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Synthesis and highly selective Diels–Alder cycloadditions of the new dienes *N*-substituted 2,3,5,6-tetrahydrobenzoxazol-2-ones

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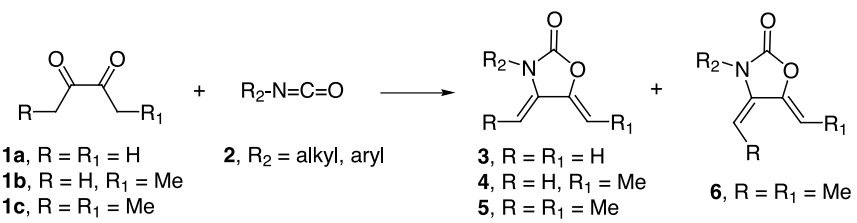
Abstract—The synthesis of the new dienes *N*-substituted 2,3,4,5-tetrahydrobenzoxazol-2-ones **8a**–**8c** is described, through a one-step convergent process from 1,2-cyclohexanedione (**7a**) and the corresponding isocyanates **2a**–**2c**. The presence of electron-donor substituents in the aryl ring of the isocyanate gave rise to the exclusive formation of the captodative olefins **10**. Diene **8a** proved to be reactive and stereoselective in Diels–Alder additions with a cyclic olefin. The reaction with acetylenic dienophiles yielded the 2,3-dihydrobenzoxazol-2-ones **21** and **24**, as the products of sequential [4+2] cycloaddition and retro-Diels–Alder reactions. Methyl vinyl ketone (**22**) underwent regio- and stereoselective tandem Diels–Alder and Michael additions to give propellane **29a**. Evidence of an endo π-pyramidalization of the central double bond of adduct **19** would rationalize the exo stereoselection in the formation of **29a**. The regioselectivity in these reactions has been rationalized in terms of FMO theory by ab initio calculations.

1. Introduction

1,3-Conjugated cyclic dienes have been widely used as privileged molecular systems for evaluating the stereospecificity, the *endo*/*exo* stereoselectivity, and π-facial control, among other features, in Diels–Alder cycloadditions.[1] In particular, heteroatom-substituted 1,3-cyclohexadienes have been found to improve the reactivity, stereoselectivity, and regioselectivity of intermolecular [4+2] cycloadditions.[2] This advantageous behavior has allowed their use as attractive and efficient synthons in organic synthesis.[3]

We have described a highly convergent synthesis of the novel *N*-substituted outer-ring dienes of 2-oxazolidinones **3** (Scheme 1).[4] The use of the unsymmetrical α-diketone **1b** led to the regio- and stereoselective formation of dienes **4**.[5] The presence of the methyl group enhanced the reactivity and regioselectivity of the Diels–Alder reaction with unsymmetrical olefins. It was noteworthy that a high *endo* stereoselectivity was also observed. When the symmetric α-diketone **1c** was used, a mixture of **5**-(4*Z*,5*Z*)/**6**-(4*E*,5*Z*) isomers was isolated, being isomer **6** the major component.[6] The presence of the *E* methyl group in the diene moiety of the latter had a significant impact on the stereoselectivity and regioselectivity in the addition toward diverse dienophiles.

The synthesis of this kind of 2-oxazolidinone dienes containing the conjugated diene inside a five- or six-membered ring would provide new insight about the factors that control not only the stereo- and regioselectivity in Diels–Alder additions of cyclic dienes, but also the performance of our method for diene formation. Therefore,



1a, R = R$_1$ = H
1b, R = H, R$_1$ = Me
1c, R = R$_1$ = Me

2, R$_2$ = alkyl, aryl

3, R = R$_1$ = H
4, R = H, R$_1$ = Me
5, R = R$_1$ = Me

6, R = R$_1$ = Me

Scheme 1.

Keywords: Tetrahydrobenzoxazol-2-ones; dienes; Diels–Alder; π-pyramidalization; Michael addition; propellanes.

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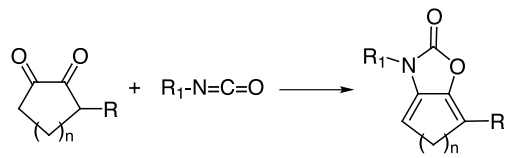


7a, R = H, n = 2 **2**, R_1 = alkyl, aryl **8**, R = H, n = 2
7b, R = Me, n = 1 **9**, R = Me, n = 1

Scheme 2.

we have intended the preparation of dienes **8** and **9** from α-diketones **7a** and **7b** with isocyanates **2** (Scheme 2), assessing the strain caused by the ring size during the intramolecular cyclization when the 1,3-oxazolidin-2-one ring is formed.[5] An evaluation of the regio- and stereoselectivity of the prepared dienes in Diels–Alder additions toward a series of dienophiles was also carried out, and the results are described herein.

2. Results and discussion

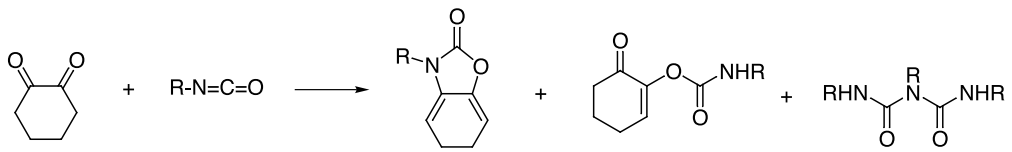
2.1. Synthesis of dienes 8a–8c

When the condensation of α-diketone **7a** with isocyanate **2a** was carried out, under similar reaction conditions to those previously used for the preparation of dienes **3** and **4**, mixtures of three different products were formed (Scheme 3). Table 1 summarizes ratios and yields of the mixtures of diene **8a**,[7] enone **10a**, and carbamoyl urea **11a** obtained after purification by column chromatography. It is noteworthy to see that the proportion of the products is mainly modified by three factors: (a) the number of molecular equivalents of the isocyanate, (b) temperature, and (c) the dehydrating agent. Only the presence of an excess of **2a** leads to the formation of diene **8a** (Table 1, entries 1 and 2). The increase of the reaction time and temperature does not produce a significant change in favor of the desired diene (Table 1, entries 2–4). Even though lithium carbonate has been found to be the optimum dehydrating agent for diene formation,[4] it was interesting to see that molecular sieves (4 Å) improved the yield of diene **8a** in particular detriment of the urea **11a** (Table 1, entry 2 vs 5).

Under these optimal conditions, derivatives **8b** and **8c** were prepared in similar fair yields, and also isolated along with the corresponding cyclohexenones **10b** and **10c**,[8] and the carbamoyl ureas **11b** and **11c** (Table 1). Carbamoyl ureas (biurets) **11** have been previously reported as by-products in the preparation of urethanes,[9] forming metallacycles with palladium and indium,[10] and they have been prepared by treating carbanilates with a base.[11]

The isolation of enones **10**, which could also be considered as cyclic captodative olefins,[7,12] represents additional support of the mechanism proposed earlier for the formation of dienes **3**–**6**, where a carbamate anion intermediate **12a** was postulated (Scheme 4).[5,6] The isocyanate undergoes addition from the base-promoted enolate of 1,2-diketone **7a**, to yield **12a**. This may lead to hemiaminal **14** (some analogous hemiaminals have been isolated and characterized)[5] by intramolecular cyclization, which can lose a molecule of water by the presence of the dehydrating agent to give the corresponding diene **8**. If the intramolecular cyclization is partially or totally inhibited, the protonation of **12a** could take place providing the observed enone **10**.

To favor the intramolecular cyclization and the formation of the diene, we used isocyanates with electron-releasing



7a

2a, R = Ph
2b, R = C_6H_4*p*-Cl
2c, R = C_2H_4Cl
2d, R = C_6H_4*p*-Me
2e, R = C_6H_4*p*-MeO

8a, R = Ph
8b, R = C_6H_4*p*-Cl
8c, R = C_2H_4Cl

10a, R = Ph
10b, R = C_6H_4*p*-Cl
10c, R = C_2H_4Cl
10d, R = C_6H_4*p*-Me
10e, R = C_6H_4*p*-MeO

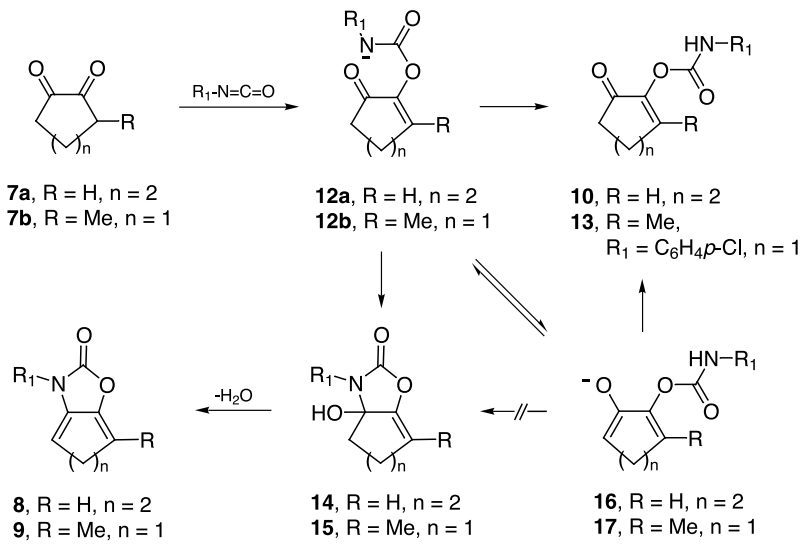
11a, R = Ph
11b, R = C_6H_4*p*-Cl
11c, R = C_2H_4Cl

Scheme 3.

Table 1. Condensation of **7a** with isocyanates **2a**–**2e**

Entry[a]	**2** (mol equiv.)	Dehydrating agent[b]	*T* (°C)	*t* (h)	**8** (%)[c]	**10** (%)[c]	**11** (%)[c]
1	**2a** (1.0)	Li_2CO_3	25	12	0	50	30
2	**2a** (2.6)	Li_2CO_3	25	12	26	22	40
3	**2a** (2.6)	Li_2CO_3	25	24	24	23	37
4	**2a** (2.6)	Li_2CO_3	50	12	20	29	37
5	**2a** (2.6)	Molecular sieves (4Å)	25	12	40	31	19
6	**2b** (2.6)	Molecular sieves (4Å)	25	12	40	30	24
7	**2c** (2.6)	Molecular sieves (4Å)	25	12	35	35	20
8	**2d** (2.6)	Molecular sieves (4Å)	25	12	0	77	0
9	**2e** (2.6)	Molecular sieves (4Å)	25	12	0	82	0

[a] Dioxane, Et_3N (1.94 mol equiv.), under N_2 atmosphere.
[b] Li_2CO_3 (1.2 mol equiv.); 0.3 g of molecular sieves.
[c] After column chromatography and recrystallization.



Scheme 4.

groups in the aromatic ring, **2d** and **2e**. In principle, the effect of the substituent R_1 in the intermediate **12a** should increase the nucleophilicity of the carbamide, improving the attack to the carbonyl group to give **14**.[4] In contrast to the expected behavior, isocyanates **2d** and **2e** gave rise to the enones **10d** and **10e**, respectively, as single products in good yields (entries 8 and 9, Table 1). Probably, when the *N*-substituent R_1 in the isocyanate has a stronger electron-donating effect, the carbamide species **12a** becomes a stronger basis as well, hence the abstraction of an α-proton of the enone moiety might be favored, leading to the conjugate enolate **16** (Scheme 4). This intermediate will then be unable to undergo intramolecular cyclization to the hemiaminal **14**, and consequently will fail to yield the wanted diene **8**. This hypothesis would support the fact that no carbamoyl ureas **11** were obtained, since the formation of **11** needs the presence of water in the reaction medium (generated in the process by dehydration of **14**) for decomposing the isocyanate to the amine R_1-NH_2.[13]

Reaction of 3-methyl-1,2-cyclopentanedione (**7b**) with *p*-chloroisocyanate (**2b**) gives rise exclusively, even under optimum reaction conditions, to the cyclopentenone **13** in 55% yield (Scheme 4). This suggests again that the intramolecular cyclization to give the heterocycle is the cumbersome step and, probably, the rate determining step as well.[5] The structure of **13** was readily established by single-crystal X-ray diffraction (CH_2Cl_2/hexane, 1:1) (Fig. 1).[14] The conformation of the carbamate moiety was out of the plane formed by the cyclopentane enone π system, but it

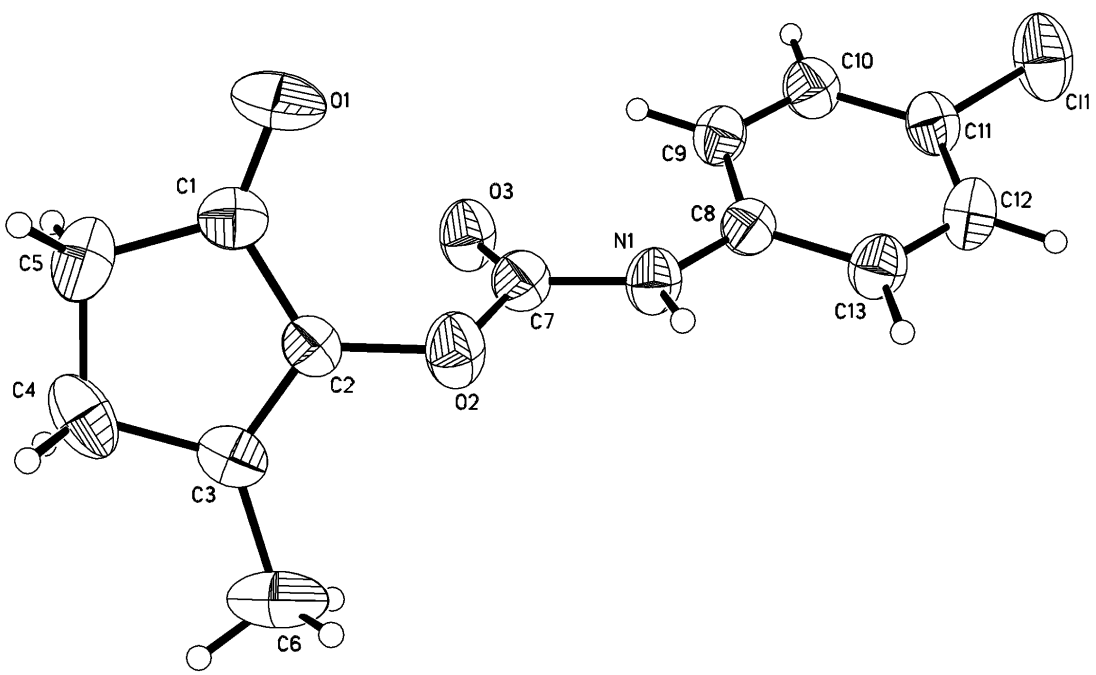
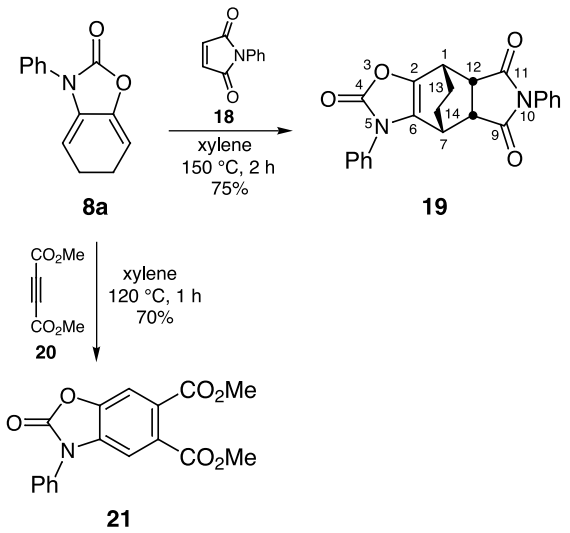


Figure 1. X-Ray structure of compound **13**.



Scheme 5.

retains coplanarity with the aryl ring. This conformation agrees with those shown by crystalline state structures of non-cyclic captodative olefins.[12,15] The crystallographic data also disclosed intermolecular N–H···O=C and Cl···H–C-5 interactions in the crystal lattice.

2.2. Diels–Alder cycloadditions

The reactivity in Diels–Alder additions of dienes **8** was assesed, and compared to that of the non-cyclic dienes **3**–**6**, by using the *N*-phenyl derivative **8a**. Thus, when the latter reacted with *N*-phenylmaleimide (**18**) under thermal conditions only the *endo* adduct **19** was obtained (Scheme 5). The temperature of the reaction was lower (150°C, 2 h) than that employed for diene **3a** (R_2=Ph, Scheme 1) (180°C, 1 h), and the same to that used for addition to diene **6c** (R_2=C_2H_4Cl), even though the reaction time for the latter was longer (3 h). Compound **19** was isolated as colorless crystals (CH_2Cl_2/hexane, 7:3), and its X-ray structure was obtained (Fig. 2).[14]

When the reaction was carried out with dimethyl acetylenedicarboxylate (**20**), the addition took place at 120°C for 1 h (Scheme 5). These conditions were milder than those used for dienes **3a** (180°C, 1 h), **4a** (R_2=Ph) (130°C, 1 h), and **5a**/**6a** (R_2=Ph) (150°C, 3 h). It is interesting to notice that the product of the reaction was not the expected bridged-bicyclic adduct but the 2,3-dihydro-1,3-benzoxazol-2-one **21**, which rises from the cleavage of the ethano bridge of the primary formed adduct by a retro Diels–Alder. The unusual mild conditions of this process can be ascribed to the stabilization gained by generation of the aromatic ring.[16]

The regioselectivity in the Diels–Alder reactions of diene **8a** was investigated with representative dienophiles bearing electron-withdrawing activating groups, such as methyl vinyl ketone (**22**) and methyl propiolate (**23**). The thermal addition of the latter readily occurred to yield a mixture of regioisomers **24**/**25** (69:31), favoring the *para* orientation (with respect to the nitrogen atom of the heterocycle) (Scheme 6). This ratio is only slightly higher than that obtained with the unsubstituted exocyclic diene **3a** (*para*/*meta*, 60:40)[5] and the (4*Z*,5*Z*)-dimethyl substituted diene **5a** (*para*/*meta*, 62:38),[6] but lower than that observed for the (4*E*,5*Z*)-dimethyl diene **6a** (*para*/*meta*, 92:8). Isomer **24** was isolated by column chromatography as a white solid in 63% yield, and characterized by NMR spectroscopy. In contrast to the last three dienes, where the [4+2] adducts were isolated, isomers **24**/**25** were found to be the corresponding aromatic rings, as previously observed for dienophile **20**. The aromatization of the ring could also be facilitated by electronic destabilizing interactions inherent to a bicyclo[2.2.2]octadiene, and angular bicyclic strain generated by the tetrasubstituted double bond of the precursor adducts **26**.[17]

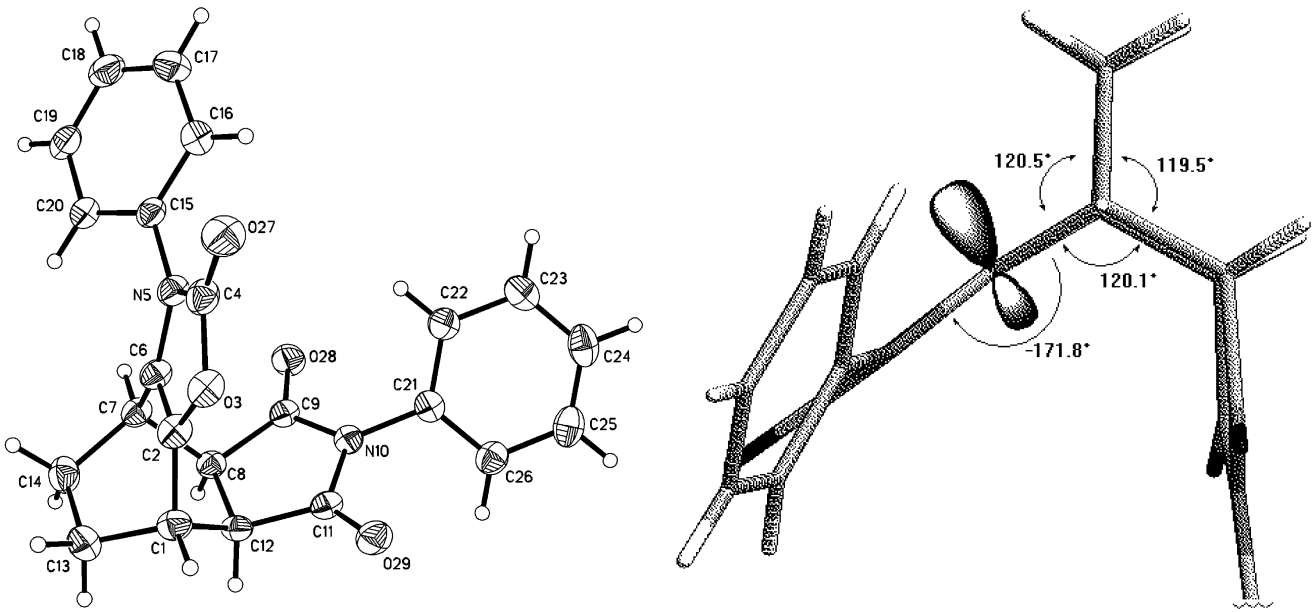
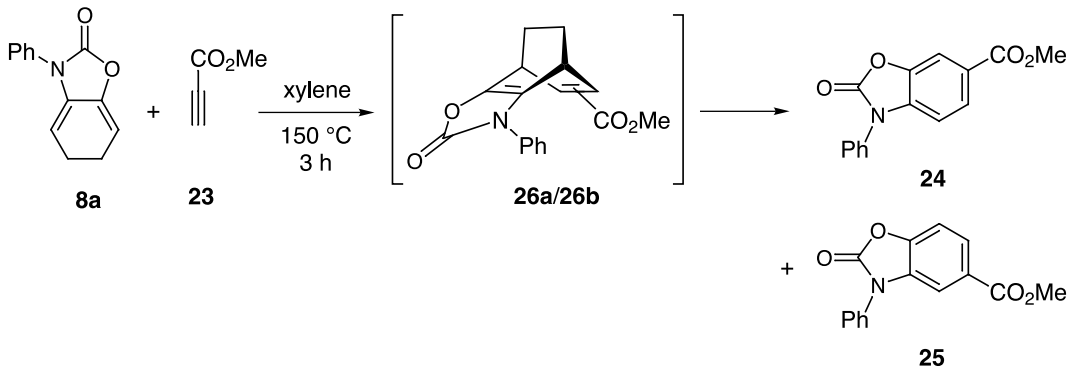


Figure 2. X-Ray structure and view of compound **19**, showing the C-2/C-6 double bond interplanar angle, and dihedral angles for the bicyclo[2.2.2]octene moiety (average values of both faces).



Scheme 6.

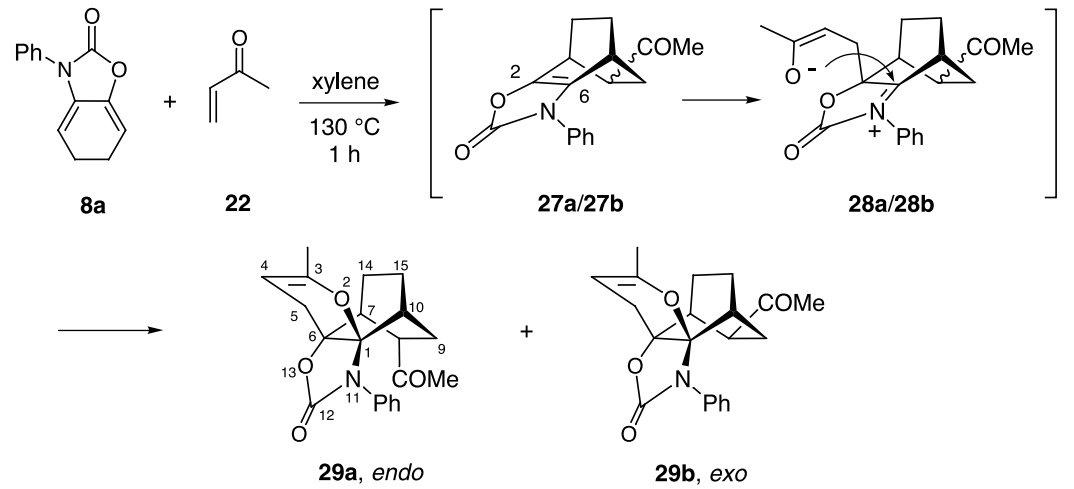
2.3. Tandem Diels–Alder/Michael additions and π-pyramidalization

When the Diels–Alder reaction was carried out with dienophile **22** (2 mol equiv.) an unexpected mixture of propellanes **29a/29b** (90:10) was furnished (Scheme 7). Although in this case it was not possible to assign unequivocally the stereochemistry of the minor isomer, the ^{1}H NMR analysis suggested it to be the propellane derivative coming from the *exo* adduct. The structure of the major isomer, which was isolated as colorless crystals by silica gel column chromatography (hexane), was established by X-ray crystallography (Fig. 3).[14] Compounds **29a/29b** were likely formed by cascade reactions, starting with the formation of the expected [4+2] adducts **27a/27b** (Scheme 7). These have an electron-rich and, probably also, strained tetrasubstituted double bond, as mentioned above for intermediates **26**. This bond behaves as a Michael donor in a conjugate addition to a second molecule of **22** to give zwitterions **28a/28b**.[18] Cyclization of these species completes the tandem Diels–Alder/Michael additions of diene **8a** towards olefin **22**. Even when just 1 mol equiv. of **22** was used, the main product was a mixture of epimers **29**. Low temperatures led to a quite low conversion of starting materials, with the presence of **29** along with polymerization of **22**, due to the longer reaction times.

The non-concerted mechanism proposed above for the last step in the propellane formation was supported by evidence provided on 4-oxazolin-2-ones, which have an analogous structure to that of intermediate **27**.[18] Thus, 4,5-dimethyl-3-phenyl-4-oxazolin-2-one reacts with **22** to give the 1,4-addition product, as suggested for intermediate **28**. However, a formal concerted hetero Diels–Alder addition cannot be completely ruled out.[19]

On the other hand, it is noteworthy that the formation of the dihydropyrane ring was regioselective to give propellanes **29a** and **29b**. Based on the proposed mechanism, this means that the 1,4-addition of the C-2/C-6 double bond of cycloadducts **27** towards the Michael acceptor **22** took place on carbon C-2. This preference could be explained by the polarization of the double bond towards carbon C-2, due to the higher electron-releasing effect of the nitrogen lone pair, in comparison to the oxygen atom of the heterocycle, as supported by an FMO study of analogous 4-oxazolin-2-ones.[18]

As shown by the X-ray structure of **29a**, the Michael addition towards the second molecule of **22** was found to take place onto the *exo* face (the opposite face of the ethano bridge bearing the acetyl group) of the bicyclic framework of **27**. This stereoselection could be attributed to steric hindrance of the acetyl group in the *endo* face, or to geometric constraints.[20] However, it could also be associated to a π-anisotropy of the double bond, increasing the electron density on the *exo* face.[1j,21] This hypothesis implicates a deviation from planarity for the double bond,



Scheme 7.

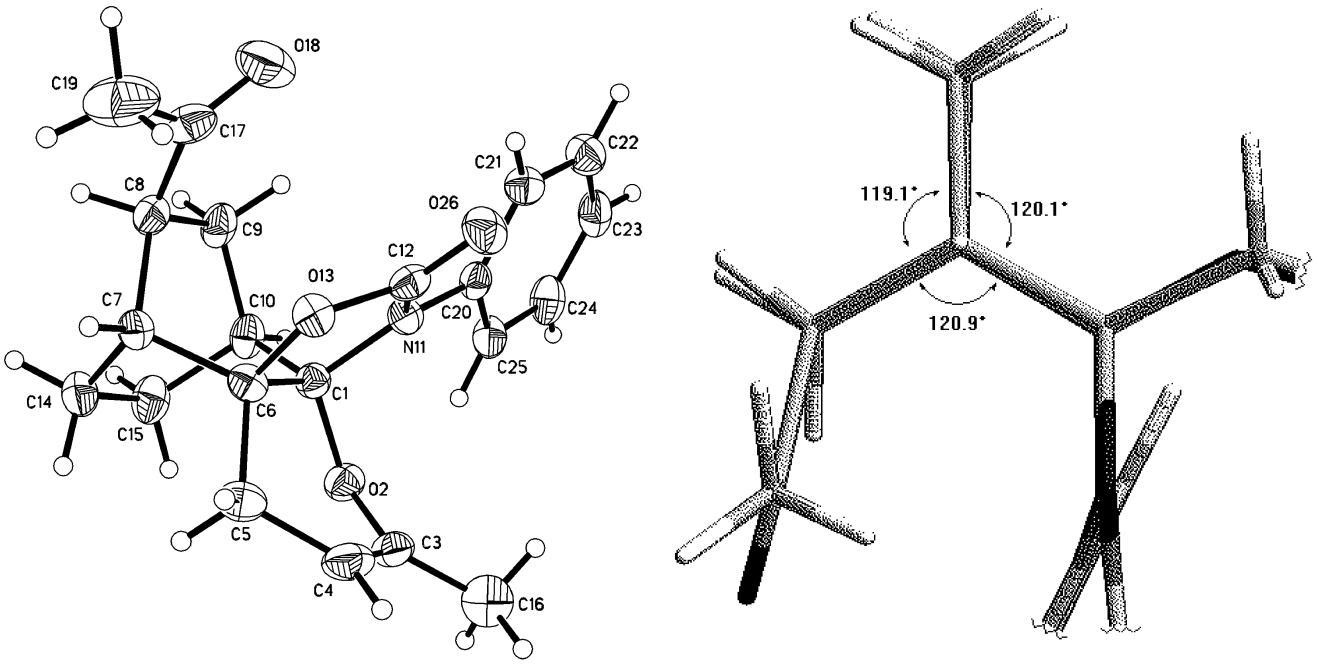


Figure 3. X-Ray structure of propellane **29a**, and a view of the dihedral angles for the bicyclo[2.2.2]octane moiety (average values of both faces).

giving rise to an *endo* pyramidalization.[22] In adduct **19**, which has an analogous structure to that of the nonisolated adduct **27**, the tetrasubstituted central C-2/C-6 double bond exhibits a π-distortion by ca. 8° from planarity with tilting occurring toward the *endo* face (Fig. 2). This deviation is appreciable for a bicyclo[2.2.2]octene, since an angle deviation from planarity in the range 3–23° has been determined from crystallography data for norbornene and bicyclo[2.2.2]octene frameworks, and in *syn*-sesquinorbornenes and related molecules.[1i,j,21b,23]

The observed olefinic pyramidalization of **19** occurred contrasterically, since the oxazolidin-2-one ring is tilted toward the *N*-phenylmaleimide ring. Electronic factors are hence predominant with respect to the steric ones, and they might be associated to hyperconjugative interactions between the π bond and the rest of the bicyclo[2.2.2]octane sigma skeleton, which can also be viewed as a puckered cyclohexane ring.[21] The stereochemistry of the *N*-phenylmaleimide moiety should be on the origin of the electron density polarization of this cyclohexane ring, promoting in consequence the π-anisotropy of the double bond toward the *exo* face.[22a,24] Therefore, the stereoselective Michael addition on the *exo* face of the likely intermediate **27**, leading to propellane **29a**, parallels the pyramidalization of the double bond.[22d,25]

In contrast with the bicyclo[2.2.1]hept-2-ene derivatives,[24c] the ethano bridges in **19** are not tilted away from the endocyclic C-2/C-6 double bond (Fig. 2). Furthermore, the ethano bridges in **29a** are not tilted either (Fig. 3), in spite of the presence of the vicinal propellane moiety, and the possibly different perturbation of the heterocycles on the puckered cyclohexane ring.

The *endo* selectivity shown by diene **8a** with dienophiles such as **18** and **22** under thermal conditions is probably due to secondary orbital interactions (SOI),[26] which stabilize this transition state preferentially, in spite of the presence of the *N*-phenyl ring. The latter appears to adopt an orthogonal conformation with respect to the heterocyclic ring in the diene,[5] and, in principle, it could increase the steric repulsion when the dienophile approach is *endo* (Fig. 4). On the other hand, the ethano bridge could generate destabilizing steric interactions in the *exo* approach,[27] favoring the *endo* adduct, as well as the SOI.[6] This stereoselection is in agreement with the thermal addition of 1,3-cyclohexadiene to similar dienophiles.[28]

From the FMO theory viewpoint, the relative higher reactivity of diene **8a** with respect to the non-cyclic dienes **3a**, **4a**, and **5a/6a** would be accounted for on the basis of relative energies of the corresponding HOMOs, when the

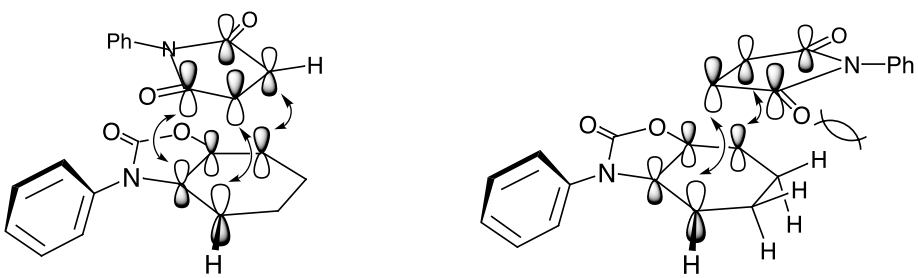
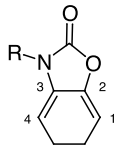
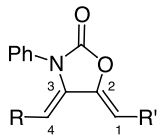


Figure 4. *endo* and *exo* Diels–Alder transition states for the addition of diene **8a** to dienophile **18**.

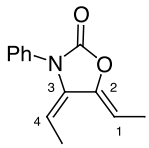
Table 2. Ab initio HF/6-31G* calculations of energies (eV) and coefficientes (C_i) of the frontier molecular orbitals for dienes **3a**, **4a**, **5a**, **6a**, and **8a**–**8c**, and olefin **22**



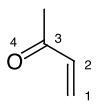
8a, R = Ph
8b, R = C_6H_4*p*-Cl
8c, R = $(CH_2)_2Cl$



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



6a



22

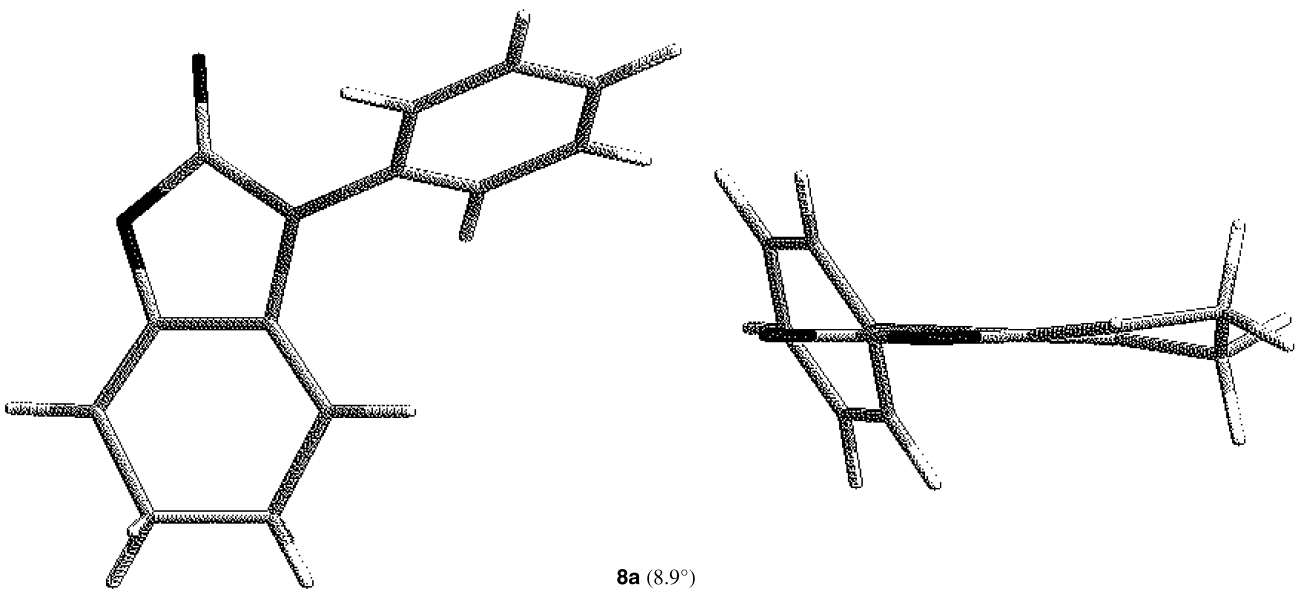
Compd[a]	*E*	HOMO				δC_i[b]	*E*	LUMO				δC_i[b]
		C_1	C_2	C_3	C_4			C_1	C_2	C_3	C_4	
8a	−8.2351	−0.2481	−0.1778	0.2136	0.3169	−0.0688	3.1847	0.2494	−0.2081	−0.2232	0.2494	0.0000
8b	−8.3869	−0.2449	−0.1772	0.2105	0.3129	−0.0680	2.9335	0.1994	−0.1609	−0.1874	0.2049	−0.0055
8c	−8.5276	−0.2617	−0.1933	0.2170	0.3222	−0.0605	3.0258	0.2793	−0.2331	−0.2442	0.2738	0.0055
3a[c]	−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[c]	−8.5804	−0.2679	−0.2084	0.2042	0.3278	−0.0599	3.1448	−0.2861	0.2345	0.2535	−0.2592	0.0269
5a[d]	−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[d]	−8.4601	−0.2154	−0.1571	0.1947	0.2782	−0.0628	3.1983	0.2532	−0.1890	−0.2005	0.2438	0.0094
22[e]	−10.4895	−0.3464	−0.3669	0.0327	0.2213	−0.0205	2.9222	0.3109	−0.2069	−0.2809	0.2549	0.1040

These are the values of the $2p_z$ coefficients, the relative $2p_z$ contributions and their δC_i are analogous.
[a] For the most stable planar *s-cis* conformation for olefin **22**.
[b] Carbon 1–carbon 4 for the dienes; carbon 1–carbon 2 for the olefin.
[c] Refs. 5,6.
[d] Ref. 6.
[e] Ref. 15a.

interaction is under normal electron demand,[29] which is indeed our case.[5,6] Frontier molecular orbitals of diene **8a** were calculated using ab initio HF theory, and employing the 6-31G* basis set.[30] The energy levels derived from these and previous calculations for the above mentioned dienes are summarized in Table 2. Thus, the more energetic HOMO of diene **8a** with respect to the other dienes would explain its higher reactivity.

The increase in energy of the HOMO of diene **8a** may be due to the hyperconjugative effect of the two methylenes forming the six-membered ring,[31] as suggested for the methyl groups in the substituted dienes **4** and **5/6**.[5,6] In fact, the geometry of **8a** was optimized (HF/6-31G*), and a dihedral angle of 9.5° for the diene moiety was calculated (HF/6-31G*) (Fig. 5). In this nonplanar geometry, two of the vicinal protons of the methylene groups adopt a pseudo-axial conformation, possibly due to the strain generated by the eclipsed methylenes when the cyclohexadiene becomes planar.[32] Therefore, it is likely that hyperconjugation between the pseudoaxial methylene protons and the diene moiety will be more efficient in the nonplanar conformation.

The relative magnitude of the coefficient of the diene



8a (8.9°)

Figure 5. Minimum potential-energy conformation of diene **8a**, showing (in parentheses) the torsion angles of the diene moiety.

terminus C_4 is bigger than that of carbon C_1 in the HOMO of diene **8a**, and for the other dienes as well (Table 2), then the *para* orientation is expected for dienophiles **22** and **23**,[5,6] in agreement with the experiments. The comparable coefficient differences (δC_i) with dienes **3a** and **8a** could explain the also similar regioisomeric ratio obtained when the reaction was carried out with olefin **23**. Nevertheless, the regioselectivity for diene **8a** was strongly improved for olefin **22**, in comparison with diene **3a**. This discrepancy may be rationalized by a larger perturbation found between **8a** and **22**, since the δE HOMOdiene–LUMOdienophile (11.1573 eV) is smaller than that found for **3a** (11.7564 eV).

3. Conclusions

The condensation reaction between the six-membered ring α-diketone **7a** and the corresponding isocyanates **2a**–**2c** gave rise to dienes **8a**–**8c**. The electron demand of the substituent in the isocyanate seems to have an effect on the outcome of diene formation, since isocyanates **2d** and **2e** yielded only the enones **10d** and **10e**, inhibiting the cyclization step that leads to the dienes. The five-membered ring α-diketone **7b** was unable to produce the expected diene **9**, stopping in the enone intermediate **13**, which could be associated to a ring strain effect during the cyclization process.

Both high reactivity and stereoselectivity in thermal Diels–Alder additions were found with symmetric dienophiles. The reaction with acetylenic dienophiles **20** and **23** yielded the 1,3-benzoxazol-2-ones, through a [4+2] addition and a subsequent ethano bridge cleavage. Methyl vinyl ketone (**22**) reacted with **8a** in a highly regio- and stereoselective cycloaddition to furnish not the expected adduct, but propellanes **29a/29b**, through a tandem reaction as well: [4+2] addition and conjugate Michael addition with two molecules of the olefin. The *exo* stereoselection in this process was rationalized in terms of π-anisotropy of the tetrasubstituted double bond C-2/C-6 of adduct **19**, which can be considered as an analogous precursor of **29**. The FMO model was useful to account for the reactivity and regioselectivity observed in these cycloadditions, as a consequence of a high interaction energy between dienes **8** and dienophiles.

4. Experimental

4.1. General

Melting points (uncorrected) were determined with an Electrothermal capillary melting point apparatus. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. ^{1}H (300 MHz) and ^{13}C (75.4 MHz) NMR spectra were recorded on a Varian Gemini-300 instrument, in $CDCl_3$, DMSO-d_6, or acetone-d_6 as solvents and TMS as internal standard. Mass spectra (MS) and high-resolution mass spectra (HRMS) were obtained, in electron impact (EI) (70 eV) mode, on a Hewlett–Packard 5971A and on a Jeol JMS-AX 505 HA spectrometers, respectively. X-Ray analyses were collected on a Siemens P4 diffractometer. Microanalyses were performed by M-H-W Laboratories (Phoenix, AZ), and Centro de Investigaciones Químicas, Universidad Autónoma de Hidalgo (Pachuca, Hgo., Mexico). Analytical thin-layer chromatography was carried out using E. Merck silica gel 60 F_{254} coated 0.25 plates, visualizing by long and short-wavelength UV lamp. Flash column chromatography was performed on a Flash40i of Biotage, Dyax Corp. All air moisture sensitive reactions were carried out under nitrogen using oven-dried glassware. Dioxane, ethyl ether, THF, toluene, and xylene were freshly distilled over sodium, and methylene chloride, ethyl acetate, acetonitrile, and DMSO over calcium hydride, prior to use. Li_2CO_3 and molecular sieves were dried overnight at 120°C prior to use. Triethylamine was distilled over sodium hydroxide. All other reagents were used without further purification.

4.2. General procedure for the preparation of dienes *N*-substituted 2,3,5,6-tetrahydrobenzoxazol-2-ones (8a–8c)

A solution of 1,2-cyclohexanedione (**7a**) (0.4 g, 3.6 mmol) in dry dioxane (3 mL) was added dropwise to a magnetically stirred solution of triethylamine (0.71 g, 7.0 mmol) in dry dioxane (2 mL) containing molecular sieves (4 Å) (0.3 g), at rt under N_2 atmosphere, and the mixture was stirred for 30 min. Then, a solution of the corresponding isocyanate (10.4 mmol) in dry dioxane (2 mL) was added dropwise and stirring was continued for 12 h at rt. The mixture was filtered and the solvent removed under vacuo. The residue was purified by column chromatography over silica gel impregnated with triethylamine (10%) in hexane (hexane/EtOAc, 9:1), (30 g/g of crude), to give dienes **8a**–**8c**.

4.2.1. 3-Phenyl-2,3,5,6-tetrahydrobenzoxazol-2-one (8a). 2-(*N*-Phenylcarbamoyloxy)-2-cyclohexen-1-one (10a). 1-(*N*-Phenylcarbamoyl)-1,3-diphenyl urea (11a). Using the general procedure with 1.24 g of phenyl isocyanate (**2a**) gave 0.30 g (40%) of **8a** as colorless crystals (CH_2Cl_2/hexane, 1:1), 0.25 g (31%) of **10a** as colorless crystals (CH_2Cl_2/hexane, 1:1), and 0.22 g (19%) of **11a** as colorless crystals (CH_2Cl_2/hexane, 1:1). Data of **8a**: R_f 0.55 (hexane/EtOAc, 7:3). Mp 81–82°C [lit.[7] 81–82°C]; IR (KBr): 1779, 1655, 1493, 1408, 1193, 1123, 993, 915, 746 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.33–2.51 (m, 4H, $2CH_2$), 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 or C-6), 21.3 (C-6 or C-5), 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), 66 (35), 64 (32), 51 (13). 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. Data of **10a**: R_f 0.47 (hexane/EtOAc, 7:3). Mp 173–174°C; IR (KBr): 3290, 3050, 1732, 1698, 1594, 1539, 1501, 1440, 1316, 1231, 1139, 1116 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05 (qi, J=6.3 Hz, 2H, H-5), 2.40–2.50 (m, 2H, H-4), 2.55 (t, J=6.3 Hz, 2H, H-6), 6.58 (t, J=4.3 Hz, 1H, H-3), 7.00–7.60 (m, 5H, PhH), 10.57 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 22.4 (C-5), 24.7 (C-4), 37.8 (C-6), 120.0 (C-9), 124.1 (C-11), 128.8 (C-10), 128.9 (C-8), 136.3 (C-3), 144.8 (C-2), 154.1 (NCO_2), 191.2 (C-1); MS (70 eV) 231 (M^+, 16), 151 (11), 140 (15), 91 (100), 65 (9). Anal. calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.93; H, 5.44; N, 5.85. Data of **11a**: R_f 0.43 (hexane/

EtOAc, 7:3). Mp 148–149°C; IR (KBr): 3400–3000, 1709, 1671, 1593, 1516, 1439, 1316, 1262, 1231, 1170, 746, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.04–7.14 (m, 2H, PhH), 7.22–7.45 (m, 10H, PhH), 7.50–7.62 (m, 3H, PhH), 8.92 (br s, 2H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 120.6, 124.4, 128.9, 129.8, 130.1, 136.5, 137.2, 153.1; MS (70 eV) 119 (M^+-212, 100), 93 (50), 91 (55), 64 (42). Anal. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.26; H, 4.94; N, 12.80.

4.2.2. 3-(4-Chlorophenyl)-2,3,5,6-tetrahydrobenzoxazol-2-one (8b). 2-[*N*-(4-Chlorophenyl)carbamoyloxy]-2-cyclohexen-1-one (10b). 1-[*N*-(4-Chlorophenyl)carbamoyl]-1,3-bis(4-chlorophenyl) urea (11b). Using the general procedure with 1.60 g of 4-chlorophenyl isocyanate (**2b**) gave 0.35 g (40%) of **8b** as colorless crystals (CH_2Cl_2/hexane, 1:1), 0.28 g (30%) of **10b** as a white powder (CH_2Cl_2/hexane, 1:1), and 0.36 g (24%) of **11b** as colorless crystals (CH_2Cl_2/hexane, 1:1). Data of **8b**: R_f 0.58 (hexane/EtOAc, 7:3). Mp 123–124°C; IR (KBr): 1780, 1665, 1496, 1359, 1207, 815 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.30–2.52 (m, 4H, $2CH_2$), 4.94–4.97 (m, 1H, H-4), 5.27–5.30 (m, 1H, H-7), 7.34–7.38 (m, 2H, ArH), 7.40–7.46 (m, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 21.2 (C-5 or C-6), 21.3 (C-6 or C-5), 95.5 (C-4), 97.0 (C-7), 126.4 (C-9), 129.6 (C-10), 131.6 (C-11), 132.2 (C-3a), 133.3 (C-8), 142.5 (C-7a), 152.8 (C-2); MS (70 eV) 249 (M^++2, 30), 247 (M^+, 100), 219 (10), 191 (17), 164 (24), 151 (36), 111 (22), 75 (18). Anal. Calcd for $C_{13}H_{10}ClNO_2$: C, 63.04; H, 4.07; N, 5.66. Found: C, 62.89; H, 4.23; N, 5.50. Data of **10b**: R_f 0.41 (hexane/EtOAc, 7:3). Mp 133–134°C; IR (KBr): 3295, 1742, 1670, 1595, 1531, 1490, 1396, 1208, 1108, 1002, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.03–2.15 (m, 2H, H-5), 2.48–2.56 (m, 2H, H-4), 2.56–2.66 (m, 2H, H-6), 6.71 (t, J=4.3 Hz, 1H, H-3), 7.15–7.19 (m, 2H, ArH), 7.27–7.31 (m, 2H, ArH), 8.00 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 22.5 (C-5), 24.8 (C-4), 38.0 (C-6), 119.8 (C-9), 128.7 (C-10, C-11), 136.1 (C-3), 137.6 (C-8), 144.5 (C-2), 151.0 (N*C*O_2), 193.6 (C-1); MS (70 eV) 265 (M^+, 1), 189 (3), 118 (18), 104 (19), 91 (16), 77 (100), 51 (90). Anal. calcd for $C_{13}H_{12}ClNO_3$: C, 58.77; H, 4.55; N, 5.27. Found: C, 58.59; H, 4.77; N, 5.30. Data of **11b**: R_f 0.46 (hexane/EtOAc, 7:3). Mp 168–169°C; IR (KBr): 3500–2900, 1743, 1719, 1678, 1601, 1537, 1496, 1402, 1214, 1108, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.40 (m, 5H, ArH), 7.40–7.46 (m, 2H, ArH), 7.47–7.56 (m, 5H, ArH), 8.84 (br s, 2H, NH); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 121.6, 127.4, 127.7, 128.1, 129.1, 129.7, 130.6, 131.0, 152.7; MS (70 eV) 155 [(M^++2)−281, 45], 153 (M^+-281, 100), 127 (15), 125 (49), 90 (41), 63 (22). Anal. calcd for $C_{20}H_{14}Cl_3N_3O_2$: C, 54.26; H, 3.25; N, 9.66. Found: C, 54.38; H, 3.51; N, 9.86.

4.2.3. 3-(2-Chloroethyl)-2,3,5,6-tetrahydrobenzoxazol-2-one (8c). 2-[*N*-(2-Chloroethyl)carbamoyloxy]-2-cyclohexen-1-one (10c). 1-[*N*-(2-Chloroethyl)carbamoyl]-1,3-bis(2-chloroethyl) urea (11c). Using the general procedure with 1.10 g of 2-chloroethyl isocyanate (**2c**) gave 0.25 g (35%) of **8c** as a white powder (CH_2Cl_2/hexane, 1:1), 0.27 g (35%) of **10c** as colorless crystals (CH_2Cl_2/hexane, 1:1), and 0.20 g (20%) of **11c** as a colorless oil. Data of **8c**: R_f 0.60 (hexane/EtOAc, 7:3). Mp 65–67°C; IR (KBr): 1766, 1701, 1437, 1331, 1255, 1090, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.30–2.46 (m, 4H, $2CH_2$), 3.66–3.74 (m, 2H, CH_2N), 3.76–3.84 (m, 2H, CH_2Cl), 4.83–4.88 (m, 1H, H-4), 5.17–5.23 (m, 1H, H-7); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 21.0 (C-5 or C-6), 21.3 (C-6 or C-5), 39.8 (N*C*H_2), 43.1 (Cl*C*H_2), 93.9 (C-4), 97.0 (C-7), 131.3 (C-3a), 142.6 (C-7a), 154.2 (C-2); MS (70 eV) 201 (M^++2, 3), 199 (M^+, 10), 164 (4), 150 (9), 136 (47), 122 (26), 103 (20), 94 (96), 80 (49), 65 (100), 63 (91). HRMS (70 eV) calculated for $C_9H_{10}ClNO_2$ $[M]^{+\cdot}$: 199.0400. Found: 199.0410. Data of **10c**: R_f 0.43 (hexane/EtOAc, 7:3). Mp 95–97°C; IR (KBr): 3335, 1730, 1690, 1523, 1235, 1175 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.00–2.12 (m, 2H, H-5), 2.45–2.60 (m, 4H, H-4, H-6), 3.50–3.71 (m, 4H, $2CH_2$), 5.57 (br s, 1H, NH), 6.65 (t, J=4.3 Hz, 1H, H-3); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 22.6 (C-5), 24.8 (C-4), 38.1 (C-6), 43.1 (*C*H_2N), 43.5 (*C*H_2Cl), 136.0 (C-3), 144.9 (C-2), 153.9 (N*C*O_2), 192.7 (C-1); MS (70 eV) 215 (M^+-2, 6), 179 (10), 166 (8), 125 (18), 112 (23), 83 (21), 70 (23), 56 (100). Anal. calcd for $C_9H_{12}ClNO_3$: C, 49.67; H, 5.56; N, 6.44. Found: C, 49.79; H, 5.72; N, 6.43. Data of **11c**: R_f 0.32 (hexane/EtOAc, 7:3); IR (film): 3600–3000, 1731, 1678, 1531, 1514, 1173, 1137, 1108, 1002 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.38–4.10 (m, 12H, $6CH_2$), 6.67 (br s, 2H, NH); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 40.7, 41.2, 42.0, 42.7, 43.3, 43.4, 155.5; MS (70 eV) 292 (M^++2, 1), 290 (M^+, 3), 199 (6), 136 (63), 122 (50), 94 (92), 80 (59), 65 (100).

4.2.4. 2-[*N*-(4-Tolyl)carbamoyloxy]-2-cyclohexen-1-one (10d). Using the general procedure with 1.38 g of 4-tolyl isocyanate (**2d**) gave 0.67 g (77%) of **10d** as a colorless oil. R_f 0.58 (hexane/EtOAc, 7:3); IR (film): 3300, 1773, 1712, 1673, 1612, 1519, 1304 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.96–2.06 (m, 2H, H-5), 2.29 (s, 3H, MeAr), 2.42 (dt, J=5.8, 5.3 Hz, 2H, H-4), 2.55 (dd, J=6.9, 6.5 Hz, 2H, H-6), 6.25 (br s, 1H, NH), 6.32 (t, J=4.2 Hz, 1H, H-3), 6.92–6.96 (m, 2H, ArH), 7.03–7.08 (m, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.7 (*C*H_3Ar), 23.0 (C-5), 24.5 (C-4), 37.7 (C-6), 115.3, 119.4, 129.7, 130.7, 136.7 (C-3), 139.2 (C-2), 154.9 (N*C*O_2), 195.6 (C-1); MS (70 eV) 245 (M^+, 96), 230 (5), 127 (70), 90 (100), 63 (12). Anal. calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.13; H, 6.22; N, 5.69.

4.2.5. 2-[*N*-(4-Anisyl)carbamoyloxy]-2-cyclohexen-1-one (10e). Using the general procedure with 1.55 g of 4-anisyl isocyanate (**2e**) gave 0.76 g (82%) of **10e** as a colorless oil. R_f 0.56 (hexane/EtOAc, 7:3); IR (film): 3286, 1775, 1728, 1680, 1510, 1280, 1200, 1150, 1000, 840, 760, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.00–2.08 (m, 2H, H-5), 2.47 (dt, J=5.7, 4.7 Hz, 2H, H-4), 2.55 (dd, J=6.9, 6.3 Hz, 2H, H-6), 3.73 (s, 3H, MeO), 6.67 (t, J=4.1 Hz, 1H, H-3), 6.73–6.85 (m, 2H, ArH), 7.23–7.40 (m, 2H, ArH), 7.88 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 22.4 (C-5), 24.7 (C-4), 38.0 (C-6), 55.3 (*C*H_3O), 114.0 (C-10), 120.5 (C-9), 130.5 (C-8), 136.9 (C-3), 144.5 (C-2), 151.4 (N*C*O_2), 155.8 (C-11), 193.2 (C-1); MS (70 eV) 261 (M^+, 1), 241 (100), 182 (47), 154 (52), 128 (20), 63 (20). Anal. calcd for $C_{14}H_{15}NO_4$: C, 64.34; H, 5.79; N, 5.36. Found: C, 64.30; H, 5.86; N, 5.56.

4.2.6. 2-[*N*-(4-Chlorophenyl)carbamoyloxy]-3-methyl-2-cyclopenten-1-one (13). Using the general procedure for

the preparation of dienes **8a**–**8c**, with 0.4 g (3.6 mmol) of 3-methyl-1,2-cyclopentanedione (**7b**) and 1.60 g of 4-chlorophenyl isocyanate (**2b**), gave 0.52 g (55%) of **13** as colorless crystals (CH_2Cl_2/hexane, 1:1). R_f 0.50 (hexane/EtOAc, 7:3). Mp 170–171°C; IR (KBr): 3273, 3120, 3058, 1762, 1655, 1604, 1541, 1401, 1301, 1208, 1093, 985, 823, 731 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.04 (s, 3H, CH_3), 2.50–2.55 (m, 2H, H-5), 2.57–2.64 (m, 2H, H-4), 7.13–7.16 (m, 2H, ArH), 7.24–7.28 (m, 2H, ArH), 8.53 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 15.3 (CH_3), 28.0 (C-4), 32.5 (C-5), 119.9 (C-9), 128.6 (C-8), 128.7 (C-10), 136.1 (C-11), 145.6 (C-2), 149.9 (C-3), 162.7 (NCO_2), 202.0 (C-1); MS (70 eV) 153 (M^+-112, 100), 125 (37), 112 (44), 90 (26), 69 (15), 63 (14), 55 (15). Anal. calcd for $C_{13}H_{12}ClNO_3$: C, 58.77; H, 4.55; N, 5.27. Found: C, 58.67; H, 4.65; N, 5.28.

4.3. General procedure for the Diels–Alder reaction of dienophiles *N*-phenylmaleimide (18), dimethyl acetylenedicarboxylate (20), methyl vinyl ketone (22), and methyl propiolate (23) with diene 8a

A mixture of diene **8a** (0.53 g, 2.5 mmol), 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 atmosphere, and in the dark. The mixture was stirred and heated until complete reaction. The solvent was removed under vacuum and the residue purified by column chromatography (hexane/EtOAc, 4:1) on silica gel (30 g/g of crude) to give the corresponding adducts.

4.3.1. (1*R,7*R**,8*S**,12*R**)-5,10-Diphenyl-3-oxa-5,10-diazatricyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-2(6)-ene-4,9,11-trione (19).** Using the general procedure with 0.86 g of **18**, and heating at 150°C for 2 h, gave 0.47 g (70%) of **19** as colorless crystals (CH_2Cl_2/hexane, 7:3). Mp 184–185°C. R_f 0.33 (hexane/EtOAc, 7:3). IR (KBr) 1757, 1712, 1595, 1419, 1383, 1190 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50–1.97 (m, 4H, H-13, H-14), 3.20–3.30 (m, 2H, H-8, H-12), 3.86–3.92 (m, 2H, H-1, H-7), 7.07–7.15 (m, 2H, PhH), 7.26–7.53 (m, 8H, PhH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.1 (C-13 or C-14), 25.8 (C-14 or C-13), 31.4 (C-1 or C-7), 32.2 (C-7 or C-1), 44.7 (C-8 or C-12), 45.1 (C-12 or C-8), 123.1, 123.3 (C-6a), 126.2, 127.2, 128.9, 129.3, 129.5, 131.2, 134.0, 137.2 (C-2), 154.2 (C-4), 175.7 (*C*ONPh), 176.3 (*C*ONPh); MS (70 eV) 386 (M^+, 90), 358 (14), 330 (24), 213 (100), 167 (18), 119 (20), 77 (72). Anal. calcd for $C_{23}H_{18}N_2O_4$: C, 71.49; H, 4.70; N, 7.25. Found: C, 71.33; H, 4.84; N, 7.18.

4.3.2. 5,6-Dimethoxycarbonyl-3-phenyl-2,3-dihydrobenzoxazol-2-one (21). Using the general procedure with 0.71 g of **20**, and heating at 150°C for 1 h, yielded 0.61 g (75%) of **21** as a white powder (CH_2Cl_2/hexane, 7:3). Mp 143–145°C. R_f 0.29 (hexane/EtOAc, 7:3). IR (KBr): 1790, 1724, 1505, 1436, 1292, 1260, 985 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.92 (s, 3H, CO_2CH_3), 3.97 (s, 3H, CO_2CH_3), 7.33 (s, 1H, H-4), 7.46–7.63 (m, 5H, PhH), 7.70 (s, 1H, H-7); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 52.8 (CO_2CH_3), 52.9 (CO_2CH_3), 109.5 (C-4 or C-7), 111.2 (C-7 or C-4), 125.2 (C-13), 127.0 (C-5 or C-6), 129.1 (C-15), 130.0 (C-6 or C-5), 130.1 (C-14), 132.7 (C-3a), 133.6 (C-12), 143.6 (C-7a), 152.7 (C-2), 166.5 (CO_2CH_3), 167.5 (CO_2CH_3); MS (70 eV) 327 (M^+, 25), 297 (16), 296 (100), 237 (16), 209 (15), 164 (11), 148 (18), 77 (60). Anal. calcd for $C_{17}H_{13}NO_6$: C, 62.39; H, 4.00; N, 4.28. Found: C, 62.18; H, 3.77; N, 3.96.

4.3.3. 6-Methoxycarbonyl-3-phenyl-2,3-dihydrobenzoxazol-2-one (24). 5-Methoxycarbonyl-3-phenyl-2,3-dihydrobenzoxazol-2-one (25). Using the general procedure with 0.42 g of **23**, and heating at 150°C for 3 h, gave a mixture of **24/25** (69:31), which was purified by column chromatography on silica gel (hexane) to yield 0.47 g (63%) of **24** as a white powder (CH_2Cl_2/hexane, 7:3). Mp 128–129°C [lit.[33] 128–129°C]. R_f 0.40 (hexane/EtOAc, 7:3). IR (KBr) 1803, 1722, 1607, 1482, 1242 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.95 (s, 3H, CO_2CH_3), 7.11 (d, J=8.1 Hz, 1H, H-4), 7.47–7.62 (m, 5H, PhH), 7.94–7.97 (m, 2H, H-5, H-7); signals attributed to minor isomer **25**: 3.91 (s, CO_2CH_3), 7.34 (d, J=8.4 Hz, H-7), 7.74 (d, J=1.8 Hz, H-4); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 52.32 (CO_2CH_3), 108.7 (C-4), 111.5 (C-7), 125.2 (2C-Ph), 125.6 (C-6), 126.3 (C-5), 128.5 (C-Ph), 130.0 (2C-Ph), 133.1 (C-3a or NC-Ph), 135.1 (NC-Ph or C-3a), 142.4 (C-7a), 153.2 (C-2), 166.0 (CO_2CH_3); signals attributed to minor isomer **25**: 52.33 (CO_2CH_3), 110.0 (C-7), 110.7 (C-4), 125.4 (C-3a), 130.2 (C-Ph); MS (70 eV) 269 (M^+, 8), 238 (20), 194 (10), 182 (7), 154 (23), 139 (10), 127 (8), 77 (100). Anal. calcd for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12; N, 5.20. Found: C, 67.17; H, 4.36; N, 5.11.

4.3.4. (1*R,6*R**,7*S**,8*R**,10*R**)-8-Acetyl-3-methyl-2,13-dioxa-11-phenyl-11-azatetracyclo[4.4.3.2^{7,10}.0^{1,6}]tridec-3-en-12-one (29a). (1*R**,6*R**,7*S**,8*S**,10*R**)-8-Acetyl-3-methyl-2,13-dioxa-11-azatetracyclo[4.4.3.2^{7,10}.0^{1,6}]tridec-3-en-12-one (29b).** Using the general procedure with 0.35 g of **22**, and heating at 130°C for 1 h, gave a mixture of **29a/29b** (90:10), which was purified by column chromatography (hexane) to yield 0.57 g (57%) of **29a** as colorless crystals (CH_2Cl_2/hexane, 7:3). Mp 206–208°C. R_f 0.29 (hexane/EtOAc, 7:3). IR (KBr) 1754, 1705, 1602, 1492, 1367, 1177, 768 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.19–1.32 (m, 2H, H-9), 1.56–1.72 (m, 1H, H-15), 1.77–1.88 (m, 4H, CH_3C=, H-15), 1.94–2.12 (m, 1H, H-14), 2.20–2.32 (m, 2H, H-10, H-5), 2.27 (s, 3H, CH_3CO), 2.44–2.56 (m, 2H, H-8, H-5), 2.68–2.72 (m, 1H, H-7), 5.11–5.20 (m, 1H, H-4), 7.18–7.25 (m, 1H, PhH), 7.36–7.43 (m, 2H, PhH), 7.80–7.86 (m, 2H, PhH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 19.25 (CH_3C=), 19.26 (C-5), 20.4 (C-9), 23.9 (C-15), 27.8 (C-14), 27.9 ($COCH_3$), 31.3 (C-10), 38.1 (C-7), 48.9 (C-8), 86.1 (C-6), 96.0 (C-1), 103.6 (C-4), 124.1 (C-Ph), 126.0 (C-Ph), 128.7 (C-Ph), 136.9 (NC-Ph), 152.4 (C-12), 163.1 (C-3), 206.4 ($COCH_3$); MS (70 eV) 283 (M^+-70, 16), 239 (12), 213 (100), 185 (14), 168 (12), 157 (20), 130 (22), 117 (37), 77 (53). Anal. calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.47; H, 6.35; N, 3.94.

4.4. Single-crystal X-ray crystallography

Single-crystal of cyclopentenone **13** was obtained by recrystallization from CH_2Cl_2/hexane, 1:1, and adducts **19** and **29a** from CH_2Cl_2/hexane, 7:3, as colorless crystals. These were mounted in glass fibers. Crystallographic

measurements were performed on a Siemens P4 diffractometer using Mo Kα radiation (graphite crystal monochromator, λ=71073 Å), and at room temperature. 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 $2<2\Theta<20°$. Intensities were corrected for Lorentz and polarization effects. No absorption correction was applied. Anisotropic temperature factors were introduced for all non-hydrogen atoms. Hydrogen atoms were placed in idealized positions and their atomic coordinates refined. Unit weights were used in the refinement. Structures were solved using the SHELXTL[34] program on a personal computer. Data for **13**: Formula: $C_{13}H_{12}ClNO_3$; molecular weight: 265.69; cryst. size: 0.42×0.54×0.94 mm^3; cryst. syst.: orthorhombic; space group: $P2_12_12_1$; unit cell parameters: a=6.709(2), b=9.6397(12), c=19.958(2) (Å); α=90, β=90, γ=90 (deg); V=1290.7(4) (Å^3); temp. (°K)=293(2); Z=4; D_x=1.367 mg/m^3; absorption coefficient: 0.295 mm^{-1}; θ scan range: 2.04–23.99 (deg); No. of reflections collected: 1681; No. of independent reflections: 1522; No. of observed reflections: 1520; R=0.0422; wR=0.0538; s=1.065. Data for **19**: Formula: $C_{23}H_{18}N_2O_4$; molecular weight: 386.39; cryst. size: 0.16×0.28×0.60 mm^3; cryst. syst.: monoclinic; space group: $P2_1/c$; unit cell parameters: a=15.840(3), b=11.857(3), c=9.970(6) (Å); α=90, β=105.03(3), θ=90 (deg); V=1808.3(12) (Å^3); temp. (°K)=293(2); Z=4; D_x=1.419 mg/m^3; absorption coefficient: 0.098 mm^{-1}; θ scan range: 1.33–28.02 (deg); No. of reflections collected: 5577; No. of independent reflections: 4374; No. of observed reflections: 4315; R=0.0524; wR=0.1127; s=1.021. Data for **29a**: Formula: $C_{21}H_{23}NO_4$; molecular weight: 353.40; cryst. size: 0.2×0.2×0.3 mm^3; cryst. syst.: monoclinic; space group: $P2_1/c$; unit cell parameters: a=7.897(2), b=15.7498(8), c=14.3996(9) (Å); α=90, β=95.250(9), θ=90 (deg); V=1783.5(4) (Å^3); temp. (°K)=293(2); Z=4; D_x=1.316 mg/m^3; absorption coefficient: 0.091 mm^{-1}; θ scan range: 1.92–26.00 (deg); No. of reflections collected: 4624; No. of independent reflections: 3512; No. of observed reflections: 3446; R=0.0617; wR=0.1437; s=1.021.

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