211. Intermolecular [4 + 2]-Cycloadditions of Nitroalkenes with Cyclic Olefins. Transformations of Cyclic Nitronates

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Nitrocyclohexene undergoes facile $SnCl_4$-induced, [4 + 2]-cycloadditions with simple cycloalkenes to produce nitronates. The nitronates can be transformed stereospecifically into a number of other functional groups (alcohol, ketone, oxime, amine) by hydrolytic, reductive, and oxidative processes. The mechanism of the [4 + 2]-cycloaddition is believed to involve formation of a zwitterionic intermediate which can collapse *via* competing pathways to form the observed products. 1,3-Dipolar cycloadditions of the nitronates are described.

Introduction. – The construction of heterocyclic compounds by cycloaddition processes falls primarily in the realm of [2 + 2]- [1] and 1,3-dipolar cycloadditions [2]. The reactive heterodienes required for a [4 + 2]-cycloaddition *(Scheme 1)* are less readily available[1]) [3a] [4]. With the exception of α,β-unsaturated carbonyl compounds [5], heterodienes must be generated *in situ* and efficiently trapped by an appropriate dienophile. Notable examples are: *i)* acylnitrilium ions [6], *ii)* amidomethylium ions [7], *iii)* nitrosoalkenes [8a] [8b], azoalkenes [8c] [8d], and *iv)* vinylnitrosonium cations [9], [14a].

Scheme 1

Recently, we reported that nitroalkenes[2]) can also act in this capacity in an intramolecular reaction when activated with $SnCl_4$ [10]. This reaction was shown to have a high degree of cycloaddition character since the configuration of both the heterodiene and the dienophile were preserved in the products. Obvious advantages of nitroalkenes are their ease of preparation [13] and stability. We now describe the extension of this reaction to the intermolecular process. Our secondary objective here was the investigation of the chemistry of the cyclic nitronates which derive from the [4 + 2]-cycloaddition. In contrast to our

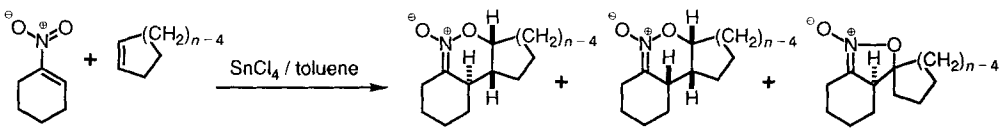
[1]) [4 + 2]-Cycloadditions using heterodienophiles have received a great deal of attention in recent years. For leading references, see [3].

[2]) Nitroalkenes have been shown to react readily with electron-rich olefins (enamines, enol ethers, enolates, allylsilanes). For a current list of examples, see [10–12]. Although under certain circumstances formal cycloadducts can be obtained, these reactions are best described as *Michael* additions and closure [11]. We thank Professors *Seebach* and *Brook* for a preprint of this manuscript.

experience with the dihydro[1,2]oxazines which result from cycloadditions of nitrosoalkenes [14b] and the tetrahydro[1,2]oxazines from vinylnitrosonium cations [14a], the cyclic nitronates offer a wealth of synthetic transformations. In particular, we discuss hydrolytic, reductive, and oxidative transformations as well as 1,3-dipolar cycloadditions.

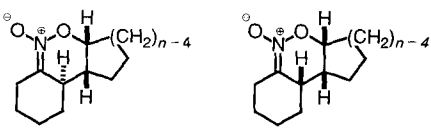
Cyclizations with 1-Nitrocyclohexene. – To facilitate exploration of the reaction conditions and simplify configurational analysis of the products, we chose as first substrates 1-nitrocyclohexene [13h] and cyclohexene. Our first attempted cycloaddition using the conditions shown in *Scheme 2* provided three crystalline products which were identified as **1b**, **2b**, and **3b** as described below.

Scheme 2



1a $n=5$ **2a** $n=5$ **3a** $n=5$
b $n=6$ **b** $n=6$ **b** $n=6$
d $n=7$ **d** $n=7$ **d** $n=7$

The two [4 + 2]-cycloadducts **1b** and **2b** showed characteristic C=N stretches in the IR for nitronic esters as well as the expected high-field ^{13}C-NMR signals for the nitronate C-atom (*Table 1*). While the low-field signal of the methine attached to the O-atom was apparent in the ^{1}H-NMR spectra for both isomers, it lacked sufficient detail to make an assignment of configuration. The assignment of the major cycloadduct **1b** as the stereoisomer arising from an *'exo'* cycloaddition, ultimately rests on a single-crystal X-ray structure determination [15]. The major (*'exo'*, **1b**) and minor (*'endo'*, **2b**) cycloadducts were also independently degraded to the known[3]) [1,1'-bicyclohexyl]-2,2'-diones (*vide infra*).



1 **2**

Table 1. *Selected Spectroscopic Data*[a])[b]) *for the Six-Ring Cycloadducts* **1** *and* **2**

Compound	n	IR [cm^{-1}] C=N	^{1}H-NMR, δ [ppm][c])		^{13}C-NMR, δ [ppm]		
			H–C–O	H–C–C=N	C=N	–C–O	H–*C*–C=N
1a	5	1609	4.61	2.95	126.6	84.34	45.19
2a	5	1613	4.67	3.12	[d])	84.59	40.71
1b	6	1609	4.26	3.02	125.70	76.73	41.35
2b	6	1605	4.38	3.15	124.35	78.72	39.66
1d	7	1607	4.42	3.12	[d])	81.54	43.29
2d	7		4.52		[d])	82.60	43.03

[a]) See *Exper. Part* for complete data.
[b]) The individual resonances of the 4 components in the **1d**/**2d** mixture could not be assigned with certainty.
[c]) All signals are unresolved *m*.
[d]) Not observed.

[3]) These diketones have been incorrectly assigned in the literature [16]. For a discussion of this assignment and a structural revision, see [15].

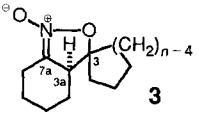


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Table 2. *Selected Spectroscopic Data*[a])[b]) *for the Five-Ring Cycloadducts* **3**

Compound	*n*	IR [cm^{-1}] C=N	^{1}H-NMR, δ [ppm][c])	^{13}C-NMR, δ [ppm]		
			H–C(3a)	C(7a)	C(3)	C(3a)
3a	5	1657	3.03	118.57	92.35	49.39
3b	6	1657	2.57	118.14	82.15	52.33
3d	7	1656	2.82	[d])	[d])	53.90

[a]) See *Exper. Part* for complete data.
[b]) The individual resonances of the 3 isomers in **3d** could not be assigned with certainty.
[c]) All signals are unresolved *m*.
[d]) Not observed.

The structure determination of the third isomeric component **3b** was facilitated by the substantially higher C=N stretch in the IR spectrum of the five-membered cyclic nitronate as well as by its higher-field ^{13}C-NMR signal for the nitronate C-atom. Also notable was the conspicuous absence of ^{1}H-NMR signals above 2.57 ppm *(Table 2)*. Further, this type of product was not unexpected since a similar species was obtained from the intramolecular cycloaddition [10].

Attempts to maximize the selectivity for the formation of **1b**/**2b** over **3b** focused on the choice of solvent and reaction temperature[4])[5]). The results of these experiments are summarized in *Table 3*. In each experiment, 1.2 equiv of $SnCl_4$ and 5 equiv. of cyclohexene were used, except the last experiment in which cyclohexene was in 20-fold excess. The ratio of the six-ring to the five-ring products was found to be virtually independent of solvent. This is surprising in view of the intramolecular precedent, but comparison could only be made at room temperature because the reaction was prohibitively slow in toluene at low temperature. The ability to run reactions at low temperatures and the high '*exo*/*endo*' selectivity made CH_2Cl_2 the solvent of choice for future experiments. This study also revealed a remarkable temperature independence of rate in CH_2Cl_2[6]).

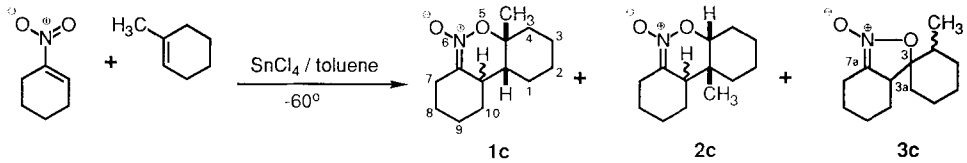
Table 3. *Solvent Effect in Cycloaddition with Cyclohexene*[a])

Solvent	Temp. [°]	Time [h][c])	Ratio of products[b]) **1b**/**2b**/**3b**
CH_2Cl_2	– 78	5	81 : 5 : 14
CH_2Cl_2	25	5	78 : 6 : 15
C_6H_5Cl	– 16	12	75 : 13 : 12
Toluene	25	8	71 : 14 : 15
Cyclohexene[d])	25	96	67 : 14 : 19

[a]) All reactions run with 1.2 equiv. of $SnCl_4$ and 5 equiv. of cyclohexene at 0.4M.
[b]) Calculated by response-factor-corrected integration of the HPLC analyses of reaction mixtures.
[c]) Time required for complete consumption of 1-nitrocyclohexene.
[d]) With 20 equiv. of cyclohexene at 0.5M.

[4]) Earlier experiments in our laboratories [10] had shown that $SnCl_4$ was the ideal *Lewis* acid for this reaction.
[5]) In the intramolecular cases, the amount of five-membered-ring nitronate was suppressed by reaction in toluene.
[6]) Extensive variable-temperature, ^{13}C-NMR studies have revealed a strong temperature dependence of the complexation equilibria between $SnCl_4$ and 1-nitrocyclohexene which may be responsible for this phenomenon. Complexation stoichiometry has been established, but the details of structure remain unclear.

Scheme 3



1c **2c** **3c**

Using these conditions, we next examined the cycloadditions of 1-nitrocyclohexene with a variety of cyclic dienophiles, *i.e.* with cyclopentene (→**1a**, **2a**, **3a**), 1-methylcyclohexene (→**1c**, **2c**, **3c**), and cycloheptene (→**1d**, **2d**, **3d**); see *Scheme 2* and *3*). The results summarized in *Table 4* illustrate several noteworthy trends. First, all of the cycloadditions proceeded more rapidly than with cyclohexene at −60°[7]). Second, the *'exo/endo'* selectivity for the three ring sizes follows the order 5 > 6 > 7. Third, 1-methylcyclohexene *(Scheme 3)* reacts more rapidly than cyclohexene but with only moderate (85:15) regioselectivity. Finally, in all cases a five-membered-ring nitronate is formed as a by-product in varying amounts (5 < 6 < 7).

Table 4. *Cycloadditions with Cyclic Olefins*[a])

Series	*n*	Temp. [°]	Time [h][b])	**1/2/3**[c])	Yield [%][d])
a	5	−60	1.5	88:7:5	81
b	6	−60	7	71:13:16	71[e])
d	7	−60	0.5	40:40:20	92

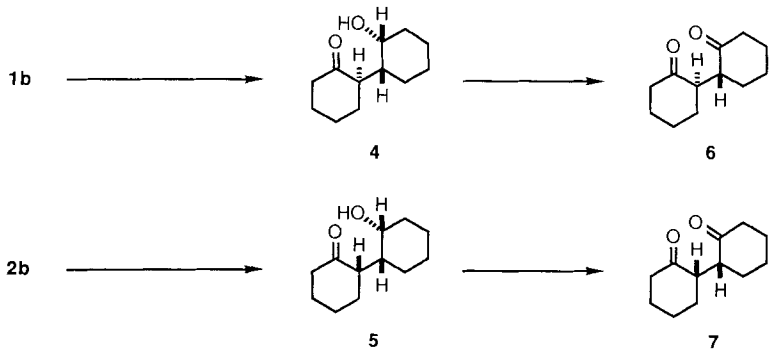
[a]) All reactions performed with 1.2 equiv. of $SnCl_4$ and 5 equiv. of alkene on a 4–6-mmol scale.
[b]) Time required for consumption of educts at −60°.
[c]) Ratio of isolated products.
[d]) Yields after chromatography.
[e]) On a 150-mmol scale, the ratio **1/2/3** was 81:6:13 (66% yield after crystallization).

Thus, we have shown that intramolecularity is not a prerequisite for nitroalkene-olefin cycloadditions. Further, these reactions provide ready access to cyclic nitronates.

Reactions of the Cyclic Nitronates. – 1. *Hydrolysis.* For the nitroalkene cycloaddition to be a useful synthetic reaction, we must be able to unmask the products without epimerization. Our first studies were directed toward a *Nef* reaction[8]) to deliver the hydroxy ketones **4** and **5** selectively from **1b** and **2b**, respectively *(Scheme 4)*. While it was possible to achieve this transformation under the usual *Nef* conditions (H_2SO_4/THF/H_2O), the products had substantially epimerized as shown by subsequent RuO_4 oxidation[9]) to the diketones **6** and **7**[10]). Variations of acid, pH, temperature, and solvents including two-phase systems were all investigated without success. Furthermore, both **4**

[7]) The reactions were monitored at −60° until completion then warmed to −10° before quenching.
[8]) For reviews of the *Nef* reaction, see [13c] [17]. For recent variants, see [18].
[9]) RuO_4 is ideal for this transformation since it is used under neutral aprotic conditions and oxidizes instantaneously and quantitatively. Pyridinium chlorochromate, pyridinium dichromate, and *Swern* oxidations were unsatisfactory.
[10]) A 2:1 mixture **6**/**7** was obtained from either **1b** or **2b**.

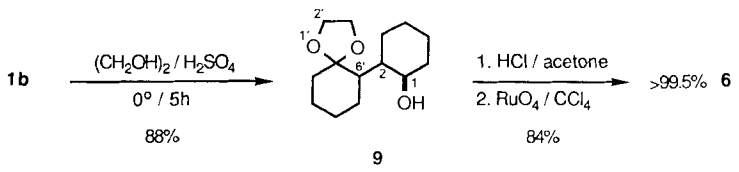
Scheme 4



and **5** underwent a facile dehydration to 2-cyclohexylidenecyclohexanone which complicated isolation. Thus, simple acidic hydrolysis of the nitronates was abandoned in favor of a transformation into a more readily hydrolyzable function.

Initial experiments with dimethylhydrazine and hydroxylamine hydrochloride were unsuccessful, but a 2,4-dinitrophenylhydrazone could be prepared in 84–86% yield. However, under the strongly acidic conditions of the reaction both **1b** and **2b** gave the same hydrazone **8** of unknown configuration (see *Formulae* **4** and **5**).

Scheme 5



A partial solution was found in the formation of ethylene acetal **9** by treatment of **1b** with ethylene glycol and H_2SO_4 (*Scheme 5*). Mild acidic hydrolysis of the acetal followed immediately by RuO_4 oxidation gave exclusively the racemic (or *l*) diketone **6** in good yield. Unfortunately, the minor cycloadduct **2b** gave a mixture of acetals under identical conditions as indicated by its ^{13}C-NMR spectrum[11]). Thus, the hydrolytic approach, while useful in preserving the different functionalities created by the cycloaddition, failed to fulfill all of the criteria for a general, stereoselective method.

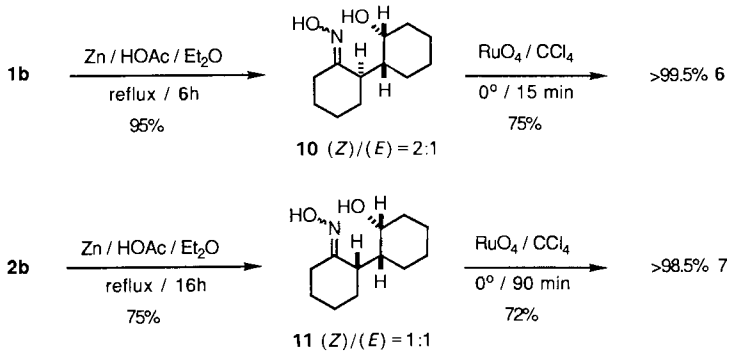
2. *Reduction.* Both nitronic acids and esters have been reduced with a variety of reagents. Some of the more recent variants of the *Nef* reaction use these methods[12]). Nitronates have been reduced to oximes with HI [19c] and to amines with H_2/Pt [19d]. We found that Zn in AcOH cleanly reduced **1b** and **2b** to their oximes **10** and **11**[13]),

[11]) The acetalization proceeded much more slowly for **2b** which may have allowed for nitronate epimerization.

[12]) *McMurry*'s $TiCl_3$ method is the best known variant [19a]. We did not try this procedure, since it was shown to simply deoxygenate a cyclic nitronate from an intramolecular cycloaddition.

[13]) The oximes were a mixture of (*E*) and (*Z*) isomers.

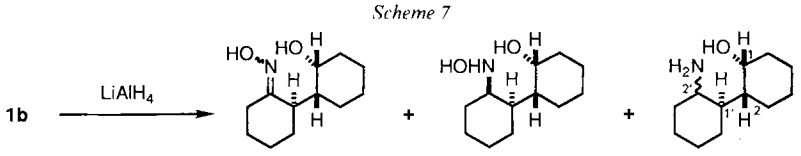
Scheme 6



respectively *(Scheme 6)*. These reductions were stereoselective as shown by subsequent RuO_4 oxidation of **10** and **11** which afforded exclusively **6** and **7**, respectively. The spectroscopic data for the diketones, particularly the ^{13}C-NMR, were in excellent agreement with the values in the literature [16] *except that the assignments were reversed!* We are certain that our assignments are correct, since *i*) there was no crossover in the degradation of **1b** and **2b**, *ii*) the structure of **1b** has been unambiguously established by X-ray crystallography, and *iii*) the pure racemic diastereoisomer **6** was resolved on a chiral chromatography column [15].

Reduction of nitronate **1b** with $LiAlH_4$ gave a variety of products depending on reaction conditions *(Scheme 7)*. At −15° in Et_2O, the reaction produced a mixture of oxime **10**, hydroxylamine **12** and amino alcohol **13** as a single stereoisomer. In refluxing THF, the nitronate was completely converted to **13**, but as a 2:1 mixture of amine

Scheme 7



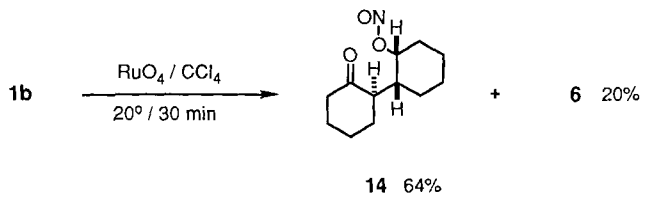
stereoisomers. The assignment of configuration for **12** and **13a** in which the NHOH and NH_2 groups are axial is based on the lack of a strong coupling to the corresponding methine protons at 4.42 and 3.08 ppm, respectively. In **13b** with an equatorial NH_2 group, the methine proton at 2.45 ppm displays two strong *trans*-diaxial couplings (J = 11.1 Hz).

3. *Oxidation.* The oxidative version of the *Nef* reaction has found many applications and can be achieved with a variety of reagents, *e.g.* O_3 [20a] [20b], $KMnO_4$ [18b], *t*-BuOOH [18g], H_2O_2 [18e], MoO_5 [18c], and iodoxybenzoic acid [18a]. A problem

inherent in oxidation of a cyclic nitronate is the fate of the N-atom. In nitronic acids or acyclic esters, nitrite or nitrate salts or esters are expendable by-products. In cyclic esters, we found that the nitrogeneous esters severely limited the utility of oxidative cleavage. This is best illustrated by the direct oxidation of **1b** with RuO_4 to give a mixture of diketone **6** and keto nitrite **14**, *(Scheme 8)*.

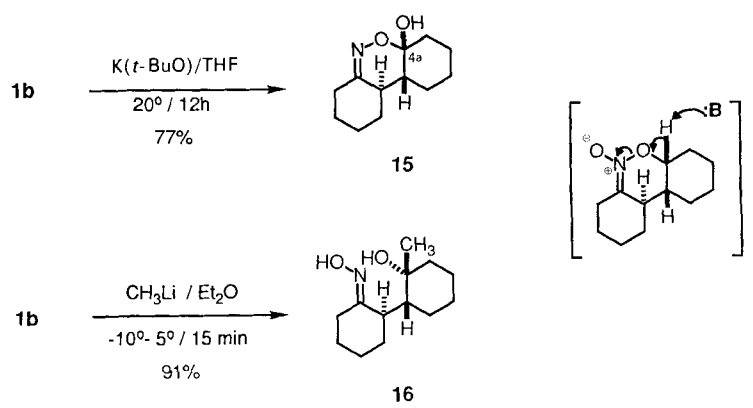
The nitrite **14** could actually be isolated and characterized, although it was extremely unstable. The thermal instability and the lack of a strong peak in the MS at *m/z* 46 ruled out the analogous alkyl nitrate. All of the oxidants examined produced **14**, albeit in poorer yields.

Scheme 8



4. *Internal Redox Reaction.* One of the most characteristic reactions of nitronates is their disproportionation to form an oxime and an aldehyde or ketone [17b] [21]. The reaction has been well examined, and base-catalyzed and thermal mechanisms have been proposed [21b]. In the cyclic case, treatment of **1b** with 25 mol-% of K(*t*-BuO) provided the internal hemiacetal **15** in 79% yield *(Scheme 9)*. While **15** is a single isomer by ^{13}C-NMR, the assignment of the configuration at C(4a) is based solely on the fact that this configuration allows for anomeric stabilization. The oximino-ketone intermediate in this reaction must be formed in the *(E)* configuration, but isomerization to the stable *(Z)* form in the hemiacetal is facile under the basic reaction conditions. We have found that it is possible to trap the oximino ketone by using a reagent which will serve both as base and nucleophile. Thus, treatment of **1b** with 2.2 equiv. of MeLi provided **16** as a single

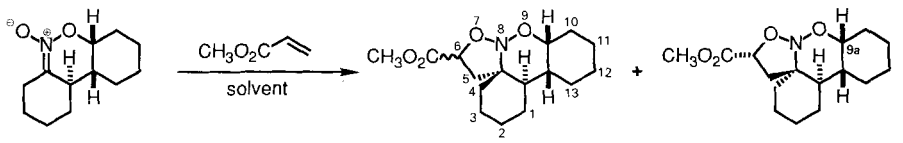
Scheme 9



stereoisomer in 91% yield, *(Scheme 9)*. The assignment of configuration is based soley on the assumption of equatorial attack by MeLi and is tentative[14]).

5. *1,3-Dipolar Cycloadditions.* The reaction of nitronates as dipoles in [3 + 2]-cycloadditions was first discovered and extensively developed by *Tartakovskii* [17b] [23]. We have recently reported that the cyclic nitronates obtained from intramolecular nitroalkene-olefin [4 + 2]-cycloadditions function very well as 1,3-dipoles for a second pericyclic reaction [10]. The tricyclic nitronates obtained in this study also underwent reaction with methyl acrylate *(Scheme 10)*, although the reactions proceeded more slowly than in the previous, less hindered cases. Also, in contrast to the rigid bicyclic system in our earlier studies, we observed little facial or *'exo/endo'* selectivity in the cycloadditions, although some dependence on the solvent used was noted (see *Scheme 10*). In addition, we

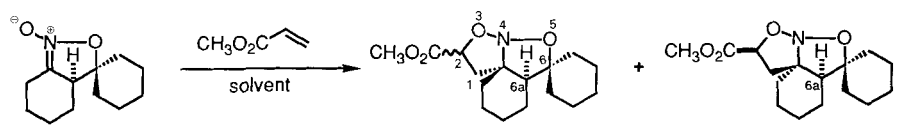
Scheme 10



1b **17/18** *α*- and *β*-CO_2CH_3, resp. **19**

CH_2Cl_2	15%:34%	30%
CH_3CN	17%:25%	39%

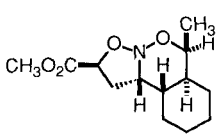
Scheme 11



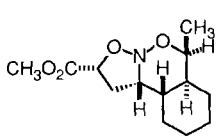
3b **20/21** *α*- and *β*-CO_2CH_3, resp. **22**

benzene	45%:2%	14%

demonstrated the use of a five-ring cyclic nitronate **3b** in the 1,3-dipolar cycloaddition *(Scheme 11)*. The configurational assignments of the products **17**–**19** and **20**–**22** were made based on ^{1}H-NMR chemical-shift and coupling-pattern comparisons to a double cycloadduct **23** obtained from an intramolecular cycloaddition [10a] whose structure was proven by X-ray crystallography[15]). The relevant data are collected in *Table 5*. For the



23



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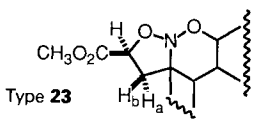
[14]) *Ashby* has shown that MeLi adds to 2-methylcyclohexanone with 88:12 equatorial/axial selectivity [22].

[15]) The ^{1}H-NMR signals for **23** were assigned using ^{1}H,^{1}H-decoupling techniques; a minor epimer **24** was also characterized which arose from an *'endo'* [3 + 2]-cycloaddition [10b].

Table 5. *Comparison of ^{1}H-NMR Data*[a])[b]) *for the Double Cycloadducts* **17**–**22** *with* **23** *and* **24**



Compound	δ [ppm]			J [Hz]		
	H	H_a	H_b	H,H_a	H,H_b	H_a,H_b
23	4.99	2.10	2.64	3.2	10.2	11.5
18	5.11	–	3.01	5.3	10.8	10.0
19	5.05	2.65	–	4.0	10.8	11.4
21	4.29	–	3.35	3.9	10.7	13.5
24	4.79	–	–	9.2	7.0	–
17	4.69	–	3.17	9.5	6.3	12.1
20	4.74	2.73	2.29	9.2	6.6	12.7
22	4.64	–	2.64	9.8	5.0	12.8

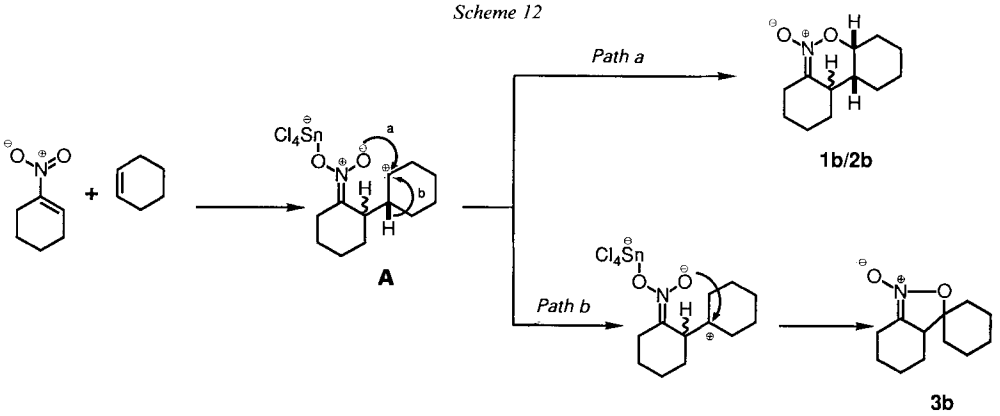
[a]) See *Exper. Part* for complete data.
[b]) Assignments of H_a and H_b are tentative.

six-membered-ring nitronates, there is good agreement among **23**, **18**, and **19** permitting assignment of the *'exo'* mode of the [3 + 2]-cycloaddition, and between **17** and **24** corresponding to the *'endo'* mode. Thus, **18** and **19** are facial isomers. The face of approach may be assigned by inspection of the ^{1}H-NMR signal for H–C(9a) which is a *q* (J = 3.6 Hz) in **18** and a *dt* (J = 12.1 and 4.9 Hz) in **19.** Conformational analysis with *Dreiding* models reveals that two stable (all-chair) conformations are available to **18** and only one to **19.** Of the two *cis-transoid-cis* conformations in **18**, only one allows a *trans*-diaxial coupling to H–C(9a). In **19**, such a relationship is rigidly enforced. Thus, we assign **19** as arising from β-face attack which produces a *cis-transoid-trans* ring system which locks the conformation of the [1,2]oxazine ring.

The analysis of the products from the five-membered-ring nitronate is less straightforward. There appears to be better agreement of the ^{1}H-NMR data from **20** and **22** with that of isomer **24** resulting from *'endo'* addition! Further, the minor cycloadduct **21** shows a coupling pattern more similar to **23**. Thus, we tentatively assign **20** and **22** as facial isomers obtained in the *'endo'* [3 + 2]-cycloaddition. The identification of facial attack was done in a similar fashion as described above. The ^{1}H-NMR signal for H–C(6a) is visible only in **20** where it appears as a *dd*. Inspection of *Dreiding* models reveals that in **20** the *cis*-fused perhydrobenzisoxazole allows some conformational mobility and the preferred, all-chair conformation has H–C(6a) bisecting the angle between the adjacent methylene H-atoms. Contrariwise, in **22** the *trans*-fused perhydrobenzisoxazole is conformationally locked with an axially oriented H–C(6a), thus mandating a large diaxial coupling constant.

Discussion. – *1-Nitrocyclohexene Cycloadditions.* The relative rates of formation and amounts of the isomeric products **1**–**3** provides insight into the nature of the cycloaddition process. For cyclohexene, the lack of a solvent dependence of the ratio **(1 + 2)/3** was surprising and suggests little charge development in the transition state. Two limiting mechanistic possibilities may be considered to account for the formation of **3**: *i)* A common zwitterionic intermediate **A** is formed which collapses *via* two separate path-

Scheme 12



ways. *Path a* to **1** and **2** by charge annihilation and *Path b* to **3** by a *Wagner-Meerwein* shift and capture of the tertiary carbocation *(Scheme 12). ii)* Alternatively, we may consider two independent competing mechanisms; concerted cycloaddition to **1** and **2** and a zwitterionic pathway which leads only to **3**. In the former mechanism, there is one rate-determining step followed by a partitioning in a product-determining step. In the latter mechanism the rate- and product-determining steps are the same for a given species. The limited amount of data from these and other experiments in the intramolecular series do not allow an unambiguous distinction between these possibilities. Nevertheless, we feel that the former mechanism can better account for the following observations: *a)* the relative rates of reaction of the three cycloalkenes ($5 \approx 7 > 6$; *Table 4*) correlate both with ring-strain energies[16]) (which may be expected for concerted reactions) and carbocation stabilities[17]), *b)* the proportion of isomer **3** from the three cycloalkenes changed regularly ($7 > 6 > 5$), and *c*) the ratio **1c**/**3c** is 87:13[18]). If the rate- and product-determining steps coincide (as in the latter mechanism), one expects a greater proportion of the isomer **3** for the faster reactions (more stable carbocation). This was not the case *(Table 4)*. If these steps are decoupled, however, we can explain these trends using carbocation stabilities to reflect the rate of reaction and using the ease of 1,2-H shifts to explain the partitioning of **A**. *Saunders et al.* [26] have discussed the effect of ring size on the rate of hydride migration in terms of optimal orbital overlap. Due to the flexibility in larger rings, one expects the proportion of isomer **3** to increase with ring size. This was observed.

On the other hand, the similarity of the ratios **1b**/**3b** and **1c**/**3c** is not completely consistent with the first mechanism. Indeed, the fact that regioisomer **2c** is formed in significant amounts argues against the formation of discrete carbocations and suggests pericyclic character in the transition state. In support of this proposal, we note the change in the percentage of *'endo'* cycloadduct **2** from the three cycloalkenes ($7 > 6 > 5$). As flexibility increases with ring size, the methylene groups can fold away in the *'endo'*-transition state thus minimizing non-bonding interactions.

In summary, the cycloaddition results to date are most consistent with a mechanism involving the formation of a common zwitterionic intermediate in the slow step followed

[16]) ΔH_f° from *Benson* [24]: cyclopentene 5.9, cycloheptene 5.4, and cyclohexene 1.4 kcal/mol.
[17]) Cycloalkyl carbocation relative stabilities may be inferred from solvolysis rates and ρ^+ [25].
[18]) We do not consider **2c** since alkyl migration is much slower than hydride migration.

by a rapid partitioning to products. The transition state leading to the zwitterion has some character of a pericyclic reaction, presumably to neutralize in part the developing charge in the zwitterion.

Reactions of Cyclic Nitronates. The ability to perform *Nef*-type hydrolyses on the cyclic nitronates to afford hydroxy ketones or hydroxy acetals represents a major advantage over the dihydro[1,2]oxazines from earlier studies. The epimerization which accompanied the hydrolyses of **1b** and **2b** may be idiosyncratic of these substrates. On the other hand, the ability to produce a protected ketone directly in the form of an acetal or oxime has obvious synthetic advantages. Further, for those objectives which require retention of the N-atom, oximes and amines are both accessible in good yield. The only transformation which does not appear to have promise is the oxidative cleavage of the nitronates, primarily due to the persistent nitrite by-product.

The nitronates prepared in the study underwent 1,3-dipolar cycloadditions with methyl acrylate with complete regioselectivity as expected. However, the *'exo/endo'* selectivity and facial selectivity were significantly diminished. *Carrié* [27] has discussed the origins of *'exo'* selectivity in [3 + 2]-cycloadditions of nitronates in terms of secondary-orbital repulsions. In the cycloadducts from **1b** this seems to hold, albeit with moderate selectivity. In the reactions of **3b,** however, the *'endo'*-mode isomer appears to predominate. We reserve comment on this result pending unambiguous assignment of configuration. The facial selectivity in nitronate [3 + 2]-cycloadditions can be interpreted in terms of the kinetic anomeric effect [28]. In rigid systems such as those leading to **23**, we observed complete facial selectivity [10]. The substrates **1b** and **3b** are conformationally mobile and can lead to products under kinetic control by attack from either face which satisfy the stereoelectronic and conformational criteria discussed by *Eschenmoser* [28a][19]. Thus, it is not surprising to observe lower selectivities in these cases.

These studies have demonstrated the ease of preparation of cyclic nitronates by cycloaddition with simple unactivated alkenes. The richness of the chemistry of nitronates augurs well for the utility of nitroalkene-olefin cycloadditions in synthesis.

We are actively pursuing many structural variations in the intramolecular series as well as the origins of activation by $SnCl_4$.

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Experimental Part

1. General. – Benzene, CH_2Cl_2, toluene, hexane, and MeCN were distilled from CaH_2. Chlorobenzene was passed through basic Alox I (act. I) prior to use. Et_2O and THF were distilled from sodium benzophenone. Methyl acrylate was distilled from $CaCl_2$. Cyclopentene, cyclohexene, 1-methylcyclohexene, and cycloheptene were distilled from Na or passed through basic Alox I. Ethylene glycol was distilled from Na. $SnCl_4$ was distilled freshly prior to use. MeLi (*Aldrich*) was titrated with diphenylacetic acid. Solns. of RuO_4 were prepared from $RuCl_3 \cdot 3H_2O$ (*Aldrich*) by the method of *Djerassi* [30a]. The 1-nitrocyclohexene was prepared according to *Corey* [13h] and distilled freshly prior to use. All other chemicals were used as supplied or purified by distillation as

[19]) The N-atom is a non-inverting stereogenic center [29].

needed. All reactions under anhydrous conditions were performed in oven(140°)- or flame-dried glassware under dry N_2. Bulb-to-bulb distillations: *Büchi GKR-50* Kugelrohr; b.p. refer to air-bath temp. and are uncorrected. Anal. TLC: *Merck* silica gel plates with *QF-254* indicator; visualization with UV light, phosphomolybdic acid, I_2, vanillin, and/or 2,4-dinitrophenylhydrazine soln. Column (flash) chromatography [31]: 32–63 μm silica gel (*Woelm*). Anal. HPLC: *Perkin-Elmer* chromatograph (series 1) with a *Perkin-Elmer-LC-75* detector; 25 × 4.5-mm column of silica gel (5 μm); retention times (t_R) and integrals from a *Hewlett Packard 3390* recorder. M.p.: *Thomas-Hoover* capillary melting point apparatus; corrected. IR spectra: *IBM-FT-IR-32* spectrometer; CCl_4 soln. unless otherwise noted; in cm^{-1} with *s* 66–100%, *m* 33–66%, and *w* 0–33% intensity. ^{1}H-NMR and ^{13}C-NMR spectra: *General-Electric-QE-300* (300 MHz (^{1}H), 75.5 MHz (^{13}C)) or *Varian-XL-200* (200 MHz (^{1}H), 50.4 MHz (^{13}C)) spectrometer; $CDCl_3$ with $CHCl_3$ as an internal standard (7.26 ppm for ^{1}H, 77.07 ppm for ^{13}C) unless otherwise stated; chemical shifts in ppm (δ), coupling constants *J* in Hz; assignments of ^{13}C resonances are supported by 75.5 MHz APT spectra. MS: *Varian-MAT-CH-5* spectrometer with ionization voltages of 10 and 70 eV; *m/z* (% rel. to base peak (= 100%)). HR-MS: *Varian-MAT-731* spectrometer. Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory.

2. Cycloadditions. – 2.1. *Nitrocyclohexene with Cyclopentene.* To a magnetically stirred soln. of 1-nitrocyclohexene (552 mg, 4.34 mmol) in dry CH_2Cl_2 (8.7 ml, 0.5M) was added cyclopentene (1.91 ml, 21.71 mmol) at 0°. The soln. was cooled to −70° and $SnCl_4$ (0.61 ml, 5.21 mmol) added rapidly. The light-yellow soln. was stirred for 1.5 h at −60°, warmed to −10°, and then poured into ice/sat. aq. $NaHCO_3$ soln. (50 ml). The white suspension was extracted with CH_2Cl_2 (50 ml), and the org. layer was washed with H_2O (2 × 50 ml) and brine (50 ml). The aq. layers were reextracted with fresh CH_2Cl_2 (2 × 50 ml) and the org. phases dried (K_2CO_3) and evaporated. The resulting orange oil was purified by flash chromatography (silica gel, benzene/acetone/hexane 3:1:1) to afford **1a–3a.** Recrystallization from hexane gave analytically pure materials.

(3aR,9aR*,9bR*)-1,2,3,3a,6,7,8,9,9a,9b-Decahydrobenzo[c]cyclopenta[e][1,2]oxazine N-Oxide* (**1a**). Yield after chromatography 606 mg (71%), after recrystallization 568 mg (67%). M.p. 100–102°. R_f 0.18 (benzene/acetone/hexane 3:1:1). IR: 2940*s*, 2859*m*, 1609*s*, 1449*m*, 1437*m*, 1366*m*, 1331*w*, 1273*m*, 1242*s*, 1221*s*, 1160*m*, 1148*m*, 1109*w*, 1088*w*, 990*w*, 955*m*, 932*w*, 911*m*, 889*m*, 862*m*. ^{1}H-NMR (300 MHz): 4.61 (*m*, H–C(3a)); 2.95 (*m*, H–C(9a)); 2.18 (*m*, H_{ax}–C(6)); 2.01–1.70 (*m*, 9H); 1.54–1.23 (*m*, 5H). ^{13}C-NMR (75.5 MHz): 126.63 (C(5a)); 84.34 (C(3a)); 45.19 (C(9a)); 37.77 (C(9b)); 33.37; 31.09; 30.00; 26.90; 24.14; 22.00. MS (10 eV): 195 (28, $M^{+\cdot}$), 95 (14), 93 (14), 81 (44), 79 (24), 69 (11), 68 (15), 67 (100), 55 (23). Anal. calc. for $C_{11}H_{17}NO_2$ (195.27): C 67.66, H 8.78, N 7.17; found: C 67.49, H 8.70, N 7.24.

(3aR,9aS*,9bR*)-1,2,3,3a,6,7,8,9,9a,9b-Decahydrobenzo[c]cyclopenta[e][1,2]oxazine N-Oxide* (**2a**). Yield after chromatography 51 mg (6%). R_f 0.17 (benzene/acetone/hexane 3:1:1). IR: 2940*s*, 2863*m*, 1613*s*, 1572*w*, 1462*w*, 1445*w*, 1277*m*, 1223*w*, 1150*m*, 982*w*, 951*w*, 918*w*, 868*w*. ^{1}H-NMR (300 MHz): 4.67 (*m*, H–C(3a)); 3.21 (*m*, H–C(9a)); 2.74 (*m*, H_{ax}–C(6)); 2.15–1.25 (*m*, 14H). ^{13}C-NMR (75.5 MHz): 84.59 (C(3a)); 40.71 (C(9a)); 36.44 (C(9b)); 30.62; 29.83; 27.30; 25.27; 24.73; 24.67; 21.45. MS (10 eV): 195 (11, $M^{+\cdot}$), 164 (39), 136 (24), 135 (100), 121 (13), 120 (11), 107 (16), 98 (71), 97 (17), 95 (11), 93 (18), 91 (15), 83 (13), 81 (28), 80 (10), 79 (28), 77 (11), 68 (11), 67 (61), 55 (21), 53 (11), 43 (15), 41 (31), 39 (15). HR-MS: 195.1250 ($C_{11}H_{17}NO_2$, calc. 195.1259).

3,3a,4,5,6,7-Hexahydrospiro[2,1-benzisoxazole-3-1'-cyclopentane] 1-Oxide (**3a**). Yield after chromatography 35 mg (4%), after recrystallization 24 mg (3%). M.p. 90–91°. R_f 0.36 (benzene/acetone/hexane 3:1:1). IR: 2942*m*, 2867*w*, 1657*s*, 1559*w*, 1539*w*, 1449*w*, 1435*w*, 1385*m*, 1337*w*, 1283*m*, 1244*m*, 1233*m*, 1144*w*, 1123*w*, 988*w*, 947*w*, 914*w*. ^{1}H-NMR (300 MHz): 3.03 (*m*, H–C(3a)); 2.80 (*m*, H_{ax}–C(7)); 2.12 (*m*, H_{eq}–C(7), 1H); 2.04–1.5 (*m*, 10H); 1.43–1.20 (*m*, 3H). ^{13}C-NMR (75.5 MHz): 118.57 (C(7a)); 92.35 (C(3)); 49.39 (C(3a)); 38.68; 33.01; 27.49; 24.39; 24.06; 23.62; 23.35; 22.82. MS (10 eV): 195 (42, $M^{+\cdot}$), 137 (10), 113 (11), 111 (22), 109 (14), 95 (12), 94 (19), 86 (10), 84 (12), 83 (16), 82 (13), 81 (100), 79 (20), 67 (20), 56 (13), 55 (50), 54 (35), 42 (14), 41 (10). HR-MS: 195.1266 ($C_{11}H_{17}NO_2$, calc. 195.1259).

2.2. *Nitrocyclohexene with Cyclohexene.* To a magnetically stirred soln. of 1-nitrocyclohexene (20.0 g, 157 mmol) in dry CH_2Cl_2 (375 ml) was added cyclohexene (64.6 g, 786 mmol) at 0°. The soln. was cooled to −78°, and $SnCl_4$ (49.1 g, 188 mmol) was added rapidly. The resulting soln. was stirred at −60° or below for 6.5 h, then warmed to −10° and poured into vigorously stirred ice/sat. aq. $NaHCO_3$ soln. (400 ml). Upon cessation of foaming, the neutralized mixture was filtered through a *Celite* pad with copious CH_2Cl_2 rinses. The filtrate was washed with additional sat. aq. $NaHCO_3$ soln. (200 ml), H_2O (400 ml), and brine (400 ml). The aq. washings were then reextracted in series with CH_2Cl_2 (2 × 400 ml) and the org. layers dried (K_2CO_3) and concentrated. The residual yellow oil was crystallized from pentane/Et_2O to give 4 g of a yellow solid which was further crystallized from hexane to give 3.6 g of off-white needles. The original pentane/Et_2O liquor was concentrated and crystallized from hexane to give an additional 4.4 g of off-white needles. All of the above mother liquors were combined, concentrated, and chromatographed on silica gel (benzene/hexane/acetone 2:2:1).

Three fractions were taken (high-R_f product, medium-R_f product, and a mixture of medium- and low-R_f products). The 3rd fraction was rechromatographed to separate the medium- and low-R_f products. The earlier obtained crystals were combined with those from the medium-R_f fractions, and all three products were separately crystallized to afford **1b, 2b** (off-white needles from hexane), and **3b** (off-white prisms from pentane/Et_2O).

(4aR,10aR*,10bR*)-2,3,4,4a,7,8,9,10,10a,10b-Decahydro-1H-dibenz[c,e][1,2]oxazine N-Oxide* (**1b**). Yield 14.1 g (43%). M.p. 86–87°. R_f 0.38 (benzene/acetone 3:1). HPLC (hexane/i-PrOH 9:1, 1.5 ml/min): t_R 11.48 min. IR: 2938*s*, 2857*s*, 1609*s* (C=N), 1447*m*, 1375*w*, 1354*w*, 1329*w*, 1294*m*, 1273*s*, 1242*s*, 1213*s*, 1144*m*, 1129*m*, 1129*m*, 1078*m*, 972*m*, 934*s*, 895*m*, 878*m*, 855*w*, 839*m*. ^{1}H-NMR (300 MHz): 4.26 (br. *s*, H–C(4a)); 3.02 (*d*, *J* = 15.2, H–C(10a)); 2.0–0.9 (*m*, 17H). ^{13}C-NMR (75.5 MHz): 125.70 (C(6a)); 76.73 (C(4a)); 41.35 (C(10a)); 37.72 (C(10b)); 33.98 (C(4)); 28.35; 28.02; 26.96; 25.48; 25.05; 24.21; 19.58. MS (10 eV): 209 (16, $M^{+\cdot}$), 97 (10), 95 (29), 93 (11), 82 (12), 81 (100), 79 (18), 69 (11), 67 (34), 55 (17). Anal. calc. for $C_{12}H_{19}NO_2$ (209.29): C 68.87, H 9.15, N 6.69; found: C 68.85, H 9.00, N. 6.72.

(4aR,10aS*,10bR*)-2,3,4,4a,7,8,9,10,10a,10b-Decahydro-1H-dibenz[c,e][1,2]oxazine N-Oxide* (**2b**). Yield 1.6 g (3%). M.p. 111–112°. R_f 0.32 (benzene/acetone 3:1). HPLC (hexane/i-PrOH 9:1, 1,5 ml/min): t_R 18.69 min. IR: 2940*s*, 2863*s*, 1605*s*, (*C=N*), 1447*s*, 1368*m*, 1354*m*, 1337*w*, 1298*w*, 1273*s*, 1244*s*, 1213*s*, 1192*m*, 1148*m*, 1130*m*, 1100*m*, 1030*w*, 992*w*, 970*m*, 934*s*, 909*s*, 880*s*, 839*s*. ^{1}H-NMR (300 MHz): 4.38 (br. *s*, H–C(4a)); 3.15 (*m*, H–C(10a)); 2.53 (*m*, H_{ax}–C(7)); 2.1–1.0 (*m* 16H). ^{13}C-NMR (75.5 MHz): 124.35 (C(6a)); 78.72 (C(4a)); 39.66 (C(10a)); 35.21 (C(10b)); 29.23; 27.59; 27.09; 24.73; 24.44; 24.31; 22.11; 19.63. MS (10 eV): 209 (21, $M^{+\cdot}$), 161 (12), 98 (12), 97 (15), 95 (37), 93 (15), 82 (14), 81 (100), 79 (17), 69, (12), 67 (36), 55 (19). Anal. calc. for $C_{12}H_{19}NO_2$ (209.29): C 68.87, H 9.15, N 6.69; found: C 69.04, H 9.18, N 6.74;

3,3a,4,5,6,7-Hexahydrospiro[2,1-benzisoxazole-3,1'-cyclohexane] 1-Oxide (**3b**). Yield 2.4 g (7%). M.p. 110–112°. R_f 0.56 (benzene/acetone 3:1). HPLC (hexane/i-PrOH 9:1, 1.5 ml/min): t_R 6.80 min. IR: 2940*s*, 2863*m*, 1657*s* (C=N), 1449*s*, 1385*s*, 1341*m*, 1281*s*, 1237*s*, 1134*m*, 1123*s*, 1090*w*, 1057*m*, 1024*w*, 990*w*, 959*m*, 914*m*, 864*s*, 847*s*. ^{1}H-NMR (300 MHz): 2.75 (*m*, H–C(3a), H_{ax}–C(7)); 2.06 (*m*, H_{eq}–C(7)); 1.97–1.69 (*m*, 4H); 1.69–1.46 (*m*, 6H); 1.46–1.08 (*m*, 6H). ^{13}C-NMR (75.5 MHz): 118.14 (C(7a)); 82.15 (C(3)); 52.33 (C(3a)); 37.04; 30.92; 25.76; 24.80; 24.07; 23.88; 23.41; 22.37; 21.82. MS (10 eV): 209 (27, $M^{+\cdot}$), 153 (13), 135 (16), 111 (20), 98 (32), 95 (12), 82 (10), 81 (100), 79 (13), 69 (19), 67 (13), 55 (21), 54 (14). Anal. calc. for $C_{12}H_{19}NO_2$: C 68.87, H 9.15, N 6.69; found: C 68.95, H 8.87, N 6.77.

2.3. *Nitrocyclohexene with 1-Methylcyclohexene.* To a magnetically stirred soln. of 1-nitrocyclohexene (818 mg, 6.43 mmol) in dry CH_2Cl_2 (13 ml, 0.5M) was added 1-methylcyclohexene (3.81 ml, 32.17 mmol). Upon addition of $SnCl_4$ (0.903 ml, 7.72 mmol) at −65°, an exothermic reaction was observed, and the resulting yellow soln. was stirred at −60° for 30 min. The soln. was then warmed to −10° and poured onto ice/sat. aq. $NaHCO_3$ (75 ml). The chalk-white suspension was extracted with CH_2Cl_2 (75 ml) and the org. phase washed with H_2O (75 ml) and brine (75 ml). Each aq. wash was reextracted with fresh CH_2Cl_2 (2 × 75 ml). The org. layers were dried (K_2CO_3) and evaporated to give an orange oil. Purification by flash chromatography (silica gel, benzene/acetone/hexane 3:1:1) afforded **1c** and **2c** as an 85:15 mixture and **3c** (mixture of 3 stereoisomers). The two fractions were recrystallized from heptane.

(4aR,10aR*,10bR*)- and (4aR*,10aS*,10bR*)-4a-Methyl-2,3,4,4a,7,8,9,10,10a,10b-decahydro-1H-dibenz-[c,e][1,2]oxazine N-Oxide* (**1c**) *and (4aR*,10aR*,10bR*)- and (4aR*,10aS*,10bR*)-10b-Methyl-2,3,4,4a,7,8,9,10,10a,10b-decahydro-1H-dibenz[c,e][1,2]oxazine N-Oxide* (**2c**). Yield 782 mg (54%) after chromatography, 661 mg (46%) after recrystallization: M.p. 76–84°. R_f 0.12–0.16 (benzene/acetone/hexane 3:1:1). IR: 2938*s*, 2865*m*, 1609*s*, 1460*w*, 1446*m*, 1379*w*, 1356*w*, 1331*w*, 1273*s*, 1242*m*, 1217*m*, 1188*m*, 1138*m*, 1111*m*, 1007*w*, 691*w*, 939*w*, 901*m*, 862*w*. ^{1}H-NMR (300 MHz): 4.36 (*m*, 0.15H, H–C(4a) of **2c**); 3.26 (*m*, 0.85H, H–C(10a) of **1c**); 2.84 (*m*, 0.15H, H–C(10a) of **2c**); 2.63–2.35 (*m*, 0.85H, H_{ax}–C(7) of **1c**); 2.19–1.11 (*m*, 19H). ^{13}C-NMR (75.5 MHz): 125.2 (C(6a)); 85.4 (C(4a) of **2c**); 82.2, 81.4 (C(4a) of **1c**); 42.47; 41.51; 39.48; 38.67; 37.29; 36.95; 33.68; 33.30; 32.44; 30.01; 28.04; 27.85; 27.58; 27.05; 25.54; 25.49; 25.46; 25.01; 24.75; 24.51; 24.07; 23.93; 23.87; 23.78; 23.25; 22.80; 22.35; 22.11; 20.68; 20.00. MS (10 eV): 223 (37, $M^{+\cdot}$), 175 (16), 135 (14), 124 (11), 111(12), 97 (14), 96 (70), 95 (100), 93 (12), 81 (82), 67 (18), 55 (15), 43 (33). Anal. calc. for $C_{13}H_{21}NO_2$ (223.33): C 69.92, H 9.48, N 6.27; found: C 69.87, H 9.62, N 6.31.

3,3a,4,5,6,7-Hexahydro-2'-methylspiro[2,1-benzisoxazole-3,1'-cyclohexane] 1-Oxide (**3c**). Yield 104 mg (7%) after chromatography, 73 mg (5%) after recrystallization: M.p. 85–87°, R_f 0.38 (benzene/acetone/hexane 3:1:1). IR: 2942*s*, 2865*m*, 1660*s*, 1583*w*, 1551*w*, 1460*w*, 1447*w*, 1436*w*, 1382*m*, 1335*w*, 1301*w*, 1284*m*, 1248*m*, 1234*m*, 1198*w*, 1143*w*, 1121*w*, 1007*w*, 971*w*, 947*w*, 894*w*, 864*w*. ^{1}H-NMR (300 MHz): 2.83–2.68 (*m*, 1.7H, H–C(3a), H–C(7)); 2.55 (*m*, 0.3H, H–C(7)); 2.11–1.18 (*m*, 16H); 0.96 (*d*, *J* = 7.03, 0.9H, CH_3–C(2')); 0.99 (*d*, *J* = 7.14, 2.1H, CH_3–C(2')). ^{13}C-NMR (75.5 MHz): 118.36 (C(7a)); 85.41, 84.49 (C(3)); 53.99, 49.01 (C(3a)); 39.04 (C(2')); 29.54; 29.09; 28.14; 27.26; 26.89; 25.19; 24.87; 24.42; 24.33; 23.77; 23.45; 22.22; 21.64; 20.83; 15.14; 13.96 (C(1')).

MS (10 eV): 223 (53, $M^{+\cdot}$), 140 (32), 137 (14), 122 (33), 113 (69), 112 (22), 111 (30), 109 (11), 97 (13), 96 (28), 95 (24), 94 (36), 86 (25), 85 (10), 84 (10), 83 (46), 82 (13), 81 (100), 79 (14), 69 (31), 68 (15), 67 (22), 56 (16), 55 (98), 54 (47), 43 (13), 42 (17), 41 (13). Anal. calc. for $C_{13}H_{21}NO_2$ (223.33): C 69.92, H 9.48, N 6.27; found: C 69.99, H 9.37, N 6.12.

2.4. *Nitrocyclohexene with Cycloheptene.* To a magnetically stirred soln. of 1-nitrocyclohexene (630 mg, 4.96 mmol) in dry CH_2Cl_2 (10 ml, 0.5M) was added cycloheptene (2.89 ml, 24.77 mmol) at −20°. Cooling was continued to −60° and $SnCl_4$ (0.696 ml, 5.95 mmol) was added rapidly. The resulting bright-yellow soln. was stirred for 30 min at low temp., warmed to −10°, and poured into sat. aq. $NaHCO_3$ soln./ice (35 ml). The cloudy, aq. suspension was extracted with CH_2Cl_2 (75 ml), and the org. phase was washed with H_2O (75 ml) and brine (75 ml). Each aq. layer was reextracted with fresh CH_2Cl_2 (2 × 75 ml), and the org. layers were dried (K_2CO_3) and evaporated affording an oil. Flash chromatography (silica gel, benzene/acetone/hexane 6:1:1) afforded **1d** and **2d** as a 43:57 mixture and **3d.** Recrystallization from hexane gave anal. pure materials.

(6aR,11aR*,11bR*)-1,2,3,4,6a,7,8,9,10,11,11a,11b-Dodecahydrobenzo[c]cyclohepta[e][1,2]oxazine* N-*Oxide* (**1d**) *and (6aR*,11bR*,11aS*)-1,2,3,4,6a,7,8,9,10,11,11a,11b-Dodecahydrobenzo[c]cyclohepta[e][1,2]-oxazine* N-*Oxide* (**2d**). Yield after chromatography 821 mg (74%), after recrystallization 675 mg (61%): M.p. 65–67° R_f 0.18 (benzene/acetone/hexane 3:1:1). IR: 2934*s*, 2859*m*, 1607*s*, 1549*w*, 1356*w*, 1329*w*, 1277*m*, 1244*m*, 1223*m*, 1148*w*, 1086*w*, 897*m*. ^{1}H-NMR (300 MHz): 4.52 (br.s, 0.43 H, H–C(5a) of **1d**); 4.42 (br. *s*, 0.57 H, H–C(5a) of **2d**); 3.12 (*m*, H–C(11a)), 2.61 (*m*, 0.43 H, H_{ax}–C(8)); 2.2–1.2 (*m*, 18.57 H). ^{13}C-NMR (75.5 MHz): 82.60, 81.54 (C(5a)); 43.29, 43.03 (C(11a)); 40.86, 39.31 (C(11b)); 33.82; 31.69; 31.06; 29.56; 28.64; 28.34; 27.73; 27.12; 27.00; 25.15; 25.07; 24.58; 24.11; 21.73; 21.68; 20.70. MS (10 eV): 223 (47, $M^{+\cdot}$), 206 (11), 175 (17), 129 (18), 113 (14), 112 (10), 111 (10), 109 (10), 97 (11), 96 (21), 95 (100), 93 (27), 83 (12), 81 (70), 79 (19), 69 (11), 68 (10), 67 (48), 55 (23). Anal. calc. for $C_{13}H_{21}NO_2$ (223.33): C 69.92, H 9.48, N 6.27; found: C 70.27, H 9.43, N 6.41.

3,3a,4,5,6,7-Hexahydrospiro[2,1-benzisoxazole-3,1'-cycloheptane] 1-Oxide (**3d**). Yield after chromatography 199 mg (18%), after recrystallization 148 mg (13%). M.p. 91–93°. R_f 0.36 (benzene/acetone/hexane 3:1:1). IR: 2934*s*, 2860*m*, 1656*s*, 1551*w*, 1459*w*, 1449*m*, 1436*w*, 1383*m*, 1347*w*, 1334*w*, 1281*s*, 1242*m*, 1160*w*, 1141*w*, 1116*w*, 1075*w*, 1017*w*, 972*w*, 947*w*, 922*w*, 856*m*. ^{1}H-NMR (300 MHz): 2.82 (*m*, H–C(3a), H_{ax}–C(7)); 2.10 (*m*, H_{eq}–C(7)); 1.94–1.23 (*m*, 17 H). ^{13}C-NMR (75.5 MHz): 53.90 (C(3a)); 41.20 (C(7)); 33.81; 29.42, 29.11; 26.39; 24.38; 23.92; 23.66; 22.27; 21.83. MS (10 eV): 223 (28, $M^{+\cdot}$), 113 (19), 111 (30), 95 (13), 83 (12), 81 (100), 79 (11), 69 (11), 68 (13), 55 (29), 54 (13). Anal. calc. for $C_{13}H_{21}NO_2$ (223.33): C 69.92, H 9.48, N 6.27; found: C 69.72, H 9.71, N 6.06.

3. Transformations of the Nitronates. – 3.1. *Reaction of* **1b** *and* **2b** *with 2,4-Dinitrophenylhydrazine.* The nitronate (0.10–1.0 mmol) was added all at once to a 0.15M 2,4 dinitrophenylhydrazine soln.[20]) (1.1 equiv.) and stirred vigorously. Steady precipitation of orange solid was observed, and TLC analysis after 30 min indicated complete consumption of starting material. The mixture was diluted with an equal volume of H_2O, and the orange precipitate was collected, rinsed thoroughly with H_2O, and recrystallized from EtOH/AcOEt. In each case, two crops were obtained, the 1st with m.p. 180–181°, and the 2nd with m.p. 176–178°. *(1'R*,2'R*)-2-(2'-Hydroxycyclohexyl)cyclohexanone 2,4-dinitrophenylhydrazone* (**8**): Yield from **1b** 86%, from **2b** 84%: M.p. 180–181°. IR ($CHCl_3$): 3633*w*, 3360*w*, 3325*w*, 3228*w*, 3100*w*, 2940*s*, 2863*m*, 1619*s*, 1592*s*, 1520*s*, 1426*s*, 1337*s*, 1210*m*, 1138*m*, 1075*m*, 972*w*, 922*w*, 833*m*. ^{1}H-NMR (200 MHz): 9.09 (*d*, *J* = 2.7, H–C(3")); 8.23 (*dd*, *J* = 9.7, 2.7, H–C(4")); 7.90 (*d*, *J* = 9.7, H–C(5")); 3.65 (br. H–C(2')); 2.97 (br. *d*, *J* = 10.0, H–C(2)); 2.48 (*m*, 1H); 2.10–1.10 (*m*, 18H). ^{13}C-NMR (50.4 MHz): 167.06 (C(4")); 164.37 (C(2")); 145.63 (C(1")); 136.74 (C(1)); 129.37; 123.59; 116.24 (C(2)); 67.82 (C(2')); 39.73 (C(2)); 39.24 (C(1')); 33.61; 33.24; 28.08; 27.75; 25.73; 23.72; 20.26; 19.26. Anal. calc. for $C_{18}H_{24}N_4O_5$ (376.21): C 57.44, H 6.43, N 14.88; found: C 57,17, H 6.22, N 15.11.

3.2. *Acetalization of* **1b** *with Ethylene Glycol.* To a cold (0°), magnetically stirred suspension of **1b** (500 mg, 239 mmol) in dry ethylene glycol (5 ml) was added conc. H_2SO_4 (18M, 0.265 ml). After 5 min, all **1b** was dissolved, and the soln. became bright blue, evolving N_2O gas, and then slowly turned green and cloudy. After 5 h, the mixture was poured into sat. aq. $NaHCO_3$ soln. (50 ml) and extracted with Et_2O (3 × 50 ml). The Et_2O extracts were washed with H_2O (50 ml) and brine (50 ml), dried (Na_2SO_4), concentrated, and chromatographed on silica gel (hexane/EtOAc 2:1). Anal. data are for a distilled sample, which showed slight decomposition on distillation. *(1R*,2R*,6'R*)-2-(1',4'-dioxaspiro[4.5]dec-6'-yl)cyclohexanol* (**9**): Yield 503 mg (88%). B.p. 100°/0.05 Torr. R_f 0.22 (hexane/EtOAc 4:1). IR: 3604*w* (OH), 3443*m*, 2938*s*, 2863*s*, 1449*s*, 1370*m*, 1306*m*, 1271*m*, 1096*s*, 1022*s*, 980*s*, 949*s*, 909*s*. ^{1}H-NMR (300 MHz): 4.06 (*m*, H–C(1)); 3.66 (*m*, 2H–C(2'), 2H–C(3')); 2.07 (*m*, H–C(6'), H–C(2)); 1.9–1.0 (*m*, 17H). ^{13}C-NMR (75.5 MHz): 108.41 (C(5')); 77.25 (C(1)); 63.09; 62.56; 44.82 (C(6')); 41.25 (C(2)); 31.45; 29.90; 25.01; 24.83; 22.17; 21.29; 21.04; 20.72. MS (10 eV): 240 (23, $M^{+\cdot}$), 197 (43), 196 (24), 180 (10), 179

[20]) Prepared by adding a soln. of 3 g of 2,4-dinitrophenylhydrazine in 15 ml of conc. H_2SO_4 to 20 ml of H_2O and 70 ml of 95% EtOH.

(72), 178 (25), 155 (10), 153 (41), 150 (14), 149 (12), 136 (11), 135 (73), 121 (10), 111 (23), 109 (12), 107 (17), 99 (17), 98 (72), 97 (23), 96 (17), 95 (24), 94 (11), 93 (11), 83 (14), 82 (17), 81 (100), 80 (19), 79 (15), 69 (10), 67 (35), 55 (14). HR-MS: 240.17263 ($C_{14}H_{24}O_3$, calc. 240.17255).

3.3. *Reduction of* **1b** *with Zn/AcOH.* To a magnetically stirred mixture of Zn dust (1.06 g, 16.2 mmol) and **1b** (340 mg, 1.62 mmol) in Et_2O (50 ml) was added 25% aq. AcOH soln. (2.5 ml), and the mixture was refluxed for 3 h. More Zn (0.5 g) was added and reflux continued for 3 h. The mixture was filtered, poured into sat. aq. $NaHCO_3$ soln. (50 ml), and extracted with Et_2O (3 × 100 ml). The Et_2O extracts were washed with H_2O (50 ml) and brine (50 ml), dried (K_2CO_3), and concentrated. The residue was crystallized from hexane/EtOAc to yield 325 mg (95%) of *(2R*,1'R*,2'R*)-2-(2'-hydroxycyclohexyl)cyclohexanone oxime* (**10**), (*E*)/(*Z*) 2:1. M.p. 126–127°. R_f 0.25 (benzene/acetone/hexane 3:1:1). IR: 3598*w* (OH), 3239*m*, 2936*s*, 2865*m*, 1650*w* (C=N), 1449*m*, 1374*w*, 1327*w*, 1285*w*, 1239*w*, 1192*w*, 1154*w*, 1136*w*, 1055*w*, 1040*w*, 974*w*, 939*w*, 907*w*, 884*w*, 857*w*, 843*w*. ^{1}H-NMR (300 MHz): 10.0 (br., C=NOH); 3.73 (br. *s*, 0.67 H, OH of (*Z*)); 3.64 (br. *s*, 0.33 H, OH of (*E*)); 3.25 (*dm*, *J* = 10.9, 0.67 H, H–C(2') of (*E*)); 3.10 (*dm*, *J* = 15.0, 0.33 H, H–C(2') of (*Z*)); 2.36 (*dm*, *J* = 10.4, 0.33 H, H–C(2) of (*Z*)); 2.27 (*dm*, *J* = 13.8, 0.67 H, H–C(2) of (*E*)); 2.1–1.0 (*m*, 17 H). ^{13}C-NMR (75.5 MHz): (*E*) isomer: 164.10 (C(1)); 67.15 (C(2')); 39.98 (C(2)); 35.24 (C(1')); 32.71; 29.41; 26.96; 26.45; 26.22; 23.68; 20.42; 19.73; (*Z*) isomer: 163.13 (C(1)); 66.12 (C(2')); 42.52 (C(2)); 40.82 (C(1')); 33.04; 28.07; 25.79; 23.93; 22.08; 21.33; 19.91; one overlap with (*E*) isomer. MS (10 eV): 211 (1, $M^{+\cdot}$), 150 (15), 136 (10), 122 (11), 113 (100), 97 (10), 96 (14), 95 (13), 81 (40), 69 (10), 67 (14), 55 (16), 54 (10). Anal. calc. for $C_{12}H_{21}NO_2$ (211.31): C 68.21, H 10.02, N 6.63; found: C 68.23, H 10.11, N 6.48.

3.4. *Reduction of* **2b** *with Zn/AcOH.* To a magnetically stirred mixture of Zn dust (1.06 g, 16.2 mmol) and **2b** (170 mg, 0.81 mmol) in Et_2O (25 ml) was added 50% aq. AcOH soln. (2.5 ml) and the mixture refluxed for 8 h. More Zn (0.5 g) was added and reflux was continued for 8h. The mixture was worked up as described above for **10** to yield 128 mg (75%) of *(2R*,1'S*,2'S*)-2-(2'-hydroxycyclohexyl)cyclohexanone oxime* (**11**), (*E*)/(*Z*) 45:55. M.p. 137–139°. R_f 0.10, 0.20 (benzene/acetone/hexane 3:1:1). IR ($CHCl_3$): 3594*m* (OH), 3245*s*, 2936*s*, 2863*s*, 1651*w* (C=N), 1555*w*, 1449*w*, 1347*w*, 1320*w*, 1296*w*, 1130*m*, 972*s*, 912*m*, 885*m*. ^{1}H-NMR (300 MHz, CD_3OD): 4.77 (br. *s*, CD_3OH); 4.05 (br. *s*, OH of (*E*) and (*Z*)); 3.58 (*dm*, *J* = 11.0, 0.45 H, H–C(2') of (*E*)); 3.03 (*dm*, *J* = 14.2, 0.55 H, H–C(2') of (*Z*)); 2.34 (*dt*, *J* = 10.7, 4.1, 0.45 H, H–C(2) of (*Z*)); 2.25–1.0 (*m*, 17.55 H). ^{13}C-NMR (75.5 MHz, CD_3OD): (*E*) isomer: 164.03 (C(1)); 65.99 (C(2')); 40.54 (C(2)); 35.05 (C(1')); 34.56; 29.73; 28.57; 27.51; 27.06; 25.14; 21.62; 20.61; (*Z*) isomer: 163.75 (C(1)); 66.13 (C(2')); 43.36 (C(2)); 40.70 (C(1')); 34.64; 29.33; 27.23; 27.02; 25.35; 22.56; 22.42; 20.56. MS (10 eV): 113 (100), 81 (28), 32 (23), 31 (84), 30 (32). Anal. calc. for $C_{12}H_{21}NO_2$ (211.31): C 68.21, H 10.02, N 6.63; found: C 67.97, H 10.02, N 6.66.

3.5. *Reduction of* **1b** *with* $LiAlH_4$. *Method A:* $LiAlH_4$ (54 mg, 1.43 mmol) was slurried in cold (–15°), magnetically stirred, dry Et_2O (4 ml). A soln. of **1b** (200 mg, 0.96 mmol) in dry Et_2O (4 ml) was added dropwise over 5 min. After 30 min, the reaction was quenched by the sequential addition of H_2O (1 ml) and 6 N NaOH (2 ml). The resulting mixture was stirred 30 min at r. t. and filtered through *Celite* with Et_2O. The filtrate was dried (K_2CO_3), concentrated, and chromatographed on silica gel (pentane/Et_2O 1:1 to 100% Et_2O gradient). Anal. data are given for samples crystallized from hexane.

Method B: The same general procedure as above was used with the following exceptions. The solvent was dry THF, the addition was performed at reflux, and the mixture was refluxed 16 h prior to cooling and quenching. The residue remaining after concentration of the filtrate was a 7:3 mixture of **13a** and **13b**, from which **13a** could be selectively crystallized from hexane. No attempt was made to further purify the 1:1 mixture remaining in soln. Spectral data for **13b** are extracted from those for the mixture.

Oxime (**10**): Yield *Method A* 52 mg (28%), *Method B* 0%, *vide supra* for characterization data.

(1R,2R*,1'R*,2'R*)-2-[2'-(Hydroxyamino)cyclohexyl]cyclohexanol* (**12**). Yield *Method A* 52 mg (26%), *Method B* 0%: M.p. 139–140°. R_f 0.35 (pentane/Et_2O 1:1). IR: 3245*m* (OH, NH), 2928*s*, 2859, 2726*w*, 1451*m*, 1420*w*, 1370*w*, 1333*w*, 1318*w*, 1211*w*, 1181*w*, 1154*w*, 1129*w*, 1102*w*, 1051*w*, 974*m*, 945*w*, 897*w*, 858*w*. ^{1}H-NMR (300 MHz): 8.9–7.8 (br. 2 OH); 5.6–4.8 (br., NH); 4.42 (br. *s*, H–C(2')); 3.64 (br. *d*, *J* = 2.1, H–C(1)); 2.24 (*dm*, *J* = 14.0, H–C(2)); 1.93 (*m*, H–C(1')); 1.8–1.1 (*m*, 16H). ^{13}C-NMR (75.5 MHz): 64.51 (C(1)); 56.33 (C(2')); 47.44 (C(1')); 45.58 (C(2)); 33.35; 27.28; 27.14; 26.41; 26.23; 25.09; 20.32; 20.01. MS (10 eV): 213 (1, $M^{+\cdot}$), 195 (17), 179 (16), 178 (100), 163 (44), 162 (27), 161 (18), 152 (24), 135 (18), 134 (15), 119 (12), 113 (12), 107 (10), 100 (47), 99 (18), 98 (15), 97 (21), 96 (47), 95 (13), 94 (13), 93 (27), 91 (17), 83 (16), 82 (25), 81 (92), 80 (11), 79 (28), 72 (41), 69 (18), 68 (10), 67 (65), 60 (14), 56 (44), 55 (23), 41 (13). Anal. calc. for $C_{12}H_{23}NO_2$ (213.32): C 67.56, H 10.87, N 6.57; found: C 67.44, H 11.14, N 6.56.

(1R,2R*,1'R*,2'R*)-2-(2'-Aminocyclohexyl)cyclohexanol* (**13a**). Yield *Method A* 44 mg (23%), *Method B* 66%[21]) (after recrystallization 75 mg (39%)). M.p. 119–121°. R_f 0.06 (Et_2O). IR: 3168*w* (OH, NH_2), 2930*s*, 2855*s*,

[21]) Yield calculated by integration of signals in the ^{1}H-NMR spectrum of a mixture **13a**/**13b**.

1580*w*, 1522*w*, 1447*m*, 1362*w*, 1331*w*, 1254*w*, 1215*w*, 1130*w*, 1076*w*, 1055*w*, 984*w*, 939*w*, 911*w*, 889*w*, 872w. ^{1}H-NMR (300 MHz): 3.90 (br. *s*, H–C(1)); 3.08 (br. *s*, H–C(2′)); 1.9–1.0 (*m*, 21 H). ^{13}C-NMR (75.5 MHz): 64.16 (C(1)); 47.35 (C(1′)); 46.46 (C(2)); 44.92 (C(2′)); 35.49; 33.84; 27.12; 26.71; 25.14; 24.89; 20.36; 19.71. MS (10 eV): 197 (4, $M^{+\cdot}$), 154 (10), 100 (17), 98 (22), 96 (12), 83 (11), 82 (16), 81 (12), 67 (11), 56 (100), 43 (11). Anal. calc. for $C_{12}H_{23}NO$ (197.32): C 73.04, H 11.75, N 7.10; found: C 73.07, H 11.85, N 7.08%.

*(1*R*,2R*,1′R*,2′S*)-2-(2′-Aminocyclohexyl)cyclohexanol* (**13b**). Yield *Method A* 0%, *Method B* 27%[21]). R_f 0.06 (Et_2O). ^{1}H-NMR[22]) (200 MHz): 3.80 (br. *s*, H–C(1)); 2.45 (*ddd*, *J* = 11.1, 11.1, 4.2, H–C(2′)). ^{13}C-NMR[22]) (50.4 MHz): 66.68 (C(1)); 52.52 (C(2′)); 48.73; 48.57; 39.58; 34.01; 32.63; 27.67; 27.22; 25.77; 25.10; 20.17.

3.6. *Oxidation of* **1b** *with* RuO_4. To a cold (0°), magnetically stirred soln. of **1b** (400 mg, 1.91 mmol) in CCl_4 (40 ml) covered with H_2O (0.4 ml) was added all at once a soln. of RuO_4 in CCl_4 (0.06M, 40 ml). From the mixture instantly precipitated a fine suspension of RuO_2, becoming opaque black. After 10 min, the reaction was quenched with i-PrOH (0.5 ml) and filtered. The precipitate was thoroughly washed with CCl_4, and the filtrate was then washed with H_2O (30 ml). The H_2O was reextracted with an additional portion of CCl_4 (30 ml), the org. layers combined, dried (Na_2SO_4), concentrated, and chromatographed on silica gel (hexane/EtOAc 4:1). The higher-R_f product was shown to be **14,** which, although stable in soln. or under vacuum, had a stability of only several seconds at r. t. and ambient pressure.

*(1*R*,2R*,1′R*)-2-(2′-Oxocyclohexyl)cyclohexyl Nitrite* (**14**). Yield 275 mg (64%). M.p. 20° (dec.). R_f 0.52 (hexane/EtOAc 4:1). IR: 2940*s*, 2859*m*, 1711*s* (C=O), 1642*s* (N=O), 1608*w*, 1461*w*, 1448*m*, 1365*w*, 1338*w*, 1312*w*, 1294*w*, 1239*w*, 1218*w*, 1201*w*, 1152*w*, 1129*m*, 1051*w*, 1039*w*, 1019*w*, 944*w*, 978*w*, 928*w*, 903*w*, 888*w*, 865*w*, 844*w*, 835*w*. ^{1}H-NMR (300 MHz): 5.71 (*s*, H–C(1)); 2.40–0.90 (*m*, 18 H). ^{13}C-NMR (75.5 MHz): 212.71 (C(1′)); 77.51 (C(1)); 51.61 (C(2′)); 42.77 (C(6′)); 38.00 (C(2)); 31.98; 31.34; 28.64; 25.56; 25.29; 23.25; 20.03. MS (70 eV): 195 (15, $M^{+\cdot}$ – NO), 179 (13), 177 (30), 159 (12), 135 (14), 133 (12), 111 (21), 107 (14), 99 (12), 98 (22), 97 (41), 95 (41), 93 (32), 91 (23), 83 (17), 81 (100), 80 (12), 79 (59), 77 (12), 69 (48), 67 (80), 57 (15), 55 (68), 54 (13), 53 (18), 43 (26), 41 (95), 39 (27), 32 (14), 30 (83, NO^+), 29 (27).

*(1*R*,1′R*)-[1,1′-Bicyclohexyl]-2,2′-dione* (**6**). Yield 75 mg (20%). See *3.9* for anal. data.

3.7. *Reaction of* **1b** *with K(t-BuO)*. Nitronate **1b** (265 mg, 1.27 mmol) was added all at once to a magnetically stirred soln. of K(*t*-BuO) (22 mg, 15 mol-%) in dry THF (5 ml). After 46 h, another portion of K(*t*-BuO) (11 mg, 8 mol-%) was added. After 4.5 days, the mixture was poured into H_2O (40 ml) and extracted with EtOAc (3 × 40 ml). The EtOAc extracts were washed with brine (40 ml), dried (K_2CO_3), concentrated, chromatographed on silica gel (EtOAc), and crystallized from hexane/EtOAc to afford *(4aR*,10aR*,10bR*)-2,3,4,4a,7,8,9,10,10a,10b-decahydro-1H-dibenz[c,e][1,2]oxazin-4a-ol* (**15**) as sparkling white needles. Yield 209 mg (79%). M.p. 182°(dec.). R_f 0.18 (hexane/EtOAc 2:1). IR: 3598*w*, 3424*w*, 2938*s*, 2859*m*, 1549*w*, 1462*w*, 1447*m*, 1433*w*, 1397*w*, 1341*w*, 1275*w*, 1260*w*, 1198*w*, 1134*m*, 1107*w*, 1065*w*, 1026*m*, 970*w*, 959*w*, 941*m*, 901*w*, 887*w*, 862*w*, 847*w*. ^{1}H-NMR (300 MHz, CD_3OD): 4.93 (*s*, CD_3OH); 2.40 (*dm*, *J* = 15.0, H–C(10a)); 2.13 (*m*, 2H–C(7)); 2.05–0.90 (*m*, 15 H). ^{13}C-NMR (75.5 MHz, CD_3OD): 162.04 (C(6a)); 95.17 (C(4a)); 43.13 ((10a)); 34.86 (C(10b)); 34.73; 31.76; 30.49; 26.24; 25.92; 25.04; 24.68; 22.41. MS (10 eV): 210 (10, $M^{+\cdot}$ + 1), 209 (53, $M^{+\cdot}$), 192 (100), 191 (16), 174 (14), 166 (22), 164 (20), 163 (31), 162 (17), 153 (16), 152 (10), 136 (13), 135 (19), 122 (12), 120 (11), 113 (37), 112 (16), 98 (11), 97 (12), 96 (12), 95 (16), 94 (15), 82 (12), 81 (53), 80 (11), 79 (15), 69 (10), 67 (23), 55 (16), 41 (14). Anal. calc. for $C_{12}H_{19}NO_2$ (209.29): C 68.87, H 9.15, N 6.69; found: C 68.90, H 8.96, N 6.58.

3.8. *Reaction of* **1b** *with MeLi*. To a cold (–12°), magnetically stirred soln. of **1b** (100 mg, 0.48 mmol) in dry Et_2O (2 ml) was added MeLi (1.20M, 0.88 ml). The mixture was warmed to 5°, quenched with H_2O (0.2 ml), dried (Na_2SO_4), concentrated, and the residue was crystallized from Et_2O/MeOH to afford *(2R*,1′R*,2′R*-E)-2-(2′-hydroxy-2′-methylcyclohexyl)cyclohexanone oxime* (**16**) as white plates. Yield 97 mg (91%). M.p. 128° (dec.). R_f 0.18 (benzene/acetone 3:1). IR: 3241*w*, 2934*d*, 2861*m*, 1597*m*, 1462*w*, 1449*m*, 1368*w*, 1258*w*, 1229*m*, 1200*m*, 1117*m*, 1090*w*, 974*w*, 932*w*, 891*w*. ^{1}H-NMR (300 MHz): 3.02 (*m*, H–C(2)); 2.38 (*m*, H_{eq}–C(6)); 1.37 (*s*, CH_3); 2.10–0.80 (*m*, 18 H). ^{13}C-NMR (75.5 MHz): 145.27 (C(1)); 74.01 (C(2′)); 47.13 (C(2)); 40.77 (C(1′)); 33.85; 30.98; 24.22; 23.47; 24.22; 23.47; 23.45; 23.01; 21.31; 21.29 (CH_3); a 13th C-atom could not be located. MS (10 eV): 226 (12, $M^{+\cdot}$ + 1), 225 (69, $M^{+\cdot}$), 208 (67), 207 (100), 193 (10), 192 (21), 191 (27), 190 (20), 181 (13), 176 (12), 165 (11), 164 (22), 153 (22), 151 (10), 150 (18), 148 (21), 135 (16), 128 (82), 124 (11), 113 (15), 112 (12), 111 (78), 110 (36), 109 (20), 98 (45), 97 (23), 96 (29), 95 (62), 94 (12), 93 (13), 86 (98), 84 (11), 83 (22), 81 (36), 73 (48), 70 (47), 68 (16), 67 (14), 57 (25), 55 (12). HR-MS: 225.1728 ($C_{13}H_{23}NO_2$, calc. 225.1278).

3.9. *(1R*,1′R*)- and (1R*,1′S*)-[1,1′-Bicyclohexyl]-2,2-diones* (**6** and **7**, resp.). *Method A:* To a cold (0°), magnetically stirred suspension of **10** or **11** in CCl_4 (0.05M) covered with a few drops of H_2O was added all at once a soln. of RuO_4 in CCl_4 (0.06M, 1.6 equiv.). When TLC analysis indicated consumption of starting material (30–90

[22]) Spectroscopic data taken from a mixture **13a**/**13b**.

min), the reaction was quenched with excess i-PrOH and filtered. The precipitate was thoroughly washed with CCl_4, and the filtrate was then washed with H_2O. The H_2O was reextracted with an additional portion of CCl_4 and the org. phase dried (Na_2SO_4), and concentrated. No further purification of products was attempted. *Method B:* Acetal **9** (250 mg, 1.04 mmol) was added all at once to a soln. of acetone (2 ml), H_2O (1 ml), and 5% aq. HCl soln. (0.022 ml) and shaken vigorously for 3 min. The soln. was then poured into sat. aq. $NaHCO_3$ soln. (30 ml) and extracted with Et_2O (3 × 30 ml). The Et_2O extracts were washed with H_2O (30 ml), brine (30 ml), dried (Na_2SO_4), and concentrated. The residue was taken up in CCl_4 (10 ml) and covered with H_2O (0.1 ml). To this magnetically stirred soln. was added all at once a soln. of RuO_4 in CCl_4 (0.06M, 10.2 ml). After 2 min, the reaction was quenched with excess i-PrOH (1 ml), and the black mixture was filtered. The precipitate was thoroughly washed with CCl_4, and the filtrate was then washed with H_2O (10 ml), dried (Na_2SO_4), concentrated, and chromatographed (hexane/EtOAc 4:1).

Data of **6:** Yield *Method A* (from **10**) 75%, *Method B* 84%. M.p. 71°. R_f 0.31 (hexane/EtOAc 4:1). IR: 2940*s*, 2865*s*, 1709*s*, 1449*s*, 1426*m*, 1345*m*, 1312*m*, 1283*m*, 1252*m*, 1229*w*, 1217*w*, 1188*w*, 1132*s*, 1111*m*, 1059*w*, 1034*w*, 1005*w*, 909*s*, 889*w*, 828*w*. ^{1}H-NMR (200 MHz): 2.85 (*m*, H–C(1), H–C(1′)); 2.34 (*m*, 2H–C(2), 2H–C(2′)); 2.15–1.0 (*m*, 12H). ^{13}C-NMR (75.5 MHz): 211.66 (C(2,2′)); 48.91 (C(1,1′)); 42.27 (C(3,3′)); 30.06; 28.01; 25.38.

Data of **7.** Yield *Method A* (from **11**) 72%. R_f 0.31 (hexane/EtOAc 4:1). IR: 2940*s*, 2865*s*, 1709*s*, 1449*s*, 1364*m*, 1339*m*, 1314*m*, 1271*m*, 1246*m*, 1231*m*, 1202*m*, 1130*s*, 1094*w*, 1059*m*, 1019*w*, 999*m*, 943*w*, 909*m*, 874*w*, 833*w*. ^{1}H-NMR (200 MHz): 2.8–1.2 (*m*, 18H). ^{13}C-NMR (75.5 MHz): 210.76 (C(2,2′)); 50.26 (C(1,1′)); 41.80 (C(3,3′)); 29.08; 26.50; 24.99.

3.10. *General Procedure for Preparation of Double Cycloadducts.* Nitronates **1b** or **3b** were dissolved in dry CH_2Cl_2, MeCN, or benzene (20 mg/1 ml). Methyl acrylate (5.0 equiv.), together with a few crystals of 2,6-di(*t*-butyl)-hydroquinone to inhibit acrylate polymerization, was added and the soln. refluxed until TLC analysis showed consumption of nitronate (1–6 days). In those instances where the reaction time was longer than 24 h, fresh methyl acrylate was added as judged necessary. Upon completion, the mixture was concentrated and chromatographed on silica gel. In several instances, an inseparable mixture of products was obtained, in which case the major isomer was fractionally crystallized from pentane/Et_2O, and the minor isomer(s) characterized by their contributions to the ^{1}H-NMR of the mixture. The yields for the minor isomers are based on integration ratios of peaks in those spectra compared to the isolated yields of the major isomers (see *Schemes 10* and *11*).

Methyl (4aR,6S*,8R*,9aS*,13aS*,13bS*)-Perhydrodibenz[c,e]isoxazolo[2,3-b][1,2]oxazine-6-carboxylate* (**17**). Yield 15–17%. R_f 0.35 (hexane/EtOAc 4:1). ^{1}H-NMR[23]) (200 MHz): 4.69 (*dd*, *J* = 9.5, 6.3, H–C(6)); 4.17 (*m*, H–C(9a)); 3.74 (*s*, CH_3O); 3.17 (*dd*, *J* = 12.1, 5.8, H_{pro-S^*}–C(5)); 2.10–0.70 (*m*, 19H).

Methyl (4aR,6R*,8R*,9aS*,13aS*,13bS*)-Perhydrodibenz[c,e]isoxazolo[2,3-b][1,2]oxazine-6-carboxylate* (**18**). Yield 25–34%. M.p. 113–114. R_f 0.35 (hexane/EtOAc 4:1). IR: 2936*s*, 2863*s*, 1761*s*, 1742*s*, 1449*m*, 1437*m*, 1354*w*, 1277*m*, 1204*s*, 1183*m*, 1157*w*, 1138*w*, 1117*m*, 1051*w*, 992*m*, 909*w*, 889*w*, 858*m*, 837*m*. ^{1}H-NMR (300 MHz): 5.11 (*dd*, *J* = 10.8, 5.3, H–C(6)); 4.27 (*q*, *J* = 3.6, H–C(9a)); 3.80 (*s*, CH_3O); 3.01 (*dd*, *J* = 11.0, 10.0, H_{pro-S^*}–C(5)); 2.10–1.05 (*m*, 19H). ^{13}C-NMR (75.5 MHz): 174.51; 78.62; 77.23; 71.64; 52.35; 41.54; 40.23; 40.02; 37.01; 30.52; 29.53; 25.35; 24.94; 21.83; 21.52. MS (10 eV): 295 (17, $M^{+\cdot}$), 236 (16), 194 (12), 187 (20), 179 (11), 167 (12), 165 (10), 135 (17), 107 (18), 95 (30), 93 (16), 82 (11), 81 (100), 79 (15), 67 (27), 55 (11). Anal. calc. for $C_{16}H_{25}NO_4$ (295.38): C 65.06, H 8.53, N 4.74; found: C 65.21, H 8.46, N 4.81.

Methyl (4aR,6R*,8R*,9aR*,13aR*,13bR*)-Perhydrodibenz[c,e]isoxazolo[2,3-b][1,2]oxazine-6-carboxylate* (**19**). Yield 30–39%. M.p. 115–116°. R_f 0.30 (hexane/EtOAc 4:1). IR: 2944*s*, 2861*s*, 1742*s*, 1456*s*, 1437*s*, 1364*m*, 1314*m*, 1283*m*, 1204*m*, 1183*s*, 1161*m*, 1129*w*, 1109*w*, 1059*s*, 1038*s*, 982*s*, 951*w*, 912*w*, 874*w*, 857*m*, 824*s*. ^{1}H-NMR (300 MHz): 5.05 (*dd*, *J* = 10.8, 4.0, H–C(6)); 3.92 (*dt*, *J* = 12.1, 4.9, H–C(9a)); 3.78 (*s*, CH_3O); 2.65 (*t*, *J* = 11.4, H_{pro-S^*}–C(5)); 2.40–2.05 (*m*, 3H); 2.00–1.60 (*m*, 8H), 1.55–1.05 (*m*, 7H); 0.85 (*m*, 1H). ^{13}C-NMR (75.5 MHz): 171.47; 79.48; 78.55; 76.51; 52.28; 36.85; 34.00; 33.03; 30.45; 25.91; 25.86; 25.86; 25.29; 25.23; 22.55; 19.61. MS (10 eV): 295 (5, $M^{+\cdot}$), 236 (13), 187 (14), 167 (15), 135 (18), 107 (18), 95 (24), 93 (14), 81 (100), 79 (14), 69 (10), 67 (25), 55 (15). Anal. calc. for $C_{16}H_{25}NO_4$ (295.38): C 65.06, H 8.53, N 4.74; found: C 64.81, H 8.57, N 5.09.

Methyl (2R,4R*,6aS*,10aS*)-Perhydrospiro[benz[c]isoxazolo[2,3-b]isoxazole-6,1′cyclohexane]-2-carboxylate* (**20**). M.p. 96–98°. R_f 0.13 (hexane/EtOAc 4:1). IR: 2938*s*, 2867*m*, 1738*s*, 1449*m*, 1437*m*, 1337*w*, 1281*m*, 1210*m*, 1105*w*, 1053*w*, 1032*m*, 1013*m*, 988*w*, 967*w*, 899*w*. ^{1}H-NMR (300 MHz): 4.74 (*dd*, *J* = 9.2, 6.6, H–C(2)); 3.76 (*s*, CH_3O); 2.73 (*dd*, *J* = 12.7, 9.2, H_{pro-S^*}–C(1)); 2.29 (*dd*, *J* = 12.7, 6.6, H_{pro-R^*}–C(1)); 2.05 (*dd*, *J* = 6.7, 2.1, H–C(6a)); 2.00–1.00 (*m*, 18H). ^{13}C-NMR (75.7 MHz): 172.39; 91.80; 78.29; 73.01; 52.35; 51.28; 41.77; 40.38; 34.31; 30.90; 25.17; 23.39; 22.08; 22.13; 21.85. MS (10 eV): 295 (2, $M^{+\cdot}$), 194 (12), 187 (10), 95 (100), 81 (21). Anal. calc. for $C_{16}H_{25}NO_4$ (295.38): C 65.06, H 8.53, N 4.74; found: C 64.91, H 8.58, N 4.83.

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[23]) Spectroscopic data taken from a mixture **17**/**18**.

Methyl (2R,4S*,6aR*,10aR*)-Perhydrospiro[benz[c]isoxazolo[2,3-b]isoxazole-6,1'-cyclohexane]-2-carboxylate* (**21**). R_f 0.13 (hexane/EtOAc 4:1). ^{1}H-NMR[24]) (200 MHz): 4.29 (*dd*, *J* = 10.7, 3.9, H–C(2)); 3.78 (*s*, CH_3O); 3.35 (*dd*, *J* = 13.5, 11.2, $H_{pro\text{-}S^*}$ + C(1)); 2.30–1.00 (*m*, 20H).

Methyl (2R,4R*,6aR*,10aS*)-Perhydrospiro[benz[c]isoxazolo[2,3-b]isoxazole-6,1'-cyclohexane]-2-carboxylate* (**22**). R_f 0.11. ^{1}H-NMR[24]) (200 MHz): 4.64 (*dd*, *J* = 9.8, 5.0, H–C(2)); 3.75 (*s*, CH_3O); 2.64 (*dd J* = 12.8, 9.8, $H_{pro\text{-}S^*}$–C(1)); 2.30–1.00 (*m*, 20H).

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