# 'Inverse-Electron-Demand' *Diels-Alder* Reactions of (*E*)-3-Diazenylbut-2-enes in Water

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The cycloadditions of (*E*)-3-diazenylbut-2-enes **1** with a variety of alkenes **2**–**6** were carried out in water as well as in organic solvents. The reactions were always faster in heterogeneous aqueous medium than in the organic solvents. These conjugated diazenyl-alkenes behave mainly as heterodienes, and the *Diels-Alder* adducts are the sole or at least main reaction products. Pyrroles derived from zwitterionic [3 + 2] cycloaddition reactions were observed in some cases. The cycloaddition of **1a** with (+)-2-(ethenyloxy)-3,7,7-trimethylbicyclo[4.1.0]heptane (**5**) is the first example of an asymmetric 'inverse electron-demand' *Diels-Alder* reaction carried out in pure water.

**Introduction.** – In recent years, 3-diazenylbut-2-enes have received much attention because they provide important synthones in organic, biological, medicinal, and agricultural chemistry [1–6].

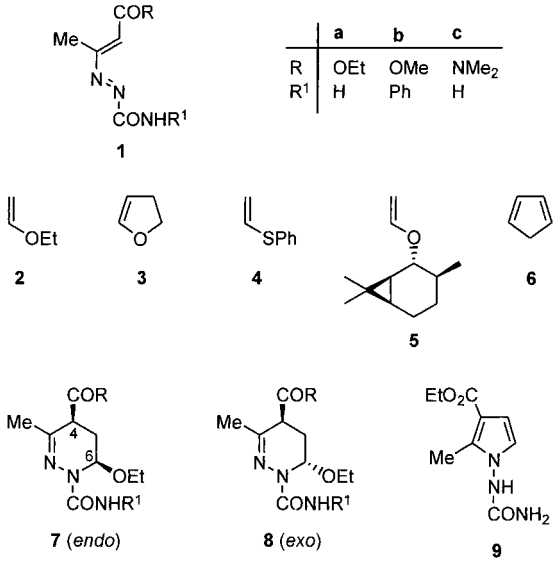
These conjugated diazenyl-alkenes are very reactive compounds, and the presence of electron-withdrawing groups on the terminal atoms of the diazenyl-ene system, renders the cycloaddition reactions more chemo- and regioselective [4][7]. Their 'inverse-electron-demand' *Diels-Alder* reaction with electron-rich dienophiles is the most common type of cycloaddition and allows preparation of 1,4,5,6-tetrahydropyridazines [1–3][6a–b][6l–n][7], which are used as herbicides [8] or as intermediates for the preparation of herbicides and fungicides [9]. The cycloadditions were carried out in organic solvents (mainly $CH_2Cl_2$, THF, and $CCl_4$) at room temperature and generally occur with high regio- and diastereoselectivity and with good yield [1–3][6a–b][6l–n][8][9]. So far, *Diels-Alder* reaction of these compounds, performed in $H_2O$, has not been reported [10].

Water as a reaction medium has attracted the attention of chemists in the last decade; unexpected results have been obtained, and many more reactions than one had imagined can be performed in this medium [11]. The low solubility of reactants is generally not an obstacle, and the reactivity and selectivity are generally improved when compared with reactions carried out in organic solvents under homogeneous conditions [12]. The possibility to use $H_2O$-tolerant *Lewis* acids [13] while controlling the pH of the reaction medium [14] allows further increase in reactivity and selectivity of the process.

Examples of 'normal-electron-demand' hetero-*Diels-Alder* reactions in aqueous medium are common in the literature [11][15], while, to our knowledge, only one

example of 'inverse-electron-demand' *Diels-Alder* reaction performed in $H_2O$ has been reported [16].

**Results and Discussion.** – We describe here the results of the 'inverse-electron-demand' hetero-*Diels-Alder* reactions of (*E*)-3-diazenylbut-2-enes **1a–c** with the alkenes **2–6** both in $H_2O$ and organic solvents. The diazenyl-alkenes **1a** and **1b** are poorly soluble in $H_2O$, while **1c** is soluble both in $H_2O$ and in organic solvents.




The cycloadditions of (*E*)-3-diazenylbut-2-enes[1]) **1a–c** with ethyl vinyl ether (**2**) were carried out at 15°, and the results are shown in *Table 1*. These cycloaddition reactions in $H_2O$ occur under heterogeneous conditions because of the low solubility of the reactants and their *Diels-Alder* adducts in $H_2O$. The cycloadditions of **1a–c** with **2–6** carried out in $CH_2Cl_2$ occur under homogeneous conditions. The diazenyl-alkenes **1a–c** are colored, and the progress of the cycloadditions was accompanied by a change in color (see *Exper. Part*).

The *Diels-Alder* reaction of **1a** with **2** in pure $H_2O$ was complete in 16 h at 15° (*Table 1*, *Entry 1*) and gave three products: **7a** (92%), **8a** (6%), and **9** (2%). The tetrahydropyridazine **7a** is a crystalline adduct, most of which was isolated in pure form by simple filtration. The cycloaddition is highly diastereoselective and the *endo*-adduct **7a** is isolated in 83% yield, while the *exo*-adduct **8a** and the *N*-(carbamoylamino)-

[1]) The configurations of diazenyl-alkenes **1a**, **1b**, and **1c** were established by $^1$H-NMR spectroscopy. The diazenyl-alkene **1d** (R = EtO, $R^1$ = *t*-BuO) was chosen as the representative compound, because both diastereoisomers are available. In (*Z*) diazenyl-alkene, the saturation of H–C(4) frequency gives a NOE effect on the H-atoms of the Me group (3%) and the saturation of frequency of the Me protons gives a NOE effect on H–C(4) (5.4%). No NOE effect was observed on the (*E*)-stereoisomer. The chemical shifts of H–C(4) and those of the Me–C(3) group of the (*E*)-isomer are at lower field ($\delta$(H–C(4)) = 6.93 ppm; $\delta$(Me) = 2.23 ppm) than those of the (*Z*)-isomer ($\delta$(H–C(4)) = 6.42 ppm; $\delta$(Me) = 1.95 ppm). Accordingly, all diazenyl-butenes are (*E*)-configured.

Table 1. Diels-Alder *Reactions of 3-Diazenylbut-2-enes* **1** *with Ethyl Vinyl Ether* (**2**) *at 15°*

| *Entry* | Diene | Medium | *t* [h] | Conversion [%][a][b]) | *endo*-**7**[b]) | *exo*-**8**[b]) | Yield [%][c]) |
|---|---|---|---|---|---|---|---|
| *1* | **1a** | $H_2O$ | 16[d]) | 100 | 92 | 8[e]) | 83 |
| *2* | | $CH_2Cl_2$ | 16 | 81 | 90 | 10 | 60 |
| *3* | | AcOEt | 16 | 22 | 77 | 23 | |
| *4* | | PhMe | 16 | 19 | 74 | 26 | |
| *5* | | THF | 16 | 16 | 75 | 25 | |
| *6* | **1b** | $H_2O$ | 13 | 100 | 89 | 11 | 75 |
| *7* | | $CH_2Cl_2$ | 13 | 79 | 91 | 9 | 55 |
| *8* | **1c** | $H_2O$ | 24 | 82 | 85 | 15 | 62[f]) |
| *9* | | $CH_2Cl_2$ | 24 | 31 | 84 | 16 | |

[a]) Reaction conversion; the complement to 100 is unreacted **1**. [b]) Percentage determined by $^1$H-NMR. [c]) Total yield of isolated main product. [d]) In the presence of $Yb(OTf)_3$ (1 mol-equiv.), the reaction time is reduced to half. [e]) Mixture of **8a**/**9** 3 : 1. [f]) Considering the recovered starting material, the yield of **7c** is 73%.

pyrrole **9** were detected by $^1$H-NMR spectroscopy. The secondary orbital interactions between the O-atom of **2** and the N(2) of diazenyl-diene system **1a** strongly favor the *endo*-addition. When the *Diels-Alder* was carried out in organic solvent (*Entries 2–5:* $CH_2Cl_2$, AcOEt, PhMe, THF) under the same experimental conditions, the reaction rate was always slower than in aqueous medium, and a large amount of the starting material was recovered. The organic solvent that led to the best results was $CH_2Cl_2$, and, therefore, it was chosen as the reference organic medium for the cycloaddition reactions of the other two diazenyl-butenes, **1b** and **1c**. The cycloaddition of **1b** and **2** gave the best yield when it was carried out in $H_2O$ (*Entries 6* and *7*). Both adducts, *endo*-**7b** and *exo*-**8b**, were isolated in pure form. The diazenyl-alkene **1c** was the least reactive of the three dienes in the cycloaddition with **2** and was not stable in $H_2O$ or in $CH_2Cl_2$ for more than 24 h at room temperature (*Entries 8* and *9*). The cycloaddition must, therefore, be stopped to avoid by-products and to achieve higher yields of the adducts. Once again, the aqueous medium allowed isolation of the *endo*-adduct **7c** with higher yield than $CH_2Cl_2$. The *exo*-adduct **8c** could not be isolated in a pure state, and its structure was assigned on the basis of the $^1$H-NMR spectrum of an enriched mixture (**7c**/**8c** 20 : 80).

It is known that the *endo*- and *exo*-adducts from [4 + 2] cycloadditions of conjugated diazenyl-alkenes with ethyl vinyl ether (**2**) can isomerize spontaneously or in solution [7]. We have checked that no *endo*/*exo*-isomerization occurs at room temperature in either $H_2O$ or in $CH_2Cl_2$.

The study was then extended to *Diels-Alder* reactions of **1a** with other vinyl ethers such as 2,3-dihydrofuran (**3**), phenyl vinyl sulfide (**4**), and (+)-2-(ethenyloxy)-3,7,7-trimethylbicyclo[4.1.0]heptane (**5**). The results of the reactions carried out at 15° in $H_2O$ and $CH_2Cl_2$ are given in *Table 2*.

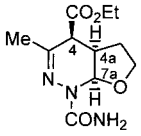
The cycloaddition of **1a** with **3** in pure $H_2O$ (*Entry 1*, *Table 2*) under heterogeneous conditions was faster than that with the simplest ethyl vinyl ether (**2**), probably because the dihydrofuran **3** is more hydrophobic than **2**, but the diastereoselectivity of the reaction was lower, and the percentage of the zwitterionic [3 + 2] cycloaddition is higher. The pyrrole derivative **12** is practically insoluble in $H_2O$, and was isolated simply by filtration at the end of the reaction; the *exo*-adduct **11** was obtained in pure form by

Table 2. Diels-Alder *Reactions of Diazenylbutene* **1a** *with Various Alkenes at 15°*

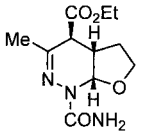
| *Entry* | Dienophile | Medium | *t* [h] | Conversion [%][a)b)] | Product [%][b)] | *endo*/*exo* | Yield [%][c)] |
|---|---|---|---|---|---|---|---|
| *1* | **3** | $H_2O$ | 3 | 100 | **10** (53) | 66:34 | [d)] |
| | | | | | **11** (27) | | 18 |
| | | | | | **12** (20) | | 20 |
| *2* | **3** | $CH_2Cl_2$ | 3 | 29 | **10** (79) | 79:21 | |
| | | | | | **11** (21) | | |
| *3* | **4** | $H_2O$ | 96 | 100 | **13** (87) | 100:0 | 50 |
| | | | | | **15** (13) | | 7 |
| *4* | **4** | $CH_2Cl_2$ | 96 | 74 | **13** (87) | 100:0 | 40 |
| | | | | | **15** (13) | | |
| *5* | **5** | $H_2O$ | 68 | 100 | **21** + **22** (83)[e)] | 83:17 | 57 |
| | | | | | **23** + **24** (17)[e)] | | 6 |
| *6* | **5** | $CH_2Cl_2$ | 72 | 100 | **21** + **22** (89)[f)] | 89:11 | 55 |
| | | | | | **23** + **24** (11)[f)] | | |
| *7* | **6** | $H_2O$ | 0.75 | 100 | **25** (100) | 100:0 | 90 |
| *8* | **6** | $CH_2Cl_2$ | 1.5 | 100 | **25** (100) | 100:0 | 90 |

For [a)] and [b)], see *Table 1*. [c)] Total yield of isolated compound. [d)] Isolated in mixture 9:1 with **11**. [e)] Reaction mixture composition: **21** (60%), **22** (23%), **23** (4%), **24** (13%); de(*endo*) 43%, de(*exo*) 53%. [f)] Reaction mixture composition: **21** (61%), **22** (28%), **23** (4%), **24** (7%); de(*endo*) 35%, de(*exo*) 25%.

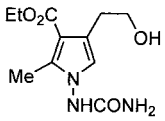
recrystallization of the remaining mixture. Chromatographic efforts did not give the *endo*-adduct **10** in pure form; a 9:1 mixture **10**/**11** was used to determine the structure of **10**. The cycloaddition of **1a** and **3** in $CH_2Cl_2$ (*Entry 2*) occurs under homogeneous conditions, leading to **10** and **11** with a higher diastereoselectivity, but low conversion rate.



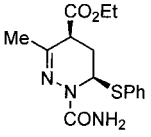

**10**



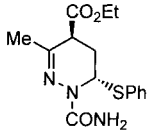

**11**



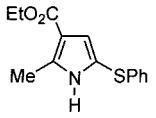

**12**




**13**




**14**

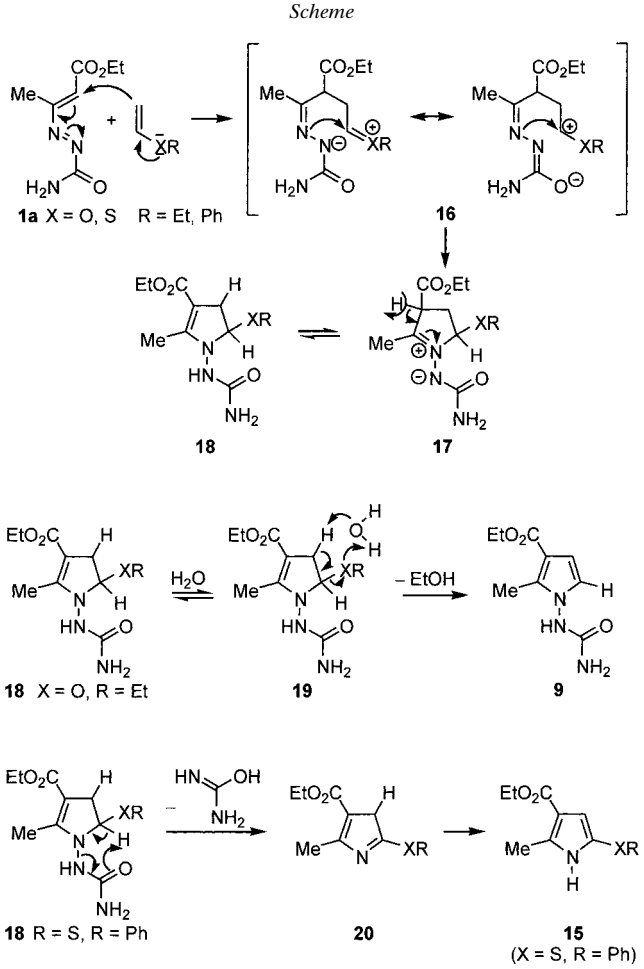



**15**

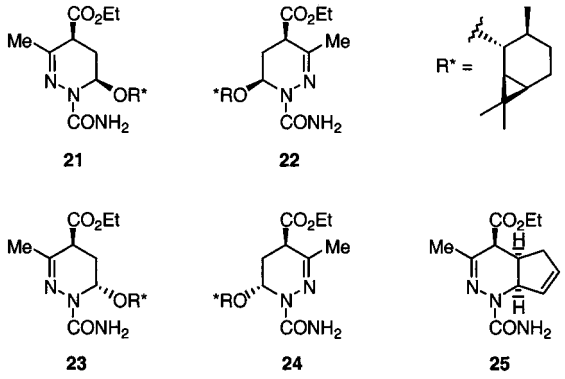
Phenyl vinyl sulfide (**4**) reacted slowly with diazenyl-alkene **1a** in aqueous medium to give the *endo*-adduct **13** and the pyrrole derivative **15** (*Table 2*, *Entry 3*). The *exo*-adduct **14** was not detected; this is due to stronger secondary orbital interactions of the S-atom with respect to the O-atom in the *endo*-transition state. The reaction carried out in $CH_2Cl_2$ (*Entry 4*) gave the same chemo- and stereoselectivity, but it was slower than that performed in aqueous medium. The formation of **15**, in contrast to that of the *N*-ureidopyrroles **9** and **12** that occurs through the cleavage of C-heteroatom bond does not occur through cleavage of the C–S bond with the elimination of thiophenol; more

likely, the N–N bond is cleaved, and urea is eliminated. On the basis of the stepwise, zwitterionic reaction mechanism proposed for [3 + 2] addition of 3-diazenylbut-2-enes with alkenes [6a–b] [6l–n], the diazenyl-alkene **1a** leads to a zwitterionic intermediate **16**, which undergoes cyclization of the lone-pair of N(2) with the electrophilic C-atom of the dienophiles (*Scheme*) to give, *via* the azomethine imide **17**, the dihydropyrroles **18**. Finally, the relative acidity of H–C(4) and H–C(5) of **18** induces the formation of **9** and **15**. As a consequence of inductive and resonance effects, in the case of X = O and R = Et, H–C(4) is more acidic than H–C(5), while the reverse is true for X = S and R = Ph. Consequently, the formation of **9**, through **19** *via* elimination of EtOH, is preferred in the first case, and the formation of tautomer **15**, through **20** *via* elimination of urea, occurs in the second case. The formation of **15** is slower than **9** (and the analogous **12**), because the carbocation **16** (X = S, R = Ph) is less stable than **16** (X = O, R = Et).

*Scheme*



The cycloaddition reaction of **1a** with (+)-2-(ethenyloxy)-3,7,7-trimethylbicyclo[4.1.0]heptane (**5**) in pure $H_2O$ (*Table 2*) required 68 h at 15° for completion and gave four products **21** (60%), **22** (23%), **23** (4%), and **24** (13%) (*Entry 5*). Analogous results were obtained when the reaction was carried out in homogeneous solution in $CH_2Cl_2$ (*Entry 6*). *endo*-Adducts **21** and **22** were separated from the *exo*-isomers **23** and **24**, respectively, by column chromatography. Fractional crystallization of the mixture **21**/**22** gave the main reaction product **21** in pure state. Efforts to obtain crystals of **21** for an X-ray diffraction analysis were unsuccessful. The assignment of the absolute configurations of **21** and its stereoisomers was tentatively achieved on the basis of the analogies of their $^1$H-NMR spectra with those of homochiral 1,2-oxazines bearing the same chiral inductor [17]. The enantioselectivities of both *endo* (de 43%) and *exo* additions (de 53%) in $H_2O$ were better than that found in $CH_2Cl_2$ (de (*endo*) 35%, de (*exo*) 25%). This is the first example of an asymmetric 'inverse-electron-demand' *Diels-Alder* reaction carried out in $H_2O$.




We then investigated whether the electron-deficient diazenyl-alkene **1a** acts as a $2\pi$ component in the presence of a highly reactive diene such as cyclopentadiene (**6**). In $H_2O$ as well as in $CH_2Cl_2$, **1a** behaved as an electron-acceptor heterodiene. The *Diels-Alder* reaction was very fast (*Table 2*, *Entries 7* and *8*), and the *endo*-adduct **25** was the sole reaction product. Again, the reaction is faster in heterogeneous aqueous medium than in homogeneous phase in $CH_2Cl_2$.

The structures of the monocyclic adducts were assigned on the basis of their $^1$H-NMR data (*Table 3*). In the *exo*-adducts **8a**, **8b**, **8c**, **23**, and **24**, H–C(4) is strongly coupled with $H_\beta$–C(5) ($J(4,5\beta) = 12.2-13.6$ Hz) indicating an axial orientation of both H-atoms. The coupling of H–C(4) with $H_\alpha$–C(5) ($J(4,5\alpha) = 6.5-6.7$ Hz) is typical for an axial/equatorial relationship. H–C(6) shows smaller, but similar vicinal coupling constants with $CH_2$(5) ($J(6,5\alpha) = 2.8-3.1$ Hz; $J(6,5\beta) = 2.4-2.7$ Hz), indicating that the EtO group occupies an axial or pseudoaxial position.

The sole inspection of coupling constants of the *endo*-adducts **7a**, **7b**, **7c**, **13**, **21**, and **22** did not allow assignment of the structures of these compounds unequivocally[2]). Therefore, NOE experiments were necessary. The adduct **7a** was chosen as a

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[2]) Reversed assignments for $H_\alpha$–C(5) and $H_\beta$–C(5), and $J$(4,5) were reported for the *endo*-adduct *cis*-6-ethoxy-4-(ethoxycarbonyl)-3-methyl-1-(*p*-tolylsulfonyl)-1,4,5,6-tetrahydropyridazine [6a].

Table 3. *$^1$H-NMR Data of the Ring H-Atoms of the Tetrahydropyridazines*

| Compound | $\delta$ [ppm] | | | | $J$ [Hz] | | | |
|---|---|---|---|---|---|---|---|---|
| | $H_\beta$–C(5) | $H_\alpha$–C(5) | H–C(4) | H–C(6) | $J(4,5\alpha)$ | $J(4,5\beta)$ | $J(6,5\alpha)$ | $J(6,5\beta)$ |
| **7a** | 1.76 | 2.72 | 2.95 | 5.79 | 1.1 | 7.4 | 2.9 | 2.3 |
| **8a** | 1.95 | 2.26 | 3.45 | 5.82 | 6.5 | 13.6 | 2.8 | 2.6 |
| **7b** | 1.80 | 2.76 | 3.03 | 5.88 | 0.8 | 7.2 | 2.7 | 2.3 |
| **8b** | 2.00 | 2.31 | 3.54 | 5.91 | 6.7 | 13.3 | 2.9 | 2.7 |
| **7c** | 1.88 | 2.42 | 3.18 | 5.76 | 1.3 | 7.8 | 2.8 | 2.9 |
| **8c** | 1.91 | 2.13 | 3.73 | 5.81 | 6.6 | 12.2 | 2.8 | 2.6 |
| **13** | 2.10 | 2.83 | 3.06 | 5.98 | 1.1 | 7.6 | 2.4 | 3.3 |
| **21** | 1.84 | 2.71 | 2.96 | 5.96 | 1.0 | 7.4 | 2.8 | 2.4 |
| **22** | 1.71 | 2.74 | 2.92 | 5.89 | 1.0 | 7.4 | 2.8 | 2.4 |
| **23** | 1.91 | 2.28 | 3.50 | 5.91 | 6.6 | 13.1 | 2.9 | 2.4 |
| **24** | 2.02 | 2.25 | 3.52 | 6.02 | 6.6 | 13.1 | 3.1 | 2.4 |

representative compound. Irradiation of H–C(4) gave a NOE effect on $H_\alpha$–C(5) (1.1%) and $H_\beta$–C(5) (3.1%). Similarly, irradiation of H–C(6) led to a NOE effect on $H_\alpha$–C(5) (1.8%) and $H_\beta$–C(5) (2.3%). Thus, H–C(4) and $H_\beta$–C(5) occupy equatorial positions, and the magnitude of the coupling constant ($J(4,5\beta) = 7.4$ Hz) indicates that the dihedral angle must be close to zero; $H_\alpha$–C(5) is in axial position and consequently should form a dihedral angle of *ca.* 90° with H–C(4) in agreement with $J(4,5\alpha) = 1.1$ Hz. The vicinal coupling constants of H–C(6) with $CH_2$(5) ($J(6,5\beta) =$ 2.3 Hz; $J(6,5\alpha) = 2.9$ Hz) indicate that the dihedral angles amount to *ca.* 60°, with the EtO group in axial position.

The $^1$H-NMR data of the bicyclic compounds **10**, **11**, and **25** (see *Exper. Part*) similarly allow assignment of the *endo*- and *exo*-configurations. The *endo*-adducts **10** and **25** show the $J(4,4a) = 5.3$ and 5.2 Hz, respectively, in agreement with an equatorial-pseudoaxial relationship of H–C(4) and H–C(4a) of a *cis*-fused bicyclic [6.5.0] system. In the *exo*-adduct **11**, the vicinal coupling constant of H–C(4) is larger than expected ($J(4,4a) = 9.3$ Hz) as a consequence of an axial-pseudoaxial relationship[3]).

The $^1$H-NMR data of pyrroles **9**, **12**, and **15** (see *Exper. Part*) are fully consistent with the assigned structures.

The $^1$H-NMR data (*Table 3*) allow us to set simple rules to assign the *cis*- or *trans*-relationship of the 4,6-disubstituted 1,4,5,6-tetrahydropyridazines: *i*) the signals for H–C(4) and H–C(6) in the *cis*-isomers appear at higher field than those of the *trans*-isomers; *ii*) $\delta(5\alpha) - \delta(5\beta)$ is higher for the *cis*- than for the *trans*-isomer; *iii*) the $J(4,5\beta)$ and $J(4,5\alpha)$ values are larger for the *trans*- than for the *cis*-adducts (*Table 3*).

Water is a unique and extraordinary reaction medium, and the main causes that have been invoked to explain its accelerating effect on the *Diels-Alder* reaction are: *i*) the hydrophobic packing of reagents [18]; *ii*) stabilizing interactions arising from the H-bonds between $H_2O$ and the activated complex [16][19]; *iii*) enforced hydrophobic interactions arising from the reduction of the hydrophobic surface area of the reactants during the activation process [16][19]; and *iv*) the high cohesive pressure of $H_2O$, which

[3]) The values for $J(4,4a)$ of **10** and **25** are higher, and that of **11** is lower than those observed in the corresponding monocyclic adducts due to variations of the dihedral angle H–C(4)–C(4a)–H.

could act as an external pressure and, therefore, favor processes with a negative activation volume [20]. All these effects are probably operative, and, at times, one or two of them may prevail depending on the reactants. The *Diels-Alder* reactions of the diazenyl-alkenes **1a** and **1b** of low solubility in $H_2O$ with **2**, which are faster and more diastereoselective than the cycloaddition reactions of $H_2O$-soluble **1c** with the same diene, indicate that, in this case, the hydrophobic interactions between the reactants and the enforced hydrophobic interactions during the activation process are the prevalent effects.

**Conclusions.** – In summary, the cycloaddition reactions of stable and easy-to-prepare [4][5] electron-deficient (*E*)-3-diazenylbutenes **1a**, **1b**, and **1c** with electron-rich olefines **2**–**5** and cyclopentadiene **6** take place in pure $H_2O$ at 15° under heterogeneous conditions and are faster than in homogeneous solution in $CH_2Cl_2$. The diazenyl-alkenes behave like heterodienes, and the *Diels-Alder* reaction is the main reaction channel that leads to tetrahydropyridazines in good yields and with high degrees of stereochemical and regiochemical control. Pyrroles arising from zwitterionic [3 + 2] cycloaddition reactions are observed in some cases. The reactions described here are the first reported of (*E*)-diazenyl-dienes in $H_2O$ and organic solvents, and rare examples of 'inverse-electron-demand' *Diels-Alder* reactions in $H_2O$. The reaction between **1a** and the optically active dienophile **5** is the first example of an asymmetric 'inverse electron-demand' [4 + 2] cycloaddition reaction carried out in aqueous medium.

## Experimental Part

*General*. $^1$H- and $^{13}$C-NMR spectra: in $CDCl_3$ soln., if not otherwise specified on *FT Bruker AC-200* and on *FT Bruker DRX-400* instruments. Column chromatography (CC): silica gel (0.04–0.063 mm, 230–240 mesh ASTM). M.p.: uncorrected. IR Spectra: in soln. or in KBr pellet on *FT Perkin Elmer 983*. The diazenyl-alkenes **1** were prepared previously [4][5]. The dienophiles **2**, **3**, **4**, and **6** are commercially available.

*Cycloaddition of Ethyl (*E*)-3-(Carbamoyldiazenyl)but-2-enoate* (**1a**) *with Ethyl Vinyl Ether* (**2**). Ether **2** (0.76 ml; $8 \cdot 10^{-3}$ mol) was added under vigorous stirring at 15° to a powdered suspension of red-colored **1a** (0.37 g, $2 \cdot 10^{-3}$ mol) in $H_2O$ (10 ml). The stirring was continued for 16 h, and the mixture was filtered under reduced pressure to give pure white crystalline **7a** (0.39 g). The mother liquors were saturated (NaCl) and extracted with AcOEt. The org. phase, which was worked up as usual, gave a mixture **7a**/**8a**/**9** (*Table 1*), which was chromatographed (silica gel; $Et_2O$) to give an additional amount of pure **7a** (0.04 g, total yield 83%) and two mixtures (0.025 g and 0.020 g), which contain **8a** and **9**, respectively as the prevailing compounds.

*Ethyl* cis-*1-Carbamoyl-6-ethoxy-1,4,5,6-tetrahydro-3-methylpyridazine-4-carboxylate* (**7a**): M.p. 177–178° (EtOH). IR (KBr): 3428, 3289 ($NH_2$), 1722 ($CO_2Et$), 1679 ($CONH_2$), 1634, 1424 (C–N). $^1$H-NMR (200 MHz): 1.05 (*t*, *J* = 7.0, *Me*$CH_2$O–C(6)); 1.28 (*t*, *J* = 7.2, *Me*$CH_2$OCO); 1.76 (*ddd*, *J* = 13.7, 7.4, 2.3, $H_\beta$–C(5)); 2.15 (*s*, Me–C(3)); 2.72 (*ddd*, *J* = 13.7, 2.9, 1,1, $H_\alpha$–C(5)); 2.95 (*dd*, *J* = 7.4, 1.1, H–C(4)); 3.52 (*m*, MeC*H*$_2$O–C(6)); 4.16 (*m*, MeC*H*$_2$OCO); 5.79 (*dd*, *J* = 2.9, 2.3, H–C(6)). $^{13}$C-NMR (200 MHz): 13.8, 14.7 (*Me*$CH_2$O–C(6), *Me*$CH_2$OCO); 24.3 (*Me*–C(3)); 26.1 (C(5)); 38.1 (C(4)); 60.9, 62.7 (Me*C*$H_2$O–C(6), Me*C*$H_2$OCO); 72.4 (C(6)); 144.6 (C(3)); 156.7 ($CONH_2$); 170.2 (*C*$O_2$Et). Anal. calc. for $C_{11}H_{19}N_3O_4$: C 51.35, H 7.44, N 16.33; found: C 51.62, H 7.41, N 16.35.

*Ethyl* trans-*1-Carbamoyl-6-ethoxy-1,4,5,6-tetrahydro-3-methylpyridazine-4-carboxylate* (**8a**): $^1$H-NMR (200 MHz): 1.14 (*t*, *J* = 7.0, *Me*$CH_2$O–C(6)); 1.31 (*t*, *J* = 7.1, *Me*$CH_2$OCO); 1.95 (*ddd*, *J* = 13.6, 13.2, 2.6, $H_\beta$–C(5)); 1.98 (*s*, Me–C(3)); 2.26 (*ddd*, *J* = 13.2, 6.5, 2.8, $H_\alpha$–C(5)); 3.45 (*dd*, *J* = 13.6, 6.5, H–C(4)); 3.61 (*m*, MeC*H*$_2$O–C(6)); 4.23 (*q*, *J* = 7.1, MeC*H*$_2$OCO); 5.82 (*dd*, *J* = 2.8, 2.6, H–C(6)).

*Ethyl 2-Methyl-1-ureido-1*H*-pyrrole-carboxylate* (**9**): $^1$H-NMR (DMSO, 200 MHz): 1.24 (*t*, *J* = 7.1, *Me*$CH_2$); 2.27 (*s*, Me–C(2)); 4.15 (*q*, *J* = 7.1, MeC*H*$_2$); 6.21 (br. *s*, $NH_2$); 6.26 (*d*, *J* = 3.2, H–C(4)); 6.63 (*d*, *J* = 3.2, H–C(5)); 9.35 (*s*, NH).

*Cycloaddition of Methyl (*E*)-3-[(Phenylcarbamoyl)diazenyl]but-2-enoate* (**1b**) *with* **2**. Ether **2** (0.76 ml, $8 \cdot 10^{-3}$ mol) was added under vigorous stirring at 15° to a powdered suspension of orange-colored **1b** (0.50 g, $2 \cdot 10^{-3}$ mol) in $H_2O$ (10 ml). The mixture was stirred for 13 h, and the red-colored suspension was saturated (NaCl) and extracted with AcOEt. The org. phase, worked up as usual, gave a mixture **7b**/**8b** (*Table 1*), which was chromatographed (silica gel; petroleum ether/$Et_2O$ 3:1) to give pure red-colored **7b** (0.475 g, yield 75%) and colorless **8b** (0.040 g) as oils.

*Methyl* cis-*6-Ethoxy-1,4,5,6-tetrahydro-3-methyl-1-(phenylcarbamoyl)pyridazine-4-carboxylate* (**7b**): IR ($CCl_4$): 3381 (NH), 1742 ($CO_2Me$), 1698 (CONHPh), 1645, 1445 (C–N). $^1$H-NMR (200 MHz): 1.07 (*t*, *J* = 7.0, *Me*$CH_2O$–C(6)); 1.80 (*ddd*, *J* = 13.7, 7.2, 2.3, $H_\beta$–C(5)); 2.22 (*s*, Me–C(3)); 2.76 (*ddd*, *J* = 13.7, 2.7, 0.8, $H_\alpha$–C(5)); 3.03 (*dd*, *J* = 7.2, 0.8, H–C(4)); 3.57 (*q*, *J* = 7.0, Me*C*$H_2O$–C(6)); 3.71 (*s*, *Me*OCO); 5.88 (*dd*, *J* = 2.7, 2.3, H–C(6)); 7.0–7.6 (*m*, 5 arom. H); 8.67 (br. *s*, NH). $^{13}$C-NMR (200 MHz): 14.9 (*Me*$CH_2O$–C(6)); 24.5 (*Me*–C(3)); 26.3 (C(5)); 38.2 (C(4)); 52.1 (*Me*OCO); 63.1 (Me*C*$H_2O$–C(6)); 72.8 (C(6)); 119.4 (C(2), C(6) of Ph); 123.1 (C(4) of Ph); 128.8 (C(3), C(5) of Ph); 138.2 (C(1) of Ph); 144.7 (C(3)); 152.5 (CONHPh); 170.8 ($CO_2Me$). Anal. calc. for $C_{16}H_{21}N_3O_4$: C 60.17, H 6.63, N 13.16; found: C 60.26, H 6.61, N 13.20.

*Methyl* trans-*6-Ethoxy-1,4,5,6-tetrahydro-3-methyl-1-(phenylcarbamoyl)pyridazine-4-carboxylate* (**8b**): IR ($CCl_4$): 3384 (NH), 1744 ($CO_2Me$), 1698 (CONHPh), 1636, 1440 (C–N). $^1$H-NMR (200 MHz): 1.15 (*t*, *J* = 7.0, *Me*$CH_2O$–C(6)); 2.00 (*ddd*, *J* = 13.3, 13.3, 2.7, $H_\beta$–C(5)); 2.04 (*s*, Me–C(3)); 2.31 (*ddd*, *J* = 13.3, 6.7, 2.9, $H_\alpha$–C(5)); 3.54 (*dd*, *J* = 13.3, 6.7, H–C(4)); 3.71 (*m*, Me*C*$H_2O$–C(6)); 3.79 (*s*, *Me*OCO); 5.91 (*dd*, *J* = 2.9, 2.7, H–C(6)); 7.0–7.6 (*m*, 5 arom. H); 8.59 (br. *s*, NH). Anal. calc. for $C_{16}H_{21}N_3O_4$: C 60.17, H 6.63, N 13.16; found: C 60.20, H 6.70, N 13.22.

*Cycloaddition of (*E*)-3-(Carbamoyldiazenyl)-*N,N*-dimethylbut-2-enamide* (**1c**) *with* **2**. The reaction of orange-colored **1c** with **2** was carried out as described for **1b**. After 24 h, the reaction was stopped, and the colorless mixture was saturated (NaCl) and extracted with AcOEt. The org. phase was concentrated under reduced pressure to give a mixture **1c**/**7c**/**8c** (*Table 1*), which, after recrystallization from AcOEt, afforded 0.257 g of pure **7c**. The mother liquors, after chromatography (silica gel; AcOEt/MeOH 19:1), gave a further 0.065 g of pure **7c** (total yield 62%) and 0.030 g of a mixture **7c**/**8c** 20:80.

cis-*1-Carbamoyl-6-ethoxy-1,4,5,6-tetrahydro-3,*$N^4$,$N^4$-*trimethylpyridazine-4-carboxamide* (**7c**): M.p. 138–140° (AcOEt). IR (KBr): 3475, 3275 ($NH_2$), 1701 ($CONH_2$), 1664 ($CONMe_2$), 1578, 1432 (C–N). $^1$H-NMR (200 MHz): 1.06 (*t*, *J* = 7.0, *Me*$CH_2$); 1.88 (*ddd*, *J* = 13.8, 7.8, 2.9, $H_\beta$–C(5)); 2.06 (*s*, Me–C(3)); 2.42 (*ddd*, *J* = 13.8, 2.8, 1.3, $H_\alpha$–C(5)); 2.93 (br. *s*, MeN); 3.05 (br. *s*, MeN); 3.18 (*dd*, *J* = 7.8, 1.3, H–C(4)); 3.53 (*m*, Me*C*$H_2$); 5.76 (*dd*, *J* = 2.9, 2.8, H–C(6)). $^{13}$C-NMR (200 MHz): 14.8 (Me); 24.4 (Me–C(3)); 26.6 (C(5)); 35.7 (MeN); 37.2 (C(4)); 37.4 (MeN); 62.7 (Me*C*$H_2$); 72.1 (C(6)); 146.5 (C(3)); 157.1 ($CONH_2$); 169.4 ($CONMe_2$). Anal. calc. for $C_{11}H_{20}N_4O_3$: C 51.55, H 7.87, N 21.86; found: C 51.70, H 7.81, N 21.91.

trans-*1-Carbamoyl-6-ethoxy-1,4,5,6-tetrahydro-3,*$N^4$,$N^4$-*trimethylpyridazine-4-carboxamide* (**8c**): $^1$H-NMR (200 MHz): 1.14 (*t*, *J* = 7.0, *Me*$CH_2$); 1.91 (*ddd*, *J* = 13.2, 12.2, 2.6, $H_\beta$–C(5)); 1.93 (*s*, Me–C(3)); 2.13 (*ddd*, *J* = 13.2, 6.6, 2.8, $H_\alpha$–C(5)); 3.01 (*s*, MeN); 3.14 (*s*, MeN); 3.61 (*m*, Me*C*$H_2$); 3.73 (*dd*, *J* = 12.2, 6.6, H–C(4)); 5.81 (*dd*, *J* = 2.8, 2.6, H–C(6)).

*Cycloaddition of* **1a** *with 2,3-Dihydrofuran* (**3**). 2,3-Dihydrofuran (**3**; 0.64 ml, $8 \cdot 10^{-3}$ mol) was added under vigorous stirring at 15° to a powdered suspension of red-colored **1a** (0.37 g, $2 \cdot 10^{-3}$ mol) in $H_2O$ (10 ml). After 3 h (*Table 2*), the mixture was filtered to give pure **12** as a white crystalline solid (0.10 g, 20%). The mother liquors were saturated (NaCl) and extracted with AcOEt ($3 \times 10$ ml). The org. phase, after workup as usual, gave a mixture **10**/**11** 66:34. Recrystallization from hexane/AcOEt gave pure **11** (0.09 g, 18%) and a 9:1 mixture **10**/**11** (0.29 g).

*Ethyl 1-Carbamoyl-1,4α,4aα,5,6,7aα-hexahydro-3-methylfuro[2,3-*c*]pyridazine-4-carboxylate* (**10**): $^1$H-NMR (200 MHz): 1.31 (*t*, *J* = 7.1, *Me*$CH_2$); 1.84 (*m*, 1 H, $CH_2$(5)); 2.12 (*s*, Me–C(3)); 2.21 (*m*, 1 H, $CH_2$(5)); 3.06 (*m*, H–C(4a)); 3.27 (*d*, *J* = 5.3, H–C(4)); 3.79 (*m*, $CH_2$(6)); 4.24 (*q*, *J* = 7.1, Me*C*$H_2$); 6.09 (*d*, *J* = 8.1, H–C(7a)).

*Ethyl 1-Carbamoyl-1,4α,4aβ,5,6,7aβ-hexahydro-3-methylfuro[2,3-*c*]pyridazine* (**11**): M.p. 175–176° (MeOH). IR (KBr): 3471, 3358 ($NH_2$), 1728 ($CO_2Et$), 1689 ($CONH_2$), 1648, 1423 (C–N). $^1$H-NMR (200 MHz): 1.32 (*t*, *J* = 7.1, *Me*$CH_2$); 1.84 (*dddd*, *J* = 12.2, 6.0, 6.0, 2.5, 1 H, $CH_2$(5)); 2.04 (*d*, *J* = 0.9, Me–C(3)); 2.23 (*m*, 1 H, $CH_2$(5)); 2.63 (*dddd*, *J* = 9.3, 7.0, 4.8, 2.5, H–C(4a)); 2.87 (*dq*, *J* = 9.3, 0.9, H–C(4)); 3.94 (*dd*, *J* = 8.5, 6.0, $CH_2$(6)); 4.26 (*q*, *J* = 7.1, Me*C*$H_2$); 5.80 (*dd*, *J* = 4.8, H–C(7a)). $^{13}$C-NMR (200 MHz): 14.4 (*Me*$CH_2$); 22.9 (Me–C(3)); 30.8 (C(5)); 37.3 (C(4a)); 45.9 (C(4)); 62.8, 65.4 (Me*C*$H_2$, C(6)); 80.4 (C(7a)); 149.6 (C(3)); 159.4 ($CONH_2$); 171.5 ($CO_2Et$). Anal. calc. for $C_{11}H_{17}N_3O_4$: C 51.76, H 6.71, N 16.46; found: C 51.68, H 6.74, N 16.49.

*Ethyl 4-(2-Hydroxyethyl)-2-methyl-1-ureido-1*H*-pyrrole-3-carboxylate* (**12**): M.p. 198–199° (MeOH). IR (KBr): 3460, 3443 (NH), 3337, 3312 ($NH_2$), 3370 (OH), 1683 ($CO_2Et$), 1651 ($CONH_2$), 1622 (C=C). $^1$H-NMR (DMSO, 200 MHz): 1.25 (*t*, *J* = 7.0, *Me*$CH_2$); 2.24 (*s*, Me–C(2)); 2.72 (*t*, *J* = 7.1, $CH_2$–C(3)); 3.50 (*dt*, *J* = 7.1, 5.2, $CH_2OH$); 4.15 (*q*, *J* = 7.1, MeC$H_2$); 4.39 (*t*, *J* = 5.2, OH); 6.12 (br. *s*, $NH_2$); 6.45 (*s*, H–C(5)); 9.19 (*s*, NH). $^{13}$C-NMR ($CD_3OD$, 200 MHz): 10.9 (*Me*$CH_2$); 14.8 (Me–C(2)); 31.0 (*C*$H_2$–C(4)); 60.5 (Me*C*$H_2$); 63.4 ($CH_2OH$); 110.3 (C(3)); 121.4 (C(4)); 121.8 (C(5)); 139.4 (C(2)); 160.9 ($CONH_2$); 167.4 ($CO_2Et$). Anal. calc. for $C_{11}H_{17}N_3O_4$: C 51.76, H 6.71, N 16.46; found: C 51.73, H 6.68, N 16.50.

*Cycloaddition of* **1a** *with Phenyl Vinyl Sulfide* (**4**). Sulfide **4** (1.04 ml, $8 \cdot 10^{-3}$ mol) was added under vigorous stirring at 15° to a powdered suspension of red-colored **1a** (0.37 g, $2 \cdot 10^{-3}$ mol) in $H_2O$ (10 ml). After 96 h (*Table 2*), the pale yellow mixture was saturated (NaCl) and extracted with AcOEt (3 × 10 ml). The org. phase, after workup as usual, gave a mixture **13**/**15** 87:13, which was chromatographed (silica gel; $Et_2O$/AcOEt 7:3) to yield the *endo*-adduct **13** as a pure yellow crystalline product (0.36 g, 50%). Elution afforded **15** as a colorless oil (0.05 g, 7%).

*Ethyl* cis*-1-Carbamoyl-1,4,5,6-tetrahydro-3-methyl-6-(phenylsulfanyl)pyridazine-4-carboxylate* (**13**): M.p. 111–112° (AcOEt). IR (KBr): 3458, 3269 ($NH_2$), 1736 ($CO_2Et$), 1683 ($CONH_2$), 1639 (C=N), 1575 (C=C of Ph). $^1$H-NMR (200 MHz): 1.34 (*t*, *J* = 7.1, *Me*$CH_2$); 2.10 (*ddd*, *J* = 14.4, 7.6, 3.3, $H_\beta$–C(5)); 2.22 (*s*, Me–C(3)); 2.83 (*ddd*, *J* = 14.4, 2.4, 1.1, $H_\alpha$–C(5)); 3.06 (*dd*, *J* = 7.6, 1.1, H–C(4)); 4.29 (*m*, MeC$H_2$); 5.98 (*ddt*, *J* = 3.3, 2.4, 0.9, H–C(6)); 7.0–7.6 (*m*, 5 arom. H). $^{13}$C-NMR (200 MHz): 13.8 (*Me*$CH_2$); 24.5 (*Me*–C(3)); 26.1 (C(5)); 38.9 (C(4)); 54.5 (C(6)); 61.6 (Me*C*$H_2$); 128.2 (C(4) of Ph); 128.8 (C(3), C(5) of Ph); 132.5 (C(1) of Ph); 134.4 (C(2), C(6) of Ph); 144.0 (C(3); 155.3 ($CONH_2$); 170.3 ($CO_2Et$). Anal. calc. for $C_{15}H_{19}N_3O_3S$: C 56.06, H 5.96, N 13.07, S 9.98; found: C 56.12, H 5.89, N 13.11, S 9.95.

*Ethyl 2-Methyl-5-(phenylsulfanyl)-1*H*-pyrrole-3-carboxylate* (**15**): IR (KBr): 3533, 3487 (NH), 1695 ($CO_2Et$), 1630 (C=C), 1565 (C=C of Ph). $^1$H-NMR (DMSO, 200 MHz): 1.26 (*t*, *J* = 7.1, *Me*$CH_2$); 1.98 (*s*, Me–C(2)); 4.21 (*q*, *J* = 7.1, MeC$H_2$); 4.58 (*s*, H–C(4)); 7.0–7.5 (*m*, 5 arom. H); 8.33 (*s*, NH).

*(+)-2-(Ethenyloxy)-3,7,7-trimethylbicyclo[4.1.0]heptane* (**5**). A mixture of (–)-2-isocaranol [21] (1.54 g, $10^{-2}$ mol), $Hg(OAc)_2$ (0.80 g, $2.5 \cdot 10^{-2}$ mol), and butyl vinyl ether (85 ml) was heated at 60° for 4.5 h. $Hg(OAc)_2$ (0.80 g, 0.025 mol) was again added, and the resulting mixture was heated further for 4.5 h at 60°. The mixture was cooled to r.t., the reaction was quenched with an aq. sat. soln. of $K_2CO_3$, and the mixture was extracted with *t*-BuOMe (3 × 30 mol). Usual workup gave a residue, which was purified by FC (silica gel pre-treated with 2.5% (*v*/*v*) $Et_3N$) eluting with hexane to give 0.81 g (45%) of pure **5** as an oil. $[\alpha]_D^{20} = +52.0$ (*c* = 1.24, $CHCl_3$). $^1$H-NMR (200 MHz): 0.66 (*m*, H–C(1), H–C(6)); 0.80 (*m*, 1 H, $CH_2$(5)); 0.93 (*d*, *J* = 6.2, Me–C(3)); 1.015, 1.020 (2*s*, 2 Me–C(7)); 1.35–1.95 (*m*, H–C(3), $CH_2$(4), H–C(5)); 3.15 (br. *d*, *J* = 10.6, H–C(2)); 4.01 (*dd*, *J* = 6.8, 1.3, $H_E$ of $CH_2$=); 4.20 (*dd*, *J* = 14.4, 1.2, $H_Z$ of $CH_2$=); 6.4 (*dd*, *J* = 14.4, 6.8, $CH_2$=C*H*). $^{13}$C-NMR (200 MHz): 15.1 (*Me*–C(7)); 16.5 (C(7)); 18.2 (C(6)); 19.0 (C(5)); 20.1 (Me–C(3)); 27.4 (*Me*–C(7)); 28.6 (C(1)); 30.1 (C(4)); 34.0 (C(3)); 78.6 (C(2)); 86.9 (*C*$H_2$=CH); 150.6 ($CH_2$=*C*H). Anal. calc. for $C_{12}H_{20}O$: C 79.94, H 11.18; found: C 79.89, H 11.21.

*Cycloaddition of* **1a** *with* **5**. Ether (**5**) (2.16 g, $12 \cdot 10^{-3}$ mol) was added at 15° under vigorous stirring to a powdered suspension of **1a** (0.74 g, $4 \cdot 10^{-3}$ mol) in $H_2O$ (20 ml), and the stirring was continued for 68 h. The mixture was saturated (NaCl) and extracted with AcOEt. The usual workup gave a mixture of four products (*Table 2*). Column chromatography hexane/AcOEt 7:3 allowed the *endo*-adducts **21** and **22** (0.84 g) to be separated from the *exo*-isomers **23** and **24** (0.09 g). Fractional recrystallizations of the *endo*-mixture at –20° from hexane/$CH_2Cl_2$ gave pure **21** as a white crystalline solid and mixtures, which were enriched with other diastereoisomer.

*Ethyl (4*S*,6*R*)-*cis*-1-Carbamoyl-6-(3,7,7-trimethylbicyclo[4.1.0]hept-2-yloxy)-1,4,5,6-tetrahydro-3-methylpyridazine-4-carboxylate* (**21**): $^1$H-NMR (400 MHz): 0.58–0.62 (*m*, H–C(1′), H–C(6′)); 0.71 (*m*, 1 H, R*); 0.71 (*d*, *J* = 6.3, Me–C(3′)); 1.00 (*m*, 1 H, R*); 0.98 (*s*, Me–C(7′)); 1.04 (*s*, Me–C(7′)); 1.29 (*t*, *J* = 7.1, *Me*–$CH_2$); 1.37 (*m*, 1 H, R*); 1.61 (*m*, 1 H, R*); 1.69 (*m*, 1 H, R*); 1.84 (*ddd*, *J* = 13.5, 7.4, 2.4, $H_\beta$–C(5)); 2.16 (*s*, Me–C(3)); 2.71 (*ddd*, *J* = 13.5, 2.8, 1.0, $H_\alpha$–C(5)); 2.96 (*dd*, *J* = 7.4, 1.0, H–C(4)); 3.10 (*d*, *J* = 10.1, H–C(2′)); 4.03 (*dq*, *J* = 10.8, 7.1, 1 H, MeC$H_2$); 4.27 (*dq*, *J* = 10.8, 7.1, 1 H, MeC$H_2$); 5.96 (*dd*, *J* = 2.8, 2.4, H–C(6)). $^{13}$C-NMR (400 MHz): 14.0 (*Me*$CH_2$); 15.3 (*Me*–C(7′)); 16.9 (C(7′)); 18.2 (C(6′)); 19.1 (C(5′)); 20.5 (*Me*–C(3′)); 24.7 (Me–C(3)); 27.7 (C(5)); 27.7 (*Me*–C(7′)); 29.2 (C(1′)); 30.4 (C(4′)); 34.3 (C(3′)); 38.4 (C(4)); 61.1 (Me*C*$H_2$); 70.9 (C(6)); 77.4 (C(2′)); 144.6 (C(3)); 156.5 ($CONH_2$); 170.3 ($CO_2Et$). Anal. calc. for $C_{19}H_{31}N_3O_4$: C 62.44, H 8.55, N 11.50; found: C 62.49, H 8.54, N 11.54.

*Ethyl (4*R*,6*S*)-*cis*-1-Carbamoyl-6-(3,7,7-trimethylbicyclo[4.1.0]hept-2-yloxy)-1,4,5,6-tetrahydro-3-methylpyridazine-4-carboxylate* (**22**): $^1$H-NMR (400 MHz): 0.42–0.50 (*m*, H–C(1′), H–C(6′)); 0.68 (*d*, *J* = 6.3, Me–C(3′)); 0.70 (*m*, 1 H, R*); 0.91 (*s*, Me–C(7′)); 0.93 (*s*, Me–C(7′)); 0.99 (*m*, 1 H, R*); 1.26 (*t*, *J* = 7.1,

*Me*$CH_2$); 1.36 (*m*, 1 H, R*); 1.65 (*m*, 1 H, R*); 1.67 (*m*, 1 H, R*); 1.71 (*ddd*, *J* = 13.4, 7.4, 2.4, $H_\beta$–C(5)); 2.13 (*s*, Me–C(3)); 2.74 (*ddd*, *J* = 13.5, 2.8, 1.0, $H_\alpha$–C(5)); 2.92 (*dd*, *J* = 7.4, 1.0, H–C(4)); 3.11 (*dd*, *J* = 10.3, 1.9, H–C(2′)); 4.12 (*m*, Me*C*$H_2$); 5.89 (*dd*, *J* = 2.8, 2.4, H–C(6)). $^{13}$C-NMR (400 MHz, $CDCl_3$): 14.0 (*Me*$CH_2$); 15.2 (*Me*–C(7′)); 16.6 (C(7′)); 18.3 (C(6′)); 19.1 (C(5′)); 20.0 (Me–C(3′)); 24.6 (*Me*–C(3)); 27.0 (C(5)); 27.7 (Me–C(7′)); 29.0 (C(1′)); 29.9 (C(4′)); 35.3 (C(3′)); 38.7 (C(4)); 61.1 (Me*C*$H_2$); 73.8 (C(6)); 79.3 (C(2′)); 144.8 (C(3)); 156.1 ($CONH_2$); 170.5 ($CO_2$Et).

*Ethyl (4*S*,6*S*)*-trans-*1-Carbamoyl-6-(3,7,7-trimethylbicyclo[4.1.0]hept-2-yloxy)-1,4,5,6-tetrahydro-3-methylpyridazine-4-carboxylate* (**23**): $^1$H-NMR (400 MHz): 0.57–0.65 (*m*, H–C(1′), H–C(6′)); 0.70 (*d*, *J* = 6.4, Me–C(3′)); 0.72 (*m*, 1 H, R*); 0.94 (*s*, Me–C(7′)); 1.03 (*s*, Me–C(7′)); 1.17 (*m*, 1 H, R*); 1.28 (*t*, *J* = 7.1, *Me*$CH_2$); 1.39 (*m*, 1 H, R*); 1.61 (*m*, 1 H, R*); 1.71 (*m*, 1 H, R*); 1.91 (*ddd*, *J* = 13.1, 13.0, 2.4, $H_\beta$–C(5)); 1.96 (*s*, Me–C(3)); 2.28 (*ddd*, *J* = 13.0, 6.6, 2.9, $H_\alpha$–C(5)); 3.13 (*dd*, *J* = 10.4, 2.3, H–C(2′)); 3.50 (*dd*, *J* = 13.1, 6.6, H–C(4)); 4.21 (*q*, *J* = 7.1, MeC$H_2$); 5.91 (*dd*, *J* = 2.9, 2.4, H–C(6)). $^{13}$C-NMR (400 MHz): 14.2 (*Me*$CH_2$); 15.2 (*Me*–C(7′)); 16.8 (C(7′)); 18.6 (C(6′)); 19.2 (C(5′)); 20.2 (Me–C(3′)); 21.9 (Me–C(3)); 27.5 (*Me*–C(7′)); 28.1 (C(5)); 29.1 (C(1′)); 30.0 (C(4′)); 35.1 (C(3′)); 40.1 (C(4)); 61.4 (Me*C*$H_2$); 73.8 (C(6)); 78.9 (C(2′)); 143.5 (C(3)); 156.3 ($CONH_2$); 172.1 ($CO_2$Et).

*Ethyl (4*R*,6*R*)*-trans-*1-Carbamoyl-6-(3,7,7-trimethylbicyclo[4.1.0]hept-2-yloxy)-1,4,5,6-tetrahydro-3-methylpyridazine-4-carboxylate* (**24**): $^1$H-NMR (400 MHz): 0.57–0.65 (*m*, H–C(1′), H–C(6′)); 0.70 (*d*, *J* = 6.4, Me–C(3′)); 0.72 (*m*, 1 H, R*); 0.94 (*s*, Me–C(7′)); 1.03 (*s*, Me–C(7′)); 1.17 (*m*, 1 H, R*); 1.28 (*t*, *J* = 7.1, *Me*$CH_2$); 1.39 (*m*, 1 H, R*); 1.61 (*m*, 1 H, R*); 1.71 (*m*, 1 H, R*); 1.96 (*s*, Me–C(3)); 2.02 (*ddd*, *J* = 13.1, 13.0, 2.4, $H_\beta$–C(5)); 2.25 (*ddd*, *J* = 12.9, 6.6, 3.1, $H_\alpha$–C(5)); 2.93 (br. *d*, *J* = 10.5, H–C(2′)); 3.52 (*dd*, *J* = 13.1, 6.6, H–C(4)); 4.21 (*q*, *J* = 7.1, MeC$H_2$); 6.02 (*dd*, *J* = 3.1, 2.4, H–C(6)). $^{13}$C-NMR (400 MHz): 14.1 (*Me*$CH_2$); 15.2 (Me–C(7′)); 16.9 (C(7′)); 18.3 (C(6′)); 19.2 (C(5′)); 20.4 (Me–C(3′)); 21.7 (*Me*–C(3)); 27.6 (*Me*–C(7′)); 28.5 (C(5)); 29.1 (C(1′)); 30.4 (C(4′)); 34.5 (C(3′)); 40.0 (C(4)); 61.4 (Me*C*$H_2$); 70.7 (C(6)); 76.1 (C(2′)); 144.1 (C(3)); 156.3 ($CONH_2$); 172.1 ($CO_2$Et).

*Cycloaddition of* **1a** *with Cyclopenta-1,3-diene* (**6**). Cyclopenta-1,3-diene (**6**; 0.528 g, $8 \cdot 10^{-3}$ mol) and powdered **1a** (0.370 g, $2 \cdot 10^{-3}$ mol) in $H_2O$ (10 ml) were vigorously stirred at 15° for 45 min (*Table 2*). The mixture was saturated (NaCl) and extracted with AcOEt. The usual workup gave pure **25** (0.42 g, 90%) as a white crystalline solid after recrystallization from hexane/$CH_2Cl_2$.

*Ethyl 1-Carbamoyl-4*α*,4a*α*,5,7a*α*-tetrahydro-3-methyl-1*H*-cyclopenta[*c*]pyridazine-4-carboxylate* (**25**): M.p. 126–129° (hexane/$CH_2Cl_2$). IR (KBr): 3448, 3343 ($NH_2$), 1740 ($CO_2$Et), 1683 ($CONH_2$), 1618 (C=N). $^1$H-NMR (400 MHz): 1.26 (*t*, *J* = 7.1, *Me*$CH_2$); 2.03 (br. *s*, Me–C(3)); 2.38 (*dm*, *J* = 17.1, 1 H, $CH_2$(5)); 2.53 (*dm*, *J* = 17.1, 1 H, $CH_2$(5)); 3.22 (*dddd*, *J* = 8.5, 5.2, 5.2, 1.0, H–C(4a)); 3.25 (br. *d*, *J* = 5.2, H–C(4)); 4.17 (*q*, *J* = 7.1, MeC$H_2$); 5.16 (br. *d*, *J* = 8.5, H–C(7a)); 5.76 (*m*, H–C(6)); 5.87 (*m*, H–C(7)). $^{13}$C-NMR (200 MHz, $CDCl_3$): 14.1 (*Me*$CH_2$); 22.6 (Me–C(3)); 35.6 (C(5)); 38.7 (C(4a)); 45.4 (C(4)); 60.8 (C(7a)); 61.2 (Me*C*$H_2$); 130.5 (C(6)); 133.0 (C(7)); 152.1 (C(3)); 157.8 ($CONH_2$); 170.4 ($CO_2$Et). Anal. calc. for $C_{12}H_{17}N_3O_3$: C 57.36, H 6.82, N 16.72; found: C 57.41, H 6.80, N 16.69.

*Cycloadditions in Organic Solvents.* A soln. of diazenyl-alkene ($2 \cdot 10^{-3}$ mol) and alkene ($8 \cdot 10^{-3}$ mol) in organic solvent (10 ml; $4 \cdot 10^{-3}$ mol and $12 \cdot 10^{-3}$ mol, resp. for the reaction of **1a** with **5** in 20 ml of $CH_2Cl_2$) was stirred at 15° for the time reported in *Tables 1* and *2*. At the end of the reaction, the mixture was concentrated, and the conversion rate and percentage of components were determined by $^1$H-NMR. If the conversion was higher than 70%, the main reaction product was isolated by CC.

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