Simple and Induced Diastereoselectivity in Intramolecular Hetero-Diels-Alder Reactions of 1-Oxa-1,3-butadienes. Experimental Data and Calculations[1]

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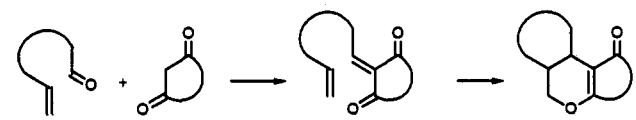
The simple and induced diastereoselectivity of the intramolecular hetero-Diels-Alder reaction of the alkylidene 1,3-dicarbonyl compounds **7a-e**, obtained *in situ* by Knoevenagel condensation of the aldehydes **5a-e** and dimethylbarbituric acid **6**, was investigated experimentally and theoretically. In all examples the selectivity is very high; thus the domino reaction of **5a** and **6** gives nearly exclusively the *trans*-fused tricyclic dihydropyran **8** (*trans*/*cis* = 98.8:1.2). In the similar reactions of the chiral aldehydes **5b-e** and **6** the *trans*-cycloadducts **28**, **33**, **36**, and **41** are the main products out of four possible diastereomers. The induced diastereoselectivity for the reaction of **5b** and **5e** with **6** is >99:1 and for the reaction of **5c** and **5d** with **6**, 95.2:3.6 and 94.1:4.7, respectively. Semiempirical AM1 calculations have been used to locate the transition structures of the intramolecular hetero-Diels-Alder reaction of **7a**. The results were employed to create new parameters for the MM2-type force-field to determine the transition structures of **7b-e**. The obtained data were compared with the experimental results of the cycloadditions and showed an excellent agreement.

Introduction

The Diels-Alder reaction[2] of 1-oxa-1,3-butadienes is a widely used method for the synthesis of the pyran moiety and its hydrogenated form, respectively, which is a structural feature of many natural products such as carbohydrates, talaromycines, milbemycins, avermectins, pheromones, iridoids, and many other natural substances. Whereas simple 1-oxa-1,3-butadienes such as α,β-unsaturated aldehydes and ketones show only low reactivity in cycloadditions, alkylidene and benzylidene 1,3-dicarbonyl compounds **3** undergo hetero-Diels-Alder reactions even with alkenes at room temperature to give the cycloadducts **4**.[3] In addition, these heterodienes **3** can be obtained quite easily by a Knoevenagel condensation[4] of an aldehyde **1** and a 1,3-dicarbonyl compound **2**; the high reactivity of these 1-oxa-1,3-butadienes is due to the electron-withdrawing group at position 3, causing a strong decrease of the LUMO energy.[3a] Furthermore the cycloadditions show



1 **2** **3** **4**

a high regio- and stereoselectivity if performed in an intramolecular mode. This can be explained by the conformational restrictions on the transition structure leading to the cycloadducts due to a 1,3-allylic strain.[5] Thus, Knoevenagel products containing a trisubstituted double bond with a geminal substitution at the sp^2 terminus always have a *cis* orientation of the substituents at the double bond; the spatial control is therefore called sp^2-geminal effect.[6] The tandem Knoevenagel hetero-Diels-Alder reaction, which was invented by us as a powerful sequential transformation, has already been used for the synthesis of several natural products.[7]

In this paper we describe the reaction of dimethylbarbituric acid **6** with the aldehyde **5a** as well as its methyl-substituted analogues **5b-e**. In the first step using ethylenediammonium diacetate as a catalyst and **5a** as a substrate the alkylidene barbiturate **7a** is formed which then gives the cycloadducts **8** and **9** in 58% yield and a ratio of 98.8:1.2. In addition 17% of the ene product **10** is obtained; this side reaction is usually found in all transformations of this type and occurs to a different extent depending on the substrates.

The aim of our studies is the determination of the simple and, in particular, the induced diastereoselection for different types of reactions such as cationic, anionic, radical, and pericyclic cyclisations; in this connection we investigate the influence of substituents at different positions of the tether as in **7b-e** in intramolecular transformations.

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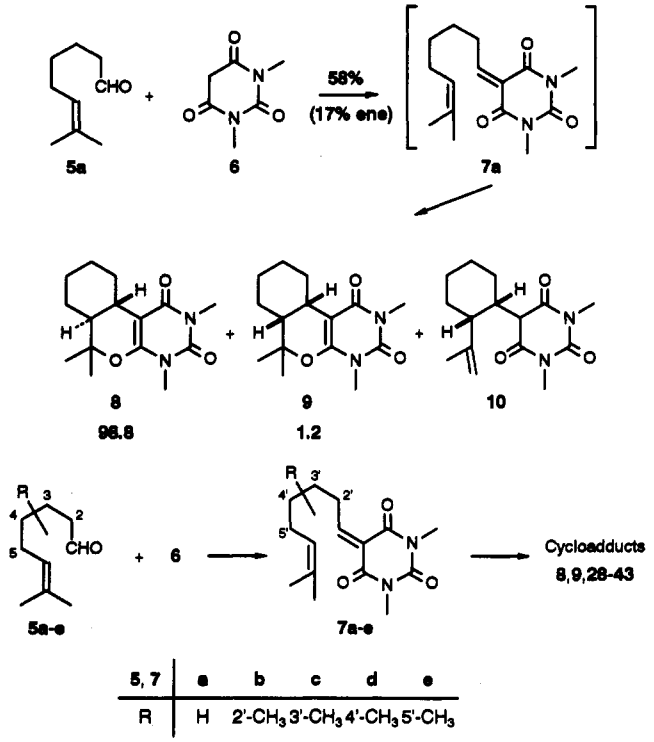
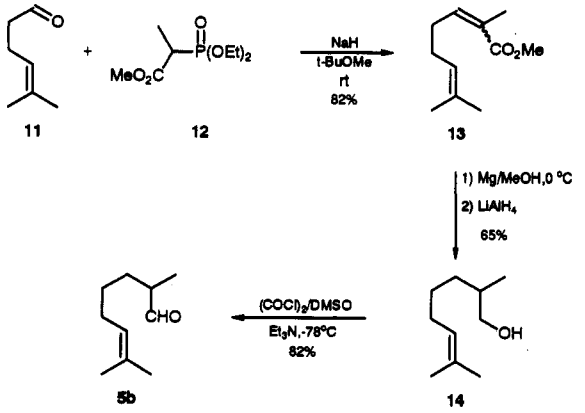


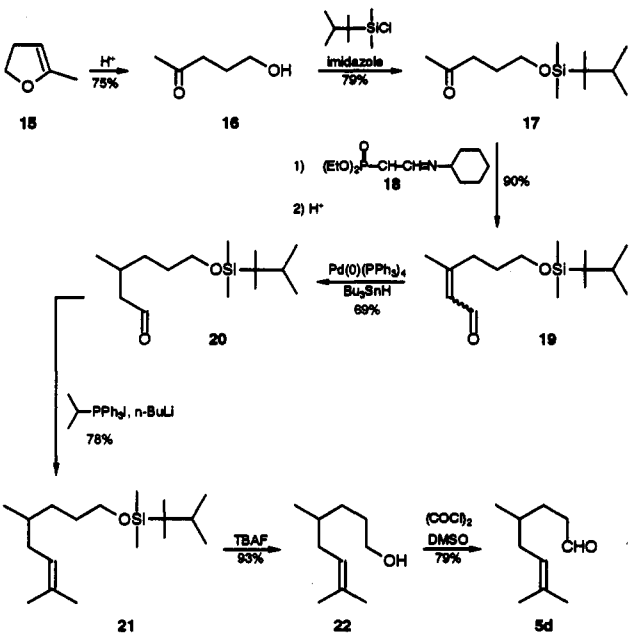
The use of substrates with a stereogenic center has been widely employed for stereocontrolled reactions, mostly with chiral compounds from the chiral pool for the synthesis of enantiomeric pure products.[8] In this respect it is quite astounding that identical substituents at a stereogenic center cause a different induced diastereoselectivity depending on the reaction type; we assume that this is due to a different geometry and bond orders in the transition structures. However, no systematic investigations on the influence of substituents in the tether on the transition structures for different reactions exist, though the influence on the conformation of molecules as cyclohexane in the ground state has been thoroughly studied.[9]

First we investigated the effect of a methyl group at different positions of the tether for the intramolecular hetero-Diels–Alder reactions of **7b–e**, which were formed *in situ* by condensation of **5b–e** and **6**. We assume that the cycloadditions proceed in a concerted way in accordance with our experiments with labeled compounds.[10] Secondly, semiempirical AM1 calculations have been used to locate the transition structures of the intramolecular hetero-Diels–Alder reaction of **7a**. The results were used to create new parameters for the MM2-type force-field to determine the transition structures for the cycloadditions of **7b-e**.[11]

Synthesis of the Aldehydes 5b–e. All chiral aldehydes were prepared and used as racemic mixtures, since in this investigation only the relative stereochemistry of the stereogenic centers in the products was of interest. The preparation of the parent aldehyde **5a** was already described by Tietze et al.[12] The aldehyde **5b** was prepared by a Wittig–Horner reaction of the aldehyde **11**[13] and the phosphonate **12**[14] to give an *E,Z*-mixture of the α,β-unsaturated ester **13** (*E*/*Z* = 3.3:1). Treatment with magnesium in methanol followed by $LiAlH_4$ afforded the alcohol **14**, which was oxidized to the desired aldehyde **5b** by Swern oxidation.[15]



Aldehyde **5c** (citronellal) was obtained from BASF and used without further purification. For the synthesis of aldehyde **5d**, 2-methyl-2,3-dihydrofuran (**15**) was cleaved by acid catalyzed hydrolysis[16] to give **16**, which was protected as the silyl ether **17**. Wittig reaction of **17** with the imine **18**[17] yielded **19** which was reduced[18] with $Bu_3SnH/Pd(0)(PPh_3)_4$ to the saturated aldehyde **20**. Wittig reaction, followed by deprotection and Swern oxidation[15] afforded **5d**.



Aldehyde **5e** was synthesized by Wittig olefination of the aldehyde ester **23**,[19] subsequent reduction of the obtained unsaturated ester **24** to the alcohol **25** with $LiAlH_4$, and transformation into the *p*-toluensulfonate **26**,

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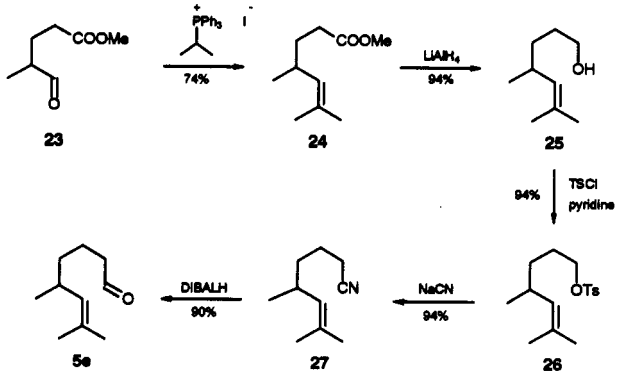
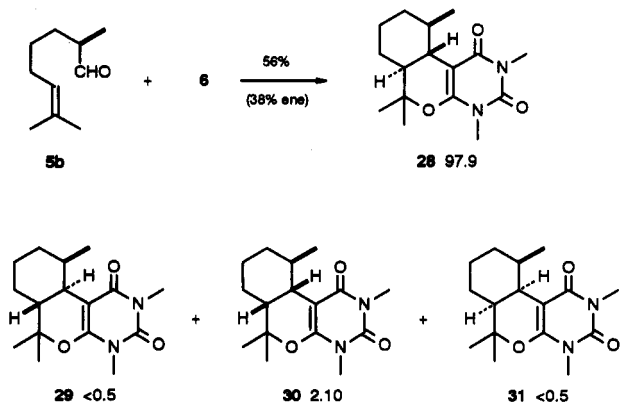
(19) The aldehyde was a gift from BASF AG, Ludwigshafen.

which was prolonged by one carbon atom with NaCN to give the nitrile **27**. This nitrile was reduced with DIBALH to the aldehyde **5e**.

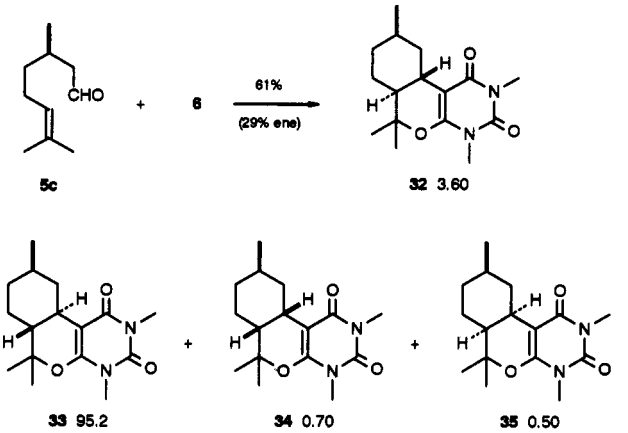


The constitution of the new aldehydes **5b,d,e** have been confirmed mainly by ^{1}H NMR spectroscopy; they all show a low-field signal at δ = 9.73–9.57 for 1-H, which appears as a doublet for **5b** and a triplet for **5d** and **5e**. 6-H resonates at δ = 5.12–4.86 as a triplet of septet for **5b** and **5d** as a broad doublet for **5e**.

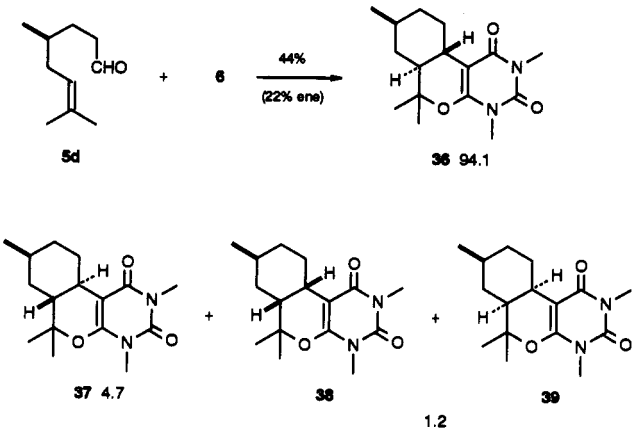
Tandem Knoevenagel Hetero-Diels–Alder Reactions of 5b–e with 6. The tandem Knoevenagel hetero-Diels–Alder reaction of the aldehydes **5b-e** with *N,N'*-dimethylbarbituric acid **6** was performed in dichloromethane at room temperature for 24 h with a catalytic amount of ethylenediammonium diacetate. The product ratio was determined by HPLC. For this purpose three reactions were carried out under identical conditions in each case, followed by three HPLC measurements of the mixtures, thus leading to nine value points for each aldehyde. Therefore the accuracy of the ratio determination is quite high with a standard deviation lower than 0.5%. Theoretically four diastereomeric cycloadducts can be formed. However, the reaction of **5b** with **6** gave only one *trans* and one *cis* cycloadduct **28** and **30** in a ratio of 97.9:2.1 in 56% yield. In addition 38% of the corresponding ene products were formed. The amount of the two other possible cycloadducts **29** and **31** was below 0.5%. The cycloadducts **28** and **30** have both been isolated by chromatography and identified by NMR spectroscopy. The induced diastereoselectivity for the formation of **28** is greater than 99.5:0.5, whereas the simple diastereoselectivity with the value of 97.9:2.1 is slighly lower than found for the reaction of **5a** with **6**.



The reaction of the aldehyde **5c** with **6** affords all four possible diastereomeric cycloadducts **32–35** in a ratio of 3.6:95.2:0.7:0.5 with 61% yield and 29% of the corresponding ene products. The four isomers were isolated by preparative HPLC and identified by NMR spectroscopy. Surprisingly the induced diastereoselectivity is quite high (95.2:3.6) in the formation of the *trans* cycloadducts **33** and **32**, whereas almost no selectivity is found for the *cis* cycloadducts. The simple diastereoselectivity corresponds well with the reaction of **5a** with **6**.

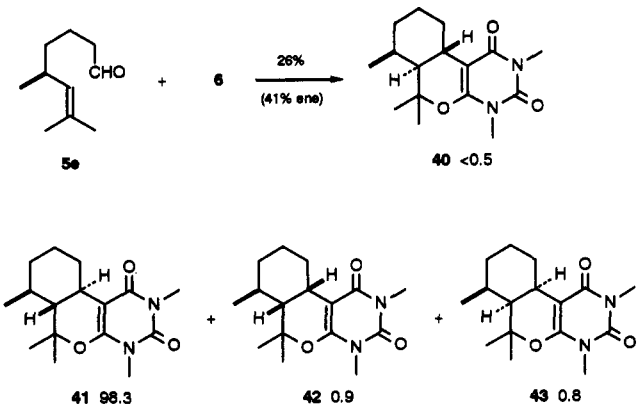


In the tandem Knoevenagel hetero-Diels–Alder reaction of **5d** and **6** only the *trans* products **36** and **37** could be isolated and the ratio was determined as 94.1:4.7; this is slighly lower than found for the reaction of **5b**. In the HPLC analysis of the mixture of the cycloadducts a third peak was observed with a similar retention time as found for **34** and **35**. We therefore assigned this peak to the *cis* products **38** and **39**, without knowing whether this is a mixture of both or represents a single compound either **38** or **39**.



The reaction of **5e** and **6** gives only 26% of the cycloadducts; the main products are the corresponding ene compounds, which are formed in 41% yield. The selectivity of the cycloaddition again is quite high; thus only one *trans* compound **41** is formed. The amount of **40** is below 0.5%. Two more peaks are observed in the HPLC analysis, which are assigned to the two *cis* cycloadducts **42** and **43** (ratio 0.9:0.8).

The structure of the new compounds was verified by NMR spectroscopy and X-ray analysis. The *trans* annelation of **8**, **28**, **32**, **33**, **36**, **37**, and **41** is determined by the coupling pattern for 10a-H with two large coupling constants. Thus, 10a-H of **8** resonates at δ = 2.19 as a doublet of a doublet of a doublet with J = 3, 11, and 11 Hz. For 10a-H of **28**, two doublets at δ = 2.18 with J = 10.5 and 9.0 Hz are found clearly indicating that the methyl group at C-10 is equatorially orientated, for 10a-H of **33**



a doublet of a doublet of a doublet at δ = 2.30 with J = 3, 10.5, and 12 Hz, for 10a-H of **36** a doublet of a triplet at δ = 2.18 with J = 3 and 11 Hz, and for 10a-H of **41** a doublet of a doublet of a doublet at δ = 2.28 with J = 3, 10, and 11 Hz are observed. 10a-H in the *cis* annulated compounds **30**, **34**, and **35** resonates at δ = 2.74–3.08; thus, there is a downfield shift by >0.4 ppm as compared to the *trans* compounds, from which an equatorial orientation of 10a-H can be deduced.

Calculations. The calculation of ground-state energies of organic molecules by force-field methods such as MM2[20] or semiempirical procedures such as AM1[21] is a well-known and in most cases highly reliable method. In contrast, calculations of transition structures are more difficult, especially with force-fields,[22] and gave in many cases only unsatisfactory results.

Our semiempirical calculations were performed using the VAMP[23] program package, which is based on AMPAC 1.0[24] and MOPAC.[25] The program package was optimized for an IBM3090/300e[26] on which the calculations were carried out. The force-field calculations were performed using PCMODEL.[27] The AM1/RHF method was used for all semiempirical calculations. This choice is based on a comparison between the X-ray structure of **33** and the structures of this compound calculated with AM1,[3] MINDO/3,[28] MNDO,[29] and also PM3.[30] The AM1/RHF structure of **33** shows by far the best correlation with the X-ray structure; the other methods are less appropriate, especially with regard to the dihedral angles (Tables I and II).

The MM2 structure of **33** is also in good agreement with the X-ray structure of **33** and in some cases the deflections are even smaller than with AM1. Transition structure geometries were obtained by using the NS01A[31] optimization routine of the VAMP package and then characterized by FORCE[32] calculations.

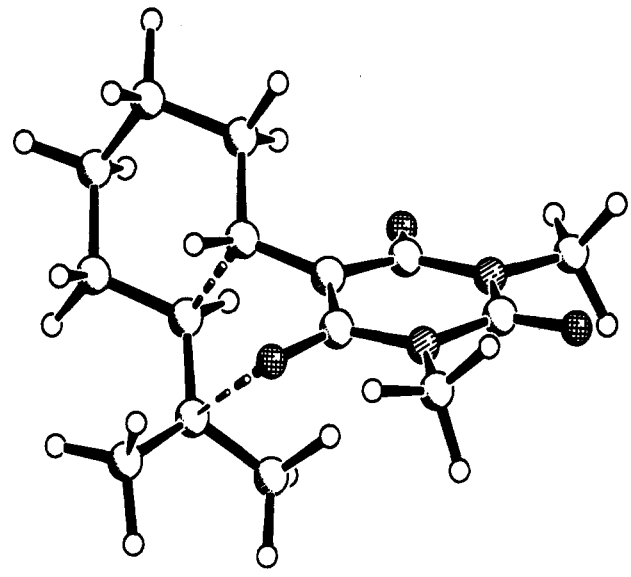


Figure 1. *Exo-E-anti* TS (**A**) (AM1/RHF).

In the cycloaddition of **7a** the four TS **A–D** have to be considered since in **7a** two oxabutadiene moieties exist, one with an (*E*)- and the other with the (*Z*)-configuration. Thus, the trans isomer **8** can be formed via the *exo-E-anti*[33] TS **A** (absolute energy: −266.5 kJ/mol) and the *endo-Z-anti* TS **D** whereas the *cis* product **9** is formed via the *exo-Z-syn* TS **C** (−256.3 kJ/mol) or the *endo-E-syn* TS **B** (−242.1 kJ/mol). The AM1/RHF calculations of these TS reveal that the *endo-Z-anti* TS **D** has the highest energy and needs not be discussed further for this type of intramolecular hetero-Diels–Alder reaction. Thus, this TS displays a high steric strain in the tether and optimization of the structure always leads to the *exo-E-anti* TS **A**. The *exo-E-anti* TS **A** to give the *trans* cycloadduct **8** is preferred by 10.2 kJ/mol compared to the *exo-Z-syn* TS **C**. Interestingly, it can be assumed that the *cis* compound **9** is nearly exclusively formed via the *exo-Z-syn* TS **C** and not the *endo-E-syn* TS **B** ($\Delta\Delta H^{\ddagger}$ = 13.0 kJ/mol).

The calculated $\Delta\Delta H^{\ddagger}$ value of 10.2 kJ/mol for the formation of the *trans* and *cis* products **8** and **9** is in excellent agreement with the experimental results($\Delta\Delta G^{\ddagger}$ = 11.1 kJ/mol). However the computation using an IBM 3090/300e was quite CPU time consuming and rendered this procedure unsuitable for routine calculations. We therefore used the AM1/RHF calculations to create new parameters for the PCMODEL force-field program. This program uses the atom-types C*, C#, O#, and C· to define a transition state of Diels–Alder reactions for the calculations and allows automatic generation of a set of parameters which depend on the bond order of the forming bonds.

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(33) The conventions used in describing the structures of the transition states are as follows: (1) *Endo/Exo* refer to the position of the tether relative to the diene moiety of the molecule. If the chain is below the diene moiety, the TS has an *endo* structure. (2) *E/Z* refer to the configuration of the C–C double bond of the oxadiene, with the higher priority given to the reacting C=O group. (3) *Syn/anti* refer to the relative positions of the hydrogens which appear at the linking positions of the newly formed ring in the product. In *ortho* additions, *syn* and *anti* give, respectively, *cis*- and *trans*-annelated products.

Table I. Comparison of X-ray Bond Length (pm), Bond Angles (deg) and Dihedral Angles (deg) for 33 with Calculated Values

	X-ray	MINDO/3	MNDO	AM1	PM3	PCModel
C(1)–N(2)	141.5	142.7	144.6	141.9	144.9	135.9
N(2)–C(3)	137.3	139.3	141.3	140.6	142.8	136.0
C(3)–N(4)	137.7	142.0	143.6	142.1	144.3	135.7
N(4)–C(4a)	138.9	138.7	140.8	139.2	142.1	137.7
C(4a)–C(10b)	134.9	140.0	138.3	137.8	136.6	134.3
C(1)–C(10b)	144.2	147.1	147.7	146.2	146.6	147.8
C(1)–O(1)	121.4	121.2	122.5	124.4	122.0	121.0
N(2)–C(21)	146.4	145.2	148.0	144.3	148.2	146.9
C(3)–O(3)	122.5	121.4	122.6	125.0	122.4	121.1
N(4)–C(41)	144.6	144.5	147.9	144.1	148.2	146.9
C(4a)–O(5)	133.8	130.9	134.7	137.6	136.0	136.5
O(5)–C(6)	148.4	139.9	143.2	146.3	145.3	141.7
C(6)–C(6a)	152.0	158.1	158.3	152.8	154.2	154.0
C(6a)–C(10a)	152.8	157.4	156.8	153.3	153.8	154.1
C(10a)–C(10b)	151.2	153.7	151.8	148.8	149.8	151.3
C(6)–C(61)	151.3	153.5	156.3	152.0	153.0	153.9
C(6)–C(62)	150.6	153.6	156.8	152.5	153.3	154.1
C(6a)–C(7)	152.4	154.1	154.8	151.9	152.6	153.8
C(7)–C(8)	152.1	151.8	154.2	151.6	152.0	153.6
C(8)–C(9)	151.4	153.8	154.8	152.2	153.0	153.7
C(9)–C(10)	152.3	154.2	153.3	152.4	153.1	154.1
C(10)–C(10a)	153.1	154.2	155.6	152.5	153.1	154.2
C(9)–C(91)	151.2	151.5	154.2	151.3	151.9	153.8
N(2)–C(1)–C(10b)	115.5	114.7	115.7	117.1	116.2	118.0
C(1)–N(2)–C(3)	125.4	125.4	120.9	122.4	120.5	121.5
N(2)–C(3)–N(4)	115.5	113.5	115.7	118.7	118.5	119.9
C(3)–N(4)–C(4a)	121.6	123.2	121.8	123.0	123.0	121.2
N(4)–C(4a)–C(10b)	123.2	118.7	116.9	119.4	117.8	120.9
C(4a)–O(5)–C(6)	117.8	130.8	122.0	115.6	116.5	118.3
O(5)–C(6)–C(6a)	107.9	108.1	108.2	108.6	109.7	108.1
C(6)–C(6a)–C(10a)	112.5	115.7	113.0	111.5	111.9	111.1
C(6a)–C(10a)–C(10b)	109.4	113.2	111.1	110.2	109.8	109.7
C(4a)–C(10b)–C(10a)	120.1	117.4	119.7	120.9	120.1	120.9
O(5)–C(4a)–C(10b)	126.3	123.2	125.1	124.9	126.8	124.4
O(1)–C(1)–C(10b)–C(10a)	4.4	12.1	20.8	4.5	16.1	7.2
N(2)–C(1)–C(10b)–C(4a)	9.3	16.3	24.0	7.3	20.7	7.8
O(3)–N(4)–C(4a)–C(10b)	0.6	16.0	19.3	0.3	14.4	2.6
N(4)–C(4a)–O(5)–C(6)	168.5	179.5	171.5	165.4	167.2	163.8
C(6)–O(5)–C(4a)–C(10b)	11.5	1.0	9.0	15.2	11.1	14.7
C(6)–C(6a)–C(10a)–C(10)	173.2	171.5	168.4	170.2	170.6	169.6

Table II. Average Deflections of Computational Methods from the X-ray Structure of 33

	MINDO/3	MNDO	AM1	PM3	PCModel
bond length (pm)	0.024	0.031	0.016	0.020	0.021
bond angles (deg)	3.2	1.8	1.8	1.8	1.7
dihedral angles (deg)	8.9	10.0	2.0	6.9	3.0

The bond orders C#–O# and C*–C* were set to 0.1 and 0.7 according to the semiempirically calculated transition state. The lacking N(sp^2)–C· bond parameter was set to r_0 = 1.32 Å and k_b = 6.32 mdyn/Å. However, the MM2 calculations with PCMODEL using the automatically generated parameter for the defined bond order showed a large deflection in the energy differences ($\Delta\Delta H^{\ddagger}$) and structure (see Table III, columns AM1 and MM2) as compared to the AM1/RHF calculations of TS A–C.

Therefore some parameters had to be changed to a obtain a better correlation. In doing so we kept the changes to a minimum (Tables IV and V).

The main reason for the failure of the automatic parameter generation was found in the generalized parameters which define the torsion angles of all TS. The C#–O# bond is too short and the torsion angle of the diene part (C*–C·–C·–O#) too small. This problem cannot be solved by decreasing the bond order of the forming C–O bond under 0.1. It can be explained by a high rigidity of the diene part (C*–C·–C·–O#), which is parameterized with the 0(all)-C·–C·–0(all) parameter. We therefore slightly decreased this parameter, which resulted in a positive modification of the structures as compared to the AM1 calculation. However there was no effect on the energy differences. A high negative variation caused a strong deformation of the dimethylbarbituric acid ring system without giving a better correspondence in the energy differences.

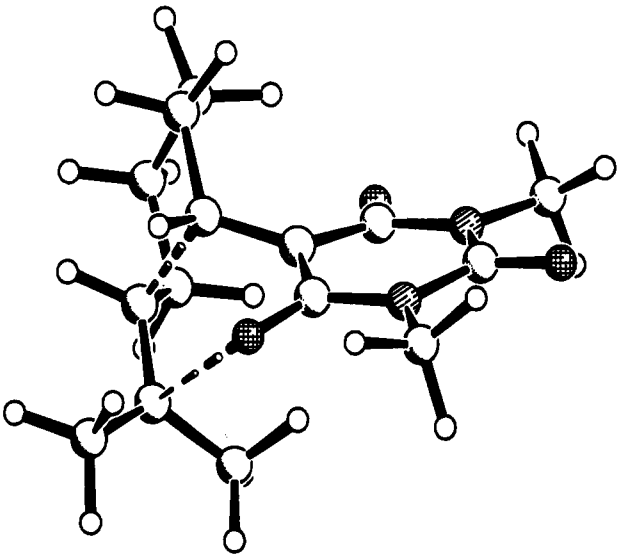


Figure 2. *Endo-E-syn* TS (B) (AM1/RHF).

Table III. Structure and Energy Comparison between AM1/RHF, MM2, and Adjusted MM2 (MM2^{ad}) Calculation

	characteristic data for the calculated TS								
	exo-E-anti TS A			*endo-E-syn* TS B			*exo-Z-syn* TS C		
	AM1	MM2	MM2^{ad}	AM1	MM2	MM2^{ad}	AM1	MM2	MM2^{ad}
C*–C* [pm]	177	175	175	178	175	175	163	176	175
C#–O# [pm]	326	310	312	314	296	306	324	292	302
C•–C•–C*–C* (deg)	101.5	93.2	97.4	98.8	82.1	89.4	99.4	78.6	87.9
C^1–C•–C*–C* (deg)	82.4	83.4	79.3	86.5	97.0	88.9	86.6	99.6	88.0
O#–C•–C•–C* (deg)	15.0	2.9	8.8	18.1	2.1	8.3	19.1	2.8	8.0
energy [kJ mol^{-1}]	−267	2	−27	−242	5	−16	−256	2	−3
ΔE [kJ mol^{-1}]	0	0	0	24.5	21.0	24.0	10.3	7.2	10.6

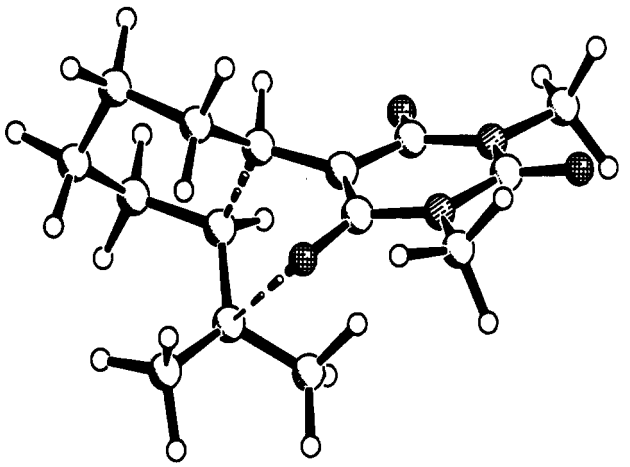


Figure 3. Exo-Z-syn TS (C) (AM1/RHF).

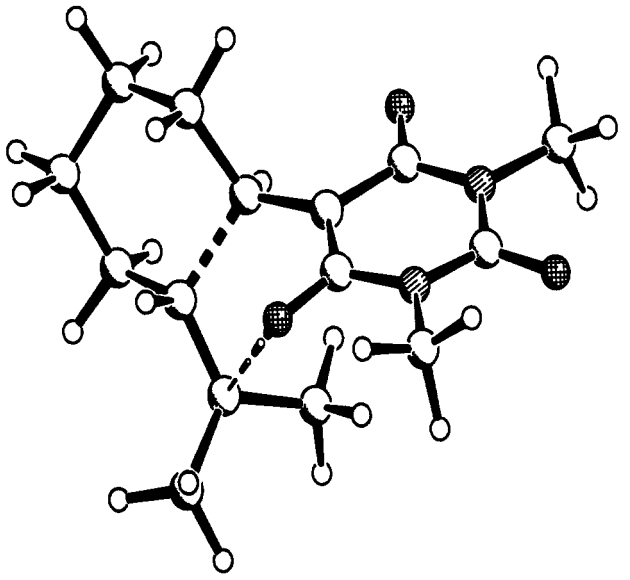
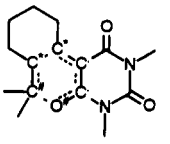


Figure 4. *Endo-Z-anti* TS (D) (adj MM).



In addition, the parameter for the dihedral angles according to the forming C–C bond in the TS were changed (Table V). This caused a positive adjustment of the energy differences and structure as compared to the AM1 calculation. This adjusted force-field (MM2^{ad}) was now used to determine the relative energies of the four TS **A–D**. As shown in Table VI the force-field calculations for the cycloaddition of **7a** are also in excellent agreement with the experimental results.

Table IV. Parameters of MM2

atom types (atom type numbers) for dihedral angle				old torsion constants V_i (kcal mol^{-1})		
				V_1	V_2	V_3
all (0)	all (0)	C* (49)	C* (49)	0	−1	0
all (0)	C• (29)	C• (29)	all (0)	0	8	0

Table V. Parameters of the Adjusted MM2 (MM2^{ad})

atom types (atom type numbers) for dihedral angle				new and modified torsion constants V_i (kcal mol^{-1})		
				V_1	V_2	V_3
C• (29)	C• (29)	C* (49)	C* (49)	0	−4	−1.86
C[C=O] (3)	C• (29)	C* (49)	C* (49)	0	−4	1
all (0)	C• (29)	C• (29)	all (0)	0	6	0

Table VI. Relative Energies (kJ/mol) of TS in the Diels–Alder Reaction of 7a

	exo-E-anti	*endo-Z-anti*	*exo-Z-syn*	*endo-E-syn*
MM2^{ad}	0	62.9	11.0	24.0
AM1/RHF	0	–	10.2	24.5
experimental	0		11.1	

For the hetero-Diels–Alder reactions of the alkylidenebarbiturates **7b–e** with a stereogenic center in the tether, which are obtained *in situ* by Knoevenagel condensation of the aldehydes **5b–e** with **6**, in each case four diastereomers may be formed. For these reactions two different *exo-E-anti*, *exo-Z-syn*, and *endo-E-syn* TS with the methyl group either in the axial or equatorial orientation have to be considered. The relative energies of these TS were calculated using the adjusted PCMODEL force-field parameters (Table VII). Again the correspondence with the experimental data is surprisingly good. The only major divergence is found for the diastereomer **35** where the calculation predicts an amount of 0.1%, whereas experimentally 0.5% was found, which may even indicate an error in the experimental determination of the ratio of the diastereomers.

Discussion

The high simple diastereoselectivity of the hetero-Diels–Alder reactions of **7a** and its methyl-substituted analogues **7b–e** is quite surprising, since the intramolecular Diels–Alder reaction of the related hydrocarbon 1,3,9-decatriene yields an approximately 1:1 mixture of the two corresponding diastereomeric cycloadducts. Houk et al. assumed that the latter reaction occurs via a nearly symmetrical transition state, and their experimental results were in good agreement with calculations on that basis.[34] We explain the observed high *trans* selectivity in the reactions of **7a–e** by the existence of a nonsymmetric

(34) Brown, F. K.; Chandra Singh, U.; Raimondi, L.; Houk, K. N.; Bock, C. W. *J. Org. Chem.* **1992**, *57*, 4862–4869.

Table VII. Relative Energies (kJ/mol) of TS in the Diels–Alder Reactions of 7b–e

	exo-E-anti CH_3eq	*exo-E-anti* CH_3ax	*exo-Z-syn* CH_3eq	*endo-E-syn* CH_3ax	*exo-Z-syn* CH_3ax	*endo-E-syn* CH_3eq
product	**28**	**29**	**30**		**31**	
MM2[ad]	0	26.9	11.1	30.4	46.1	26.6
experimental	0	>15	9.1		>15	
product	**33**	**32**	**35**		**34**	
MM2[ad]	0	8.0	10.8	52.3	19.8	25.0
experimental	0	8.1	13.0		12.1	
product	**36**	**37**	**38**		**39**	
MM2[ad]	0	6.9	11.1	32.7	34.0	23.6
experimental	0	7.37	10.8		>15	
product	**41**	**40**	**43**		**42**	
MM2[ad]	0	21.8	15.6	41.5	15.1	22.9
experimental	0	>15	12.1		11.7	

TS with a chairlike arranged tether. Thus, AM1-RHF calculations of the *exo-E-anti* TS to **8** show bond orders for the forming C–C bond of 0.7 and for the C–O bond of 0.1.

In addition to the excellent simple diastereoselectivity also a high diastereofacial differentiation was observed for the intramolecular hetero-Diels–Alder reactions of **7b–e**. Two contributions must be taken into account for these transformations, which can either act in the same direction or oppose each other. (1) "Steric and electrostatic interactions" of the substituents with the diene or dienophile moiety (see below). (2) "Conformational effects" of the tether e.g. by 1,3-diaxial interactions of the substituents. Thus, the high induced diastereoselectivity of >99:1 for the *trans* cycloadducts **28** and **41** in the reactions of the aldehydes **5b** and **5e**, which contain a methyl group in α-position to the diene and the dienophile moiety, respectively, can be attributed to steric interactions between the methyl group and the diene or dienophile moiety of the molecule. The methyl group must have an equatorial orientation in the TS to avoid severe 1,3-allylic strain. However quite surprisingly, in the formation of the *cis* cycloadducts **42** and **43** only a low diastereoselectivity is observed (0.8:0.9). This can nicely be explained by the calculated TS to **42** and **43** from which we can deduce that the allylic strain for both structures should be almost identical because of an isoclinal orientation of the methyl groups at C-5′ and C-7′ (*Z*).

In the reaction of the aldehydes **5c** and **5d** with the methyl group at the β-position relative to the diene or dienophile moiety "conformational effects" are dominant. Thus, the methyl groups prefer an equatorial orientation in the TS with a chairlike arranged tether. Surprisingly the selectivity for the *trans*-disubstituted cycloadducts **33** and **36** is much higher than expected (**33**/**32** = 95.2:3.6; **36**/**37** = 94.1:4.7). Thus the ratio of **33** and **32** even exceeds that of the two conformers of methylcyclohexanes (95.0:5.0). Again, an explanation is given by the calculated TS to **32** and **33**. The plots show that the hydrogen at C-1′ is turned "inwardly", which would increase the 1,3-diaxial interaction having an axial methyl group in the TS as compared to methylcyclohexane. The calculations of the TS leading to the cycloaddducts are in excellent agreement with the experimental data. They even explain experimental results which we did not understand beforehand. Thus, the data show the feasibility of using the adjusted force-field model for the transition state calculations of intramolecular Diels–Alder reactions of 1-oxa-1,3-butadienes. Furthermore, the calculations support the assumption of a concerted mechanism for these cycloadditions with a highly unsymmetric transition state as has also been shown experimentally.[35] It seems to be quite clear that the high *exo*-selectivity is due to the difference in the bond length of the forming C–C and C–O bond. Force-field calculations with similar bond orders for both bonds resulted in a much worse selectivity which is caused by a smaller energy difference between the *exo-E-anti* and the *endo-E-syn* transition state. The unsymmetric transition state causes the *endo-E-syn* transition state to have a higher energy than the *exo-Z-syn* TS and especially the *exo-E-anti* TS.

Thus, the *cis* cycloadduct **9** and its methylated analogoues **30**, **34**, **35**, **38**, **39**, **42**, and **43** must be formed via an *endo-Z-syn* transition structure; the energy of the *exo-E-syn* geometry, which also would lead to the *cis* diastereomer **9** is higher in energy by 13.0 kJ/mol (AM1/RHF; see Table VI). In our former publications we had assumed that the *cis* diastereomers formed in the tandem Knoevenagel hetero-Diels–Alder reaction of aliphatic aldehydes and 1,3-dicarbonyl compounds occur via an *endo-E-syn* transition structure. This has now been disproved by the calculations. However, for the intramolecular hetero-Diels–Alder reaction of benzylidenepyrazolones it has been shown experimentally that the *cis* diastereomers as the main products are formed via an *endo-E-syn* geometry.[36]

Experimental Section

(4*RS*)-4-Methyl-5-oxopentanoic acid methyl ester (**23**) was a gift by the BASF AG, Ludwigshafen.

(2*RS*)-2,7-Dimethyl-octa-2,6-dienoic Acid Methyl Ester (13). A solution of 2-(diethoxyphosphoryl)propionic acid methyl ester (**12**) (52.5 g, 235 mmol) in 20 mL of *t*-BuOMe was slowly added to a suspension of NaH (5.8 g, 240 mmol) in 100 mL of *t*-BuOMe at 10 °C. After stirring the mixture at room temperature for 1 h, 5-methylhex-4-enal (**11**) (26 g, 232 mmol) in 20 mL of *t*-BuOMe was added within 30 min at 10 °C. After 1 h at room temperature the reaction was quenched with 50 mL of water and extracted twice with *t*-BuOMe. The combined organic layers were washed with brine and dried over $MgSO_4$. After removing the solvent, distillation (60–70 °C, 0.1 Torr) of the residue resulted in 34.5 g (82%) of a colorless fluid **13**: ^{1}H-NMR ($CDCl_3$) δ 1.60 (s, 3H, 8-H_3), 1.69 (s, 3H, 8-H_3), 1.76–1.82 (m, 3H, 2-CH_3), 2.00–2.54 (m, 4H, 4-H_2, 5-H_2), 3.75 (s, 3H, OCH_3), 4.96–5.26 (m, 1H, 6-H), 5.82–6.08 (m, 0.23H, 3-H (*Z*-isomer)), 6.62–6.90 (m, 0.77H, 3-H (E-isomer)); ^{13}C-NMR ($CDCl_3$) δ 12.40 (2-CH_3 (*E*)), 17.65 (7-CH_3 *cis*), 20.71 (2-CH_3 (*Z*)), 25.71 (7-CH_3 *trans*), 27.18 (C-5 (*E*)), 27.97 (C-5 (*Z*)), 29.10 (C-4 (*E*)), 29.92 (C-4 (*Z*)), 51.10 (OCH_3 (*Z*)), 51.57 (OCH_3 (*E*)), 123.42 (C-6 (*E*)), 123.88 (C-6 (*Z*)), 127.12 (C-2 (*Z*)), 127.79 (C-2 (*E*)), 132.12 (C-7 (*Z*)), 132.55 (C-7 (*E*)), 142.17 (C-3 (*E*)), 143.11 (C-3 (*Z*)), 168.34 (C-1 (*Z*)), 168.59 (C-1

(35) Tietze, L. F.; Brumby, T.; Brand, S.; Bratz, M. *Chem. Ber.* **1988**, *121*, 499–506.

(36) Tietze, L. F.; Brumby, T.; Pretor, M.; Remberg, G. *J. Org. Chem.* **1988**, *53*, 810–820.

(*E*)); MS (70 eV) 182 (11%) [M⁺], 151 (7), 150 (7), 114 (68), 69 (100). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.52; H, 10.03.

(2*RS*)-2,7-Dimethyloct-6-en-1-ol (14). (a) Reduction of the 2,3 Double Bond with Magnesium in Methanol. To a solution of **13** (30 g, 165 mmol) in 500 mL of methanol were added magnesium cuttings (20.0 g, 825 mmol). After the evolution of H_2 started (10 min) the reaction mixture was cooled in an ice bath, stirred for 6 h and then poured into 600 mL of ice-cold 3 N HCl, and then extracted with CH_2Cl_2. The combined organic layers were washed with an aqueous solution of NH_4Cl and brine and dried with $MgSO_4$. After removal of the solvent on a rotary evaporator, the crude saturated ester was obtained as an oil.

(b) Reduction of the Ester with $LiAlH_4$. A solution of the crude ester (10.5 g, 56.5 mmol) in 30 mL of *t*-BuOMe was slowly added to a boiling solution of $LiAlH_4$ (1.5 g, 40 mmol) in 75 mL of *t*-BuOMe under nitrogen atmosphere. After 6 h of reflux the reaction was carefully quenched with 20 mL of 10% aqueous KOH and extracted with *t*-BuOMe. The combined organic layers were washed with brine and dried with $MgSO_4$. After removing the solvent, distillation (68 °C, 1.6 Torr) of the residue resulted in 16.8 g (65%) of a colorless fluid, which was identified as **14**: ^{1}H-NMR ($CDCl_3$) δ 0.93 (d, J = 7 Hz, 3H, 2-CH_3), 1.00–2.20 (m, 7H), 1.61 (s, 3H, 8-H_3), 1.70 (s, 3H, 8-H_3), 1.86 (s, 1H, OH), 3.30–3.60 (m, 2H, 1-H_2), 5.00–5.24 (mc, 1H, 6-H); ^{13}C-NMR ($CDCl_3$) δ 16.78 (2-CH_3), 17.65 (7-CH_3 *cis*), 25.72 (7-CH_3 *trans*), 27.52 (C-4), 28.55 (C-5), 33.19 (C-3), 35.86 (C-2), 67.87 (C-1), 124.99 (C-6), 130.97 (C-7); MS (70 eV) 156 (5%) [M⁺], 138 (2), 123 (6), 109 (3), 95 (20), 82 (68), 69 (73), 55 (28), 41 (100). Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.96; H, 12.80.

(2*RS*)-2,7-Dimethyloct-6-enal (5b). A solution of DMSO (6.63 g, 85.0 mmol) in 30 mL of CH_2Cl_2 was slowly added to oxalyl chloride (5.46 g, 43.0 mmol) in 25 mL of CH_2Cl_2 at −70 °C with stirring. To this solution was added **14** (5.95 g, 38 mmol) in 25 mL of CH_2Cl_2 within 15 min and stirring was continued for 15 min. Then the reaction was quenched with 30 mL of Et_3N and the mixture was allowed to warm up. After addition of 200 mL of water and extraction with CH_2Cl_2, the combined organic layers were washed with brine and dried over $MgSO_4$. Evaporation of the solvent and Kugelrohr distillation afforded 4.8 g (82%) of a colorless fluid, which was identified as **5b**: ^{1}H-NMR ($CDCl_3$) δ 1.08 (d, J = 7 Hz, 3H, 2-CH_3), 1.20–1.80 (m, 4H, 3-H_2, 4-H_2), 1.60 (d, J = 1 Hz, 3H, 7-CH_3 *cis*), 1.70 (d, J = 1 Hz, 3H, 7-CH_3 *trans*), 2.02 (q, J = 7 Hz, 2H, 5-H_2), 2.20–2.45 (dq, J = 2 Hz, J = 7 Hz, 1H, 2-H), 5.12 (t sept, J = 1 Hz, J = 7 Hz, 1H, 6-H), 9.57 (d, J = 2 Hz, 1H, 1-H); ^{13}C-NMR ($CDCl_3$) δ 13.34 (2-CH_3), 17.70 (7-CH_3 *cis*), 25.72 (7-CH_3 *trans*), 27.21, 27.97 (C-5, C-4), 30.15 (C-3), 46.31 (C-2), 124.05 (C-6), 131.90 (C-7), 205.20 (C-1); MS (70eV) 156 (5) [M⁺], 138 (2), 123 (6), 109 (3), 95 (29), 82 (68), 69 (73), 55 (28), 41(100). Anal. Calcd for 2,4-dinitrophenylhydrazone of **5b** ($C_{16}H_{22}N_4O_4$): C, 57.47; H, 6.63; N, 16.76. Found: C, 57.64; H, 6.67; N, 16.66.

5-(Dimethylthexylsiloxy)pentan-2-one (17). 5-Hydoxypentan-2-one (5.47 g, 53.6 mmol) was added to a solution of dimethylthexylsilyl chloride (9.58 g, 53.6 mmol) and imidazole (5.47 g, 80.4 mmol) in 67 mL of CH_2Cl_2 at 0 °C. After stirring for 12 h the reaction mixture was quenched with ice-cold water washed with brine and extracted thrice with ether. The organic layers were dried with $MgSO_4$, the solvent was removed, and the residue was distilled yielding 10.35 g (79%) of **17**: ^{1}H-NMR ($CDCl_3$) δ 0.04 (s, 6H, $Si(CH_3)_2$), 0.80 (s, 6H, $SiC(CH_3)_2$), 0.84 (d, J = 7 Hz, 6H, $SiCCH(CH_3)_2$), 1.58 (sept, J = 7 Hz, 1H, $Si(CH_3)_2C(CH_3)_2CH(CH_3)_2$), 1.74 (tt, J = 6, 7 Hz, 2H, 4-H_2), 2.11 (s, 3H, 1-H_3), 2.48 (t, 2H, J = 7 Hz, 3-H_2), 3.56 (t, 2H, J =6 Hz, 5-H_2); ^{13}C-NMR ($CDCl_3$) δ −3.570 ($SiCH_3$), 18.41 (1′-$(CH_3)_2$), 20.24 (2′-$(CH_3)_2$), 25.02 (C-1′), 26.74 (C-4), 29.74 (C-1), 34.10 (C-2′), 40.05 (C-3), 61.72 (C-5), 208.87 (C-2); MS (70 eV) 161 (5), 160 (13), 159 (100), 158 (9), 145 (5), 141 (9), 102 (11), 101 (9), 85 (13), 84 (10), 75 (79), 73 (20), 59 (6), 57 (24.3), 43 (20), 41 (16); IR (film) 2958, 2868, 1720, 1466, 1376, 1366, 1252, 1104, 830 cm^{-1}. Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.55. Found: C, 64.06; H, 11.60.

(*E*/*Z*)-3-Methyl-6-(dimethylthexylsiloxy)hex-2-enal (19). NaH (348 mg, 14.5 mmol) was suspended in 15 mL of THF. To this mixture a solution of [2-(cyclohexylimino)ethyl]phosphonic acid diethyl ester[17] (3.78 g, 14.5 mmol) in 30 mL of THF was added at 0 °C. After 15 min a solution of **17** (2.95 g, 12.1 mmol) in 30 mL of THF was added dropwise and the reaction mixture was stirred for 3 h at room temperature. Then it was poured onto ice-water and extracted three times with ether. The combined organic layers were washed with brine and water, and the solvent was removed. The residue was dissolved in 30 mL of THF, and 1 M oxalic acid (15.5 mL, 15.5 mmol) was added. After 3 h 75 mL of ether, 75 mL of hexane, and 75 mL of water were added, and the organic layer was separated. The aqueous phase was extracted with ether, and the combined organic layers were washed with water and dried with $MgSO_4$. After removal of the solvent, chromatography on silica gel (20 g, 63–200 μm, ethyl acetate/hexane 1:10) afforded 2.77 g (85%) of a colorless fluid, which was used as such in further reactions. ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 2H, $Si(CH_3)_2$ (*Z*)), 0.08 (s, 4H, $Si(CH_3)_2$ (*E*)), 0.83 (s, 2H, $SiC(CH_3)_2$ (*Z*)), 0.85 (s, 4H, $SiC(CH_3)_2$ (*E*)), 0.88 (d, J = 7 Hz, 6H, $SiCCH(CH_3)_2$ (*E*/*Z*)), 1.62 (sept, J = 7 Hz, 1H, thexyl-CH (*E*/*Z*)), 1.55–1.85 (m, 2H, 5-H_2 (*E*/*Z*)), 1.98 (d, 1H, J = 1.5 Hz, 3-CH_3 (*Z*)), 2.18 (d, 2H, J =1.5 Hz, 3-CH_3 (*E*)), 2.29 (t, J = 7 Hz, 1.3H, 4-H_2 (*E*)), 2.66 (t, J = 1.5 Hz, 0.7H, 4-H_2 (*Z*)), 3.60 (t, J = 6.5 Hz, 2H, 6-H (*E*)), 3.62 (t, J = 6.5 Hz, 1H, 6-H (*Z*)), 5.88 (sext d, J =1.5 Hz, J = 8 Hz, 2-H (*E*/*Z*)), 9.97 (d, J = 8 Hz, 0.35H, 1-H (*Z*)), 10.00 (d, J = 8 Hz, 0.75H, 1-H (*E*)); ^{13}C-NMR ($CDCl_3$) δ −3.56 ($Si(CH_3)_2$), 17.53 (3-CH_3 (*E*)), 18.42 (1′-$(CH_3)_2$), 20.24 (2′-$(CH_3)_2$), 24.90 (3-CH_3 (*Z*)), 24.99 (C-1′), 28.99 (C-5 (*Z*)), 30.20 (C-5 (*E*)), 31.64 (C-4 (*Z*)), 34.12 (C-2′), 37.05 (C-4 (*E*)), 61.52 (C-6 (*Z*)), 61.78 (C-6 (*E*)), 127.24 (C-2 (*E*)), 128.55 (C-2 (*Z*)), 164.02 (C-3 (*E*)), 164.21 (C-3 (*Z*)), 190.90 (C-1 (*Z*)), 191.14 (C-1 (*E*)); MS (70 eV) 185 (3), 160 (9), 159 (70), 145 (8), 141 (21), 101 (8), 93 (9), 85 (21), 84 (10), 77 (18), 76 (17), 75 (100), 73 (25), 69 (11), 67 (13), 59 (14), 45 (11), 43 (53), 41 (22); IR (film) 2958, 2868, 1718, 1678, 1466, 1444, 1406, 1380, 1252, 1102, 832 cm^{-1}.

(3*RS*)-3-Methyl-6-(dimethylthexylsiloxy)hexanal (20). To tetrakis(triphenylphosphine)palladium(0) (0.91 g, 0.79 mmol) and 2,6-di-*tert*-butyl-4-methylphenol (0.35 g, 1.58 mmol) in 5 mL of THF was added 7.0 g of **19** in 80 mL of THF. Within 18 h Bu_3SnH (11.5 g, 39.4 mmol) was added dropwise at room temperature with the help of a syringe pump. After the addition of 20 mL of aqueous NH_4Cl the mixture was stirred for 10 min and extracted four times with CH_2Cl_2. The combined organic layers were washed with aqueous NH_4Cl, aqueous $NaHCO_3$, and brine and were dried over $MgSO_4$. After evaporation of the solvent the obtained oil was purified by flash chromatography on silica gel (160 g, 32–63 μm, ethyl acetate/hexane 1:10) to give 4.95 g (69%) of a pale yellow oil, which was identified as **20**: ^{1}H-NMR ($CDCl_3$) δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.76 (s, 6H, $SiC(CH_3)_2$), 0.80 (d, J = 7 Hz, 6H, $SiCCH(CH_3)_2$), 0.90 (d, J = 7 Hz, 3H, 3-CH_3), 1.05–1.67 (m, 6H, 2′-H, 3-H, 4-H_2, 5-H_2), 2.20 (dd, J = 2.5, 7.5 Hz, 1H, 2-H), 2.30 (dd, J = 2 Hz, J = 6 Hz, 1H, 2-H), 3.50 (t, J = 6 Hz, 2H, 6-H_2), 9.68 (t, J = 2 Hz, 1H, 1-H); ^{13}C-NMR ($CDCl_3$) δ −3.48 ($Si(CH_3)_2$), 18.44 (1′-$(CH_3)_2$), 19.89 (4-CH_3), 20.29 (2′-$(CH_3)_2$), 25.04 (C-1′), 27.90 (C-3), 30.08 (C-5), 33.06 (C-4), 34.15 (C-2′), 50.98 (C-2), 62.72 (C-6), 202.71 (C-1); IR 2956, 2870, 1728, 1464, 1252, 1096, 832, 774 cm^{-1}; HRMS calcd for $C_{15}H_{32}O_2Si$ 272.2172, found 272.2172.

(5*RS*)-2,5-Dimethyl-8-(dimethylthexylsiloxy)oct-2-ene (21). Isopropyltriphenylphosphonium iodide (9.40 g, 21.8 mmol) was suspended in 70 mL of THF. A 1.6 M solution of *n*-butyllithium in hexane (12.5 mL, 20 mmol) was added dropwise at 0 °C and the red mixture was stirred for 30 min at 0 °C and/or 90 min at room temperature. **20** (4.95 g, 18.2 mmol) in 5 mL of THF was then added at −78 °C and after 10 min at this temperature the mixture was slowly warmed to 30 °C over the course of 1 h. The precipitate was filtered off and extracted four times with pentane. The combined organic layers were washed twice with brine and dried with $MgSO_4$. After evaporation of the solvent, chromatography on silica gel (40 g, 63–200 μm, hexane) afforded 3.89 g (72%) of a colorless fluid, which was identified as **21**: ^{1}H-NMR ($CDCl_3$) δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.77 (s, 6H, $Si(CH_3)_2$), 0.81 (d, J = 6.5 Hz, 6H, $SiCCH(CH_3)_2$), 0.82 (d, J = 6.5 Hz, 3H, 5-CH_3), 1.15–1.67 (m, 6H, 7-H_2, 6-H_2, 5-H, 2′-H), 1.51 (sbr, 3H, 1-H_3), 1.62 (sbr, 3H, 2-CH_3), 1.82 (m_c, 2H, 4-H_2), 3.49 (t, J = 6.5 Hz, 2H, 8-H_2), 5.06 (t sept, J = 1.5 Hz, J = 7 Hz, 1H, 3-H); ^{13}C-NMR ($CDCl_3$) δ −3.37 ($Si(CH_3)_2$), 17.81 (C-1), 18.52 (1′-$(CH_3)_2$), 19.63 (5-CH_3), 20.38 (2′-$(CH_3)_2$), 25.13 (C-1′), 25.85 (2-CH_3), 30.51 (C-7), 32.73 (C-6), 33.54 (C-5), 34.24 (C-2′), 35.46 (C-4), 63.27 (C-8), 123.45 (C-3), 131.79 (C-2); MS (70 eV) 298 (0.8) [M⁺, ^{28}Si], 214

(19), 213 (75), 205 (18), 157 (14), 137 (36), 95 (33), 84 (39), 81 (83), 75 (100), 69 (43); IR 2958, 2930, 2868, 1462, 1380, 1252, 1098, 832 cm^{-1}; HRMS calcd for $C_{18}H_{38}OSi$ 298.2692, found 298.2692.

(4*RS*)-4,7-Dimethyloct-6-en-1-ol (22). At 0 °C **21** (3.89 g, 13.1 mmol) in 20 mL of THF was added dropwise to a solution of TBAF·$3H_2O$ (5.37 g, 17.0 mmol) in 30 mL of THF. After stirring 12 h at room temperature the solvent was evaporated and the obtained oil was purified by chromatography on silica gel (60 g, 63–200 μm, ether/hexane 1:1). An amount of 1.90 g (93%) of a pale yellow oil was obtained, which was identified as **22**: ^{1}H-NMR ($CDCl_3$) δ 0.85 (d, J = 2 Hz, 3H, 4-CH_3), 1.08–1.72 (m, 6H, 2-H_2, 3-H_2, 4-H, OH), 1.59 (sm, 3H, 8-H_3), 1.70 (sm, 3H, 7-CH_3), 1.92 (m_c, 2H, 5-H_2), 3.63 (t, J = 6.5 Hz, 2H, 1-H_2), 5.13 (t sept, J = 1 Hz, J = 7 Hz, 1H, 6-H); ^{13}C-NMR ($CDCl_3$) δ = 17.84 (C-8), 19.56 (4-CH_3), 25.96 (7-CH_3), 30.47, 32.63 (C-3, C-5), 33.62 (C-4), 35.38 (C-2), 63.29 (C-1), 123.25 (C-6), 132.04 (C-7); IR 3348, 2956, 2870, 1668, 1456, 1378, 1200, 1112, 1060 cm^{-1}; MS (70 eV) 156 (7) [M^+], 95 (14), 86 (18), 84 (19), 75 (58), 69 (94), 68 (11), 67 (13), 57 (24), 56 (13), 55 (22), 41 (100). Anal. Calcd for phenylurethane of **22** (mp 31–33 °C, recrystallized from hexane) ($C_{17}H_{25}NO_2$): C, 74.14; H, 9.15; N, 5.09. Found: C, 74.24; H, 9.21; N, 5.12.

(4*RS*)-4,7-Dimethyloct-6-enal (5d). Following the same procedure as for the oxidation of **14** to **5b**, 1.90 g (12.2 mmol) of **5d** was obtained. Chromatography of the crude product on silica gel (90 g, 32–63 μm, ether/hexane 1:10) resulted in 1.49 g (79%) of a colorless fluid, which was identified as **5d**: ^{1}H-NMR ($CDCl_3$) δ 0.87 (d, J = 6 Hz, 3H, 4-CH_3), 1.33–1.54 (m, 3H, 3-H_2, 4-H), 1.58 (sm, 3H, 7-CH_3), 1.70 (d, J = 1.0 Hz, 3H, 8-H_3), 1.77–2.06 (m, 2H, 5-H_2), 2.38–2.48 (m_c, 2H, 2-H_2), 5.12 (t sept, J = 1.5 Hz, J = 7 Hz, 1H, 6-H), 9.77 (t, J = 2 Hz, 1H, 1-H); ^{13}C-NMR ($CDCl_3$) δ 13.34 (4-CH_3), 17.70 (7-CH_3 *cis*), 25.72 (7-CH_3 *trans*), 27.21, 27.97 (C-5, C-4), 30.15 (C-3), 46.31 (C-2), 124.05 (C-6), 131.90 (C-7), 205.20 (C-1); MS (70 eV) 156 (5) [M^+], 138 (2), 123 (6), 109 (3), 95 (29), 82 (68), 69 (73), 55 (28), 41(100); IR ν 2962, 2924, 2718, 1726, 1676, 1454, 1380, 842 cm^{-1}. Anal. Calcd for 2,4-dinitrophenylhydrazone of **5d** (mp 63- 68 °C, recrystallized from ethyl acetate) ($C_{16}H_{22}N_4O_4$): C, 57.47; H, 6.63; N, 16.76. Found: C, 57.29; H, 6.57; N, 16.65.

(4*RS*)-4,6-Dimethylhept-5-enoic Acid Methyl Ester (24). To a stirred solution of the ylide obtained from 4.75 g (11.0 mmol) of isopropyltriphenylphosphonium iodide and 6.25 mL (10.0 mmol) of *n*-butyllithium (1.6 M) in THF was added 1.30 g (9.00 mmol) **23** at –78 °C and warmed up to room temperature within 60 min. After filtration the residue was treated with pentane and filtered three times followed by extraction with pentane for 24 h. The organic phases were washed with water and dried (Na_2SO_4). After evaporation, chromatography (ether/pentane, 1:4) yielded 1.13 g (74%) of a volatile colorless oil: R_f 0.53 (ether/hexane, 1:2); ^{1}H NMR (100 MHz, $CDCl_3$) δ 0.93 (d, J = 6.5 Hz, 3 H, 4-CH_3), 1.1–1.9 (m, 2 H, 3-H_2), 1.59 (d, J = 1.5 Hz, 3 H, 6-CH_3), 1.68 (d, J = 1.5 Hz, 3 H, 7-H_3), 2.1–2.58 (m, 3 H, 2-H_2, 4-H), 3.67 (s, 3 H, OCH_3), 4.82 (d sept, J = 9.5, 1.5 Hz, 1 H, 5-H); ^{13}C NMR (20 MHz, $CDCl_3$) δ 17.93 (C-7), 21.30 (4-CH_3), 25.81 (6-CH_3), 32.26 (C-4), 32.26 and 32.86 (C-2 and C-3), 51.21 (OCH_3), 130.42 (C-5), 131.01 (C-6), 174.10 (C-1); MS (70 eV) 170 (17) [M^+], 155 (2), 139 (6), 96 (58), 83 (100); IR (film, cm^{-1}) 2940, 2910, 2850, 1735, 1445, 1430, 1370, 1250, 1190, 1160, 840. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H 10.66. Found: C, 70.50; H, 10.60.

(4*RS*)-4,6-Dimethylhept-5-en-1-ol (25). An amount of 1.70 g (10.0 mmol) of **24** diluted in 20 mL of THF was added to a stirred suspension of 0.28 g (7.50 mmol) lithium aluminum hydride in 30 mL of THF at 0 °C. After stirring for 15 h at room temperature the excess $LiAlH_4$ in the reaction mixture was hydrolyzed with 100 mL of ice-cooled saturated aqueous ammonium chloride solution at 0 °C and extracted with ether (4 × 30 mL). The combined etheral phases were successively washed with saturated sodium hydrogen carbonate solution (20 mL), water (20 mL), and brine (20 mL) and dried ($MgSO_4$). After removal of the solvent, the crude product was purified by chromatography (ether) to yield 1.37 g (96%): R_f 0.27 (ether/hexane 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.93 (d, J = 6.5 Hz, 3H, 4-CH_3), 1.09–1.58 (m, 4H, 2-H_2, 3-H_2), 1.48 (s, 1H, OH), 1.61 (d, J = 1.5 Hz, 3H, 7-H_3), 1.67 (d, J = 1.5 Hz, 3H, 6-CH_3), 2.32 (m_c, 1H, 4-H), 3.67 (t, J = 7 Hz, 2H, 1-H_2), 4.86 (d br, J = 10 Hz, 1H, 5-H); ^{13}C-NMR (20 MHz, $CDCl_3$) δ 17.68 (C-7), 21.15 (4-CH_3), 25.52 (6-CH_3), 30.52 and 33.70 (C-2 and C-3), 32.13 (C-4), 62.58 (C-1), 129.71 (C-6), 131.05 (C-5); MS (70eV) 142 (8) [M^+], 124 (1), 109 (10), 83 (100); IR (film, cm^{-1}) 3342, 2954, 2926, 2866, 1448, 1376, 1062, 838. Anal. Calcd for $C_9H_{18}O$: C, 76.00; H, 12.75. Found: C, 75.89; H, 12.87.

Toluene-4-sulfonic Acid 4,6-Dimethylhept-5-enyl Ester (26). An amount of 4.68 g (27.5 mmol) of **25** was diluted with 8.00 mL (110 mmol) of pyridine at 0 °C. An amount of 6.3 g (33.0 mmol) *p*-toluenesulfonyl chloride were added successively, and the mixture was stirred for 23 h. After dilution with 350 mL of ice-cooled 2 N hydrochloric acid solution, the reaction mixture was extracted with ether (4 × 50 mL). The combined etheral phases were washed twice with 2 N hydrochloric acid, saturated sodium hydrogen carbonate, and once with water and brine and dried ($MgSO_4$). Removing the solvent yielded 8.03 g (94%) of crude product which was pure enough to be used in further reactions: R_f 0.28 (petroleum ether/ether, 10:1).

(5*RS*)-5,7-Dimethyloct-6-enenitrile (27). An amount of 8.46 g (26.0 mmol) of **26** and 1.66 g (33.8 mmol) of sodium cyanide were dissolved in 25 mL of DMSO and warmed to 90 °C for 2.5 h. The orange-red reaction mixture was extracted with petroleum ether (3 × 10 mL), and the combined organic phases were washed with brine twice and dried ($MgSO_4$). After evaporation of the solvent, column chromatography (petroleum ether/ether, 10:1) yielded 3.65 g (93%) of a colorless unpleasant smelling liquid: R_f 0.46 (petroleum ether/ether, 10:1); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.94 (d, J = 6.5 Hz, 3H, 5-CH_3), 1.22–1.75 (m, 4H, 3-H_2, 4-H_2), 1.59 (d, J = 1.5 Hz, 3H, 8-H_3), 1.67 (d, J = 1.5 Hz, 3H, 7-CH_3), 2.25 (t, J = 6.5 Hz, 2H, 2-H_2), 2.34 (m_c, 1H, 5-H), 4.85 (dbr, J = 10 Hz, 1H, 6-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.25 (C-2), 17.97 (C-8), 21.33 (5-CH_3), 23.55 (C-3*), 25.77 (C-9), 31.96 (C-5), 36.65 (C-4*), 119.90 (C-1), 130.24 (C-6), 130.85 (C-7); MS (70 eV) 151 (14) [M^+], 136 (18), 83 (100); IR (film, cm^{-1}) 2960, 2924, 2868, 2244, 1452, 1378, 1318, 1220, 1150, 1098, 1062. Anal. Calcd for $C_{10}H_{17}N$: C, 79.40; H, 11.34; N, 9.26. Found: C, 79.44; H, 11.40; N, 9.25.

(5*RS*)-5,7-Dimethyloct-6-enal (5e). A volume of 35.3 mL (53.0 mmol) of DIBAH (1.5 M in toluene) was added to a stirred solution of 3.65 g (24.1 mmol) of **27** in THF at –78 °C. The reaction mixture was warmed up to room temperature within 16 h and was hydrolyzed with methanol (5 mL), water (20 mL), and 2 N sulfuric acid solution (100 mL) at 0 °C. The mixture was extracted with petroleum ether (6 × 40 mL), and the combined organic phases were washed with water (40 mL), saturated sodium hydrogen carbonate solution (50 mL), and brine (40 mL) and dried. After evaporation of the solvent and flash chromatography (petroleum ether/ether, 10:1), 3.35 g (90%) of a light yellow oil was obtained: R_f 0.49 (petroleum ether/ether, 10:1); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.91 (d, J = 7 Hz, 3H, 5-CH_3), 1.12- 1.45 (m, 2H, 4-H_2), 1.50–1.67 (m, 2H, 3-H_2), 1.59 (d, J = 1.5 Hz, 3H, 8-H_3), 1.68 (d, J = 1.5 Hz, 3H, 7-CH_3), 2.22–2.45 (m, 1H, 5-H), 2.39 (dt, J = 2, 7 Hz, 2H, 2-H_2), 4.86 (dbr, J = 9 Hz, 1H, 6-H), 9.73 (t, 1H, J = 2 Hz, CHO); MS (70 eV) 154 (4) [M^+], 139 (6), 95 (26), 83 (100, M); IR (film, cm^{-1}) 2956 , 2924, 2868, 2720, 1726, 1452, 1380, 1108, 842; HRMS calcd for $C_{10}H_{18}O$ 154.1358, found 154.1358.

Tandem-Knoevenagel–Hetero-Diels–Alder Reactions. One equivalent of aldehyde **5a–e** was stirred with 1.1 equiv of *N,N'*-dimethylbarbituric acid (**6**) and 0.01 equiv ethylenediammonium diacetate (EDDA) in dichlormethane for 24 h at room temperature. The reaction mixture was filtered over silica gel, the solvent evaporated, and the residue separated either by column chromatography, preparative HPLC (Fa. Knauer, 250 × 4 mm column with 30 × 4 mm precolumn, Nucleosil 7C18, solvent acetonitrile/water 1:1, flow 1 mL/min, detection at 240 nm) or by fractional crystallization.

Reaction of 5a with 6. The pure isomers were obtained by crystallization and are already described by Tietze et al.[35]

Reaction of 5b with 6. (6a*RS*,10*SR*,10a*RS*)-4,6,6a,7,8,9,-10,10a-Octahydro-2,4,6,6,10-pentamethyl-1*H*-[2]benzopyrano[3,4-*d*]pyrimidine-1,3(2*H*)-dione (28). mp 115–116 °C (recrystallized from hexane); ^{1}H-NMR ($CDCl_3$) δ 1.08 (d, J = 6 Hz, 3H, 10-CH_3), 1.10 (s, 3H, 6-CH_3 ax), 1.04–1.19 (m, 1H), 1.30–1.49 (m, 2H), 1.44 (s, 3H, 6-CH_3 eq), 1.49–1.65 (m, 2H, 6a-H, 10-H), 1.71–1.94 (m, 3H), 2.18 (dd, J = 10.5 Hz, J = 9.0 Hz, 1H, 10a-H), 3.31 (s, 3H, NCH_3), 3.34 (s, 3H, NCH_3); ^{13}C-NMR ($CDCl_3$) δ 18.73 (6-CH_3 ax), 22.47 (10-CH_3), 26.25 (C-8), 27.11 (6-CH_3 eq), 28.06

(N-CH_3), 28.10 (C-7), 28.47 (N-CH_3), 36.29 (C-9), 39.93 (C-10), 42.37 (C-10a), 51.23 (C-6a), 84.10 (C-6), 91.10 (C-10b), 151.21 (C-3), 155.64 (C-4a), 163.41 (C-1); MS (70 eV) 292 (100) [M^+], 277 (43), 249 (40), 235 (27), 223 (16), 221 (24), 207 (16), 169 (51), 157 (31), 136 (31); IR (KBr) 1710, 1655, 1620, 1200 cm^{-1}; UV (CH_3CN) λ_{max} 263 nm (log ϵ 3.96). Anal. Calcd for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27; N, 9.58. Found: C, 65.53; H, 8.37; N, 9.61.

(6a*SR*,10*SR*,10a*RS*)-4,6,6a,7,8,9,10,10a-Octahydro-2,4,6,6,-10-pentamethyl-1*H*-[2]benzopyrano[3,4-*d*]pyrimidine-1,3-(2*H*)-dione (30): mp 127–131 °C (recrystallized from hexane); ^{1}H-NMR ($CDCl_3$) δ 0.96–1.04 (m, 1H), 1.05 (d, J = 7 Hz, 3H, 10-CH_3), 1.20–1.35 (m, 1H), 1.26 (s, 3H, 6-CH_3 ax), 1.38–1.60 (m, 2H), 1.43 (s, 3H, 6-CH_3 eq), 1.64–1.84 (m, 3H), 2.74 (m, 1H, 10a-H), 3.31 (s, 6H, NCH_3), 3.44–3.62 (m, 1H, 10-H); ^{13}C-NMR ($CDCl_3$) δ 18.08 (10-CH_3), 18.66 (C-8), 22.82 (C-7), 25.12 (C-10), 25.58, 25.78 (6-CH_3), 26.52 (C-9), 27.85, 28.69 (N-CH_3), 34.80 (C-6a), 35.93 (C-10a), 83.24 (C-6), 87.38 (C-10b), 151.24 (C-3), 155.56 (C-4a), 163.07 (C-1); MS (70 eV) 292 (100) [M^+], 277 (46), 249 (25), 235 (28), 223 (12), 221 (47), 169 (31), 157 (16), 136 (14); IR (KBr) 1700, 1640, 1615, 1190 cm^{-1}; UV (CH_3CN) λ_{max} 262 nm (log ϵ 3.97); HRMS calcd for $C_{16}H_{24}N_2O_3$ 292.1787, found 292.1787.

(6a*SR*,9*RS*,10a*RS*)-4,6,6a,7,8,9,10,10a-Octahydro-2,4,6,6,9-pentamethyl-1*H*[2]benzopyrano[3,4-*d*]pyrimidine-1,3(2*H*)-dione (34): mp 142–144 °C (recrystallized from hexane); ^{1}H-NMR ($CDCl_3$) δ 0.90 (d, J = 6.5 Hz, 3H, 9-CH_3), 1.03–1.18 (m, 2H, 10-H ax, 8-H ax), 1.43 (s, 3H, 6-CH_3 ax), 1.48 (s, 3H, 6-CH_3 eq), 1.53–1.65 (m, 2H, 9-H, 8-H eq), 1.74–1.88 (m, 2H, 7-H ax, 7-H eq), 1.96 (ddd, J = 6.5 Hz, J = 6.0 Hz, J = 3.0, 1H, 6a-H), 2.33 (mc, 1H, 10-H eq), 2.81 (ddd, J = 12.0, 6.0, 5.0 Hz, 1H, 10a-H), 3.32 (s, 3H, NCH_3), 3.35 (s, 3H, NCH_3); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 21.87 (9-CH_3), 24.56 (C-7), 25.99 (6-CH_3 ax), 27.67, 28.44 (NCH_3), 29.12 (6-CH_3 eq), 30.57 (C-9), 30.88 (C-8), 30.88 (C-10a), 34.66 (C-10), 38.72 (C-6a), 85.14 (C-6), 89.97 (C-10b), 151.60 (C-3), 154.25 (C-4a), 162.91 (C-1); MS (70 eV) 292 (100), 277 (10), 249 (21), 235 (2), 223 (5), 209 (6), 207 (12), 169 (19), 157 (25), 136 (27); HRMS calcd for $C_{16}H_{24}N_2O_3$ 292.1787, found 292.1787. IR (KBr) 1700, 1640, 1200, 760 cm^{-1}; UV (CH_3CN) λ_{max} 262 nm (log ϵ 3.97).

(6a*RS*,9*RS*,10a*SR*)-4,6,6a,7,8,9,10,10a-Octahydro-2,4,6,6,9-pentamethyl-1*H*[2]benzopyrano[3,4-*d*]pyrimidine-1,3(2*H*)-dione (35): mp 138–140 °C (recrystallized from hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.86 (d, J = 7.0 Hz, 3H, 9-CH_3), 0.91 (tdd, J = 13.0, 12, 4.0 Hz, 1H, 8-H ax), 1.01 (ddd, J = 13.0, 12.0, 4.0 Hz, 1H, 10-H ax, 1.10 (tdd, J = 13.0, 12.0, 4.0 Hz, 1H, 7-H ax), 1.13–1.23 (m, 1H, 9-H), 1.30 (s, 3H, 6-CH_3 ax), 1.43 (s, 3H, 6-CH_3 eq), 1.56 (ddd, J = 12.0, 5.0, 4.0 Hz, 1H, 6a-H), 1.69 (dm, J = 12.0 Hz, 1H, 8-H eq), 1.78 (dm, J = 13.0 Hz, 1H, 7-H eq), 3.08 (ddd, J = 5.0, 4.0, 3.0 Hz, 1H, 10a-H, 3.25 (dq, J = 13.0, 3.0 Hz, 1H, 10-H eq), 3.31 (s, 3H, NCH_3), 3.32 (s, 3H, NCH_3); ^{13}C-NMR ($CDCl_3$) δ 222.28 (9-CH_3), 222.92 (C-7), 25.31, 25.75 (6-CH_3), 26.91 (C-9), 27.85, 28.70 (NCH_3), 29.61 (C-10a), 34.28 (C-10), 35.28 (C-8), 41.02 (C-6a), 82.81 (C-6), 86.91 (C-10b), 151.27 (C-3), 155.53 (C-4a), 162.90 (C-1); MS (70 eV) 292 (100), 277 (21), 249 (41), 235 (11), 223 (12), 221 (12), 209 (15), 207 (27), 169 (43), 157 (67), 136 (52); HRMS calcd for $C_{16}H_{24}N_2O_3$ 292.1787, found 292.1787; IR (KBr) 1685, 1630, 1610, 1190, 1140 cm^{-1}; UV (CH_3CN) λ_{max} 262 nm (log ϵ 3.98).

(6a*SR*,9*RS*,10a*SR*)-4,6,6a,7,8,9,10,10a-Octahydro-2,4,6,6,9-pentamethyl-1*H*[2]benzopyrano[3,4-*d*]pyrimidine-1,3(2*H*)-dione (32): mp 159–160 °C (recrystallized from hexane); ^{1}H-NMR ($CDCl_3$) δ 1.12 (ddd, J = 13.0, 12.0, 5.0 Hz, 1H, 10-H ax), 1.13 (d, J = 7.5 Hz, 3H, 9-CH_3), 1.20 (s, 3H, 6-CH_3 ax), 1.30–1.42 (m, 2H), 1.47 (s, 3H, 6-CH_3 eq), 1.55–1.72 (m, 3H), 2.06–2.22 (m, 1H, 9-H), 2.52 (ddd, J = 12.0, 10.5, 3.0 Hz, 1H, 10a-H), 3.01 (ddd, J = 13.0, 3.0, 2.0 Hz, 1H, 10-H eq), 3.34 (s, 6H, NCH_3); ^{13}C-NMR ($CDCl_3$) δ 18.49 (9-CH_3), 19.83 (6-CH_3 ax), 22.32 (C-7), 26.92 (6-CH_3 eq), 27.34 (C-9), 27.66 (NCH_3), 27.87 (C-10a), 28.56 (NCH_3), 32.00 (C-8), 35.13 (C-10), 49.20 (C-5a), 83.80 (C-6), 89.59 (C-10b), 151.3 (C-3), 155.3 (C-4a), 162.5 (C-1); MS (70 eV) 292 (100) [M^+], 277 (17), 249 (47), 223 (13), 209 (18), 207 (26), 169 (41), 157 (63), 136 (47); HRMS calcd for $C_{16}H_{24}N_2O_3$ 292.1787, found 292.1787; IR (KBr) 1700, 1640, 1630 cm^{-1}; UV (CH_3CN) λ_{max} 262 (log ϵ 4.00).

(6a*RS*,8*RS*,10a*RS*)-4,6,6a,7,8,9,10,10a-Octahydro-2,4,6,6,8-pentamethyl-1*H*-[2]benzopyrano[3,4-*d*]pyrimidine-1,3(2*H*)-dione (36): mp 177–179 °C (recrystallized from ethyl acetate); ^{1}H-NMR ($CDCl_3$) δ 0.66–0.90 (m, 1H, 10-H ax), 0.96 (d, J = 6.5 Hz, 3H, 8-CH_3), 0.90–1.10 (m, 1H, 7-H ax), 1.17 (s, 3H, 6-CH_3 ax), 1.10–1.30 (m, 1H, 9-H ax), 1.46 (s, 3H, 6-CH_3 eq), 1.34–1.60 (m, 2H, 6a-H, 8-H), 1.70–1.90 (m, 2H, 9-H eq, 7-H eq), 2.18 (td, J = 11.0, 3.0 Hz, 1H, 10a-H), 3.10–3.24 (m, 1H, 10-H eq), 3.34 (s, 6H, N-CH_3); ^{13}C-NMR ($CDCl_3$) δ 19.68 (6-CH_3 ax), 22.51 (8-CH_3), 26.90 (6-CH_3 eq), 27.52, 28.44 (NCH_3), 29.38 (C-10), 33.10 (C-8), 33.81 (C-10a), 34.62 (C-9), 36.00 (C-7), 48.31 (C-6a), 83.70 (C-6), 89.32 (C-10b), 151.09 (C-3), 155.03 (C-4a), 162.40 (C-1); MS (70 eV) 292 (77) [M^+], 277 (5), 249 (28), 169 (50), 157 (81), 136 (100); IR (KBr) 1705, 1645, 1625, 1255 cm^{-1}; UV (CH_3CN) λ_{max} 262 nm (log ϵ 3.98). Anal. Calcd for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27; N, 9.58. Found: C, 65.56; H, 8.21; N, 9.66.

(6a*RS*,7*RS*,10a*RS*)-4,6,6a,7,8,9,10,10a-Octahydro-2,4,6,6,7-pentamethyl-1*H*-[2]benzopyrano[3,4-*d*]pyrimidine-1,3(2*H*)-dione (41): mp 155–156 °C (recrystallized from hexane); ^{1}H-NMR ($CDCl_3$) δ 0.85 (tdd, J = 13.0, 11.0, 4.0 Hz, 1H, 10-H ax), 1.05 (d, J = 6.5 Hz, 3H, 7-CH_3), 1.18–1.35 (m, 2H), 1.21 (s, 3H, 6-CH_3 ax), 1.36–1.57 (m, 2H), 1.60 (s, 3H, 6-CH_3 eq), 1.71–1.87 (m, 2H), 2.28 (ddd, J = 11.0, 10.0, 3.0 Hz, 1H, 10a-H), 3.11 (d, J = 13 Hz, 1H, 10-H eq), 3.31 (s, 3H, NCH_3), 3.33 (s, 3H, NCH_3); ^{13}C-NMR ($CDCl_3$) δ 19.68 (6-CH_3 ax), 22.51 (8-CH_3), 26.90 (6-CH_3 eq), 27.52, 28.44 (N-CH_3), 29.38 (C-10), 33.10 (C-8), 33.81 (C-10a), 34.62 (C-9), 36.00 (C-7), 48.31 (C-6a), 83.70 (C-6), 89.32 (C-10b), 151.1 (C-3), 155.0 (C-4a), 162.4 (C-1); MS (70 eV) 292 (92), 277 (5), 249 (32), 209 (28), 195 (47), 182 (77), 169 (52), 157 (36), 136 (41), 83 (100); IR 1705, 1640, 1210, 1105 cm^{-1}; UV (CH_3CN) λ_{max} 262 nm (log ϵ 4.00). Anal. Calcd for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27; N, 9.58. Found: C, 65.56; H, 8.21; N, 9.66.

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Supplementary Material Available: Copies of ^{1}H NMR spectra of **5e**, **20**, **21**, **30**, **32**, **34**, and **35** (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.