Inter- and Intramolecular *hetero* Diels-Alder Reactions, XXI[1]

Intramolecular *hetero* Diels-Alder Reaction of Alkylidene-1,3-dicarbonyl Compounds. Experimental Evidence for an Asymmetric Transition State

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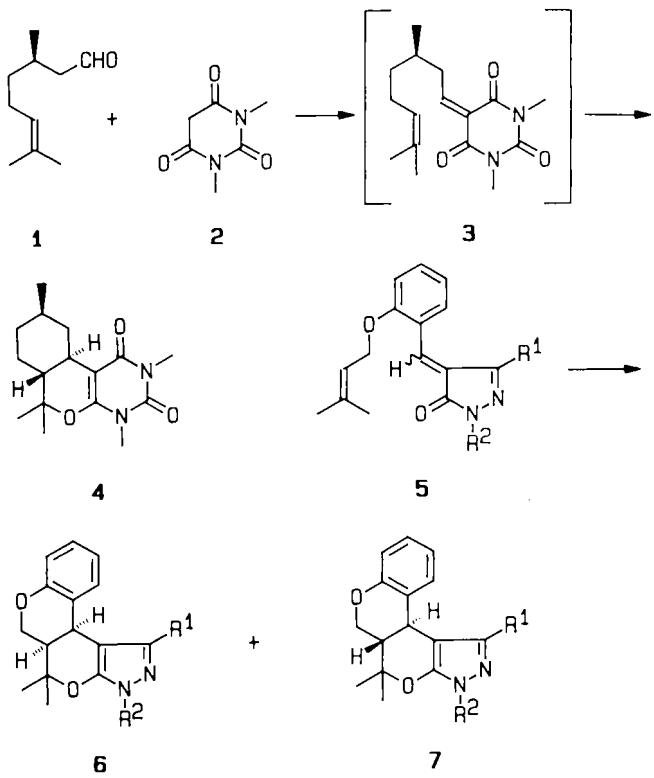
The intramolecular *hetero* Diels-Alder reaction of heterodienes **13** is described. The heterodienes, which are obtained in situ by Knoevenagel condensation of aldehydes **12a–e** with dimethylbarbituric acid (**2**), yield the cycloadducts **14a–e/15a–e** and the ene adducts **16a, c–e/17a, c–e**. The ratio of **14/15** was determined by HPLC. The resulting data are interpreted as experimental evidence of an asymmetrical transition state of the Diels-Alder reaction.

Inter- und Intramolekulare *hetero*-Diels-Alder-Reaktionen, XXI[1]. – Intramolekulare *hetero*-Diels-Alder-Reaktionen von Alkyliden-1,3-dicarbonyl-Verbindungen. Experimenteller Beweis für das Vorliegen eines nicht symmetrischen Übergangszustandes.

Die intramolekulare *hetero*-Diels-Alder Reaktion der Heterodiene **13**, die durch Knoevenagel-Kondensation der Aldehyde **12a–e** mit Dimethylbarbitursäure (**2**) in situ gebildet werden, ergibt die diastereomeren Cycloaddukte **14a–e/15a–e** und die En-Produkte **16a, c–e/17a, c–e**. Das Verhältnis von **14/15** wurde durch HPLC bestimmt. Die so erhaltenen Daten lassen sich als experimenteller Beweis eines unsymmetrischen Übergangszustandes bei der Diels-Alder Reaktion werten.

The intramolecular *hetero* Diels-Alder[2] reaction of α,β-unsaturated carbonyl compounds[3] which are activated by electron-accepting substituents at C-1 or C-2 (positions 2 and 3, respectively, in the heterodiene) is a valuable and highly selective method for the formation of annulated dihydropyrans. The scope of this transformation is enormous, since the heterodienes can be formed in situ by a condensation of aldehydes with 1,3-dicarbonyls and analogous compounds. In addition, simple alkenes can act as dienophiles and the induced and non-induced diastereoselectivity exceeds 90% in most cases[4,5].



Thus, condensation of citronellal (**1**) and dimethylbarbituric acid (**2**) gives the alkylidene-1,3-dicarbonyl compound **3**, which immediately reacts nearly exclusively to give the cycloadduct **4**. The reaction goes to completion within 60 min and shows a ni-de value of more than 98% and an i-de of 92%[6].

In our investigations concerning the transition state of this reaction we were able to show that normally (*E*)-heterodienes react preferably. Thus, *Z*-**5** with a (*Z*)-heterodiene moiety isomerizes to yield *E*-**5** prior to the cycloaddition, even in the case where R^1 is *tert*-butyl[7]. Therefore, the ratio of the obtained cycloadducts **6** and **7** does not depend on the ground state configuration of the educts. Also, it has been shown that the transformation proceeds in a concerted manner[8]. This resulted in a model for the transition state; thus, the observed diastereoselectivity can best be explained by assuming an asynchronous asymmetric approach of the dienophile to the β-carbon of the heterodiene along a trajectory of 109°[9].

Asynchronous transition states have already been proposed for the inter- and intramolecular Diels-Alder reaction in terms of steric hinderance of unsymmetrical addends[10]. In this paper we show experimentally that the degree of asynchronism must be different for the *endo*- and *exo*- transition state and that asynchronism must not only be caused by steric but also by stereoelectronic effects[9a].

For this reason we investigated the *tandem* Knoevenagel-*hetero*-Diels-Alder reaction of aldehydes **12** and dimethylbarbituric acid (**2**).

Results

The synthesis of the aldehydes **12a–e** was accomplished through Wittig reaction[11] of formylester **8** with the phosphonium salts **9a–e** to give the unsaturated esters **10a–e**,

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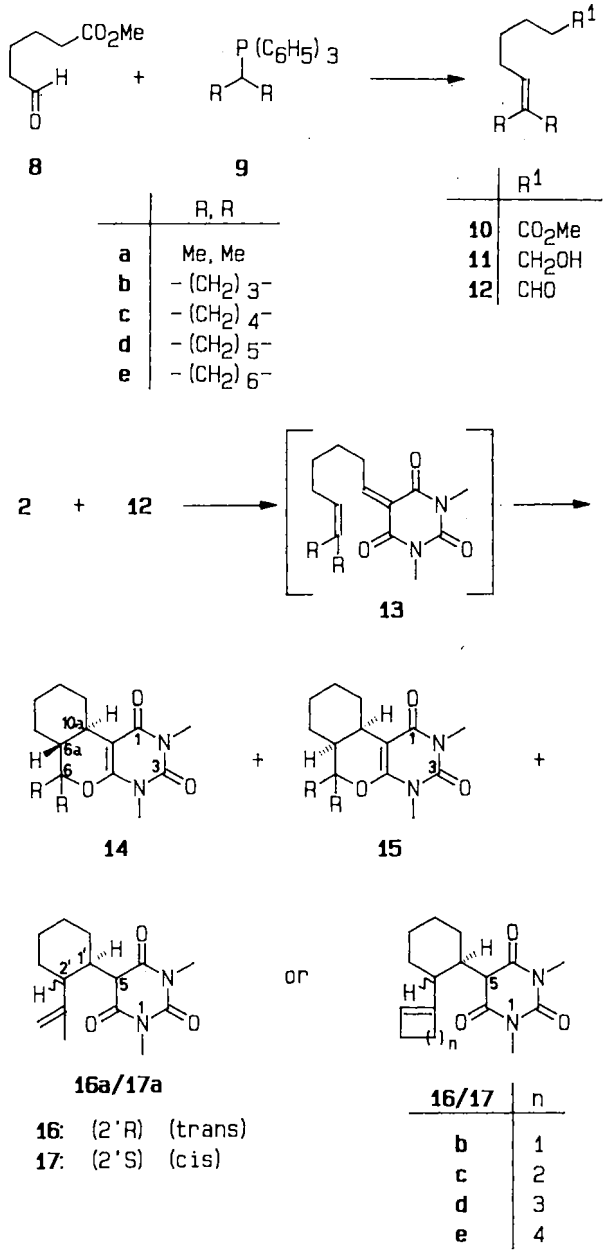


which were reduced to the corresponding alcohols **11a–e** with lithium aluminium hydride. The final oxidation was carried out using the method of Swern et al.[12]. This efficient reaction has the particular advantage of completely avoiding acidic conditions during the synthesis of the highly acid-sensitive aldehydes **12a–e**. The overall yield from **8** was about 40% in all cases, the sequence was not optimised.

The Knoevenagel condensation of **12a–e** with **2** was performed in acetonitrile at room temperature using ethylene-diammonium diacetate (EDDA) as catalyst[13]. All attempts to isolate the heterodienes **13** were unsuccessful because of the fast formation of the cycloadducts **14/15**. Therefore, the condensation–cycloaddition sequence was run as an "one pot" reaction, providing **14/15** and **16/17** with good overall yields. Interestingly, during the transformation an intense yellow colour appeared, which faded as the final products were formed. This indicates the intermediate occurence of a π complex[2g]. The ratio of Diels-Alder to ene products was not always reproducible, whereas the overall yield remained nearly constant for a given system (Tab. 1).

Table 1. Yields of cycloadducts **14/15** and ene products **16/17**

Entry	Educts	14/15 (%)	16/17 (%)	Overall Yield (%)	Ratio 14/15:16/17
1	**2** + **12a**	58	17	75	3.4:1
2	**2** + **12b**	42	–	42	–
3	**2** + **12c**	59	40	99	1.5:1
4	**2** + **12d**	58	19	77	3.1:1
5	**2** + **12e**	48	44	92	1.1:1

This may be due to a small but different content of acetic acid in the reaction mixtures, which stems from the Knoevenagel catalyst. Thus, it can be assumed that the reaction rate of both transformations is differently influenced by the acid. The ratio of **14/15**, which is the prime interest of this investigation, however, is not affected and was found constant in different experiments with the same substrate (Tab. 2).

The ene products **16/17** can be cyclised quantitatively to give **14/15** with BF_3-Et_2O at room temperature. This allows us to determine the selectivity of the ene reaction, since an isomerization does not take place during this transformation.

Table 2. Ratios of Diastereomers **14** and **15** and ni-de values of the Diels-Alder reaction

Entry	Educts	Ratio 14:15 (%)	ni-de[5] (%)
1	**2** + **12a**	98.76:1.24 (0.01)[a]	97.5
2	**2** + **12b**	93.32:6.78 (0.01)	86.4
3	**2** + **12c**	97.07:2.93 (0.02)	94.2
4	**2** + **12d**	99.25:0.75 (0.01)	98.5
5	**2** + **12e**	98.19:1.91 (0.02)	96.2

[a] Values in parentheses give standard deviations.

As an example, the cyclisation of **16e/17e** yielded **14e** and **15e** in a ratio of 99.22:0.78. This corresponds to ni-de of 98.4%. Thus, the ene reaction appears to be more selective than the corresponding Diels-Alder reaction (ni-de 96.2%).

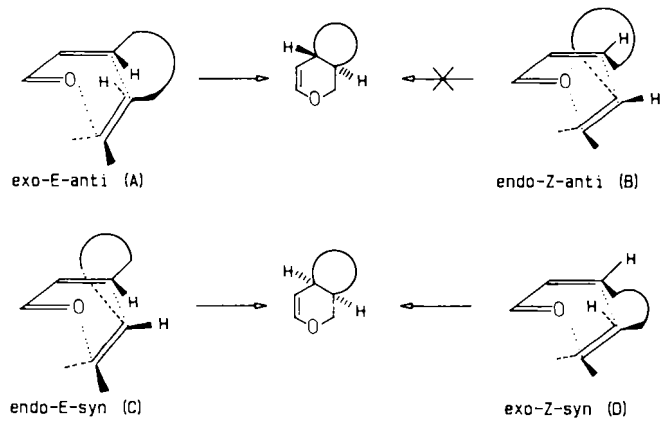
Isolation and Structure Determination of the Products 14, 15, and 16

The main reaction products **14** and **16** were obtained pure by crystallisation after flash chromatography. The identification of **15** posed a problem because the amount of this product usually did not exceed 3%. However, we were able to increase the amount of **15b** to 12% by fractional crystallisation of the main isomer **14b**. From this mixture, **15b** could be isolated by preparative HPLC and its structure determined.

The configuration of the cycloadducts **14a–e** and **15b** was determined by ^{1}H- and ^{13}C-NMR spectroscopy. In the ^{1}H-NMR spectra of the *trans*-annulated compounds **14**, 10a-H shows two large and one small couplings ($J_{10a,6a}$ = $J_{10a,10ax}$ = 11.0 Hz, $J_{10a,10eq}$ = 3.0 Hz). This pattern is only compatible with a *trans*-diaxial relationship between 6a-H and 10a-H. In the spectrum of **15b** a small multiplett is found for 10a-H. The absence of any large couplings indicates the equatorial position of this proton and thus the *cis* stereochemistry in this compound. In the spectrum of **14b** the absorption of 10a-H could not be observed, since the signal was masked by the peaks for the cyclobutane ring. In this, as in all other cases, ^{13}C-NMR data are equally well qualified to determine the stereochemistry of the cycloadducts. Thus, a signal in the range of δ = 44.8 to 51.0 is observed for C-6a in the *trans* compounds **14**[14], whereas C-6a in the *cis*-annulated cycloadducts **15** absorbs at δ = 39.2 to 41.1. A similar effect is observed for the C-10a resonance (*trans*: δ = 33.5 to 35.3; *cis* δ = 27.7 to 29.2). The upfield shift of the signals of the two carbons at the ring junction in *cis*-fused systems has already been observed on decalins[14] and cycloadducts of type **6**[7]. In the ^{1}H-NMR spectra of the ene adducts **16**, the absorption of 1′-H is used to determine the stereochemistry at the cyclohexane. Thus, two large and two small couplings ($J_{1',2'}$ = $J_{1',6'ax}$ = 11.0 to 11.5 Hz, $J_{1',5}$ = 2.0 Hz, $J_{1',6'eq}$ = 3.5 Hz) are observed for this proton, which clearly indicates the *trans*-orientation of the substituents.

Discussion

For the intramolecular *hetero* Diels-Alder reaction of alkylidene-1,3-dicarbonyls of type **13** an *exo-E-anti* (A), an *endo-E-syn* (C), and an *exo-Z-syn* (D) orientation in the transition state can be taken into consideration. The former one would give a *trans*- and the two latter a *cis*-fused compound. The *endo-Z-anti* (B) orientation is unlikely for geometrical reasons. Since we have shown that only an *E*-heterodiene in compounds of type **5** reacts, we feel entitled to omit also the *exo-Z-syn*-transition state in our further discussion. In the reaction of **13** the *trans*-fused compounds **14** are formed preferentially; this is due to a strong steric interaction between one hydrogen at C-3 of the chain and the CO group at position 3 of the heterodiene in an *endo-E-syn* transition state with a chairlike conformation of the chain. However, if one assumes a symmetric orientation of the heterodiene and the dienophile in the *endo*- and *exo*-transition state (e.g. angle 90°, distance 2.2 Å)[2g], no change in the ratio of *trans*- and *cis*-fused adducts **14** and **15** should be observed by a symmetric alteration of the substituents R in the dienophile. In contrast to this, the experimental results clearly show that there is a dependence of the ratio of **14**/**15** on the size of the ring at the dienophile, thus the formation of the *cis* product **14** increases in the row: 6-ring, dimethyl, 7-ring, 5-ring, 4-ring. It can be assumed that all reactions proceed via a concerted mechanism, as it has been shown for **5**[8], since in all examples **11a–e**, alkyl substituents are located at the dienophile moiety[15]. Therefore, the best explanation for the obtained results is a different degree of asymmetry in the *endo*- and the *exo*-transition state. Since it is quite unlikely that the *endo*-transition state is symmetric and the *exo* not and vice versa, both transition states should be asymmetric. This again would be in agreement with our conception that in the *hetero* Diels-Alder reaction of alkylidene- and benzylidene-1,3-dicarbonyl and similar compounds the dienophile approaches C-4 of the heterodiene at a trajectory of about 109°. In addition, it can be assumed that the dienophile is tilted to the plane of the heterodiene or vice versa in order to minimize steric interaction and to optimize overlap of the appropriate orbitals. The degree of deviation from planarity may be different in the *exo*- and *endo*-transition state.



The conclusions drawn from these experiments are only valid if the *hetero* Diels-Alder reactions of **2** and **12** proceed with kinetic control. Therefore, the pure cycloadducts **14** were kept under reaction conditions for 24 h, an isomerization was not observed.

For the ene reaction we also assume an asynchronous transition state. This is in agreement with the results, that **13c** gives the highest amount of ene product. The geometry of **13b** should be similarly favourable for an ene reaction[16], but an ene product was not found in the transformation of this compound. However, in this reaction a large amount of undefined material was observed, which may stem from a primarily formed highly strained cyclobutene moiety by decomposition under the reaction conditions.

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Experimental

^{1}H NMR and ^{13}C NMR: Varian XL-200, VXR-200, and FT-80A, multiplicities were determined with the APT pulse sequence. – MS: Varian MAT 311A; high resolution: Varian MAT 731. – IR: Perkin-Elmer 297. – UV: Varian Cary 219. – Melting points: Kofler melting point apparatus (corrected values). – HPLC: Varian LC 5000 (Vista CDS 401 Datasystem), Knauer HPLC-system (Merck-Hitachi Integrator D 2000). – Elemental analyses were carried out in the analytical laboratory of the university. – All solvents were distilled prior to use. Acetonitrile used for the Diels-Alder reactions was filtered through basic alumina (Alumina Woelm B super I, Fa.

Woelm Pharma, Eschwege) before use. – Products were generally isolated by flash chromatography[17] (FC) on SiO_2 (Silica Woelm 32–63 active, Fa. Woelm Pharma, Eschwege) using ether/petroleum ether mixtures as eluent. – Acetonitrile for HPLC was purchased from J. T. Baker Chemical Co., water was bidistilled in quartz vessels. The solvents were manually mixed and filtered through a membrane filter (0.2 μm) prior to use. – All chiral compounds are obtained as racemic mixtures.

Synthesis of the Esters **10a–e**. – *General Procedure I. – Wittig Reaction with n-Butyl Lithium:* A suspension of phosphonium salt (100 mmol) in dry THF (200 ml) is cooled to 0°C and a solution of *n*-butyl lithium (10 ml, 10 M in hexane) slowly added. The resulting red solution is stirred at this temperature for 45 min and then cooled to −78°C. A solution of aldehyde **8** (97 mmol) in THF (50 ml) is added *quickly*[18]. The solution is then allowed to warm to room temperature and stirred overnight. For workup, water (100 ml) is added and the phases are separated. After carefull extraction of the aqueous phase with petroleum ether, the combined extracts are washed with satd. aqueous NH_4Cl and brine and dried with Na_2SO_4. The crude product obtained after removal of the solvent in vacuo is purified by distillation.

General Procedure II. – Wittig Reaction with Potassium tert-Butylate: To a mechanically stirred mixture of potassium *tert*-butylate (KOtBu) (100 mmol) in dry *tert*-butyl methyl ether (tBuOMe) (200 ml) the phosphonium salt (100 mmol) is added. The resulting very viscous mixture is refluxed for 15 min and allowed to cool to room temperature (30 min). *Quick*[18] addition of a solution of aldehyde **8** (100 mmol) in tBuOMe (20 ml) causes the temperature to rise again. The reaction mixture is stirred overnight. Workup as in procedure I.

Methyl 7-Methyl-6-octenoate (**10a**): 14.4 g (100 mmol) of **8** and 38.6 g (100 mmol) of **9a** are treated according to procedure I. Distillation (97°C, 10 Torr) afforded 9.70 g (57%) of **10a**. – IR (film): ν = 1740 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 1.20–1.75 (m, 4H), 1.54 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.92 (q, J = 7 Hz, 2H, 5-CH_2), 2.25 (t, J = 7 Hz, 2H, 2-CH_2), 3.58 (s, 3H, OCH_3), 5.02 (tm, J = 7 Hz, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 17.65 (CH_3 *cis*), 24.66 (C-3), 25.72 (CH_3 *trans*), 27.67 (C-4), 29.41 (C-5), 34.07 (C-2), 51.43 (OCH_3), 124.3 (C-6), 131.7 (C-7), 174.2 (C-1).

$C_{10}H_{18}O_2$ (170.2) Calcd. C 70.55 H 10.65
Found C 70.61 H 10.72

Methyl 6-Cyclobutylidenehexanoate (**10b**): 15.0 g (104 mmol) of **8**, 50.0 g (105 mmol) of (4-bromobutyl)triphenylphosphonium bromide and 23.0 g (205 mmol!) KOtBu were treated according to procedure II. Distillation (66°C, 0.5 Torr) gave 9.30 g (49%) of **10b**. – IR (film): ν = 1740 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 1.30–2.90 (m, 14H), 3.67 (s, 3H, OCH_3), 5.03 (m_c, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 17.18 (C-3′), 24.68 (C-3), 27.68, 29.37 (C-5, C-4, C-2′ *cis*), 30.99 (C-2′ *trans*), 34.04 (C-2), 51.33 (OCH_3), 120.0 (C-6), 140.2 (C-1′), 174.0 (C-1).

$C_{11}H_{18}O_2$ (182.3) Calcd. C 72.49 H 9.95
Found C 72.62 H 9.97

Methyl 6-Cyclopentylidenehexanoate (**10c**): 5.80 g (400 mmol) of **8** and 19.0 g (46.0 mmol) of **9c** were treated according to procedure II. Kugelrohr distillation (120°C, 1 Torr) afforded 6.00 g (77%) of **10c**. – IR (film): ν = 1740 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 1.25–1.80 (m, 8H), 1.85–2.45 (m, 8H), 3.66 (s, 3H, OCH_3), 5.21 (t quint, J = 7, J = 2.5 Hz, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 24.78 (C-3), 26.49, 26.54 (C-3′), 28.69, 29.33 (C-4, C-5, C-2′ *cis*), 33.66 (C-2′ *trans*), 34.08 (C-2), 119.8 (C-6), 143.4 (C-1′), 174.0 (C-1).

$C_{12}H_{20}O_2$ (196.3) Calcd. C 73.41 H 10.29
Found C 73.33 H 10.28

Methyl 6-Cyclohexylidenehexanoate (**10d**): 17.5 g (122 mmol) of **8** and 52.0 g (122 mmol) of **9d** were treated according to procedure I. Distillation (94°C, 2 Torr) afforded 14.0 g (55%) of **10d**. – IR (film): ν = 1740 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 1.20–1.80 (m, 1H), 1.85–2.20 (m, 6H), 2.31 (t, J = 7 Hz, 2H, 2-H), 3.68 (s, 3H, OCH_3), 5.04 (t, br., J = 7 Hz, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 24.75 (C-3), 26.89, 27.25, 28.10, 28.94, 29.89 (C-4, C-5, C-2′ *cis*, C-3′, C-4′), 33.99 (C-2), 37.44 (C-2′ *trans*), 51.17 (OCH_3), 121.1 (C-6), 139.8 (C-1′), 173.6 (C-1).

$C_{13}H_{22}O_2$ (210.3) Calcd. C 74.24 H 10.54
Found C 74.14 H 10.34

Methyl 6-Cycloheptylidenehexanoate (**10e**): 10.0 g (69 mmol) of **8** and 32.0 g (72 mmol) of **9e** were treated according to procedure I. Distillation (118°C, 2 Torr) afforded 6.5 g (42%) of **10e**. – IR (film): ν = 1740 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 1.20–1.80 (m, 12H), 1.80–2.10 (m, 2H), 2.10–2.40 (m, 6H), 3.69 (s, 3H, OCH_3), 5.11 (t, quint, J = 7, J = 1 Hz, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 24.93 (C-3), 27.49 (C-4′ *cis* and *trans*), 29.36, 29.62, 29.72 (C-4, C-2′ *cis*, C-5), 30.21 (C-3′ *cis* and *trans*), 34.00 (C-2), 38.08 (C-2′ *trans*), 51.12 (OCH_3), 124.9 (C-6), 141.3 (C-1′), 173.5 (C-1).

$C_{14}H_{24}O_2$ (224.3) Calcd. C 74.95 H 10.78
Found C 75.08 H 10.82

Synthesis of the Alcohols **11a–e**. – *General Procedure III. – Reduction of the Esters* **10a–e**: To a suspension of lithium aluminium hydride (720 mg, 20 mmol) in refluxing tBuOMe is slowly added a solution of ester **10** (40 mmol) in tBuOMe (20 ml). The solution is then refluxed until the educt cannot be detected anymore by TLC. After careful addition of water (5 ml) to hydrolyse the surplus hydride, 10% KOH (20 ml) is added. The phases are separated, and the aqueous phase is extracted with tBuOMe. The combined organic phases are washed with brine and dried with sodium sulfate. The solvent is removed under reduced pressure and the crude product purified by distillation.

7-Methyl-6-octen-1-ol (**11a**): 8.50 g (50.0 mmol) of **10a** was reduced according to procedure III. Distillation (61°C, 0.8 Torr) gave 6.84 g (96%) of **11a**. – ^1H NMR ($CDCl_3$): δ = 1.10–2.20 (m, 8H), 1.60 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 2.94 (s, br., 1H, OH), 3.60 (t, J = 6.5 Hz, 2H, 1-CH_2), 5.52 (tm, J = 7 Hz, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 17.67 (CH_3 *cis*), 25.45 (C-3), 25.74 (CH_3 *trans*), 28.00 (C-4), 29.71 (C-2), 32.71 (C-5), 62.88 (C-1), 124.6 (C-6), 131.4 (C-7).

$C_9H_{18}O$ (142.2) Calcd. C 75.99 H 12.76
Found C 75.81 H 12.83

6-Cyclobutylidene-1-hexanol (**11b**): 9.30 g (51.0 mmol) of **10b** was reduced according to procedure III. Distillation (69°C, 0.02 Torr) gave 6.30 g (80%) of **11b**. – ^1H NMR ($CDCl_3$): δ = 1.20–1.70 (m, 6H), 1.80–2.15 (m, 5H, 5-H, 3′-H, OH), 2.50–2.80 (m, 4H, 2′-H), 3.62 (t, J = 7 Hz, 2H, 1-H), 5.03 (m_c, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 17.13 (C-3′), 25.51 (C-3), 27.98 (C-5), 29.31, 29.69 (C-2′ *cis*, C-4), 30.94 (C-2′ *trans*), 32.71 (C-2), 62.58 (C-1), 120.4 (C-6), 139.8 (C-1′).

$C_{10}H_{18}O$ (154.3) Calcd. C 77.87 H 11.76
Found C 77.94 H 11.81

6-Cyclopentylidene-1-hexanol (**11c**): 2.30 g (12.0 mmol) of **10c** was reduced according to procedure III. Kugelrohr distillation (150°C, 0.03 Torr). gave 1.67 g (84%) of **11c**. – ^1H NMR ($CDCl_3$): δ = 1.25–1.85 (m, 11H), 1.90–2.40 (m, 6H), 3.64 (t, J = 6 Hz, 2H, 1-H), 5.24 (m_c, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 25.66 (C-3), 26.46, 26.53 (C-3′), 28.65, 29.69 (C-5, C-4, C-2′ *cis*), 32.74 (C-2), 33.62 (C-2′ *trans*), 62.52 (C-1), 120.2 (C-6), 143.0 (C-1′).

$C_{11}H_{20}O$ (168.3) Calcd. C 78.51 H 11.98
Found C 78.40 H 12.17

6-Cyclohexylidene-1-hexanol (**11d**): 14.0 g (66.7 mmol) of **10d** was reduced according to procedure III. Distillation (105°C, 0.01 Torr) gave 12.0 g (98%) of **11d**. – ^{1}H NMR ($CDCl_3$): δ = 1.20–1.80 (m, 12H), 1.85–2.25 (m, 7H), 3.60 (t, *J* = 6.5 Hz, 2H, 1-H), 4.90–5.15 (m, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 25.57 (C-3), 27.14, 27.97, 28.81 (C-2′ *cis*, C-3′, C-5), 30.17 (C-4), 32.70 (C-2), 37.31 (C-2′ *trans*), 62.37 (C-1), 121.4 (C-6), 139.4 (C-1′).

$C_{12}H_{22}O$ (182.3) Calcd. C 79.06 H 12.16
Found C 79.24 H 12.17

6-Cycloheptylidene-1-hexanol (**11e**): 5.50 g (25.0 mmol) of **10e** was reduced according to procedure III. Distillation (107°C, 1 Torr) gave 2.30 g (49%) of **11e**. – ^{1}H NMR ($CDCl_3$): δ = 1.20–1.80 (m, 15H, 2-H, 3-H, 4-H, 3′-H *cis* and *trans*, 4′-H *cis* and *trans*, OH), 1.90–2.40 (m, 6H, 5-H, 2′-H *cis* and *trans*), 3.65 (t, *J* = 7.0 Hz, 2H, 1-H), 5.12 (t, quint, *J* = 7.0, *J* = 1.2 Hz, 1H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 25.69 (C-3), 27.31, 27.68, 29.20, 29.54, 29.87, 30.07 (C-2′ *cis*, C-3′ *cis* and *trans*, C-4′ *cis* and *trans* C-5, C-4), 32.75 (C-2), 37.93 (C-2′ *trans*), 62.60 (C-1), 125.1 (C-6), 141.0 (C-1′).

$C_{13}H_{24}O$ (196.3) Calcd. C 79.53 H 12.32
Found C 79.54 H 12.32

Synthesis of the Aldehydes **12a–e**. – *General Procedure IV.* – *Oxidation of the Alcohols* **11a–e**: To a stirred solution of oxalyl chloride (1.0 ml, 11 mmol) in dry methylene chloride at –78°C is added dropwise a solution of DMSO (1.7 ml, 22 mmol) in 5 ml of methylene chloride. The rate of addition is controlled to achieve a steady gas evolution. 2 min after the end of this period, a solution of alcohol **9** (10 mmol) in methylene chloride (10 ml) is added over 15 min at –78°C and the mixture is stirred for 15 min at this temperature, then triethylamine (7 ml) is added. After additional 5 min, the mixture is allowed to warm to room temperature. Water (5 ml) is then added, and the phases are separated. The aqueous phase is carefully extracted with methylene chloride, and the combined organic phases are washed with brine. Drying (Na_2SO_4) and removal of the solvent in vacuo affords the crude product. All aldehydes **12** have a very persistent and disgusting odour!

7-Methyl-6-octenal (**12a**): 1.42 g (10 mmol) of **11a** was treated according to procedure IV. FC (ether/petroleum ether, 1:9, R_f = 0.29) gave 1.38 g (97%) of **12a**. – IR (film): ν = 1740 cm^{-1} (C=O). – ^{1}H NMR ($CDCl_3$): δ = 1.30–2.60 (m, 8H), 1.59 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 5.06 (tm, *J* = 7 Hz, 1H, 6-H), 9.72 (t, *J* = 1.5 Hz, 1H, 1-H). – ^{13}C NMR ($CDCl_3$): δ = 17.66 (CH_3 *cis*), 21.73 (C-3), 25.69 (CH_3 *trans*), 27.71 (C-4), 29.38 (C-5), 43.85 (C-2), 124.1 (C-6), 131.8 (C-7), 202.7 (C-1).

$C_9H_{16}O$ (140.2) Calcd. C 77.09 H 11.50
Found C 77.18 H 11.45

3.10 g (20.0 mmol) of **11b** was treated according to procedure IV. FC (ether/petroleum ether, 1:20) afforded two fractions.

Fraction 1. – *6-(Cyclobutylidene)hexyl (Methylthio)methyl Ether*: R_f = 0.35, yield 80 mg (1.9%). – ^{1}H NMR ($CDCl_3$): δ = 1.20–2.20 (m, 10H), 2.13 (s, 3H, SCH_3), 2.50–2.80 (m, 4H), 3.50 (t, *J* = 7 Hz, 2H, OCH_2), 4.61 (s, 2H, OCH_2S), 5.03 (m_c, 1H, =C–H). – ^{13}C NMR ($CDCl_3$): δ = 13.81 (SCH_3), 17.09 (C-3′), 25.87 (C-3), 27.89, 29.27, 29.37, 29.56, 30.90 (C-2′ *cis*, C-2′ *trans*, C-2, C-4, C-5), 68.08 (C-1), 75.15 (O–CH_2–S), 120.3 (C-6), 139.7 (C-1′). – MS (70 eV): *m/z* (%) = 214 (3) [M^+], 199 (23) [M – CH_3], 186 (5) [M – C_2H_4 or M – CO], 167 (5) [M – SCH_3], 153 (7) [M – C_2H_5S], 81 (100).

$C_{12}H_{22}OS$ Calcd. 214.1391 Found 214.1391 (MS)

Fraction 2. – *6-Cyclobutylidenehexanal* (**12b**): R_f = 0.20, yield 2.80 g (91%). – IR (film): ν = 1730 cm^{-1} (C=O). – ^{1}H NMR ($CDCl_3$): δ = 1.25–2.15 (m, 8H), 2.30–2.80 (m, 6H), 5.0 (m_c, 1H, 6-H), 9.72 (t, *J* = 2 Hz, 1H, 1-H). – ^{13}C NMR ($CDCl_3$): δ = 17.11 (C-3′), 21.70 (C-3), 27.67, 29.30 (C-4, C-5, C-2′ *cis*), 30.93 (C-2′ *trans*), 43.87 (C-2), 119.8 (C-6), 140.3 (C-1′), 202.5 (C-1).

$C_{10}H_{16}O$ (152.2) Calcd. C 78.90 H 10.59
Found C 78.78 H 10.30

6-Cyclopentylidenehexanal (**12c**): 4.70 g (28 mmol) of **11c** was treated according to procedure IV. FC (ether/petroleum ether, 1:10, R_f = 0.22) afforded 2.95 g (63%) of **12c**. – IR (film): ν = 1735 cm^{-1} (C=O). – ^{1}H NMR ($CDCl_3$): δ = 1.30–1.50 (m, 2H), 1.50–1.80 (m, 6H), 1.92–2.08 (m, 2H, 5-H), 2.10–2.30 (m, 4H, 2′-H), 2.44 (td, *J* = 7.0, *J* = 1.9 Hz, 2H, 2-H), 5.22 (t, quint, *J* = 7.0, *J* = 2.5 Hz, 2H, 6-H), 9.77 (t, *J* = 1.9 Hz, 1H, 1-H). – ^{13}C NMR ($CDCl_3$): δ = 21.78 (C-3), 26.37, 26.44 (C-3′), 28.65 (C-4), 29.21, 29.28 (C-5, C-2′ *cis*), 33.58 (C-2′ *trans*), 43.89 (C-2), 119.4 (C-6), 143.7 (C-1′), 202.8 (C-1).

$C_{11}H_{18}O$ (166.3) Calcd. C 79.46 H 10.91
Found C 79.28 H 11.03

6-Cyclohexylidenehexanal (**12d**): 1.80 g (10 mmol) of **11d** was treated according to procedure IV. FC (ether/petroleum ether, 1:9, R_f = 0.28) gave 1.50 g (80%) of **12d**. – IR (film): ν = 1730 cm^{-1} (C=O). – ^{1}H NMR ($CDCl_3$): δ = 1.20–2.20 (m, 16H), 2.30–2.50 (m, 2H, 2-H), 5.03 (t, br., *J* = 7 Hz, 1H, 6-H), 9.72 (t, *J* = 2 Hz, 1H, 1-H). – ^{13}C NMR ($CDCl_3$): δ = 21.83 (C-3), 26.92, 27.20, 28.05, 28.89, 29.85 (C-4, C-5, C-2′ *cis*, C-3′, C-4′), 37.41 (C-2′ *trans*), 43.90 (C-2), 120.9 (C-6), 139.9 (C-1′), 201.5 (C-1).

$C_{12}H_{20}O$ (180.3) Calcd. C 79.94 H 11.18
Found C 80.05 H 11.17

6-Cycloheptylidenehexanal (**12e**): 2.00 g (10 mmol) of **11e** was treated according to procedure IV. FC (ether/petroleum ether, 1:10, R_f = 0.26) gave 1.21 g (61%) of **12e**. – IR (film): ν = 1735 cm^{-1} (C=O). – ^{1}H NMR (C_6D_6): δ = 1.00–1.65 (m, 12H), 1.70–2.0 (m, 4H), 2.05–2.35 (m, 4H), 5.11 (t, quint, *J* = 7.0, *J* = 1.2 Hz, 1H, 6-H), 9.38 (t, *J* = 2.0 Hz, 1H, 1-H). – ^{13}C NMR (C_6D_6): δ = 22.03 (C-3), 27.53, 27.64, 29.38, 29.63, 29.78, 30.25 (C-4, C-5, C-2′ *cis*, C-3′ *cis* and *trans*, C-4′ *cis* and *trans*), 38.14 (C-2′ *trans*), 43.82 (C-2), 125.0 (C-6), 141.3 (C-1′), 200.5 (C-1).

$C_{13}H_{22}O$ (194.3) Calcd. C 80.35 H 11.41
Found C 80.51 H 11.53

General Procedure V. – *Reaction of Aldehydes* **12a–e** *with 1,3-Dimethylbarbituric Acid* (**2**): To a suspension of dimethylbarbituric acid (DMBA) (1.07–1.12 mmol) and ethylene diammonium diacetate (EDDA) (0.02–0.05 mmol) in dry acetonitrile (20 ml) is added a solution of aldehyde **12** (1.00 mmol) in 10 ml of the same solvent. The resulting solution turns yellow as the alkylidene compound **13** is formed. The reaction is stirred for the time given, the solution usually becomes colourless after completion of the cycloaddition. The solvent is then removed under reduced pressure and the mixture flash-chromatographed in the solvent stated. The Diels-Alder fraction is analysed by HPLC and ^{13}C-NMR spectroscopy. The other data are obtained after crystallisation, the ene fraction is crystallised directly. The yields refer to chromatographically pure compounds.

Reaction of **12a**: 770 mg (5.50 mmol) of **12a**, 27 mg (0.13 mmol) of EDDA, and 780 mg (5.00 mmol) of DMBA were treated according to procedure V (reaction time: 60 min). FC (ether/petroleum ether, 2:1) gave 236 mg (17%) of **16a**/**17a** and 806 mg (58%) of **14a**/**15a**.

1,3-Dimethyl-5-[2-(1-methylethenyl)cyclohexyl]-1,3-pyrimidine-2,4,6(1H,3H,5H)-trione (**16a**): R_f = 0.72 (ether/petroleum ether,

2:1). – IR (film): ν = 1750 cm^{-1} (C=O), 1680 (br., C=O). – UV (acetonitrile): λ_{max} (lg ε) = 224 nm (3.83), 266 (3.04). – ^{1}H NMR ($CDCl_3$): δ = 1.20–1.80 (m, 6H), 1.72 (m_c, 3H, CH_3), 2.38–2.50 (m_c, 2H, 1'-H, 2'-H), 3.28 (s, 3H, NCH_3), 3.38 (s, 3H, NCH_3), 3.60 (s, br., 1H, 5-H), 4.88 (m_c, 2H, $=CH_2$). – MS (70 eV): *m/z* (%) = 278 (17) [M$^+$], 235 (4) [M – C_3H_7], 157 (100) [$C_6H_9N_2O_3$], 122 (100) [C_9H_{14}], 107 (43) [122 – CH_3].

$C_{15}H_{22}N_2O_3$ (278.4) Calcd. C 64.73 H 7.97 N 10.06
Found C 64.75 H 7.97 N 10.07

(6aRS,10aRS)-4,6,6a,7,8,9,10,10a-Octahydro-2,4,6,6-tetramethyl-1H-[2]benzopyrano[3,4-d]pyrimidine-1,3(2H)-dione (**14a**): R_f = 0.25 (ether/petroleum ether, 2:1), m.p. 142–144°C (ether). – IR (film): ν = 1705 cm^{-1} (C=O, imide), 1640 (C=O, conj.), 1625 (C=C), 1210, 1140. – UV (acetonitrile): λ_{max} (lg ε) = 261.5 nm (4.03). – ^{1}H NMR ($CDCl_3$): δ = 0.82 (qm, *J* = 12 Hz, 1H, 10-H_{ax}), 1.00–1.50 (m, 4H, 6a-H, 7-H_{ax}, 8-H_{ax}, 9-H_{ax}), 1.15 (s, 3H, 6-CH_{3ax}), 1.42 (s, 3H, 6-H_{eq}), 1.65–1.90 (m, 3H, 7-H_{eq}, 8-H_{eq}, 9-H_{eq}), 2.19 (td, *J* = 11, *J* = 3 Hz, 1H, 10a-H), 3.14 (d, br., *J* = 13 Hz, 1H, 10-H_{eq}), 3.30 (s, 3H, NCH_3), 3.31 (s, 3H, NCH_3). – MS (70 eV): *m/z* (%) = 278 (100) [M$^+$], 263 (16) [M – CH_3], 235 (58) [M – C_3H_7], 221 (10) [M – CH_3NCO], 209 (21) [M – $C_5H_9^+$], 195 (20) [M – C_6H_{11}], 182 (44) [$C_8H_{10}N_2O_3$], 169 (56) [$C_7H_9N_2O_3^+$], 157 (70) [$C_6H_9N_2O_3$], 122 (52) [C_9H_{14}], 107 (21) [M – $C_8H_{11}^+$], 95 (21) [C_7H_{11}], 79 (31) [C_6H_7].

$C_{15}H_{22}N_2O_3$ (278.4) Calcd. C 64.72 H 7.97 N 10.07
Found C 64.73 H 8.04 N 10.17

Reaction of **12b**: 965 mg (6.19 mmol) of **12b**, 23 mg (0.11 mmol) of EDDA, and 1.4 mg (6.67 mmol) of DMBA were treated according to procedure V (reaction time: 22 h). FC (ether/petroleum ether, 1:1, R_f = 0.20) gave 754 mg (42%) of **14b/15b**. The diastereomers were separated by preparative HPLC: acetonitrile/water, 1:1, nucleosil 5 C18 (250 × 8 mm), 0.6 ml/min, 70 bar, UV (254 nm), automatic injection (*c* = 2.5 mg/ml in acetonitrile/water 62:38, 3 mg per separation), t_r(**14b**) = 90 min, t_r(**15b**) = 97 min.

(6aSR,10aRS)-6a,7,8,9,10,10a-Hexahydro-2,4-dimethylspiro[6H-[2]benzopyrano[3,4-d]pyrimidine-6,1'-cyclobutane]-1,3(2H,4H)-dione (**15b**) (*cis*): M.p. 160–161°C (hexane). – UV (acetonitrile): λ_{max} (lg ε) = 263 nm (3.97). – IR (KBr): ν = 1700 cm^{-1} (C=O, imide), 1640 (C=O, conj.), 1620 (C=C), 1200 (C–O–C), 778, 760. – ^{1}H-NMR ($CDCl_3$): δ = 0.90–1.55 (m, 5H), 1.60–2.20 (m, 7H), 2.22–2.40 (m, 2H), 2.95–3.25 (m, 2H, 10-H_{eq}, 10a-H), 3.31 (s, 3H, NCH_3), 3.36 (s, 3H, NCH_3). – MS (70 eV): *m/z* (%) = 290 (100) [M$^+$], 262 (21) [M – C_2H_4], 247 (17) [M – C_3H_7], 233 (5) [M – $OCNCH_3$], 157 (6) [$C_6H_9N_2O_3^+$], 134 (3) [$C_{10}H_{14}$].

$C_{16}H_{22}N_2O_3$ Calcd. 290.1631 Found 290.1630 (MS)

(6aRS,10aRS)-6a,7,8,9,10,10a-Hexahydro-2,4-dimethylspiro[6H-[2]-benzopyrano[3,4-d]pyrimidine-6,1'-cyclobutane]-1,3(2H,4H)-dione (**14b**) (*trans*): M.p. 133.5–135.5°C (hexane). – UV (acetonitrile): λ_{max} (lg ε) = 262 nm (3.99). – IR (KBr): ν = 1705 cm^{-1} (C=O, imide), 1640 (C=O, conj.), 1625 (C=C), 1200 (C–O–C), 780, 772, 758. – ^{1}H-NMR ($CDCl_3$): δ = 0.80–0.98 (m, 1H, 10-H_{ax}), 1.10–2.50 (m, 13H), 3.13 (d, br., *J* = 12 Hz, 1H, 10-H_{eq}), 3.31 (s, 3H, NCH_3), 3.37 (s, 3H, NCH_3). – MS (70 eV): *m/z* (%) = 290 (100) [M$^+$], 262 (54) [M – C_2H_4], 247 (41) [M – C_3H_7].

$C_{16}H_{22}N_2O_3$ (290.4) Calcd. C 66.19 H 7.64 N 9.65
Found C 66.26 H 7.74 N 9.55

Reaction of **12c**: 1) 225 mg (1.34 mmol) of **12c**, 6 mg (0.03 mmol) of EDDA, and 235 mg (1.51 mmol) of DMBA were treated according to procedure V (reaction time: 3.5 h). FC (ether/petroleum ether, 2:1) gave 240 mg (59%) of **16c/17c** and 136 mg (40%) of **14c/15c**.

2) 173 mg (1.04 mmol) of **12c**, 10 mg (0.05 mmol) of EDDA, and 174 mg (1.12 mmol) of DMBA were treated according to procedure V (reaction time: 2.7 h). FC (ether/petroleum ether, 2:1) gave 170 mg (54%) of **16c/17c** and 126 mg (40%) of **14c/15c**.

5-[2-(1-Cyclopentenyl)cyclohexyl]-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**16c**): M.p. 96–98°C (hexane). – UV (acetonitrile): λ_{max} (lg ε) = 225 nm (3.82), 267 (3.05). – IR (KBr): ν = 1745 cm^{-1} (C=O, imide), 1690, 1670 (C=O), 760. – ^{1}H-NMR ($CDCl_3$): δ = 1.16–1.54 (m, 4H), 1.56–2.00 (m, 6H), 2.18–2.31 (m, 4H, $CH_2C=$), 2.41 (tdd, *J* = 11.5, *J* = 3.5, *J* = 2.0 Hz, 1H, 1'-H), 2.30–2.48 (m, 1H, 2'-H), 3.28 (s, 3H, NCH_3), 3.30 (s, 3H, NCH_3), 3.48 (d, *J* = 3.5 Hz, 1H, 5-H), 5.47 (s, br., 1H, CH=); double resonance: δ = 3.48→2.41 (td, *J* = 11.5, *J* = 2.0 Hz, 1H, 1'-H). – MS (70 eV): *m/z* (%) = 304 (12) [M$^+$], 157 (40) [$C_6H_9N_2O_3^+$], 148 (100) [$C_{11}H_{16}$].

$C_{17}H_{24}N_2O_3$ (304.4) Calcd. C 67.08 H 7.95 N 9.20
Found C 67.00 H 7.88 N 9.19

(6aRS,10aRS)-6a,7,8,9,10,10a-Hexahydro-2,4-dimethylspiro[6H-[2]benzopyrano[3,4-d]pyrimidine-6,1'-cyclopentane]-1,3(2H,4H)-dione (**14c**): M.p. 104–106°C (tBuOMe/hexane) – UV (acetonitrile): λ_{max} (lg ε) = 262 nm (4.00). – IR (KBr): ν = 1700 cm^{-1} (C=O, imide), 1635 (C=O, conj.), 1620 (C=C), 1210. – ^{1}H-NMR ($CDCl_3$): δ = 0.71–1.18 (m, 2H), 1.20–2.10 (m, 15H), 2.23 (td, *J* = 11.0, *J* = 3.0 Hz, 1H, 10a-H), 3.13 (d, br., *J* = 11 Hz, 1H, 10-H_{eq}), 3.30 (s, 3H, NCH_3), 3.32 (s, 3H, NCH_3); double resonance: δ = 3.13→2.23 (t, *J* = 11.0 Hz, 1H, 10a-H). – MS (70 eV): *m/z* (%) = 304 (19) [M$^+$], 157 (39) [$C_6H_9N_2O_3^+$], 148 (100) [$C_{11}H_{16}$].

$C_{17}H_{24}N_2O_3$ (304.4) Calcd. C 67.08 H 7.95 N 9.20
Found C 66.95 H 7.97 N 9.08

Reaction of **12d**: 1) 413 mg (2.29 mmol) of **12d**, 10 mg (0.05 mmol) of EDDA, and 438 mg (2.81 mmol) of DMBA were treated according to procedure V (reaction time: 2.8 h). FC (ether/petroleum ether, 1:2) gave 211 mg (29%) of **16d/17d** and 350 mg (48%) of **14d/15d**.

2) 409 mg (2.27 mmol) of **12d**, 13 mg (0.06 mmol) of EDDA, and 380 mg (2.44 mmol) of DMBA were treated according to procedure V (reaction time: 3.3 h). FC (ether/petroleum ether, 1:2) gave 137 mg (19%) of **16d/17d** and 419 mg (58%) of **14d/15d**.

5-[2-(1-Cyclohexenyl)cyclohexyl]-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**16d**): R_f = 0.36 (ether/petroleum ether, 1:2), m.p. 102–105°C (hexane). – UV (acetonitrile): λ_{max} (lg ε) = 225 nm (3.82), 268 (3.04). – IR (KBr): ν = 1745 cm^{-1}, 1690, 1675 (C=O), 760. – ^{1}H-NMR ($CDCl_3$): δ = 1.10–1.78 (m, 12H), 1.84–2.00 (m, 4H), 2.14–2.34 (m, 1H, 2'-H), 2.44 (tdd, *J* = 11.5, *J* = 3.5, *J* = 2.0 Hz, 1H, 1'-H), 3.28 (s, 3H, NCH_3), 3.30 (s, 3H, NCH_3), 3.50 (d, *J* = 2.0 Hz, 1H, 5-H), 6.50–6.60 (m, 1H, =CH). – MS (70 eV): *m/z* (%) = 318 (2) [M$^+$], 162 (100) [M – $C_6H_8N_2O_3$], 157 (32) [$C_6H_9N_2O_3^+$].

$C_{18}H_{26}N_2O_3$ (318.4) Calcd. C 67.90 H 8.23 N 8.80
Found C 68.11 H 7.99 N 8.89

(6aRS,10aRS)-6a,7,8,9,10,10a-Hexahydro-2,4-dimethylspiro[6H-[2]benzopyrano[3,4-d]pyrimidine-6,1'-cyclohexane]-1,3(2H,4H)-dione (**14d**): R_f = 0.15 (ether/petroleum ether, 1:2), m.p. 165–168°C (hexane). – UV (acetonitrile): λ_{max} (lg ε) = 262 nm (3.98). – IR (KBr): ν = 1700 cm^{-1} (C=O, imide), 1640 (C=O, conj.), 1600 (C=C). – ^{1}H-NMR ($CDCl_3$): δ = 0.80–1.50 (m, 7H), 1.50–2.00 (m, 11H), 2.28 (td, *J* = 11.0, *J* = 3.0 Hz, 1H, 10a-H), 3.16 (d, br., *J* = 12 Hz, 1H, 10-H_{eq}), 3.34 (s, 3H, NCH_3), 3.40 (s, 3H, NCH_3). – MS (70 eV): *m/z* (%) = 318 (24) [M$^+$], 162 (100) [M – $C_6H_8N_2O_3$], 157 (40) [$C_6H_9N_2O_3^+$].

$C_{18}H_{26}N_2O_3$ (318.4) Calcd. C 67.90 H 8.23 N 8.80
Found C 67.84 H 8.23 N 8.81

Reaction of **12e**: 1) 147 mg (0.76 mmol) of **12e**, 4 mg (0.02 mmol) of EDDA, and 100 mg (0.64 mmol) of DMBA were treated according to procedure V (reaction time: 15 h). FC (ether/petroleum ether, 3:1) gave 81 mg (32%) of **16e/17e** and 124 mg (49%) of **14e/15e**.

2) 196 mg (1.01 mmol) of **12e**, 8 mg (0.04 mmol) EDDA and 180 mg (1.15 mmol) DMBA were treated according to procedure V (reaction time: 16 h). FC (ether/petroleum ether, 3:1) gave 148 mg (44%) of **16e/17e** and 161 mg (48%) of **14e/15e**.

3) 57 mg (0.29 mmol) of **12e**, 5 mg (0.02 mmol) of EDDA, and 53 mg (0.34 mmol) of DMBA were treated according to procedure V (reaction time: 16 h). FC (ether/petroleum ether, 3:1) gave 39 mg (41%) of **16e/17e** and 41 mg (43%) of **14e/15e**.

5-[2-(1-Cycloheptenyl)cyclohexyl]-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**16e**): R_f = 0.42 (ether/petroleum ether, 1:3), m.p. 79–81°C (hexane). – UV (acetonitrile): λ_{max} (lg ε) = 225 nm (3.84), 268 (2.94). – IR (KBr): ν = 1745 cm^{-1} (C=O), 1690–1675 (C=O, C=C). – ^{1}H-NMR ($CDCl_3$): δ = 1.10–1.90 (m, 14H), 1.90–2.20 (m, 4H), 2.20–2.45 (m, 2H, 1′-H, 2′-H), 3.30 (s, 6H, NCH_3), 3.55 (s, br., 1H, 5-H), 5.73 (dd, J = 7.0, J = 6.0 Hz, 1H, 2″-H). – MS (70 eV): *m/z* (%) = 332 (6) [M^+], 177 (49) [$C_{13}H_{21}^+$], 176 (100), [$C_{13}H_{20}$], 157 (69) [$C_6H_9N_2O_3^+$].

$C_{19}H_{28}N_2O_3$ (332.4) Calcd. C 68.65 H 8.49 N 8.43
Found C 68.58 H 8.51 N 8.43

(6aRS,10aRS)-6a,7,8,9,10,10a-Hexahydro-2,4-dimethylspiro-[6H-[2]benzopyrano[3,4-d]pyrimidine-6,1′-cycloheptane]-1,3(2H,4H)-dione (**14e**): R_f = 0.32 (ether/petroleum ether, 1:3), m.p. 129–132°C (hexane). – UV (acetonitrile): λ_{max} (lg ε) = 262 nm (4.03). – IR (KBr): ν = 1710 cm^{-1} (C=O, imide), 1640 (C=O, conj.), 1625 (C=C), 1200 (C–O–C), 770, 750. – ^{1}H-NMR ($CDCl_3$): δ = 0.74–0.90 (m, 1H), 1.04–1.24 (m, 1H), 1.25–2.10 (m, 15H), 2.22 (td, J = 11.0, J = 3.0 Hz, 1H, 10a-H), 3.52 (d, br., J = 13 Hz, 1H, 10-H_{eq}), 3.30 (s, 3H, NCH_3), 3.35 (s, 3H, NCH_3). – MS (70 eV): *m/z* (%) = 332 (31) [M^+], 176 (100) [$C_{13}H_{20}$], 157 (37) [$C_6H_9N_2O_3^+$].

$C_{19}H_{28}N_2O_3$ (332.4) Calcd. C 68.65 H 8.49 N 8.43
Found C 68.39 H 8.47 N 8.46

Cyclisation of the Ene Product (**16e**): To a solution of **16e** (39 mg, 0.12 mmol) in dry methylene chloride (10 ml) under argon were added three drops of freshly distilled BF_3–Et_2O. The mixture was stirred overnight at room temperature and then quenched with methanol (2 ml). The solvent was removed in vacuo and the product isolated by FC (ether/petroleum ether, 1:3). Yield: 39 mg (100%). The HPLC analysis gave a ratio **14e/15e** of 127.3(1.9):1.

Table 3. Separation parameters for the cycloadducts **14a–e** and **15a–e**[a]

Reaction of **2** and	Flow [ml/min]	Pressure [bar]	t_R (**14**) [min]	t_R (**15**) [min]	α	*R*	Ratio **14/15**
12a	0.5	55	19.6	21.5	1.11	1.6	79.7 (0.3) 79.8 (0.9)
12b	0.9	100	19.2	21.7	1.14	2.5	13.8 (0.1)
12c	0.9	110	27.0	29.7	1.11	2.3	33.1 (0.1)
12d	0.9	100	39.2	43.0	1.10	2.0	131.6 (1.6)
12e	1.5	280	21.2	23.5	1.12	1.5	51.4 (0.7) 53.3 (1.2) 51.7 (1.3)
16e (BF_3–Et_2O)							127.3 (1.9)[b]

[a] All separations were run on nucleosil 7 C18 (0.4 × 25 cm) with acetonitrile/water, 50:50 (v/v). Detection: UV at 263 nm. – [b] Ratio obtained from the cyclisation of **16e**. – The structures of **16a**, **16c–e** were assigned by analogy to **16b** on the basis of their very similar chromatographic behaviour and their spectroscopic data in ^{13}C-NMR spectra of the reaction mixtures.

Table 4. ^{13}C-NMR data of the cycloadducts **14a–e** and **15a, b**

	14a	**14b**	**14c**	**14d**	**14e**	**15a**[a]	**15b**
C-1	162.60	162.49	162.65	162.61	162.38	162.91	162.64
C-3	151.28	151.21	151.31	151.34	151.19	151.28	151.06
C-4a	155.28	154.73	155.02	154.69	154.70	155.68	155.17
C-6	83.81	85.91	95.65	84.64	89.92*	83.21	87.59*
C-6a	48.58	44.83	45.21	48.70	50.98	41.07	39.22
C-7	27.57	27.02	27.50	27.50	27.25*	22.89*	21.23*
C-8	26.57	26.40	26.42	26.68	26.79	25.38*	25.26*
C-9	25.82	25.82	25.89	25.88*	25.87*	21.35*	21.33*
C-10	29.72	30.37*	29.82	29.94	29.34	26.83*	26.65*
C-10a	34.16	33.52	35.30	33.62	34.14	29.23	27.65
C-10b	89.63	90.44	90.43	89.87	88.25*	86.66	86.04*
N-CH3	27.71	27.68	27.72	27.72	27.64	27.79	27.72
	28.51	28.56	28.44	28.50	28.51	28.68	28.79
R	26.94	30.48*	35.65	34.44	39.47	28.63	33.92
	19.71	29.42*	31.00	26.76*	30.69	27.66	31.11
	-	12.82	24.30	25.43	29.89	-	12.79
	-	-	23.97	21.41	29.89	-	-
	-	-	-	21.41	22.87	-	-
	-	-	-	-	22.45	-	-

[a] Data were obtained from a ^{13}C-NMR spectrum of the mother liquor after crystallisation of **14a** by subtraction of the data for **14a**.

Table 5. ^{13}C-NMR data of the ene products **16a, c–e**

	16a	**16c**	**16d**	**16e**
C-2	151.78	151.75	151.85	151.60
C-4	167.88*	167.98*	168.10*	167.92*
C-5	51.02	51.64	51.59	51.60
C-6	169.40*	169.19*	169.28*	169.08*
C-1′	45.41*	45.58	48.16	49.94
C-2′	47.83*	41.95	44.88	44.81
C-3′	32.42	32.34*	32.32	32.85
C-4′	25.76	29.70	26.47*	28.38*
C-5′	26.50	26.30*	25.98*	26.30*
C-6′	28.87	25.66*	25.34*	25.66*
N-CH3	28.42	28.20	28.32	28.18
	28.10	28.35	28.32	28.25
C-1″	147.81	145.77	139.87	146.31
C-2″	112.77	126.46	124.17	129.6 (b)
C-3″	19.25	31.35	25.00*	31.8 (b)
C-4″		23.06	22.99*	27.13*
C-5″		32.12*	21.62*	29.67*
C-6″			30.14*	27.07*
C-7″				31.8 (b)

* denotes ambiguous assignments, (b) broad signals.

CAS Registry Numbers

2: 769-42-6 / **8**: 6654-36-0 / **9a**: 47180-35-8 / **9c**: 111998-10-8 / **9d**: 62941-13-3 / **9e**: 111998-11-9 / **10a**: 111998-05-1 / **10b**: 111998-06-2 / **10c**: 111998-07-3 / **10d**: 111998-08-4 / **10e**: 111998-09-5 /

11a: 646-17-3 / **11b**: 111998-12-0 / **11c**: 111998-13-1 / **11d**: 111998-14-2 / **11e**: 111998-15-3 / **12a**: 70512-12-8 / **12b**: 111998-17-5 / **12c**: 111998-18-6 / **12d**: 111998-19-7 / **12e**: 111998-20-0 / **14a**: 111998-23-3 / **14b**: 111998-25-5 / **14c**: 111998-28-8 / **14d**: 112020-98-1 / **14e**: 112021-00-8 / **15a**: 111998-24-4 / **15b**: 112020-96-9 / **15c**: 112020-97-0 / **15d**: 112020-99-2 / **15e**: 112021-01-9 / **16a**: 111998-21-1 / **16c**: 111998-26-6 / **16d**: 111998-29-9 / **16e**: 111998-32-4 / **17a**: 111998-22-2 / **17c**: 111998-27-7 / **17d**: 111998-30-2 / **17e**: 111998-31-3 / (6-cyclobutylidene)hexyl (methylthio)methyl ether: 111998-16-4 / (4-bromobutyl)triphenylphosphonium bromide 7333-63-3

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[15] The *hetero* Diels-Alder reaction of heterodienes **13** with different substituents R (e.g. ethyl and methyl) has also been investigated. There is no change of the configuration at the dienophile moiety. However, using compounds with R = phenyl and methyl, the configuration is contained with the (*E*) dienophile and not contained with the (*Z*) dienophile, indicating that in the latter case a carbocation or a radical may be formed as an intermediate. This experiment is quite important, since it shows that principally a rotation about a single bond formed in the intermediate is possible. L. F. Tietze, S. Brand, unpublished results.

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[18] Slow addition of the aldehyde resulted in isolation of the aldol adducts as main products.

[270/87]