-(*p*-Anisyl)-2,8-diphenyl-1,6-dioxa-2,8-diazaspiro[4.4]nonane-7,9-dione (26a).** A mixture of 0.05 g (0.26 mmol) of **8a**, 0.12 g (0.53 mmol) of **24a**, and hydroquinone (3 mg) in dry benzene (1.5 mL), was placed in a threaded ACE glass pressure tube with a sealed Teflon screw cap, under an N_2 atmosphere, and in the dark. The mixture was stirred and heated to 60 °C for 12 h. The solvent was removed under vacuum, and the residue was purified by column chromatography on silica gel (8 g, hexane/EtOAc, 99:1) to give 0.075 g (68%) of a mixture of **25a**/**26a** (72:28). This mixture was recrystallized (hexane/CH_2Cl_2, 2:1) to give **25a** as a white crystalline powder: R_f 0.5 (hexane/EtOAc, 7:3); mp 179-180 °C; IR (KBr) 1826, 1749, 1501, 1417, 1250, 1170 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.02 (dd, J = 13.8, 8.2 Hz, 1H, H-4β), 3.47 (dd, J = 13.8, 8.1 Hz, 1H, H-4α), 3.84 (s, 3H, MeO), 4.68 (dd, J = 8.2, 8.1 Hz, 1H, H-3), 6.91-6.96 (m, 2H, ArH), 7.10-7.15 (m, 3H, PhH), 7.23-7.29 (m, 2H, PhH), 7.41-7.46 (m, 2H, ArH), 7.47-7.56 (m, 5H, PhH); signals attributed to isomer **26a**: 3.25 (dd, J = 12.9, 11.4 Hz, H-4), 4.79 (dd, J = 11.4, 5.9 Hz, H-3); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 47.6 (C-4), 55.5 (MeO), 71.6 (C-3), 105.3 (C-5), 114.6, 119.8, 125.7, 125.8, 128.8, 128.9, 129.0, 129.4, 129.6, 130.7, 148.0, 152.1 (C-7), 160.0, 167.2 (C-9); signals attributed to isomer **26a**: 69.3, 118.5, 125.7, 128.7; MS (70 eV) m/z 189 (M^+-227, 27), 119 (100), 91 (48), 77 (10). Anal. Calcd for $C_{24}H_{20}N_2O_5$: C, 69.22; H, 4.84; N, 6.73. Found: C, 69.23; H, 5.03; N, 6.64.

(3*R,5*R**)-2-Benzyl-3-(*p*-anisyl)-8-phenyl-1,6-dioxa-2,8-diazaspiro[4.4]nonane-7,9-dione (25b). (3*S**,5*R**)-2-Benzyl-3-(*p*-anisyl)-8-phenyl-1,6-dioxa-2,8-diazaspiro[4.4]nonane-7,9-dione (26b).** The same procedure as for **25a** was used, with 0.025 g (0.13 mmol) of **8a** and 0.064 g (0.265 mmol) of **24b** in dry benzene (1.0 mL). The reaction was carried out at 80 °C for 24 h. Column chromatography on silica gel (5 g, hexane) yielded 0.045 g (80%) of a mixture of **25b**/**26b** (57:43) as a white powder. This mixture was recrystallized (hexane/CH_2Cl_2, 2:1) to give **25b** as a white crystalline powder: R_f 0.53 (hexane/EtOAc, 7:3); mp 167-168 °C; IR (KBr) 1822, 1745, 1514, 1413, 1248, 1177, 1147 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.91 (dd, J = 13.7, 9.8 Hz, 1H, H-4β), 3.28 (dd, J = 13.7, 7.6 Hz, 1H, H-4α), 3.82 (s, 3H, MeO), 3.90 (d, J = 15.0 Hz, 1H, CH_2Ph), 4.04-4.30 (m, 2H, H-3, CH_2Ph), 6.91-6.96 (m, 1H, ArH), 7.23-7.54 (m, 12H, ArH); signals attributed to **26b**: 3.15 (dd, J = 12.9, 11.4 Hz, H-4), 3.82 (s, MeO); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 47.6 (C-4), 55.4 (MeO), 59.7 (CH_2Ph), 71.1 (C-3), 105.4 (C-5), 114.4, 125.6, 127.5, 128.3, 128.4, 128.7, 129.2, 129.4, 129.7, 130.7, 136.7, 152.6 (C-7), 160.1, 167.9 (C-9); signals attributed to **26b**: 68.5, 127.6, 127.7, 127.8, 129.0, 136.4, 160.0; MS (70 eV) m/z 189 (M^+-241, 48), 119 (100), 91 (43). Anal. Calcd for $C_{25}H_{22}N_2O_5$: C, 69.76; H, 5.15; N, 6.51. Found: C, 69.60; H, 5.14; N, 6.50.

X-Ray Structure Determination of Compound 15a. Crystal data: $C_{18}H_{19}NO_4$; M = 313.34; monoclinic; space group $P2_1/c$; a = 6.9818(7), b = 10.3225(9), c = 22.655(2) Å; α = 90°, β = 90.961(8)°, γ= 90°; V = 1632.5(3) $Å^3$, Z = 4; D = 1.275 mg/m^3; No. of reflections collected: 4062, No. of observed reflections: 2873; R = 0.0441, R_w = 0.0661; goodness of fit on F^2 = 1.049; largest residual peak = 0.210 e $Å^{-3}$.[25]

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