Stereoselective Synthesis of 4,5-Diethylidene-Oxazolidinones as New Dienes in *Diels-Alder* Reactions

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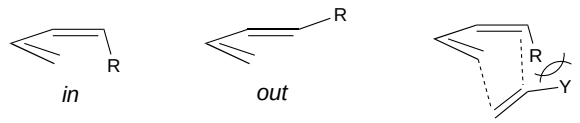
The *N*-substituted isomeric (4*Z*,5*Z*)- and (4*E*,5*Z*)-4,5-diethylideneoxazolidin-2-ones **5** and **6** were synthesized, the latter being favored during the one-step process from the α-diketone **1c** and different isocyanates. The steric interaction between the *N*-substituent and the Me group attached to the exocyclic diene moiety plays a decisive role in controlling the observed stereoselectivity, as suggested by the calculated free energies of the two isomers. Both dienes undergo efficient additions to symmetric dienophiles in thermal *Diels-Alder* reactions to yield the adducts **11** and **13**, respectively. These molecules displayed interesting C–H$\cdots\pi$, and C–H$\cdots$X (X = O, Cl) interactions according to their X-ray crystal structures. Isomers **6** suffered highly stereo- and regioselective additions with nonsymmetrical dienophiles such as methyl vinyl ketone or methyl propiolate. Steric interactions, promoted by the inward-pointing Me group in **6**, seem to explain such selectivity. These results have also been rationalized by *ab initio* calculations in terms of the FMO theory.

1. Introduction. – Both the reactivity and stereoselectivity of the *Diels-Alder* reaction depend on an interplay of several factors, *e.g.*, the electronic demand of the substituents in both diene and dienophile, the anchimeric assistance of polar substituents, the presence of *Lewis* acid catalysts, the polarity of the medium, the π-facial differentiation, and pressure [1]. The perturbation produced by these variables on the stability of the *endo* and *exo* transition states, and on the regioselectivity as well, has been attributed to effects such as secondary orbital interactions [2], electrostatic forces [3], steric hindrance [4], hydrogen bonding [5], and attractive *Van der Waals* interactions [6].

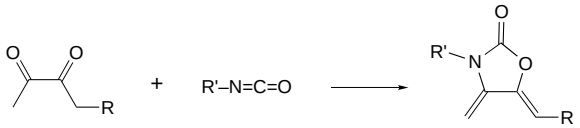
Frontier-molecular-orbital (FMO) theory has commonly been used to explain the rate and regioselectivity of the *Diels-Alder* reaction [1a][7]. This theory and other models have been particularly successful for dienes and dienophiles that are not substituted by more than two functional groups [8]. In particular, the *endo* preference has been traditionally rationalized by stabilizing secondary orbital interactions in the transition state [1b][2]. However, this preference might also be justified [9] either by dominant steric repulsions in the *exo* transition state [10], or by electronic repulsions between π-diene and lone-pair electrons of heterosubstituents at the olefin [3d], or even by stabilizing σ-π interactions between the diene and alkyl substituents of the olefin [6]. In other words, the reactivity in *Diels-Alder* reactions is not only controlled by orbital interactions but also influenced by other factors, for example, by the substitution pattern in the diene [4a][11]. The presence of a substituent in the '*in*-position' of the diene, as compared to the corresponding '*out*-diene', depletes the reactivity towards dienophile addition [12]. Consequently, both the stereo- and

regioselectivity of the reaction may also be altered, involving steric and electrostatic interactions in the transition state [13].



Recently, we have described a tandem condensation reaction between the aliphatic 1,2-diketone **1a** and some isocyanates **2** to yield the corresponding *N*-substituted *exo*-oxazolidin-2-ones **3** (*Scheme 1*) [14]. The use of the unsymmetrical 1,2-diketone **1b** conduced to the regio- and stereoselective formation of the dienes **4** [15]. The presence of the additional Me group enhanced both the reactivity and regioselectivity of the *Diels-Alder* reaction with nonsymmetrical olefins. Thereby, a high *endo*-stereoselectivity was observed.

Scheme 1



1a R = H
1b R = Me

2 R' = alkyl, aryl

3 R = H
4 R = Me

With the aim of further exploring the effect of the geometry of substituted exo heterocyclic dienes on the stereochemical course of the *Diels-Alder* reaction, we now report the preparation of the isomeric 1,4-dimethyl dienes **5** and **6** (*Scheme 2*), which were reacted with a series of dienophiles. Calculated electronic energies and FMO analyses were examined to explain the stereochemical outcome of both diene formation and *Diels-Alder* reaction.

2. Results and Discussion. – 2.1. *Synthesis and Stereoselectivity in the Formation of 4,5-Diethylideneoxazolidin-2-ones* **5** *and* **6**. The condensation of the 1,2-diketone **1c** with a variety of isocyanates **2** was carried out in dioxane at room temperature in the presence of Et_3N and Li_2CO_3 (*Scheme 2*). In *Table 1*, the yields and ratios of the isomers **5**/**6**, obtained after purification by column chromatography, are given. Interestingly, only two of the four possible isomers were formed, *i.e.*, the dienes **7** and **8** were not detected in the crude mixtures by ^{1}H-NMR. The isomer ratio **5**/**6** was found to be dependent on the substituent R of the isocyanates. However, the (4*E*,5*Z*)-isomer **6** was always the major component. Moreover, the presence of an alkyl group in **2g** induced the exclusive formation of a single isomer (**6g**). Nevertheless, in the case of aryl-substituted compounds it seems that there is no correlation between the electronic nature of the *N*-phenyl group and the stereochemical outcome of this reaction (*vide infra*).

Scheme 2

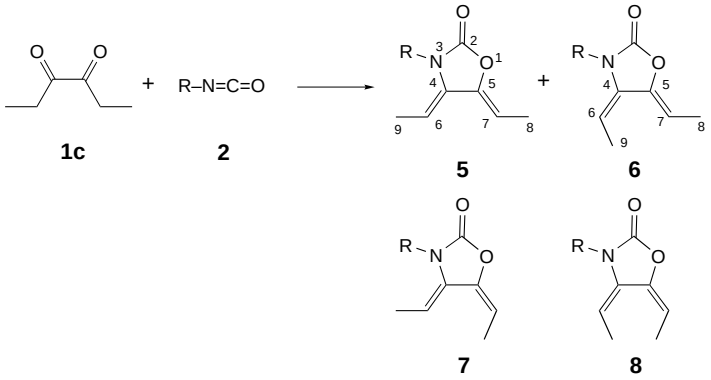


Table 1. *Condensation of* **1c** *with Isocyanates* **2a**–**2g**[a])

Entry	Isocyanate (R)	Dienes (ratio)[b])	Yield [%][c])
1	**2a** (Ph)	**5a**/**6a** (29 : 71)	50
2	**2b** (4-Cl-C_6H_4)	**5b**/**6b** (28 : 72)	46
3	**2c** (4-Cl-C_6H_4)	**5c**/**6c** (37 : 63)	67
4	**2d** (4-Me–C_6H_4)	**5d**/**6d** (32 : 68)	39
5	**2e** (4-Me–C_6H_4)	**5e**/**6e** (40 : 60)	58
6	**2f** (4-MeO–C_6H_4)	**5f**/**6f** (26 : 74)	24
7	**2g** (CH_2CH_2Cl)	**6g**	64

[a]) Dioxane, Et_3N (2.0 mol-equiv.), Li_2CO_3 (1.2 mol-equiv.), r.t., 12 h. [b]) Determined by ^{1}H-NMR from the crude mixture. [c]) For the mixture **5**/**6**.

Partial separation of some of the **5**/**6** mixtures was accomplished only either by high-performance liquid chromatography (HPLC) (*LiChrospher*, MeCN/H_2O 8 : 2, 1 ml/min), or by flash chromatography (FC) in a SiO_2-prepacked column performed on a *Chromatoflash Flash40i*® instrument (5 kbar of N_2, hexane). These compounds were characterized spectroscopically, and the configurational assignment was established by NOE experiments (*Fig. 1*). Additional evidence came from the chemical shift observed for *H*–C=C(4) and for *Me*CH=C(4). Thus, in the isomers **6**, the signal for *H*–C=C(4) was shifted upfield with respect to **5**. Similarly, the resonance of *Me*CH=C(4) was shifted upfield in **5** compared to **6**. This is probably due to the diamagnetic anisotropic effect of the aryl ring attached to the N-atom. X-Ray crystal-structure analysis of the

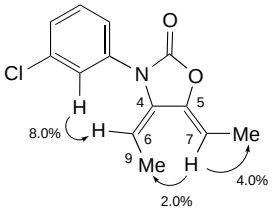
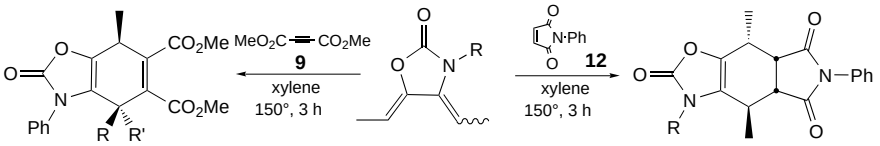


Fig. 1. *NOEs observed upon irradiation of protons in diene* **6b**

dienes **4** has shown the aryl ring in an orthogonal position with respect to both the heterocycle and the diene [15]. Therefore, the aryl ring is expected to shield the spatial region of the mentioned H-atoms in **6** and **5**. This effect is more pronounced for the Me group ($\Delta\delta \approx 0.6$ ppm) than for the olefinic H ($\Delta\delta \approx 0.2$ ppm), since the former is closer to the center of the aromatic ring.

2.2. *Reactivity of the Dienes* **5** *and* **6** *in Stereoselective* Diels-Alder *Reactions.* The thermal *Diels-Alder* reaction (150°, 3 h) of a mixture of the dienes **5a**/**6a** (28:72) with dimethyl acetylenedicarboxylate (**9**) yielded the corresponding mixture of the adducts **10**/**11** (32:68) (*Scheme 3*). No difference in reactivity was observed between **5a** and **6a**, since a similar product distribution was determined by ^{1}H-NMR monitoring. Reactions at lower temperatures were conducted, but the reaction time greatly increased. The reactivity of the above dienes was estimated to lie between those of the dienes **3** and **4**, taking into account the optimum temperature for the addition to the same dienophiles [15].

Scheme 3



10 R = Me, R' = H
11 R = H, R' = Me

5a (4*Z*), R = Ph
6a (4*E*), R = Ph
6g R = CH_2CH_2Cl

13 R = CH_2CH_2Cl

Both the adducts **10** and **11** showed in their ^{1}H-NMR spectra a strong shielding effect of the *Me*-C(4) group vicinal to the *N*−Ph group compared to the other Me group (Me−C(7)), similar to **5** and **6**. The major diastereoisomer **11** was recrystallized from CH_2Cl_2/hexane, and its structure was established by single-crystal X-ray diffraction (*Fig. 2*). Indeed, the analysis of this structure revealed an intramolecular C−H$\cdots\pi$ interaction between *Me*−C(4) and the centroid (Cg) of the Ph ring (distance H$\cdots$Cg = 3.16 Å; γ angle = 33.10°; C−H$\cdots$Cg = 148.20°). This distance is typical for such weak interactions (2.5–3.7 Å) [16]. The interatomic distance between the H-atom of *Me*−C(4) and the aromatic *ipso*-C-atom was 2.67 Å, which also fits the average value for an intramolecular CH/Ar contact forming a six-membered ring (2.70 Å) [17]. The intramolecular C−H$\cdots\pi$ interaction has been supported by a second analysis of the X-ray data of **11** by the *SHELX97* package [18], which compared the bond distances, angles, and the intramolecular distance of the H-atom of *Me*−C(4) to the centroid of the benzene ring with the database of the *Cambridge Crystallographic Data Centre*. The analysis of the X-ray data supports the hypothesis that the orientation of the *N*-Ph ring and the pertinent Me group is maintained both in solution and in the crystalline state.

In addition, three different intermolecular C−H$\cdots$O interactions in the crystal lattice of **11** were observed (*Fig. 3*): *a*) H-bonding between one of the *ortho*-protons of the Ph group with the O-atom of the oxazolidinone C=O group; *b*) interaction between one of the two remaining H-atoms of *Me*−C(4) and the O-atom of the MeO_2C group at C(5); and *c*) H-bonding between one of the H-atoms of the Me group of

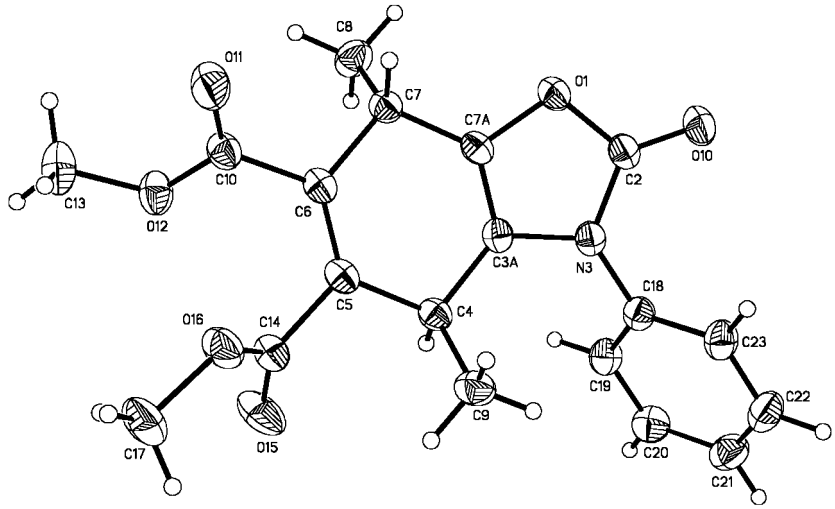


Fig. 2. *X-Ray structure of compound* **11**, *ORTEP representation* (ellipsoids with 30% probability)

MeO_2C at C(6) with the ester C=O group at C(6) in a neighboring molecule. The interaction of type *b*) is probably favored by the polarization of the C-atom due to the intramolecular $C-H\cdots\pi$ interaction with the Ph ring.

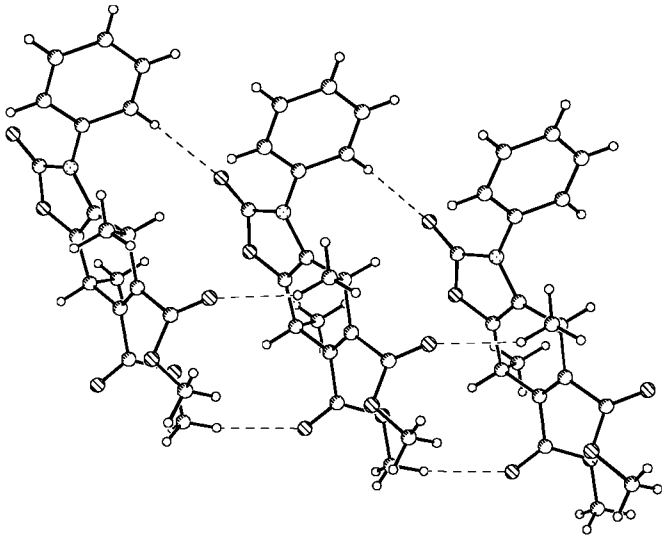


Fig. 3. *View of the unit cell of compound* **11**, *showing the intermolecular* $C-H\cdots O$ *interactions*

When the diene **6g** reacted with *N*-phenylmaleimide (**12**) under thermal conditions, only the *endo*-adduct **13** was obtained (*Scheme 3*). Its X-ray crystal structure [16] (*Fig. 4*) revealed an interesting feature: the crystal packing was stabilized by $C-H\cdots O$, $Cl\cdots O$, and C-H $\cdots$ Cl interactions between two molecules of $CHCl_3$ (the crystallization

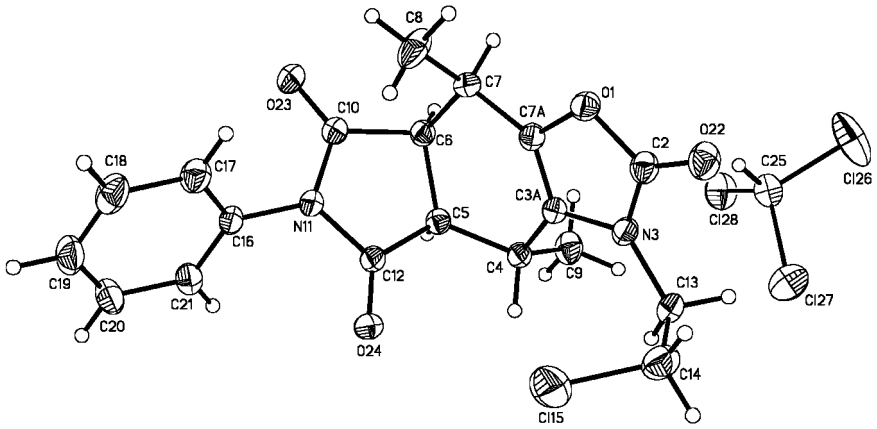


Fig. 4. *X-Ray structure of compound* **13**, *ORTEP representation* (ellipsoids with 30% probability)

solvent) and three molecules of **13** (*Fig. 5*). The C–H···O interaction is observed between the O-atom of the oxazolidinone C=O group and the $H-CCl_3$. The same O-atom forms a second contact with a Cl-atom, whereas the third contact takes place

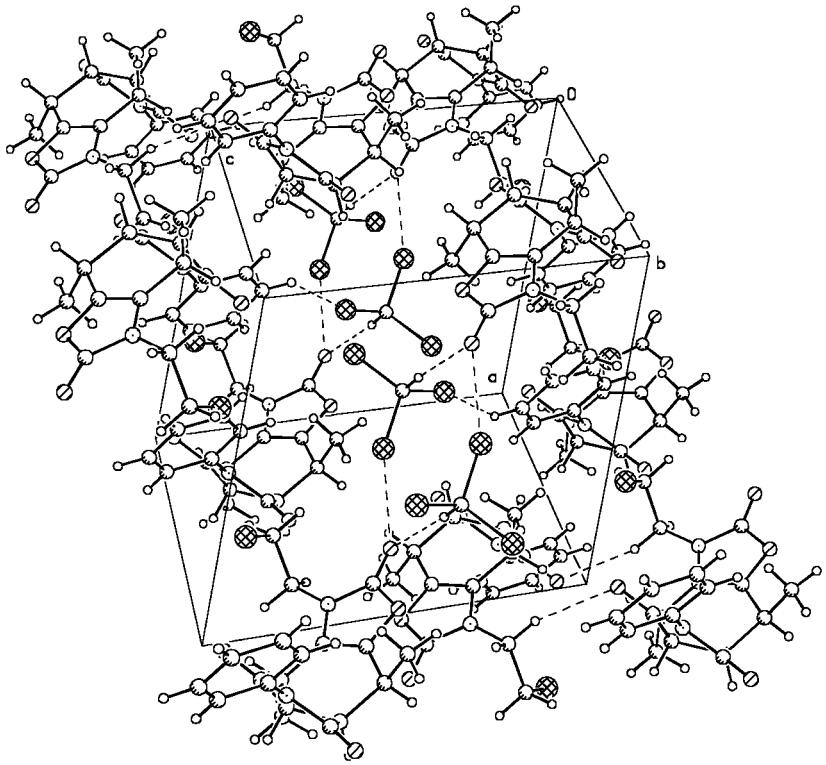
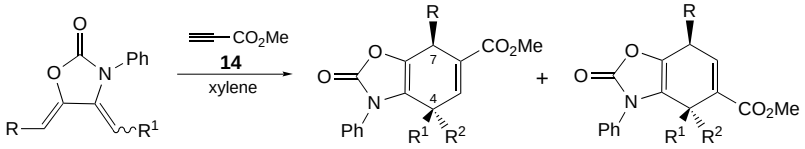


Fig. 5. *Unit-cell packing diagram of compound* **13**, *showing the C–H···O, Cl···O, and C–H···Cl interactions with two molecules of* $CHCl_3$

between another Cl-atom and the H-atom in the *meta*-position of the maleimide *N*–Ph ring of a third molecule of **13**. An additional C–H···O interaction is observed between one of the H-atoms of the *N*-methylene group of the oxazolidinone and the O-atom of one of the C=O groups of the maleimide. This result is noteworthy in so far as 85% of all known organic crystals do not contain crystallization solvent [19]. Clathrate formation is generally associated with strong solvent-solute interactions, promoted by an enthalpic factor that counterbalances the entropic gain due to solvent expulsion from the crystal lattic. This is probably the case in the structure of **13**, since H-bonds with $CHCl_3$ belong to the strongest C–H···O interactions known [20].

As shown in *Scheme 4*, the thermal reaction of a mixture of **5a**/**6a** (29:71) with methyl propiolate (**14**) furnished a mixture of the regioisomers **17** and **18** *vs.* **19** and **20** (84/16). This ratio is higher than that of the starting mixture, indicating a higher reactivity of **6a**. Moreover, the regioselectivity depends on the configuration of the diene, since the ratio **17**/**18** of 92:8, resulting from the '*in*-diene' **6a**, is higher than that of **19**/**20** (62:38), resulting from the '*out*-diene' **5a**. The former ratio is comparable to that observed for the reaction with **4a**, but higher than that for **3a** (*Table 2*, *Entries 1–3*). However, the ratio **19**/**20** is similar to the regioselectivity observed in reactions with **3a**.

Scheme 4



5a (4*Z*), R = R^1 = Me
6a (4*E*), R = R^1 = Me
4a R = Me, R^1 = H
3a R = R^1 = H

17 R = R^2 = Me, R^1 = H **18**
19 R = R^1 = Me, R^2 = H **20**
21 R = R^2 = H, R^1 = Me **22**
23 R = R^1 = R^2 = H **24**

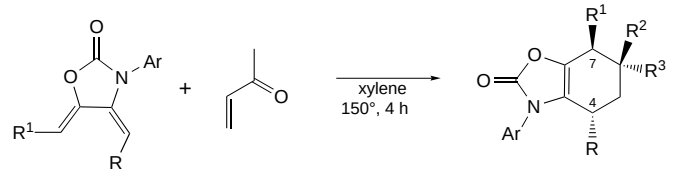
Table 2. *Cycloaddition Reaction of Dienes* **5** *and* **6** *with Olefins* **2a**–**2g**[a])

Entry	Diene (ratio)	Dienophile[b])	*T* [°C]	*t* [h]	Adducts (ratio)[c])	Yield [%][d])
1	**5a**/**6a** (29:71)	**14**	150	4.0	**17/18/19/20** (77:7:10:6)	63
2	**4a**	**14**	130	1.0	**21/22** (93:7)	90[e])
3	**3a**	**14**	120	6.0	**23/24** (64:40)	44[e])
4	**6c**	**15**	150	4.0	**25/26** (62:38)	60
5	**4b**	**15**	130	1.0	**27/28** (96:4)	91[e])
6	**6b**	**16**	150	8.0	**29/30** (51:49)	38
7	**4a**	**16**	120	8.0	**31/32** (80:20)	60

[a]) Xylene, hydroquinone (1–2%), N_2 atmosphere. [b]) 2.0 mol-equiv. [c]) Determined by ^{1}H-NMR or GC/MS (entry 1) of the crude mixture. [d]) For the major isomer after column chromatography and recrystallization. [e]) See [15].

When the diene **6c** reacted with methyl vinyl ketone (MVK, **15**), a single regioisomer as a mixture of *endo*/*exo*-stereoisomers was found (*Scheme 5*). In contrast, for diene **3b** (R′ = 4-Cl–C_6H_4) a mixture of regioisomers was obtained [15]. The

Scheme 5



6c Ar = 4-Cl–C_6H_4, R = R^1 = Me
4b Ar = 4-Cl–C_6H_4, R = H, R^1 = Me

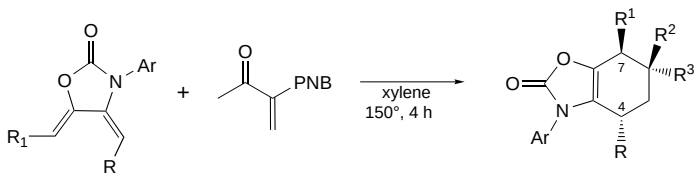
15

25 *endo* Ar = 4-Cl–C_6H_4, R = R^1 = Me, R^2 = Ac, R^3 = H
26 *exo* Ar = 4-Cl–C_6H_4, R = R^1 = Me, R^2 = H, R^3 = Ac
27 *endo* Ar = 4-Cl–C_6H_4, R = H, R^1 = Me, R^2 = Ac, R^3 = H
28 *exo* Ar = 4-Cl–C_6H_4, R = H, R^1 = Me, R^2 = H, R^3 = Ac

endo-stereoselectivity, however, was not as pronounced in the case of **4b** (*Table 2*, *Entries 4* and *5*).

The captodative dienophile (1-acetylvinyl) 4-nitrobenzoate (PNB, **16**) [21] has proven to be both highly reactive and regioselective in *Diels-Alder* [22] and in 1,3-dipolar [23] cycloadditions. Indeed, upon reaction with the diene **4a** (*Scheme 6*), high regio- and *endo*-stereoselectivities were found (*Table 2*, *Entry 7*). In contrast, the addition of **16** to the diene **6b** provided a single regioisomer, but no stereoselectivity was observed (*Table 2*, *Entry 6*).

Scheme 6



6b Ar = 3-Cl–C_6H_4, R = R^1 = Me
4a Ar = C_6H_5, R = H, R^1 = Me

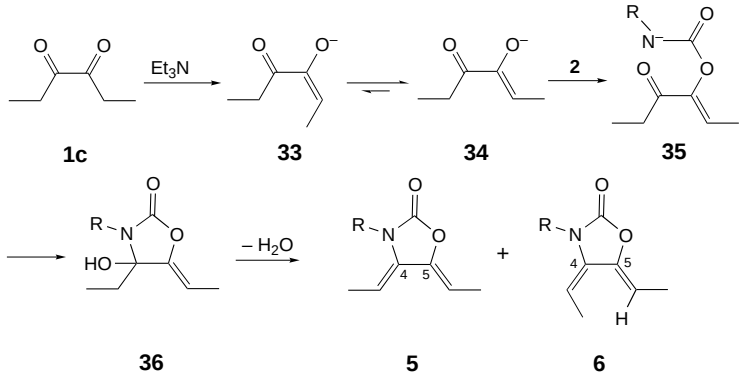
16 PNB: 4-Nitrobenzoyloxy

29 Ar = 3-Cl–C_6H_4, R = R^1 = Me, R^2 = Ac, R^3 = PNB
30 Ar = 3-Cl–C_6H_4, R = R^1 = Me, R^2 = PNB, R^3 = Ac
31 Ar = C_6H_5, R = H, R^1 = Me, R^2 = Ac, R^3 = PNB
32 Ar = C_6H_5, R = H, R^1 = Me, R^2 = PNB, R^3 = Ac

Both NOE and 2D-NMR experiments were used to establish the structures of the major isomers obtained in these cycloadditions suggesting, a half-chair conformation for the cyclohexene moiety in the adducts **25**, **29**, and **31**, as observed for analogous compounds [15][22]. The Me groups $H_3C(8)$ and $H_3C(9)$ are in pseudo-axial positions, with the Ac group lying in an equatorial position, even in the case of **29** and **31**, where the preferred conformation of the 4-nitrobenzoyloxy (PNB) group is axial.

2.3. *Mechanism for the Stereoselective Formation of* **5** *and* **6**, *Including Calculations of Electronic and Conformational Energies.* The exclusive formation of the (5*Z*)-stereoisomers **5** and **6** supports a mechanism proposed earlier for the one-pot reaction leading to **3** and **4** [15]. As shown in *Scheme 7* the thermodynamically more stable (*Z*)-enolate **34** of the 1,2-diketone **1c**, preferentially undergoes addition to isocyanate **2**. Therefore, the configuration of the ethylidene fragment at C-(4) should be established in the final step, when dehydration of the intermediate **36** takes place (*Scheme 7*). This

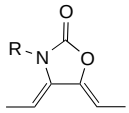
Scheme 7



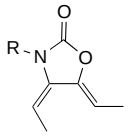
hypothesis was supported after isolating **36f** (R = 4-MeO–C_6H_4) in 17% yield during the preparation of the dienes **5f**/**6f**, and by the isolation of alcohol **36j** (R = 3-MeO–C_6H_4) as the only product, when the reaction was carried out with (3-methoxyphenyl) isocyanate. Therefore, the ratio of the isomers **5** and **6** should depend on their relative thermodynamic stabilities, which are mainly influenced by two possible steric interactions: *a*) the repulsive interaction between *Me*–CH=C(4) and the N-substituent for isomer **5**, and *b*) the steric repulsion between the (*E*)-configured Me group (*Me*–C=C(4)) and the (*Z*)-configured olefinic H (*H*–C=C(5)) in the case of isomer **6**. Consequently, the lower proportion of **5** in the reaction mixture suggests that the interaction between the Me group and the N-substituent are dominant.

This hypothesis was confirmed by *ab initio* (*HF/3-21G** and *6-31G**) [24] calculations for both the isomers **5** and **6**. The relative electronic energies for the prepared dienes **5a**/**6a**, **5f**/**6f**, **5g**/**6g**, and for the unknown dienes **5h**/**6h** and **5i**/**6i** are reported in *Table 3*. In all cases, isomer **6** was found to be more stable than **5**, except for

Table 3. *Relative Electronic Energies* (ΔE, [kcal/mol]) *Calculated for* **5** *and* **6**[a])



5a R = Ph
5f R = 4-MeO–C_6H_4
5g R = C_2H_4Cl
5h R = H
5i R = *t*-Bu



6a R = Ph
6f R = 4-MeO–C_6H_4
6g R = C_2H_4Cl
6h R = H
6i R = *t*-Bu

	ΔE				
Level	**5a**–**6a**	**5f**–**6f**	**5g**–**6g**	**5h**–**6g**	**5i**–**6i**
3-21G*	1.27	1.32	1.85	–2.01	4.11
6-31G*	1.22	1.31	1.78	–2.08	4.19

[a]) As a difference between the values of electronic energies for each pair of dienes.

the unsubstituted dienes **5h**/**6h**. The largest difference was calculated for the bulky *N*-(*tert*-butyl) derivatives, suggesting that the larger the N-substituent, the less stable isomer **5** is. Hence, it appears that an energy difference of *ca*. 1.8 kcal/mol could be enough to shift the thermodynamic equilibrium toward the '*in*-diene', as suggested by the fact that **6g** was obtained as the single stereoisomer.

These calculations prompted us to attempt the preparation of the dienes **5i**/**6i** by treatment of **1c** with *tert*-butyl isocyanate under optimized reaction conditions; however, no conversion was detected. This is probably due to the same steric effect, but now affecting the intramolecular cyclization from the intermediate **35** to the oxazolidinone **36**, which seems to be the rate-determining step (*Scheme 7*) [15].

Fig. 6 depicts the minimum-potential-energy conformations for **5a**/**6a**, **5g**/**6g**, and **5i**/**6i**, showing a heavily twisted heterocyclic ring for both the *N*-(*t*-Bu) derivatives **5i**/**6i** in order to relieve the steric strain between the diene and the N-substituent. Dienes **5a**/**6a** avoid such repulsive interactions by imposing an almost 90° torsion angle between the phenyl ring and the π-plane of the diene, as observed by X-ray-analysis even for the less strained dienes **4** [15]. As expected, in the derivatives **5g**/**6g**, the chloroethyl chain rotates as far away as possible, leaving just one H close to the diene, with the chloromethyl substituent adopting an orthogonal conformation with respect to the

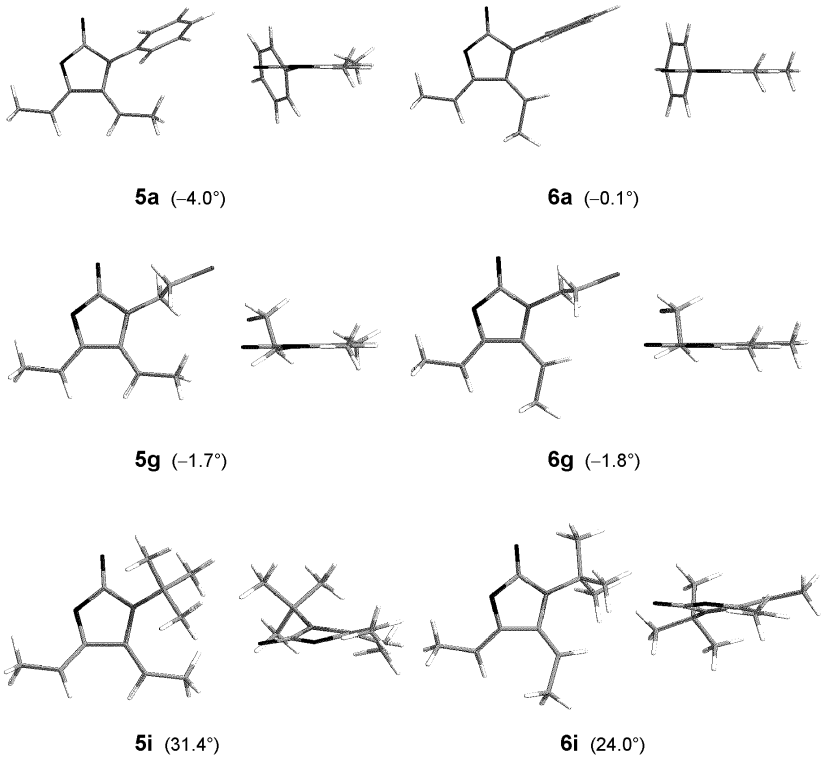


Fig. 6. *Minimum-potential-energy conformations of* **5a**–**6a**, **5g**–**6g**, *and* **5i**–**6i**, *showing* (in parentheses) *the torsion angles of the diene moieties*

plane of the heterocycle. The calculated torsion angle of the diene moiety was 24.0° for the '*in*-diene' **6i**, and 31.4° for the '*out*-diene' **5i**, indicating that the strain generated by the Me group in **6i** is less significant compared to **5i**. This would explain the relatively small effect, produced by additional '*in*-Me'/'*in*-H'-repulsions in the diene moiety of **6**, on the distance between the 1,4-dimethylene C-atoms with respect to **5** (the calculated 1,4-distances for **5a** and **6a** are 3.14 and 3.25 Å, respectively). In any case, the possible difference in reactivity towards a dienophile might not be due to this factor, as it has been suggested for explaining the lower reactivity of the '*in*-isomer' of exocyclic dienes, substituted with a Cl-atom [12e]. However, the presence of a non-zero torsion angle in the diene moiety might have an impact on the reaction rate, since the *Diels-Alder* reaction requires the diene to adopt the s-*cis*-conformation [1d][3h][11][12d][25].

2.4. *Steric and Electronic Effects in the* Diels-Alder *Reactions of* **5** *and* **6**. The high *endo*-selectivity in reactions of the dienes **3** and **4** with dienophiles such as **15** under thermal conditions is not well-understood. Perhaps secondary orbital-interactions are taking place, stabilizing this particular transition-state preferentially in spite of the presence of an *N*-aryl ring [15]. Similar effects might play a role in the reaction of diene **6g** with dienophile **12**, which exclusively yielded the *endo*-isomer **13**. In addition, destabilizing steric interactions may be involved with the (*E*)-configured Me group during the *exo*-approach (*Fig. 7*). This factor also seems to contribute to the *endo*/*exo*-ratio for cycloadditions with the captodative dienophile **16**, since the high *endo*-preference observed for reactions with **4a** (*Table 2*, *Entry 7*) was lost with **6b** (*Table 2*, *Entry 6*).

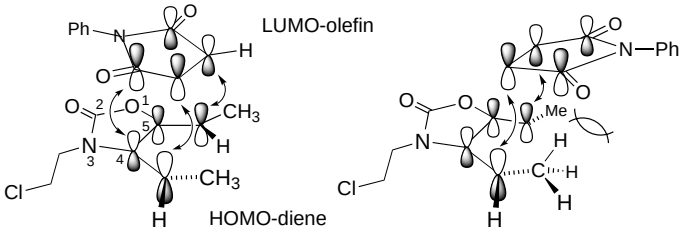
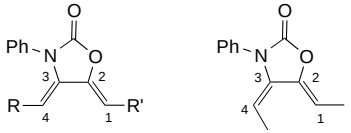


Fig. 7. endo *and* exo Diels-Alder *transition states for the addition of diene* **6g** *to olefin* **12**, *showing possible effects that control the* endo *preference*

Furthermore, these steric interactions with the '*in*-Me group' may be also at the origin of the higher regioselectivity in reactions between **14** and **6a** (**17**/**18** 92:8) as compared to **14** and **5a** (**19**/**20** 62:38) (*Table 2*). The polarizability of the π-orbital in **5a** should be similar to that of the unsubstituted dienes **3**, since the hyperconjugation effect of the Me groups in **5a** is outbalanced, leaving the control of the orientation of the cycloaddends to the electronic effect of the heteroatoms. The results seem to be in agreement with this hypothesis, because the reaction between **3a** (R′ = Ph) and **14** led to a mixture of regioisomers in similar amounts (**23**/**24** 60:40) (*Table 2*).

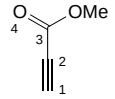
To evaluate the electronic contribution to the regioselectivity of the *Diels-Alder* reaction, we calculated the FMO coefficients (*C*) for both **5a** and **6a** at the *6-31G** level and compared them with those of **3a** and **4a** (*Table 4*). We found that the relative magnitude of the coefficient C_4 was bigger than C_1 for the HOMO of both the dienes **5a** and **6a**. However, ΔC was larger for **6a**, suggesting an enhancement of regioselectivity.

Table 4. Ab Initio *6-31 G* Calculated Energies* [eV] *and Coefficients* (C_i) *of the Frontier Molecular Orbitals of the Dienes* **5a**, **6a**, **3a** *and* **4a**, *and the Olefins* **14**, **15**, *and* **16**[a])

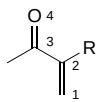


5a R = R' = Me
3a R = R' = H
4a R = H, R' = Me

6a



14



15 R = H
16 R = 4-NO_2–C_6H_4COO

		HOMO[b])						LUMO[c])				
Compd[d])	*E*	C_1	C_2	C_3	C_4	ΔC_1[e])	*E*	C_1	C_2	C_3	C_4	ΔC_1[e])
5a	– 8.2675	– 0.2573	– 0.1883	0.2210	0.3164	– 0.0591	3.2832	0.2630	– 0.2250	– 0.2342	0.2763	– 0.0133
6a	– 8.4601	– 0.2154	– 0.1571	0.1947	0.2782	– 0.0628	3.1983	0.2532	– 0.1890	– 0.2005	0.2438	0.0094
3a[f])	– 8.8342	0.2591	0.1758	– 0.2173	– 0.3339	– 0.0748	2.9470	– 0.2690	0.2501	0.2470	– 0.2625	0.0065
4a[f])	– 8.5804	– 0.2679	– 0.2084	0.2042	0.3278	– 0.0599	3.1448	– 0.2861	0.2345	0.2535	– 0.2592	0.0269
14[f])	– 11.4648	– 0.3746	– 0.3944	0.0343	0.1924	– 0.0198	3.2972	0.2895	– 0.1830	– 0.3391	0.2786	0.1065
15[g])	– 10.4895	– 0.3464	– 0.3669	0.0327	0.2213	– 0.0205	2.9222	0.3109	– 0.2069	– 0.2809	0.2549	0.1040
16[g])	– 11.0123	– 0.3593	– 0.3565	0.0236	0.1676	0.0028	2.4588	0.2940	– 0.2386	– 0.2889	0.2800	0.0554

[a]) These are the values of the p_z coefficients; the relative p_z contributions and their ΔC are analogous. [b]) Energies and coefficients of the NHOMO of olefin **14** and of the 2NHOMO of olefin **16**; the corresponding HOMOs do not have any p_z contribution. [c]) Energy and coefficients of the NLUMO of olefin **16**. [d]) For the most stable planar s-*cis*-conformation for **15**, and nonplanar s-*trans*-conformation for **16**. [e]) For olefins: C(1) – C(2), for dienes: C(1) – C(4). [f]) See [15]. [g]) See [26].

This, however, is inconsistent with the HOMO energies (*Table 4*), whose relative values indicate that **5a** should be more reactive than **6a**. Moreover, in terms of perturbation theory, **5a** should also be more selective than **6a** [7g][27]. This apparent contradiction can be solved if steric repulsions from the '*in*-Me group' are considered. The latter prevents the approach of the methoxycarbonyl group of the dienophile towards the diene moiety in the minor isomer **18** as compared to the major isomer **17**, in which the pertinent groups are further away from one another. This hypothesis is also supported by the fact that **6c** ($R' = 4\text{-}ClC_6H_4$) reacts with MVK to exclusively yield the regioisomer **25**/**26**, whereas the thermal addition of **3a** or **3c** ($R' = Ph$ or $4\text{-}ClC_6H_4$) with the same dienophile provided a mixture of regioisomers (8:2) [15].

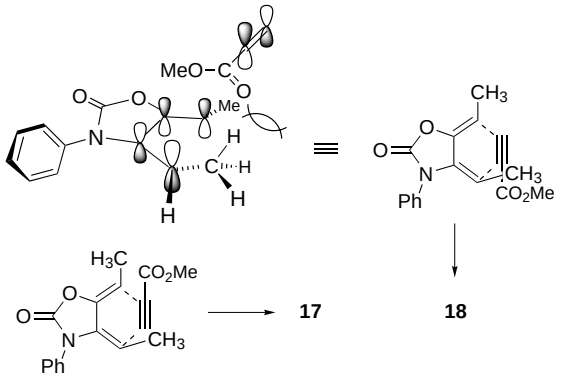


Fig. 8. Diels-Alder *transition states for the addition of diene* **6a** *to olefin* **14**, *showing possible effects that control the preferred* para-*arrangement*

From the FMO-theory viewpoint, the observed regioselectivity would be explained on the basis of coefficient differences for the energetically more favorable HOMO/LUMO interaction (*Table 4*). Assuming that the largest FMO coefficients determine bond formation in the transition state [7], and considering that the relative magnitude of C_4 is bigger than that of C_1 in the HOMO of both **5a** and **6a**, – a '*para*-orientation' is expected, in agreement with the experiment. The same prediction can be made for the dienes **6b**,**c** used in the cycloadditions, since a negligible contribution of the *N*-aryl substituent to the polarizability of the π-system is expected for **3** and **4** [15]. Therefore, for these dienes, the regioselectivity in *Diels-Alder* reactions cannot be explained simply on the basis of electronic effects, but has to be in part explained by steric interactions, especially for the '*in*-substituted' dienes.

3. Conclusions. – The stereoselective condensation of the 1,2-diketone **1c** with several isocyanates gave rise to the 4,5-diethylidene-1,3-oxazolidin-2-one **5**/**6**, whose structure differs in the geometry of the ethylidene fragment at C-(4). The formation of the preferred '*in*-geometry' of **6a**–**g** was thermodynamically controlled during the dehydration of the intermediate **36** due to the steric strain between the N-substituent of the oxazolidine and the Me group of the exocyclic diene moiety. Compounds **6** proved

to be highly regio- and stereoselective in thermal *Diels-Alder* cycloadditions with both the symmetric and unsymmetric olefins **12** and **14**–**16**. FMO-theory, based on *ab initio* calculations, seems to predict the observed regioselectivities. However, the steric interactions between the '*in*-Me group' of the diene and the substituents in the dienophiles, better explain the high selectivity of such processes.

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Experimental Part

General. Anal. TLC: *Merck* silica gel *60* F_{254}-coated plates, visualization by a long- and short-wavelength UV lamp. Flash chromatography (FC): *Flash40i* apparatus of *Biotage*, *Dyax Corp*. All moisture-sensitive reactions were carried out under N_2 in oven-dried glassware. Dioxane, Et_2O, THF, toluene, and xylene were freshly distilled from Na, CH_2Cl_2, AcOEt, MeCN, and Me_2SO from CaH_2 prior to use. Li_2CO_3 was dried overnight at 120° prior to use. Et_3N was distilled from NaOH. All other reagents were used without further purification.

M.p.: uncorrected; *Electrothermal* capillary melting-point apparatus. IR Spectra: *Perkin-Elmer 1600* spectrophotometer. ^{1}H- (300 MHz) and ^{13}C-NMR (75.4 MHz) Spectra: *Varian Gemini-300* instrument in $CDCl_3$, $(CD_3)_2SO$ or $(CD_3)_2CO$ with Me_4Si as internal standard. MS: EI mode (70 eV); *Hewlett-Packard 5971A* spectrometer. X-Ray Analyses were performed with a *Siemens P4* diffractometer. Microanalyses: *M-H-W Laboratories* (Phoenix, AZ), and *Centro de Investigaciones Químicas*, *Universidad Autónoma de Hidalgo* (Pachuca, Hgo., Mexico). *Abbreviations:* ID = internal diameter, IT = initial temp., FT = final temp., t_R = retention time.

General Procedure for the Preparation of N-*Substituted (4Z,5Z)- and (4*E,*5Z)-Diethylidene-1,3-oxazolidin-2-ones* **5a**–**5g** *and* **6a**–**6g**. A soln. of 3,4-hexanedione (**1c**) (0.4 g, 3.5 mmol) in anh. dioxane (3 ml) was added dropwise to a magnetically stirred soln. of Et_3N (0.71 g, 7.0 mmol) in anh. dioxane (2 ml) containing dried Li_2CO_3 (0.3 g, 4.2 mmol). The mixture was stirred at r.t. under N_2, for 30 min. Then, a soln. of the corresponding isocyanate (5.2 mmol) in anh. dioxane (2 ml) was added dropwise, and stirring was continued for 12 h. The mixture was filtered and the solvent was removed *in vacuo*. The residue was prepurified by CC using SiO_2, conditioned with Et_3N (10%) in hexane, eluant: hexane/AcOEt 9:1. The isomeric mixtures were separated by HPLC (*LiChrospher*; MeCN/H_2O, 8:2, 1 ml/min) or by FC (column: 10 × 3 cm, 5 kBar N_2 pressure, hexane).

*(4Z,5Z)- and (4*E,*5Z)-4,5-Diethylidene-3-phenyl-1,3-oxazolidin-2-one* (**5a** and **6a**). The reaction with 0.62 g of phenyl isocyanate (**2a**) gave 0.38 g (50%) of a mixture of **5a**/**6a** (29:71) as a pale yellow oil, which was separated by HPLC.

Data of **6a**: R_f 0.52 (hexane/AcOEt 9:1). IR (film): 1779, 1665, 1496, 1403, 1310, 1251, 1191, 1092, 1016, 782, 718. ^{1}H-NMR (300 MHz, $CDCl_3$)[1]): 1.76 (br. *d*, *J* = 7.6, 3 H–C(9)); 1.92 (br. *d*, *J* = 7.2, 3 H–C(8)); 4.83 (*q*, *J* = 7.6, 1 H–C(6)); 5.29 (*q*, *J* = 7.2, H–C(7)); 7.26–7.51 (*m*, 5 arom. H); signals attributed to the minor isomer **5a**: 1.15 (*d*, *J* = 7.8, 3 H–C(9)); 2.00 (*d*, *J* = 7.8, 3 H–C(8)); 5.05 (*q*, *J* = 7.6, H–C(6)); 5.18 (*q*, *J* = 7.3, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 10.6 (C(8)); 12.0 (C(9)); 97.8 (C(6)); 103.8 (C(7)); 127.4, 128.6, 129.3, 130.9 (6 arom. C); 133.0 (C(4)); 143.3 (C(5)); 152.1 (C(2)); selected signals attributed to **5a**: 9.8 (C(8)); 10.8 (C(9)); 94.5 (C(6)); 94.7 (C(7)); 128.5; 128.8; 135.1 (C(4)); 143.9 (C(5)); 153.4 (C(2)). EI-MS (70 eV): 215 (100, M^+), 200 (12), 170 (35), 156 (36), 132 (40), 130 (47), 104 (15), 91 (16), 77 (75). Anal. calc. for $C_{13}H_{13}NO_2$: C 72.54; H 6.09; N 6.51; found: C 72.52, H 6.31, N 6.39.

*(4Z,5Z)- and (4*E,*5Z)-4,5-Diethylidene-3-(3-chlorophenyl)-1,3-oxazolidin-2-one* (**5b** and **6b**). The reaction with 0.80 g of (3-chlorophenyl) isocyanate (**2b**) yielded 0.4 g (46%) of a mixture of **5b**/**6b** (28:72), which was separated by FC.

Data of **6b**: Colorless crystals. R_f 0.51 (hexane/AcOEt 9:1). M.p. 126–127° (CH_2Cl_2/hexane, 1:1). IR (KBr): 1770, 1711, 1589, 1478, 1372, 1101, 1074, 761. ^{1}H-NMR (300 MHz, $CDCl_3$)[1]): 1.78 (br. *d*, *J* = 7.6, 3 H–C(9)); 1.92 (br. *d*, *J* = 7.2, 3 H–C(8)); 4.87 (*q*, *J* = 7.6, H–C(6)); 5.30 (*q*, *J* = 7.2, H–C(7)); 7.20–7.50

[1]) Trivial numbering of atoms according to *Scheme 2* was used both in ^{1}H- and ^{13}C-NMR assignments.

(*m*, 4 arom. H); signals attributed to the minor isomer **5b**: 1.21 (*d*, *J* = 7.8, 3 H–C(9)); 1.81 (*d*, *J* = 6.8, 3 H–C(8)); 5.09 (*q*, *J* = 7.8, H–C(6)); 5.21 (*q*, *J* = 6.8, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 11.1 (C(8)); 12.4 (C(9)); 98.3 (C(6)); 103.6 (C(7)); 126.1, 128.1, 128.9, 130.7 (4 arom. C); 133.0 (C(4)); 134.5, 135.3 (2 arom. C); 143.4 (C(5)); 152.5 (C(2)); selected signals attributed to **5b**: 10.2 (C(8)); 11.6 (C(9)); 95.2 (C(6)); 95.8 (C(7)); 127.3; 130.1; 142.8 (C(5)). EI-MS (70 eV): 251 (26, $[M+2]^+$), 249 (100, M^+), 204 (19), 190 (20), 166 (43), 154 (12), 138 (14), 125 (12), 111 (36), 75 (30), 67 (27). Anal. calc. for $C_{13}H_{12}ClNO_2$: C 62.53, H 4.84, N 5.61; found: C 62.41, H 5.00, N 5.42.

*(4Z,5Z)- and (4*E*,5Z)-4,5-Diethylidene-3-(4-chlorophenyl)-1,3-oxazolidin-2-ones* (**5c** and **6c**). The reaction with 0.58 g of (4-chlorophenyl) isocyanate (**2c**) yielded 0.58 g (67%) of a mixture of **5c**/**6c** (37:63), which was separated by FC.

Data of **6c**: Colorless crystals. R_f 0.59 (hexane/AcOEt 9:1) M.p. 120–121° (CH_2Cl_2/hexane 1:1). IR (KBr): 1785, 1667, 1493, 1403, 1089. ^{1}H-NMR (300 MHz, $CDCl_3$)[1]): 1.77 (br. *d*, *J* = 7.6, 3 H–C(9)); 1.92 (br. *d*, *J* = 7.2, 3 H–C(8)); 4.83 (*q*, *J* = 7.6, H–C(6)); 5.29 (*q*, *J* = 7.2, H–C(7)); 7.22–7.28 (*m*, 2 arom. H); 7.42–7.49 (*m*, 2 arom. H); selected signals attributed to the minor isomer **5c**: 1.19 (*d*, *J* = 7.8, 3 H–C(9)); 1.80 (*d*, *J* = 7.2, 3 H–C(8)); 5.06 (*q*, *J* = 7.8, H–C(6)); 5.19 (*q*, *J* = 7.2, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 11.1 (C(8)); 12.4 (C(9)); 98.2 (C(6)); 103.6 (C(7)); 129.1, 130.0, 131.9 (3 arom. C); 133.1 (C(4)); 134.5 (arom. C); 143.9 (C(5)); 152.4 (C(2)); selected signals attributed to **5c**: 10.2 (C(8)); 11.5 (C(9)); 94.9 (C(6)); 95.6 (C(7)); 129.4; 132.9; 134.1; 144.0 (C(5)); 152.8 (C(2)). EI-MS (70 eV): 251 (32, $[M^+ + 2]$), 249 (100, M^+), 234 (9), 204 (7), 190 (16), 166 (40), 151 (11), 138 (17), 125 (15), 111 (27), 75 (18). Anal. calc. for $C_{13}H_{12}ClNO_2$: C 62.53, H 4.84, N 5.61; found: C 62.40, H 4.78, N 5.60.

*(4Z,5Z)- and (4*E*,5Z)-4,5-Diethylidene-3-(3-methylphenyl)-1,3-oxazolidin-2-one* (**5d** and **6d**). The reaction with 0.69 g of (2-methylphenyl) isocyanate (**2d**) yielded 0.31 g (39%) of a mixture of **5d**/**6d** (32:68), which was separated by FC:

Data of **6d**: Pale yellow oil. R_f 0.56 (hexane/AcOEt 9:1). IR (film): 1785, 1669, 1491, 1251, 1027. ^{1}H-NMR (300 MHz, $CDCl_3$)[1]): 1.76 (br. *d*, *J* = 7.6, 3 H–C(9)); 1.92 (br. *d*, *J* = 7.2, 3 H–C(8)); 2.39 (*s*, *Me*C_6H_4); 4.81 (*q*, *J* = 7.6, H–C(6)); 5.27 (*q*, *J* = 7.2, H–C(7)); 7.07–7.39 (*m*, 4 arom. H); selected signals attributed to the minor isomer **5d**: 1.16 (*d*, *J* = 7.8, 3 H–C(9)); 2.37 (*s*, *Me*C_6H_4); 5.03 (*q*, *J* = 7.8, H–C(6)); 5.17 (*q*, *J* = 7.5, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 11.1 (C(8)); 12.4 (C(9)); 21.2 (*Me*C_6H_4); 98.0 (C(6)); 104.2 (C(7)); 124.8, 128.3, 129.6, 130.9 (5 arom. C); 133.1 (C(4)); 139.8 (arom. C); 143.6 (C(5)); 152.7 (C(2)); selected signals attributed to **5d**: 10.2 (C(8)); 14.0 (C(9)); 22.9 (*Me*C_6H_4); 94.6 (C(6)); 95.1 (C(7)); 124.9, 128.4, 129.5 (4 arom. C); 133.3 (C(4)); 139.3 (arom. C). EI-MS (70 eV): 229 (84, M^+), 214 (14), 184 (28), 170 (68), 146 (84), 144 (82), 131 (25), 118 (25), 105 (20), 91 (100), 65 (67). Anal. calc. for $C_{14}H_{15}NO_2$: C 73.34, H 6.59, N 6.11; found: C 73.17, H 6.23, N 5.96.

*(4Z,5Z)- and (4*E*,5Z)-4,5-Diethylidene-3-(4-methylphenyl)-1,3-oxazolidin-2-one* (**5e** and **6e**). The reaction with 0.69 g of (4-methylphenyl) isocyanate (**2e**) gave 0.54 g (67%) of a mixture of **5e**/**6e** (40:60), which was separated by FC.

Data of **6e**: Pale yellow oil. R_f 0.55 (hexane/AcOEt 9:1). IR (film): 1741, 1512, 1360, 1218, 750. ^{1}H-NMR (300 MHz, $CDCl_3$)[1]): 1.75 (br. *d*, *J* = 7.6, 3 H–C(9)); 1.91 (br. *d*, *J* = 7.2, 3 H–C(8)); 2.39 (*s*, *Me*C_6H_4); 4.81 (*q*, *J* = 7.6, H–C(6)); 5.27 (*q*, *J* = 7.2, H–C(7)); 7.14–7.32 (*m*, 4 arom. H); selected signals attributed to the minor isomer **5e**: 1.16 (br. *d*, *J* = 7.6, 3 H–C(9)); 1.80 (br. *d*, *J* = 7.2, 3 H–C(8)); 2.38 (*s*, *Me*C_6H_4); 5.02 (*q*, *J* = 7.6, H–C(6)); 5.17 (*q*, *J* = 7.2, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 11.0 (C(8)); 12.3 (C(9)); 21.1 (*Me*C_6H_4); 97.9 (C(6)); 104.1 (C(7)); 127.6, 130.3, 130.5 (5 arom. C); 133.5 (C(4)); 138.7 (1 arom. C); 143.6 (C(5)); 152.8 (C(2)); selected signals attributed to **5e**: 10.2 (C(8)); 20.4 (*Me*C_6H_4); 94.5 (C(6)); 95.0 (C(7)); 127.4 (2 arom. C); 129.9 (2 arom. C); 144.2 (C(5)); 154.2 (C(2)). EI-MS (70 eV): 229 (100, M^+), 214 (32), 184 (29), 170 (53), 146 (83), 144 (80), 118 (33), 105 (35), 91 (96), 65 (71). Anal. calc. for $C_{14}H_{15}NO_2$: C 73.34, H 6.59, N 6.11; found: C 73.18, H 6.49, N 6.33.

*(4Z,5Z)- and (4*E*,5Z)-4,5-Diethylidene-3-(4-methoxyphenyl)-1,3-oxazolidin-2-one* (**5f** *and* **6f**) *and (5Z)-4-Ethyl-5-ethylidene-4-hydroxy-3-(4-methoxyphenyl)-1,3-oxazolidin-2-one* (**36f**). The reaction with 0.77 g of (4-methoxyphenyl) isocyanate (**2f**) gave 0.38 g (44%) of a mixture of **5f**/**6f** (26:74) and 0.16 g (17%) of **36f** as a white powder. The mixture of **5f**/**6f** was separated by FC.

Data of **6f**: Pale yellow oil. R_f 0.50 (hexane/AcOEt, 9:1). IR (film): 1778, 1513, 1249, 1020. ^{1}H-NMR (300 MHz, $CDCl_3$)[1]): 1.76 (br. *d*, *J* = 7.6, 3 H–C(9)); 1.91 (br. *d*, *J* = 7.2, 3 H–C(8)); 3.83 (*s*, *Me*O); 4.76 (*q*, *J* = 7.6, H–C(6)); 5.27 (*q*, *J* = 7.2, H–C(7)); 6.92–7.04 (*m*, 2 arom. H); 7.18–7.24 (*m*, 2 arom. H); selected signals attributed to the minor isomer **5f**: 1.20 (br. *d*, *J* = 7.2, 3 H–C(9)); 1.82 (br. *d*, *J* = 7.2, 3 H–C(8)); 5.01 (*q*, *J* = 7.2, H–C(6)); 5.17 (*q*, *J* = 7.2, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 11.1 (C(8)); 12.3 (C(9)); 55.5 (MeO); 97.9 (C(6)); 104.2 (C(7)); 114.2, 125.7, 129.1 (5 arom. C); 133.8 (C(4)); 143.6 (C(5)); 152.9 (C(2)); 159.6 (arom. C);

signals attributed to **5f**: 10.2 (C(8)); 10.9 (C(9)); 94.4 (C(6)); 95.1 (C(7)); 114.3, 129.2 (4 arom. C). EI-MS (70 eV): 245 (100, M^+), 230 (10), 214 (6), 200 (13), 186 (31), 162 (31), 134 (23), 108 (17), 92 (15), 77 (14). Anal. calc. for $C_{14}H_{15}NO_3$: C 68.56, H 6.16, N 5.71; found: C 68.31, H 5.89, N 5.51.

Data of **36f**: colorless crystals. R_f 0.42 (hexane/AcOEt 8:2). M.p. 108–109° (CH_2Cl_2/hexane 7:3). IR (KBr): 3366, 1760, 1707, 1601, 1490, 1240, 1149. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.76 (*t*, *J* = 7.5, 3 H–C(9)); 1.69 (*d*, *J* = 7.2, 3 H–C(8)); 1.67–1.85 (*m*, 2 H–C(6)); 3.80 (*s*, MeO); 4.22 (br. *s*, OH); 5.00 (*q*, *J* = 7.2, H–C(7)); 6.86–6.89 (*m*, 2 arom. H); 7.36–7.40 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 8.0, 9.9 (C(9), C(8)); 29.7 (C(6)); 55.4 (MeO); 91.3 (C(4)); 100.0 (C(7)); 114.2, 126.3, 127.9 (5 arom. H); 149.1 (C(5)); 153.6 (C(2)); 158.6 (arom. H). EI-MS (70 eV): 245 (100, $[M-18]^+$), 214 (5), 186 (33), 162 (30), 134 (28), 108 (25), 77 (14), 64 (14). Anal. calc. for $C_{14}H_{17}NO_4$: C 63.85, H 6.51, N 5.32; found: C 63.68, H 6.36, N 5.37.

*(4*E*,5*Z*)-3-(2-Chloroethyl)-4,5-diethylidene-1,3-oxazolidin-2-one* (**6g**). The reaction with 0.55 g of (2-chloroethyl) isocyanate (**2g**) yielded, after purification by CC (SiO_2; hexane), 0.45 g (64%) of **6g** as a pale yellow oil. R_f 0.36 (hexane/AcOEt 9:1). IR (film): 1768, 1658, 1417, 1323, 1088, 1009, 754. ^{1}H-NMR (300 MHz, $CDCl_3$)[1]): 1.82 (br. *d*, *J* = 7.5, 3 H–C(9)); 1.87 (br. *d*, *J* = 7.2, 3 H–C(8)); 3.64 (*t*, *J* = 6.7, CH_2N); 3.81 (*t*, *J* = 6.7, CH_2Cl); 4.95 (*q*, *J* = 7.5, H–C(6)); 5.25 (*q*, *J* = 7.2, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 11.1 (C(8)); 12.5 (C(9)); 39.1 (CH_2N); 42.3 (CH_2Cl); 96.5 (C(6)); 105.0 (C(7)); 131.1 (C(4)); 143.3 (C(5)); 153.5 (C(2)). EI-MS (70 eV): 203 (30, $[M+2]^+$), 201 (100, M^+), 186 (11), 166 (56), 152 (17), 124 (16), 111 (16), 83 (21), 56 (70). Anal. calc. for $C_9H_{12}ClNO_2$: C 53.60, H 12.10, N 6.95; found: C 53.79, H 12.32, N 6.77.

*(5*Z*)-4-Ethyl-5-ethylidene-4-hydroxy-3-(3-methoxyphenyl)-1,3-oxazolidin-2-one* (**36j**). The reaction with 0.77 g of (3-methoxyphenyl) isocyanate (**2j**) gave 0.42 g (45%) of **36j** as colorless crystals. R_f 0.43 (hexane/AcOEt 8:2). M.p. 105–106° (CH_2Cl_2/hexane, 1:1). IR (KBr): 3370, 1763, 1706, 1598, 1490, 1387, 1253, 1073, 1011. ^{1}H-NMR (300 MHz, $CDCl_3$)[1]): 0.78 (*t*, *J* = 7.5, 3 H–C(9)); 1.77 (*d*, *J* = 7.2, 3 H–C(8)); 1.88–2.01 (*m*, 2 H–C(6)); 3.56 (br. *s*, OH); 3.80 (*s*, MeO); 5.06 (*q*, *J* = 7.2, H–C(7)); 6.84–6.91 (*m*, 1 arom. H); 7.14–7.21 (*m*, 2 arom. H); 7.28–7.34 (*m*, 1 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 8.1 (C(8)); 10.0 (C(9)); 29.9 (C(6)); 55.3 (MeO); 91.6 (C(4)); 100.1 (C(7)); 111.9, 113.0, 118.2, 129.7, 129.9 (5 arom. C); 139.8 (C(5)); 152.9 (C(2)); 164.2 (arom. C). EI-MS (70 eV): 245 (90, $[M-18]^+$), 214 (5), 186 (20), 162 (100), 134 (20), 92 (21), 77 (37), 55 (23). Anal. calc. for $C_{14}H_{17}NO_4$: C 63.85, H 6.51, N 5.32; found: C 63.65, H 6.43, N 5.37.

General Procedures for the Diels-Alder *Reaction of the Dienophiles Dimethyl Acetylene-1,2-dicarboxylate* (**9**), *N-Phenylmaleimide* (**12**), *Methyl Propiolate* (**14**), *Methyl Vinyl Ketone* (**15**), *and (1-Acetylvinyl) 4-Nitrobenzoate* (**16**) *with the Dienes* **4a, 5a**/**6a**, **6b**, *and* **6c**. A mixture of the diene (2.5 mmol), the dienophile (5.0 mmol), and hydroquinone (0.003 g) in dry xylene (3 ml) was placed in a threaded *ACE* glass pressure-tube with a sealed teflon screw-cap under N_2 and in the dark. The mixture was stirred and heated until the reaction was complete. The solvent was removed *in vacuo*, and the residue was purified by CC (hexane/AcOEt 4:1) on SiO_2 (30 g/g of crude material).

*(4*R**,7*S**)- and (4*R**,7*R**)-2,3,4,7-Tetrahydro-5,6-Bis[(methoxy)carbonyl]-4,7-dimethyl-3-phenyl[1,3]benzoxazol-2-one* (**10** and **11**). The reaction between a mixture of **5a**/**6a** (29:71, 0.54 g) and dimethyl acetylenedicarboxylate (**9**) (0.71 g) at 150° for 3 h gave a mixture of **10**/**11** (32:68), which was separated to yield 0.53 g (60%) of **11** as colorless crystals. R_f 0.30 (hexane/AcOEt, 7:3). M.p. 156–157° (CH_2Cl_2/hexane 7:3). IR (KBr): 1769, 1725, 1594, 1496, 1261, 1212, 1033. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.84 (*d*, *J* = 6.6, *Me*–C(4)); 1.36 (*d*, *J* = 6.6, *Me*–C(7)); 3.79 (*s*, CO_2*Me*); 3.84 (*s*, CO_2*Me*); 3.74–3.90 (*m*, H–C(4), H–C(7)); 7.30–7.55 (*m*, 5 arom. H); selected signals attributed to the minor isomer **10**: 1.03 (*d*, *J* = 6.5, *Me*–C(4)); 1.47 (*d*, *J* = 6.6, *Me*–C(7)); 3.81 (*s*, CO_2Me); 3.85 (*s*, CO_2Me). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 17.3, 18.0, *Me*–C(4,7)); 30.0, 30.2 (C(4,7)); 52.4 (CO_2*Me*); 52.5 (CO_2*Me*); 120.6 (C(3a)); 125.6, 128.3, 129.8 (5 arom. C); 134.1, 134.4 (C(5,6)); 135.4 (arom. C); 136.6 (C(7a)); 154.2 (C(2)); 167.15, 167.20 (2 *C*O_2Me). EI-MS (70 eV): 357 (13, M^+), 310 (100), 283 (16), 252 (18), 194 (9), 91 (7), 77 (29). Anal. calc. for $C_{19}H_{19}NO_6$: C 63.86, H 5.36, N 3.92; found: C 63.55, H 5.54, N 3.68.

*(4*R**,4a*S**,7a*R**,8*R**)-3-(2-Chloroethyl)-3,4,4a,5,6,7,7a,8-octahydro-4,8-dimethyl-6-phenyl-2*H*-[1,3]oxazolo[4,5-f]isoindole-2,5,7-trione* (**13**). The reaction between **6g** (0.54 g) and *N*-phenylmaleimide (**12**) (0.86 g) at 150° for 3 h gave 0.76 g (82%) of **13** as colorless crystals. R_f 0.33 (hexane/AcOEt 7:3). M.p. 91–92° (CH_2Cl_2/hexane 7:3). IR (KBr) 1770–1695, 1509, 1455, 1381, 1210, 825. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.30, 1.32 (2*d*, *J* = 6.6, 6.8, Me–C(4,8)); 3.16 (*dd*, *J* = 8.2, 1.0, H–C(4a)); 3.19–3.30 (*m*, H–C(4)); 3.52–3.60 (*m*, CH_2N); 3.60–3.71 (*m*, H–C(8)); 3.71–3.76 (*m*, CH_2Cl); 3.91–4.00 (*m*, H–C(7a)); 7.18–7.23 (*m*, 2 arom. H); 7.34–7.45 (*m*, 3 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 15.2, 20.6 (Me–C(4,8)); 23.7, 25.8 (C(4,8)); 40.6 (CH_2N); 42.0 (C(4a) or C(7a)); 44.0 (CH_2Cl); 47.5 (C(7a) or C(4a)); 123.0 (C(3a)); 126.1, 128.8, 129.3, 131.4 (6 arom. C); 134.6 (C(8a)); 155.4 (C(2)); 175.1, 176.1 (C(5,7)). EI-MS (70 eV): 376 (29, $[M+2]^+$), 374 (84, M^+), 359 (35),

226 (14), 201 (100), 166 (34), 111 (14), 77 (33). Anal. calc. for $C_{19}H_{19}ClN_2O_4 \cdot CHCl_3$: C 48.50, H 4.27, N 5.66; found: C 48.32, H 4.17, N 5.72.

*(4*R*,7*R*) and (4*R*,7*S*)-2,3,4,7-Tetrahydro-6-[(methoxy)carbonyl]-4,7-dimethyl-3-phenyl[1,3]benzoxazol-2-one* (**17** and **19**) *and (4*R*,7*R*)- and (4*R*,7*S*)-2,3,4,7-Tetrahydro-5-[(methoxy)carbonyl]-4,7-dimethyl-3-phenyl[1,3]benzoxazol-2-one* (**18** and **20**). The reaction between a mixture of **5a**/**6a** (29:71, 0.54 g) and methyl propiolate (**9**) (0.71 g) at 150° for 4 h gave a mixture of **17**/**18**/**19**/**20** (77:7:10:6) [GC/MS, 5% PhMe Siloxane (ID: 0.25 mm, 30 m), IT = 70°C, 20°C/min, FT = 220°C, 80 ml/min: t_R 22.80, 22.17, 22.89, 22.01, resp., which was separated to yield 0.47 g (63%) of **17** as a white powder. R_f 0.44 (hexane/AcOEt 7:3). M.p. 128–129° (CH_2Cl_2/hexane 7:3). IR (KBr): 1768, 1721, 1594, 1496, 1396, 1250, 1041, 978. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.85 (*d*, *J* = 7.0, *Me*–C(4)); 1.40 (*d*, *J* = 6.7, *Me*–C(7)); 3.50–3.62 (*m*, H–C(4)); 3.67–3.80 (*m*, H–C(7)); 3.81 (*s*, CO_2Me); 6.81 (*dd*, *J* = 3.4, 1.4, H–C(5)); 7.32–7.54 (*m*, 5 arom. H); selected signals attributed to the minor isomer **19**: 0.91 (*d*, *J* = 6.9, Me–C(4)); 1.35 (*d*, *J* = 6.9, Me–C(7)); 3.45–3.63 (*m*, H–C(4)); 3.62–3.77 (*m*, H–C(7)); 3.78 (*s*, CO_2Me). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 18.8, 19.1 (*Me*–C(4,7)); 28.6, 29.2 (C(4,7)); 52.0 (CO_2*Me*); 120.6 (C(3a)); 125.5, 128.1, 129.6 (5 arom. C); 131.3 (C(6)); 134.4 (arom. C); 136.7 (C(7a)); 139.6 (C(5)); 154.2 (C(2)); 166.3 (*C*O_2Me). EI-MS (70 eV): 299 (96, M^+), 284 (100), 268 (15), 252 (50), 240 (80), 225 (78), 180 (55), 121 (38), 77 (44). Anal. calc. for $C_{17}H_{17}NO_4$: C 68.22, H 5.72, N 4.68; found: C 68.47, H 5.80, N 4.64.

*(4*R*,6*R*,7*R*)- and (4*R*,6*S*,7*R*)-6-Acetyl-3-(4-chlorophenyl)-2,3,4,5,6,7-hexahydro-4,7-dimethyl[1,3]benzoxazole-2-one* (**25** and **26**). The reaction between **6c** (0.62 g) and methyl vinyl ketone (**15**) (0.35 g) at 150° for 3 h gave a mixture of **25**/**26** (73:27), which was purified by CC (hexane) to yield 0.48 g (60%) of **25** as a yellow oil. R_f 0.29 (hexane/AcOEt 7:3). IR (film): 1768, 1711, 1495, 1376, 975. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6.9, Me–C(4)); 1.05 (*d*, *J* = 6.8, Me–C(7)); 1.63–1.70 (*m*, 1 H–C(5)); 2.04–2.25 (*m*, 1 H–C(5)); 2.24 (*s*, MeC=O); 2.76–2.84 (*m*, H–C(4)); 3.03 (*ddd*, *J* = 12.6, 5.4, 2.4, H–C(6)); 3.16–3.26 (*m*, H–C(7)); 7.22–7.31 (*m*, 2 arom. H); 7.40–7.50 (*m*, 2 arom. H); selected signals attributed to the minor isomer **26**: 0.74 (*d*, *J* = 6.7, Me–C(4)); 1.17 (*d*, *J* = 6.7, Me–C(7)); 1.33–1.45 (*m*, H–C(5)); 2.26 (*s*, MeCO); 2.54–2.63 (*m*, H–C(6)); 2.82–2.97 (*m*, H–C(4)); 3.00–3.14 (*m*, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.7 (*Me*–C(7)); 17.9 (*Me*–C(4)); 24.0 (C(4)); 25.7 (C(7)); 27.9 (C(5)); 28.3 (*Me*C=O); 46.3 (C(6)); 124.1 (C(3a)); 126.9, 129.4, 132.1, 133.7 (6 arom. C); 137.1 (C(7a)); 153.9 (C(2)); 207.5 (Me*C*=O); selected signals attributed to the minor isomer **26**: 14.2 (*Me*–C(7)); 18.4 (*Me*–C(4)); 24.5 (C(4)); 26.4 (C(6)); 28.4 (C(7)); 30.9 (*Me*C=O); 46.9 (C(5)); 124.3 (C(3a)); 128.9, 129.6, 129.9, 137.5 (6 arom. C); 144.6 (C(7a)); 154.9 (C(2)); 208.0 (Me*C*=O). EI-MS (70 eV): 321 (27, $[M+2]^+$), 319 (80, M^+), 304 (4), 276 (10), 249 (100), 232 (42), 166 (20), 138 (22), 111 (23), 95 (33). Anal. calc. for $C_{17}H_{18}ClNO_3$: C 63.85, H 5.67, N 4.38; found: C 64.00, H 5.57, N 4.37.

*(4*R*,6*R*,7*R*)- and (4*R*,6*S*,7*R*)-6-Acetyl-3-(3-chlorophenyl)-2,3,4,5,6,7-hexahydro-4,7-dimethyl-6-[(4-nitrobenzoyl)oxy][1,3]benzoxazol-2-one* (**29** and **30**). The reaction between **6b** (0.62 g) and (1-acetylvinyl) 4-nitrobenzoate (**16**) (1.17 g) at 150° for 8 h gave a mixture of **29**/**30** (51:49), which was separated to yield 0.46 g (38%) of **29** and 0.35 g (29%) of **30** as pale yellow crystals (CH_2Cl_2/hexane 1:1).

Data of **29**: R_f 0.61 (hexane/AcOEt 7:3). M.p. 232–233°. IR (KBr): 1766, 1721, 1591, 1523, 1483, 1348, 1280, 1099. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.64 (*d*, *J* = 7.2, Me–C(4)); 1.16 (*d*, *J* = 7.0, Me–C(7)); 2.22 (*s*, MeC=O); 2.56 (br. *d*, *J* = 15.6, 1 H–C(5)); 2.68 (*dd*, *J* = 15.6, 6.6, 1 H–C(5)); 2.97–3.09 (*m*, H–C(4)); 3.23 (*q*, *J* = 7.0, H–C(7)); 7.25–7.43 (*m*, 4 arom. H); 8.18–8.45 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 15.3 (*Me*–C(7)); 18.1 (*Me*–C(4)); 24.1 (C(4)); 24.6 (*Me*C=O); 28.7 (C(5)); 34.9 (C(7)); 88.0 (C(6)); 123.1 (C(3a)); 123.8; 123.9; 126.0; 128.7; 130.6; 131.1; 134.1; 135.0; 135.1; 135.3; 151.0 (C–NO_2); 154.5 (C(2)); 164.2 (Ar*C*=O); 203.0 (Me*C*=O). EI-MS (70 eV): 486 (0.5, $[M+2]^+$), 484 (2, M^+), 319 (43), 317 (100), 304 (25), 302 (79), 276 (18), 274 (50), 262 (16), 260 (47), 150 (8), 121 (6). Anal. calc. for $C_{24}H_{21}ClN_2O_7$: C 59.45, H 4.37, N 5.78; found: C 59.39, H 4.48, N 5.71.

Data of **30**: R_f 0.58 (hexane/AcOEt 7:3). M.p. 230–231°. IR (KBr): 1764, 1723, 1589, 1528, 1480, 1352, 1277, 1097. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.79 (*d*, *J* = 6.7, Me–C(4)); 1.16 (*d*, *J* = 7.0, Me–C(7)); 2.00 (*dd*, *J* = 15.0, 10.4, 1 H–C(5)); 2.24 (*s*, MeC=O); 2.49–2.61 (*m*, H–C(4)); 2.80 (*ddd*, *J* = 15.0, 5.6, 1 H–C(5)); 3.21 (*q*, *J* = 7.0, H–C(7)); 7.10–7.40 (*m*, 4 arom. H); 8.18–8.46 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 15.1 (*Me*–C(7)); 17.6 (*Me*–C(4)); 24.0 (C(4)); 24.7 (*Me*C=O); 31.5 (C(5)); 35.0 (C(7)); 87.7 (C(6)); 123.1 (C(3a)); 123.6; 124.0; 125.9; 128.6; 130.6; 131.0; 134.0; 135.3; 135.7; 136.0; 151.2 (C–NO_2); 154.7 (C(2)); 163.8 (Ar*C*=O); 202.9 (Me*C*=O). EI-MS (70 eV): 486 (0.4, $[M+2]^+$), 484 (2, M^+), 319 (40), 317 (100), 304 (22), 302 (66), 276 (18), 274 (50), 262 (15), 260 (46), 150 (10), 121 (7). Anal. calc. for $C_{24}H_{21}ClN_2O_7$: C 59.45, H 4.37, N 5.78; found: C 59.47, H 4.52, N 5.69.

*(6*R*,7*R*)- and (6*R*,7*S*)-6-Acetyl-2,3,4,5,6,7-hexahydro-7-methyl-6-[(4-nitrobenzoyl)oxy]-3-phenyl[1,3]benzoxazol-2-one* (**31** and **32**). The reaction between **4a** (0.59 g) and (1-acetylvinyl) 4-nitrobenzoate (**16**) (0.61 g, 2.6 mmol) at 120° for 8 h gave a mixture of **31**/**32** (80:20), which was separated to yield 0.56 g (60%) of

31 as colorless crystals. R_f 0.61 (hexane/AcOEt 7:3). M.p. 145–146° (CH_2Cl_2/hexane, 7:3). IR (KBr): 1767, 1718, 1522, 1397, 1353, 1277, 1081, 715. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.16 (*d*, *J* = 7.0, Me–C(7)); 2.20–2.45 (*m*, 2 H–C(4), 1 H–C(5)); 2.25 (*s*, MeC=O); 2.70–2.84 (*m*, 1 H–C(5)); 3.18–3.32 (br. *q*, *J* = 7.0, H–C(7)); 7.28–7.53 (*m*, 5 arom. H); 8.20–8.42 (*m*, 4 arom. H); selected signals attributed to the minor isomer **32**: 1.32 (*d*, *J* = 7.0, Me–C(7)); 2.29 (*s*, MeC=O); 3.47–3.51 (*m*, H–C(7)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.9 (*Me*–C(7)); 17.1 (C(4)); 21.8 (C(5)); 24.8 (*Me*C=O); 34.9 (C(7)); 88.0 (C(6)); 119.4 (C(3a)); 123.9; 124.8; 127.8; 129.5; 131.0; 131.5; 133.9; 135.8; 151.1 (C–NO_2); 154.3 (C(2)); 163.7 (Ar*C*=O); 203.1 (Me*C*=O). EI-MS (70 eV): 436 (6, M^+), 269 (100), 254 (31), 226 (96), 201 (14), 150 (70), 120 (13), 77 (15). Anal. calc. for $C_{23}H_{20}N_2O_7$: C 63.30, H 4.62, N 6.42; found: C 63.49, H 4.60, N 6.26.

Single-Crystal X-Ray Crystallography. Crystals of **11** and **13** were obtained from CH_2Cl_2/hexane 7:3, and from $CHCl_3$/hexane 1:1, respectively, and were mounted on glass fibers. Crystallographic measurements were performed on a *Siemens P4* diffractometer using Mo K_α radiation (graphite crystal monochromator, λ = 0.71073 Å) at r.t. Three standard reflections were monitored periodically; they showed no change during data collection. Unit-cell parameters were obtained from least-squares refinement of 26 reflections in the range $2 < \theta < 20°$. Intensities were corrected for *Lorentz* and polarization effects. No absorption correction was applied. Anisotropic temperature factors were introduced for all non-H-atoms. H-Atoms were placed in idealized positions and their atomic coordinates refined. Unit weights were used in the refinement. Structures were solved using the *SHELXTL* [28] program on a personal computer.

Data for **11**: Formula: $C_{19}H_{19}NO_6$; molecular weight: 357.35; cryst. size: 0.16 × 0.48 × 0.60 mm; cryst. syst.: monoclinic; space group: *C*2/c; unit-cell parameters: *a* 28.894(3), *b* 5.978(2), *c* 22.641(2) (Å); α 90, β 114.443(6), γ 90 (deg); *V* = 3560(2) (Å^3); temp. (K): 293 (2); *Z:* 8; D_x = 1.333 mg/m^3; absorption coefficient: 0.100 mm^{-1}; θ scan range: 1.55–27.00 (deg); No. of reflections collected: 4923; No. of independent reflections: 3888; No. of observed reflections: 3854; *R:* 0.0537; *wR* = 0.1392; *s:* 1.029.

Data for **13** · $CHCl_3$: Formula: $C_{20}H_{20}Cl_4N_2O_4$; molecular weight: 494.18; cryst. size: 0.2 × 0.4 × 0.85 mm; cryst. syst.: triclinic; space group: P-1; unit-cell parameters: *a* 9.467(2), *b* 11.1261(14), *c* 11.6520(11) (Å); α 76.308(9), β 76.538(10), γ 69.412(12) (deg); *V* = 1101.1(2) (Å^3); temp. (K): 293 (2); *Z:* 2; D_x = 1.491 mg/m^3; absorption coefficient: 0.567 mm^{-1}; θ scan range: 1.82–28.00 (deg); No. of reflections collected: 6178; No. of independent reflections: 5227; No. of observed reflections: 5182; *R:* 0.0663; *wR* = 0.1780; s: 1.084.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the *Cambridge Crystallographic Data Centre*, as deposition No. CCDC-168422, for **11**, and CCDC-168421, for **13**. Copies of the data can be obtained, free of charge, on application to the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

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