Carbohydrate-derived dienes for intramolecular and asymmetric Diels–Alder reactions †

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Received (in Cambridge, UK) 27th July 2000, Accepted 13th February 2001
First published as an Advance Article on the web 19th March 2001

3-Acyloxydienes **2** and **10**, derived from tri-*O*-acetyl-D-glucal are converted into appropriate substrates to perform intramolecular Diels–Alder reactions, thus yielding *cis*- or *trans*-fused bicyclic compounds. Attempts are made to rationalize the observed ratios between cycloadducts, as well as those previously reported in the literature for related experiments, by theoretical studies at the PM3 semiempirical level. In addition, the new chiral diene **9** derived from D-galactose or D-mannose, *via* an *aldehydo*-heptose, is obtained; the Diels–Alder reaction of **9** with *N*-phenylmaleimide is studied, and the observed asymmetric induction is explained by PM3 and B3LYP/6-31G* calculations.

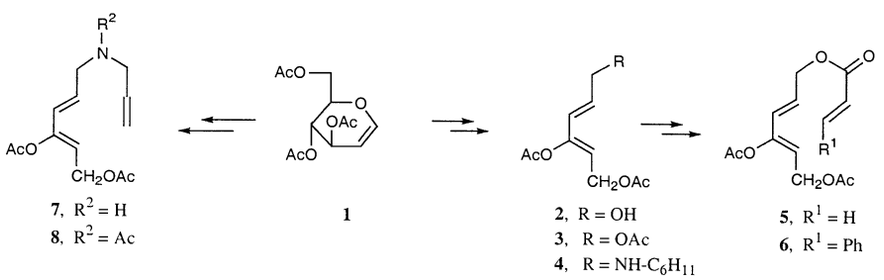
Introduction

The preparation of novel dienes, together with the study of their applications in Diels–Alder reactions, is still an important challenge in synthetic organic chemistry. However, the use of carbohydrates as starting materials for these syntheses has been scantily investigated,[1a] especially in those cases where the product could be adequate to carry out intramolecular Diels–Alder reactions.[1b] There are literature examples in which: (*a*), a sugar fragment, thus operating as chiral auxiliary, is incorporated on a pre-existing diene,[2] or (*b*), the dienic moiety is constructed on a sugar framework or constitutes an extension thereof.[3] Although dienes we have used in the present work could be considered of the second type, the methodology followed for their preparation has been rather different from the more general procedure, where the dienic system is constructed by a Wittig reaction on a suitably functionalized sugar;[3b–e] in addition, they are stable 2-acyloxydienes, a type of substance for which examples of Diels–Alder reactions are rather scarce,[4] probably as a consequence of difficulties in their preparation,[5–7] and of their sometimes described instabilities.[8]

In the course of our study on the use of unsaturated sugar derivatives in Diels–Alder reactions, we have described[9] the syntheses of dienes **3** and **4** from tri-*O*-acetyl-D-glucal **1** (Scheme 1), together with some examples of their applications for intermolecular [4+2] cycloaddition reactions; thus, we obtained adducts that were converted, in some cases, into cyclohexanone derivatives.[10] Now, as an extension of these investigations, we report here on the preparation of trienes **5**–**8**, as well as of chiral diene **9**, either starting from **1** or from an aldohexose (D-galactose or D-mannose), respectively.

Since compounds **5**–**8** present both a dienophilic double bond and a dienic system in appropriate positions, intramolecular Diels–Alder reactions have been performed upon them, thus leading to their corresponding bicyclic adducts. On the other hand, an asymmetric cycloaddition between chiral diene **9** and *N*-phenylmaleimide has been accomplished, and a pair of stereoisomeric adducts were obtained. In each case, the stereoselectivity was determined by ^{1}H NMR studies of the crude mixtures at the end of the reaction; also, theoretical computer-assisted calculations have been performed in order to justify the results.

† Transition structures for intramolecular cycloadditions of compounds **5**, **6** and **25**–**31** are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p1/b0/b006078j/

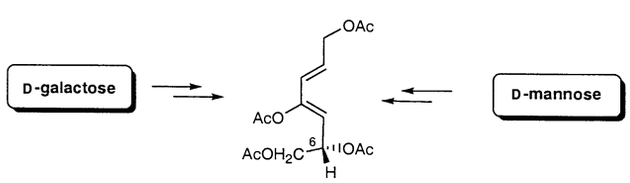


7, R^2 = H
8, R^2 = Ac

1

2, R = OH
3, R = OAc
4, R = NH-C_6H_{11}

5, R^1 = H
6, R^1 = Ph



9

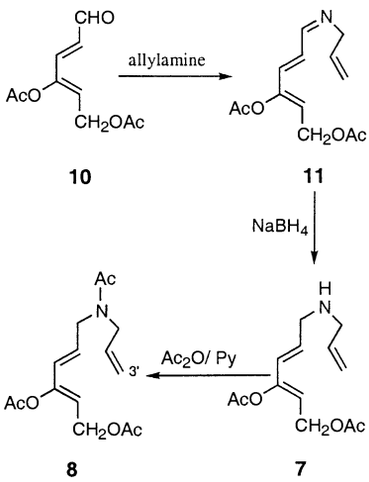
Scheme 1

 DOI: 10.1039/b006078j

Results and discussion

Synthesis of trienes. Intramolecular Diels–Alder reactions

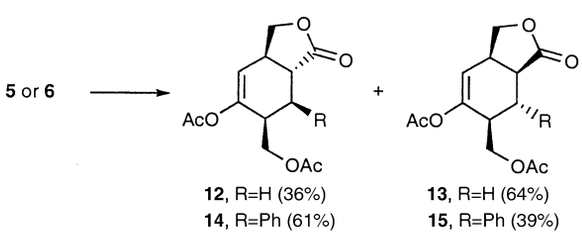
Treatment of (2*E*,4*Z*)-4,6-diacetoxyhexa-2,4-dien-1-ol[9b,11] **2** with acryloyl or cinnamoyl chloride led to trienes **5** and **6**, respectively (Scheme 1). Furthermore, to modify the functionality at C-1 on the acyloxydienic system, we accomplished the reaction of (2*E*,4*Z*)-4,6-diacetoxyhexa-2,4-dienal[9a,11] **10** with allylamine, thus leading to the imine **11** (Scheme 2). Selective



Scheme 2

sodium borohydride reduction of this last compound yielded an unstable amine (**7**) which, on treatment with acetic anhydride in pyridine, led to the acetamide **8**. The ^{1}H NMR spectra of either $CDCl_3$ or DMSO-d_6 solutions of **8**, registered at room temperature, showed two groups of signals that were present in almost the same 1 : 0.65 ratio in both solvents; although we could not correlate each compound with their corresponding signals, they were attributable to the *Z* and *E* isomers of the acetamido group (enolic tautomer), since the temperature of coalescence (DMSO-d_6) was 70 °C. As expected,[12] we found that the most significant differences ($\Delta\delta > 3$ ppm) between ^{13}C NMR chemical shifts of equivalent carbons of *Z*-**8** and *E*-**8** correspond to those adjacent to the amide nitrogen, these differences being smaller when atoms are progressively more distant.

Intramolecular cycloadditions of trienes **5** and **6** were performed in refluxing benzonitrile, thus leading to a 36 : 64 mixture of **12** and **13** in the first case, and to a 61 : 39 mixture of **14** and **15** in the second (Scheme 3). The observed stereoselectivity



Scheme 3

in these reactions was rather low, probably as a consequence of high temperatures and relatively long times that were necessary to carry out the processes. To our knowledge, no results have been reported about intramolecular cycloadditions of analogous esters bearing aromatic substituents on the terminal carbon of the dienophilic moiety;[13] on the other hand, previous data for acryloyl esters related to **5** indicate a low Diels–Alder reactivity,[14] caused by extensive polymerization of the substrate.

The assignment of the stereochemistry for adducts **12**–**15** was based on their coupling constants and nuclear Overhauser

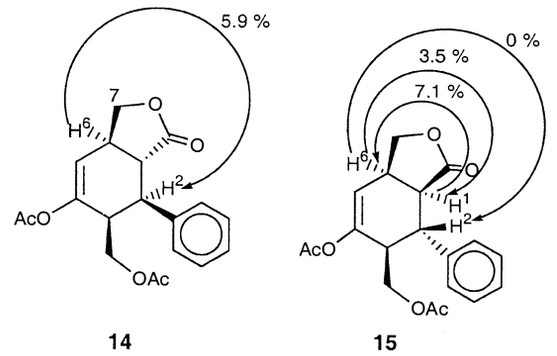
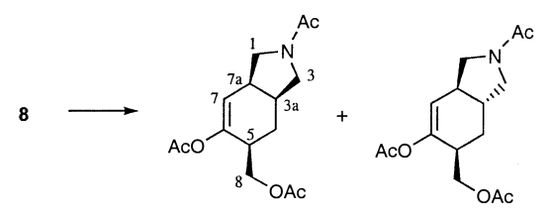


Fig. 1 Selected NOE correlations for the adducts **14** and **15**.

enhancement (NOE) experiments for **14** and **15** (Fig. 1). Thus, $J_{1,6}$-values for **12** and **14** (≈13 Hz) supported[15] a *trans*-fusion between rings; furthermore, we observed a 7.1% NOE from H-1 to H-6 in compound **15**, and an absence of this effect from H-2 to H-6, in agreement with a *cis*-fusion. On the other hand, the isomer **14** gave a 5.9% NOE from H-2 to H-6, thus supporting the *cis* relationship of these hydrogens. Concerning ^{13}C NMR data, differences between chemical shifts for carbons C-1, C-6 and C-7 in both *cis*- and *trans*-isomers were similar to those previously reported[16] for structurally related compounds.

Although compound **7** also reacted under the same conditions that were used for intramolecular cycloadditions of **5** and **6**, it led to a rather complex mixture from which inseparable *cis* and *trans* adducts (1 : 1 ratio) were isolated in low (5%) yield. In contrast (Scheme 4), acetyl derivative **8** reacted cleanly,

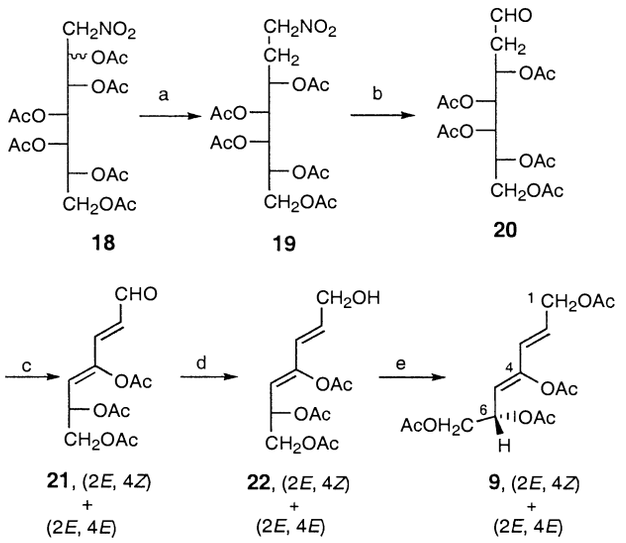


Scheme 4

yielding quantitatively **16** and **17** as an inseparable 1 : 1 mixture; its ^{1}H and ^{13}C NMR spectra showed four groups of signals (≈1 : 1 : 1 : 1 proportions) that were assigned to the respective *Z* and *E* acetamido isomers of each cycloadduct. Thus, the H-7 olefinic protons for *cis*-isomers (**16**-*Z*/*E*) appear at δ 5.53 and 5.50 ppm as two double doublets ($J_{5,7}$ 2.2 and $J_{7,7a}$ 5.1 Hz), and as two broad singlets at δ 5.72 and 5.68 for *trans*-isomers (**17**-*Z*/*E*). The coupling constants $J_{7,7a}$ are in good agreement with previous data[14,17] that reported values of 4.0 Hz and 1.5 Hz, respectively, for related *cis* and *trans* compounds.

Synthesis of chiral diene 9 and its Diels–Alder reaction with *N*-phenylmaleimide

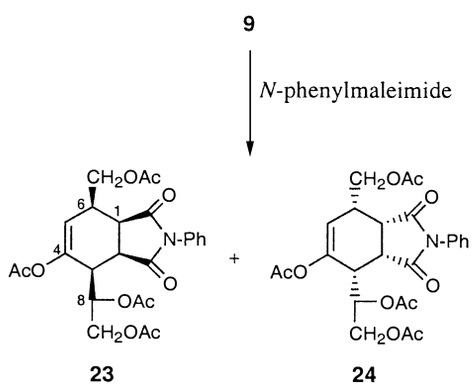
Besides the above described processes, in which achiral substrates were used, we have also attempted an asymmetric Diels–Alder reaction with chiral diene **9**. As indicated in Scheme 5, this compound has been prepared from D-galactose which, on treatment with nitromethane followed by acetylation, yielded the pair of per-acetylated nitropolyols **18**.[18] Selective elimination of the acetate group on C-2 to give compound **19**[19] was accomplished by the procedure of Martin *et al.*[20] and it probably occurs through the corresponding *in situ*-formed nitroalkene; then, $KMnO_4/MgSO_4$ oxidation[21] of **19** afforded the *aldehydo*-heptose **20**. Although this substance was found to be a recrystallizable compound, its tendency to eliminate acetic acid to give an α,β-unsaturated *aldehydo*-heptose[9a] prompted us to characterize it as its 2,4-dinitrophenylhydrazone. Reaction



Scheme 5 *Reagents and yields*: (a) $NaBH_4$, EtOH, 1,4-dioxane (68%); (b) $KMnO_4$, $MgSO_4$ (75%); (c) DBU (64%); (d) $NaBH_4$ (77%); (e) Ac_2O, Py (70%).

of **20** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) yielded diene **21**[9a] as a mixture of 2*E*,4*Z*- and 2*E*,4*E*-isomers. In contrast with other hitherto described methods, it is noteworthy that the dienic system has been generated in only one step, probably through the corresponding α,β-unsaturated *aldehydo*-heptose. Finally, reduction of the aldehyde group in **21** with $NaBH_4$ and conventional acetylation of the resulting alcohol **22** led to a 15 : 1 mixture (^{1}H NMR) of chiral diene **9** (2*E*,4*Z*) and its minor 2*E*,4*E*-isomer.‡ In a similar way, compounds **21**, **22** and **9** have also been obtained from D-mannose.

Diels–Alder reaction of diene **9** with *N*-phenylmaleimide (Scheme 6) was carried out in toluene at reflux for five days,



Scheme 6 Non-systematic numbering scheme.

yielding a separable 1.7 : 1 mixture of the cycloadducts **23** and **24**, respectively. We did not observe any reaction for the minor 2*E*,4*E*-isomer of **9**, probably because of steric hindrance that would arise in its required *s-cis* conformation.

As depicted in Fig. 2, the sugar side-chains in both **23** and **24** show conformations in which H-3 and H-8 hydrogens are in *anti*-periplanar relationships ($J_{3,8}$ 11.4 and 10.5 Hz). The proximity of the acetoxymethylene group on C-8 to the vinylic acetate in **23** (or one of the carbonyl groups in the imide ring of **24**) is consistent with NOEs from protons H-9 or H′-9 to H-2, which were observed only in the case of **24**.

‡ With the exception of H-3 (δ 6.6) and H-7,7′ (δ 4.7), ^{1}H NMR signals for protons of the minor isomer were hidden behind those of compound **9** (2*E*,4*Z*).

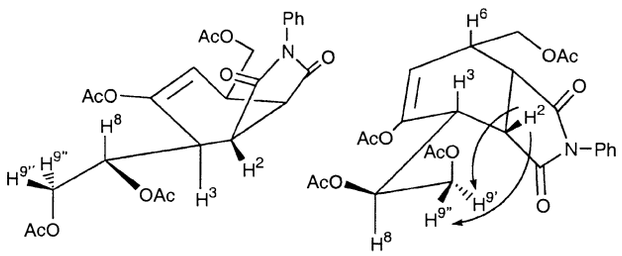


Fig. 2

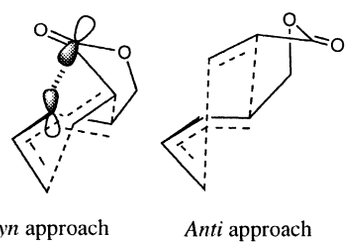


Fig. 3 *syn* and *anti* approaches for intramolecular Diels–Alder reactions.

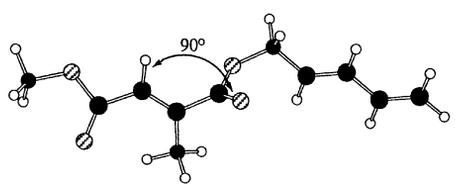


Fig. 4 PM3-optimized structure for triene **28**.

Theoretical calculations

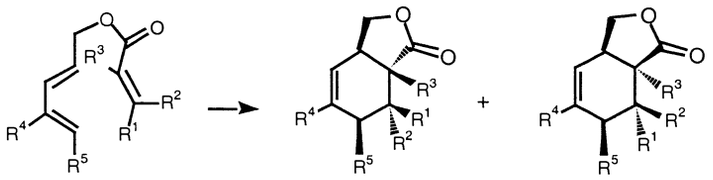
Concerning ratios of *cis*- or *trans*-fused bicyclic adducts that were formed in this type of intramolecular cycloaddition, it can be observed (Table 1) that our data from compounds **5** and **6**, as well as those available in the literature[13,22] from **25**–**31**, are hardly understandable as a whole; thus, in an attempt to rationalize these results, we have made a theoretical study at the PM3[23] semiempirical level with the Gaussian94 package of programs.[24]

Although the regiochemistry of these cycloadditions is conditioned by their intramolecular nature, the ratios of *cis* and *trans* adducts could be determined in each case by the secondary interactions between orbitals on the carbonyl carbon and the dienic fragment, which would be stabilizing for the *syn* approach (Fig. 3), thus leading to *cis* cycloadducts.

From energies and coefficients of frontier orbitals involved in cycloadditions (Table 2), we observed that compounds **28**–**30** showed very small values for coefficients of C-1′. As shown in Fig. 4 for triene **28**, this may be because the R^3 substituent is a methyl group that prevents coplanarity, and hence conjugation, between the ester carbonyl group and the dienophilic double bond. In these cases, secondary orbital interactions would be negligible and steric interactions should probably be considered.

Since the PMO theory did not explain satisfactorily all the experimental results shown in Table 1, we accomplished a search of stationary points in those processes at the semiempirical level. By considering the more stable *s-trans* conformations of the dienic moiety of each reactant, we have performed a complete optimization of the structures. Also, in order to verify that transition structures (TS) have one and only one imaginary frequency, they have been characterized by frequency calculations. Table 3 collects the energies of the starting

Table 1 *trans* : *cis* ratios and yields for adducts formed from trienes **5**, **6** and **25**–**31**

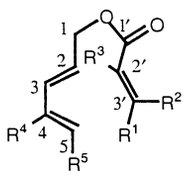


Triene *trans*-fused adduct *cis*-fused adduct

Triene	R^1	R^2	R^3	R^4	R^5	*Trans* : *cis* ratios	Yield (%)
5	H	H	H	OAc	CH_2OAc	36 : 64	80
6	Ph	H	H	OAc	CH_2OAc	62 : 38	70
25	Me	COOH	H	H	Me	0 : 100 [a]	32
26	Me	COOMe	H	H	H	100 : 0	55 [b]
27	Me	COOMe	H	H	Me	100 : 0	40
28	COOMe	H	Me	H	H		0
29	COOMe	H	Me	H	Me	82 : 18	85
30	H	COOH	Me	H	Me		0 [b]
31	COOMe	Me	H	H	Me	82 : 18 [c]	83

[a] An explanation for this result is given in refs. 22*b* and 25. [b] The starting material polymerizes. [c] Tentative structural assignments.

Table 2 Energies and coefficients of the frontier orbitals involved in cycloadditions



Compound	MO	Energy/eV	C-2	C-3	C-4	C-5	C-1′	C-2′	C-3′
5	HOMO	−9.33	−0.21	−0.21	0.33	0.40			
	LUMO	−0.12					−0.32	−0.38	0.51
6	HOMO	−9.30	−0.33	−0.29	0.40	0.48			
	LUMO	−0.85					−0.22	−0.43	0.43
25	HOMO	−9.32	−0.42	−0.32	0.37	0.43			
	LUMO	−0.97					−0.36	−0.54	0.61
26	HOMO	−9.37	−0.48	−0.40	0.35	0.45			
	LUMO	−0.49					−0.35	−0.57	0.67
27	HOMO	−9.11	−0.46	−0.36	0.39	0.46			
	LUMO	−0.48					−0.35	−0.57	0.67
28	HOMO	−9.46	−0.39	−0.31	0.28	0.36			
	LUMO	−0.42					−0.03	−0.62	0.54
29	HOMO	−9.19	−0.37	−0.27	0.32	0.36			
	LUMO	−0.40					−0.035	−0.64	0.55
30	HOMO	−9.08	−0.42	−0.33	0.35	0.42			
	LUMO	−0.62					−0.015	−0.22	0.20
31	HOMO	−9.15	−0.48	−0.38	0.41	0.48			
	LUMO	−0.35					−0.31	−0.42	0.46

materials, activation energies, and lengths of forming bonds in cycloadditions; for *cis*- and *trans*-TS arising from trienes **6**, **25**, **27**, and **31**, the differences ($d1 \sim d2$) between lengths are of the order ≈0.2–0.3 Å, thus suggesting a certain degree of asynchronicity in these processes; however, more synchronous cycloadditions should occur in the rest of the cases, where the differences were of the order ≈0.1 Å.

Although the calculated $\Delta\Delta E^{\ddagger}$ values are rather small, they are in relatively good agreement with experimental *trans*/*cis* ratios indicated in Table 1; surprisingly, in spite of processes involving **28** and **30** showing the lowest $\Delta E^{\ddagger}$-values, no Diels–Alder reaction was observed for these substrates. Here, other causes, for example, polymerization of starting material or subtle substituent effects,[22b] could be responsible for the lack of reactivity.

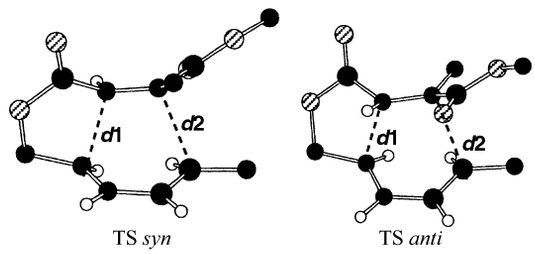
Also, we have performed theoretical calculations to rationalize the asymmetric induction observed for the reaction of chiral diene **9** with *N*-phenylmaleimide. Fig. 5 shows the optimized structures corresponding to the *endo*-(**32**‡ and **33**‡) and the hypothetic *exo*-(**34**‡ and **35**‡) transition states, their relative energies being collected in Table 4; at the PM3 level, the calculated values were much too similar to explain satisfactorily the observed diastereoselectivity. Since our adducts have an excessive number of atoms to allow us to perform a full optimization at the *ab initio* level, we have performed single-point energy calculations at the B3LYP/6-31G*//PM3 level;[26] in this way, we found values which revealed a greater stability for the *endo* transition states (**32**‡ and **33**‡), in agreement with our experimental data. This fact discloses that the B3LYP/6-31G* method constitutes an appropriate tool to explain the course of cycloaddition processes.

Experimental

General

Silica Gel 60 (Merck, 230–400 mesh ASTM for flash chromatography) was used for column chromatography, which was

Table 3 Heats of formation of trienes and TSs, activation energies (kcal mol^{-1})[a] and lengths (Å) of forming bonds in cycloadditions. As example, TS *syn* and TS *anti* from triene **25** are shown. For clarity, hydrogen atoms have been omitted, except those involved in the ring fusion



TS *syn* TS *anti*

	Heat of formation			Activation energy ($\Delta E^{\ddagger}$)		$\Delta\Delta E^{\ddagger}$	TS *syn*		TS *anti*	
Compound	Triene	TS *syn*	TS *anti*	TS *syn*	TS *anti*	*syn* − *anti*	*d*1	*d*2	*d*1	*d*2
5	201.74	168.20	167.43	33.54	34.31	−0.77	2.14	2.15	2.12	2.16
6	179.65	140.39	139.54	39.26	40.11	−0.85	2.08	2.24	2.03	2.28
25	139.29	100.42	99.43	38.87	39.86	−0.99	2.03	2.34	2.01	2.34
26	120.79	82.89	84.22	37.90	36.57	1.33	2.12	2.22	2.09	2.24
27	131.22	92.29	93.64	38.93	37.58	1.35	2.03	2.33	1.97	2.34
28	121.54	86.50	85.09	35.03	36.45	−1.42	2.20	2.14	2.16	2.16
29	131.99	93.91	92.27	38.08	39.72	−1.64	2.13	2.21	2.10	2.21
30	139.09	102.41	103.08	36.68	36.01	0.67	2.13	2.20	2.10	2.21
31	131.47	94.67	94.75	36.81	36.72	0.09	2.05	2.31	2.02	2.31

[a] 1 cal = 4.184 J.

Table 4 Energy differences (kcal mol^{-1})[a] and bond distances (Å) for TSs **32**–**35**

TS	ΔE^{b}	a	b	ΔE^{c}
32‡	0	2.163	2.163	0
33‡	2.6	2.184	2.165	4.3
34‡	2.4	2.152	2.176	6.0
35‡	2.2	2.141	2.186	11.5

[a] 1 cal = 4.184 J. [b] At PM3 level. [c] At B3LYP/6-31G*//PM3 level.

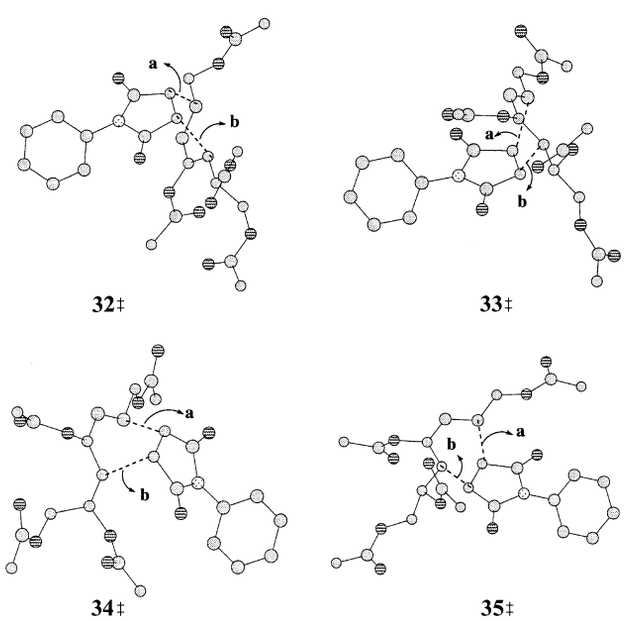


Fig. 5 Transition structures for the cycloaddition of **9** with *N*-phenylmaleimide.

carried out using flash mode. TLC was performed on pre-coated Merck Kieselgel 60 GF_{254} aluminium-backed plates; bands were visualized by UV light. Reagents were used as supplied by Aldrich Chemical Co. NMR spectra were taken on a Bruker AC/PC instrument (400.13 MHz for ^{1}H and 100.62 MHz for ^{13}C), with deuteriochloroform as solvent. Chemical shifts are reported in δ (ppm) with reference to Me_4Si (δ 0.00) for ^{1}H spectra or $CDCl_3$ (δ_C 77.00) for ^{13}C spectra as internal standards. Coupling-constant-values J are recorded in Hz. Characterization of NMR signals is based on spin decoupling, heteronuclear chemical-shift correlation spectroscopy and distortionless enhancement by polarization transfer (DEPT) experiments. HR (chemical ionization) mass spectra were recorded on a VG Autospec spectrometer; only significant fragment ions are reported. IR spectra were recorded on a Perkin-Elmer 399 and an FT-IR MIDAC Corporation spectrophotometer. Solid samples were run as KBr disks and liquids as thin films on NaCl plates. Details are reported as ν_{max}/cm^{-1}. Mps were determined in open capillary tubes on an Electrothermal 8100 capillary melting point apparatus and are uncorrected. Extracts were dried over anhydrous magnesium sulfate.

(2*E*,4*Z*)-4,6-Diacetoxyhexa-2,4-dienyl acrylate 5

To a stirred solution of a 15 : 1 mixture of (2*E*,4*Z*)-4,6-diacetoxyhexa-2,4-dien-1-ol[9b] **2** and its (2*E*,4*E*)-isomer (1.83 g, 8.56 mmol) in diethyl ether (40 mL) was added dropwise a mixture of pyridine (1.4 mL) and acryloyl chloride (1.4 mL, 17.12 mmol) in diethyl ether (3 mL). After stirring at room temperature for 45 min, the reaction mixture was treated with 5% aq. sodium hydrogen carbonate (15 mL) and then extracted with diethyl ether (50 mL). The extract was washed with brine (15 mL), dried, and concentrated to give 1.4 g (70%) of title ester **5**;[11] ν_{max}(film)/cm^{-1} 3020 (=C–H), 2920 (C–H aliphatic), 1755 (C=O vinyl ester), 1730 (C=O ester), 1710 (C=C–C=O), 1635 (C=C) and 1250 (C–O–C); δ_H 6.43 (dd, $J_{3't,2'}$ 17.5, $J_{3't,3'c}$ 1.5, 1H, H-3′*trans*), 6.21 (dt, $J_{3,1}$ 1.4, $J_{3,2}$ 15.5, 1H, H-3), 6.14 (dd, $J_{2',3't}$ 17.5, $J_{2',3'c}$ 10.5, 1H, H-2′), 5.86 (dd, $J_{3'c,3't}$ 1.5, $J_{3'c,2'}$ 10.5, 1H, H-3′*cis*), 5.84 (dt, $J_{2,1}$ 5.9, $J_{2,3}$ 15.5, 1H, H-2), 5.57 (t, $J_{5,6}$ 7.0, 1H, H-5), 4.72 (d, $J_{1,2}$ 5.9, 2H, H_2-1), 4.57 (d, $J_{6,5}$ 7.0, 2H, H_2-6), 2.28 (s, 3H, 4-OAc), 2.05 (s, 3H, 6-OAc); δ_C 170.7 (6-O*C*OCH$_3$), 168.0 (4-O*C*OCH$_3$), 165.6 (C-1′), 147.2 (C-4), 131.2 (C-3′), 128.0, 127.1 (C-2′, -2), 125.3 (C-3), 116.3 (C-5), 63.6 (C-1), 58.6 (C-6), 20.8, 20.4 (2 × OCO*C*H$_3$); *m*/*z*(CI) 268 (M + H, 5%), 209 (M + H − OAc, 18), 167 (27), 137 (15), 112 (27), 95 (100) (Found: M$^+$, 268.0978. $C_{13}H_{16}O_6$ requires *m*/*z*, 268.0946).

(2*E*,4*Z*)-4,6-Diacetoxyhexa-2,4-dienyl cinnamate 6

To a stirred solution of a 15 : 1 mixture of (2*E*,4*Z*)-4,6-

diacetoxyhexa-2,4-dien-1-ol[9b] **2** and its (2*E*,4*E*)-isomer (0.78 g, 3.6 mmol) in dry toluene (4 mL) was added dropwise a mixture of pyridine (0.3 mL) and a solution of cinnamoyl chloride (0.6 g, 3.6 mmol) in dry toluene (3 mL). After stirring at 85 °C for 1 h, the reaction mixture was filtered, diluted with toluene, and washed successively with water (10 mL), 2 M sodium hydrogen carbonate (10 mL), 1 M hydrochloric acid (10 mL) and water (10 mL). The organic extract was dried and concentrated to give title ester **6**[11] (1 g, 80%); ν_{max}(film)/cm^{-1} 3030 (=C–H), 2930 (C–H aliphatic), 1760 (C=O vinyl ester), 1735 (C=O ester), 1710 (C=C–C=*O*), 1635 (C=C), 1600 and 1490 (C=Carom); δ_H 7.71 (d, $J_{3',2'}$ 16.1, 1H, H-3′), 7.54–7.52 (m, 2H, ArH), 7.40–7.38 (m, 3H, ArH), 6.45 (d, $J_{2',3'}$ 16.1, 1H, H-2′), 6.25 (dt, $J_{1,3} < 1$, $J_{3,2}$ 15.6, 1H, H-3), 5.88 (dt, $J_{2,1}$ 5.7, $J_{2,3}$ 15.6, 1H, H-2), 5.58 (t, $J_{5,6}$ 7.0, 1H, H-5), 4.77 (d, $J_{1,2}$ 5.7, 2H, H_2-1), 4.57 (d, $J_{6,5}$ 7.0, 2H, H_2-6), 2.28 (s, 3H, 4-OAc), 2.05 (s, 3H, 6-OAc); δ_C 170.7 (6-O*C*OCH$_3$), 168.0 (4-O*C*OCH$_3$), 166.4 (C-1′), 147.3 (C-4), 145.4 (C-2′), 134.3 (C-1arom), 130.4 (C-2), 128.9 (C-2arom, -6arom), 128.1 (C-3arom, -5arom), 127.1 (C-4arom), 125.6 (C-3), 117.6 (C-3′), 116.3 (C-5), 63.6 (C-1), 58.7 (C-6), 20.8, 20.4 (2 × OCO*C*H$_3$); *m*/*z*(CI) 345 (M + H, 50%), 131 (COCH=CHPh, 100), 95 (65) (Found: [M + H]$^+$, 345.1329. $C_{19}H_{21}O_6$ requires *m*/*z*, 345.1338).

(2*E*,4*Z*)-4,6-Diacetoxy-*N*-allylhexa-2,4-dienimine 11

To a stirred solution of a 9 : 1 mixture of (2*E*,4*Z*)-4,6-diacetoxyhexa-2,4-dienal[9a] **10** and its (2*E*,4*E*)-isomer (1.10 g, 5.12 mmol) in diethyl ether (20 mL) were added molecular sieves (Merck, 4 Å) and allylamine (0.39 mL, 5.19 mmol). The reaction mixture was stirred at 0 °C for 3 h and at room temperature for 1 h; it was then filtered, dried, and concentrated to give a mixture of title imine **11** and its (2*E*,4*E*)-isomer as an inseparable 9 : 1 oily mixture (1.24 g, 95%); ν_{max}(film)/cm^{-1} 1760 (C=O vinyl ester), 1740 (C=O ester), 1640 (C=N, C=C diene) and 1225 (C–O–C); δ_H 7.92 (dd, $J_{1,2}$ 7.3, $J_{1,3}$ 1.0, 1H, H-1), 6.49 (dd, $J_{3,2}$ 15.7, $J_{3,1}$ 1.0, 1H, H-3), 6.40 (dd, $J_{2,3}$ 15.7, $J_{2,1}$ 7.3, 1H, H-2), 5.97 (m, $J_{2',1'}$ 5.8, 1H, H-2′), 5.74 (t, $J_{5,6}$ 6.9, 1H, H-5), 5.16 (m, 2H, C=CH_2), 4.61 (d, $J_{6,5}$ 6.9, 2H, H_2-6), 4.12 (br d, $J_{1',2'}$ 5.8, 2H, H_2-1′), 2.28 (s, 3H, 4-OAc), 2.07 (s, 3H, 6-OAc); δ_C 170.6 (6-O*C*OCH$_3$), 167.9 (4-O*C*OCH$_3$), 162.1 (C-1), 147.3 (C-4), 135.2, 134.6 (C-2′, -3), 129.5 (C-2), 119.7 (C-5), 116.5 (C-3′), 63.4 (C-1′), 58.7 (C-6), 20.8, 20.3 (2 × OCO*C*H$_3$).

(2*E*,4*Z*)-4,6-Diacetoxy-*N*-allylhexa-2,4-dienamine 7

To a stirred solution of a 9 : 1 mixture of **11** and its (2*E*,4*E*)-isomer (1.24 g, 4.94 mmol) in methanol (16 mL) at 0 °C was added sodium borohydride (187 mg, 4.94 mmol) and the mixture was kept for 20 min. The reaction mixture was diluted with water (35 mL), extracted with methylene dichloride (4 × 20 mL), and the extracts washed successively with saturated aq. sodium hydrogen carbonate (2 × 40 mL) and water (40 mL). The organic extracts were dried and concentrated to give 1.31 g (74%) of amine **7** and its (2*E*,4*E*)-isomer as an inseparable 9 : 1 oily mixture; ν_{max}(film)/cm^{-1} 3500–3100 (NH), 2950 (C–H aliphatic), 1760 (C=O vinyl ester), 1750 (C=O ester), 1650 (C=C diene), 1220 and 1030 (C–O–C); δ_H 6.10 (br d, $J_{3,2}$ 15.5, 1H, H-3), 5.90 (m, $J_{2,3}$ 15.5, $J_{2,1}$ 6.2, 1H, H-2), 5.80 (m, $J_{2',3't}$ 17.1, $J_{2',3'c}$ 10.1, $J_{2',1'}$ 6.1, 1H, H-2′), 5.48 (t, $J_{5,6}$ 7.1, 1H, H-5), 5.17 (dd, $J_{3't,2'}$ 17.1, $J_{3't,3'c}$ 1.6, 1H, H-3′*trans*), 5.10 (br d, $J_{3'c,2'}$ 10.1, $J_{3'c,3't}$ 1.6, 1H, H-3′*cis*), 4.56 (d, $J_{6,5}$ 7.1, 2H, H-6), 3.33 (br d, $J_{1,2}$ 6.2, 2H, H_2-1), 3.23 (br d, $J_{1',2'}$ 6.1, 2H, H_2-1′), 2.26 (s, 3H, 4-OAc), 2.05 (s, 3H, 6-OAc); δ_C 170.8 (6-O*C*OCH$_3$), 168.2 (4-O*C*OCH$_3$), 148.1 (C-4), 136.5 (C-2′), 130.9 (C-3), 125.0 (C-2), 116.2 (C-3′), 114.4 (C-5), 58.7 (C-6), 51.8, 50.2 (C-1, -1′), 20.8, 20.5 (2 × OCO*C*H$_3$).

(2*E*,4*Z*)-4,6-Diacetoxy-*N*-acetyl-*N*-allylhexa-2,4-dienamine 8

A solution of a 9 : 1 mixture of amine **7** and its 2*E*,4*E*-isomer (1.18 g, 4.66 mmol) in pyridine (3 mL) was treated with acetic anhydride (0.66 mL), and kept in the dark at room temperature for 4 h. After pouring onto ice–water (100 mL), the reaction mixture was extracted with methylene dichloride (5 × 20 mL) and washed successively with 2 M hydrochloric acid (2 × 100 mL), saturated sodium hydrogen carbonate (3 × 100 mL), and water (2 × 100 mL). The organic layer was dried and concentrated to give **8** and its 2*E*,4*E*-isomer as a 15 : 1 oily mixture (0.53 g, 38%). Column chromatography (ethyl acetate) allowed isolation of an analytical sample of pure **8** (*Z*/*E*-acetamido isomeric mixture, in the respective ratio of 1 : 0.65); ν_{max}(film)/cm^{-1} 3550–3300 (NH), 1750 (C=O vinyl ester), 1730 C=O (ester), 1650 (C=O amide), 1225 and 1010 (C–O–C); δ_H (*Z*/*E*-major isomer) 6.01 (br d, $J_{3,2}$ 15.6, 1H, H-3), 5.70 (m, $J_{2,1}$ 6.4, $J_{2,3}$ 15.6, $J_{2',1'}$ 4.7, 2H, H-2, -2′), 5.50 (t, $J_{5,6}$ 7.1, 1H, H-5), 5.23–5.12 (m, 2H, H_2-3′), 4.55 (d, $J_{6,5}$ 7.1, 2H, H_2-6), 4.04 (br d, $J_{1,2}$ 6.4, 2H, H-1), 3.83 (d, $J_{1',2'}$ 4.7, 2H, H_2-1′), 2.26 (s, 3H, 4-OAc), 2.09 and 2.05 (2 s, 6H, NAc and 6-OAc); δ_H (*Z*/*E*-minor isomer) 5.52 (t, $J_{5,6}$ 7.0, 1H, H-5), 4.57 (d, $J_{6,5}$ 7.0, 2H, H_2-6), 3.97 (br d, $J_{1,2}$ 6.1, 2H, H_2-1), 3.95 (d, $J_{1',2'}$ 5.1, 2H, H_2-1′), 2.28 (s, 3H, 4-OAc), 2.06 (s, 6H, 2 × Ac); δ_C (*Z*/*E*-couple) 170.7, 170.5 (N*C*OCH$_3$ and 6-O*C*OCH$_3$), 168.1, 168.0 (4-O*C*OCH$_3$), 147.6, 147.4 (C-4), 133.0, 132.5 (C-2′), 127.2, 126.6, 126.5, 125.4 (C-2, -3), 117.6, 116.8 (C-3′), 115.8, 115.2 (C-5), 58.7 (C-6), 50.1, 48.7, 47.8, 46.4 (C-1, -1′), 20.8, 20.4 (2 × OCO*C*H$_3$); *m*/*z*(CI) 296 (M + H, 22%), 253 (M + H − Ac, 15), 236 (M + H − AcOH, 18), 194 (M + H − Ac − OAc, 89), 152 (24), 82 (100) (Found: [M + H]$^+$, 296.1480. $C_{15}H_{22}NO_5$ requires *m*/*z*, 296.1497).

Intramolecular Diels–Alder reaction of (2*E*,4*Z*)-4,6-diacetoxyhexa-2,4-dienyl acrylate 5

To a solution of a 15 : 1 mixture of compound **5** and its 2*E*,4*E*-isomer (0.08 g, 0.30 mmol) in benzonitrile (4 mL) was added hydroquinone (catalytic amount). After reflux for 36 h, TLC (hexane–ethyl acetate 1 : 1) showed the absence of starting material and the appearance of two new products with R_f 0.43 (**12**) and R_f 0.30 (**13**) (ratio 1 : 1.8, respectively, ^{1}H NMR). The solvent was evaporated off to leave an oil (0.065 g, 80%), which was subjected to column chromatography (hexane–ethyl acetate 2 : 1) to afford pure isobenzofuranones **12** and **13** as colourless oils.

Data for compound **12**: ν_{max}(film)/cm^{-1} 2950 (CH aliphatic), 1765 (C=O vinyl ester), 1740 (C=O ester), 1720 (C=O lactone), 1660 (C=C) and 1245 (C–O–C); δ_H 5.75 (dd, $J_{5,3}$ 1.6, $J_{5,6}$ 3.3, 1H, H-5), 4.49 (dd, $J_{7,6}$ 6.9, $J_{7,7'}$ 8.1, 1H, H-7), 4.19 (dd, $J_{8,3}$ 3.5, $J_{8,8'}$ 11.2, 1H, H-8), 4.08 (dd, $J_{8',3}$ 7.6, $J_{8',8}$ 11.2, 1H, H′-8), 3.96 (dd, $J_{7',6}$ 11.5, $J_{7',7}$ 8.1, 1H, H′-7), 3.02 (m, $J_{6,5}$ 3.3, $J_{6,7}$ 6.9, $J_{6,7'}$ 11.5, 1H, H-6), 2.92 (m, $J_{3,8}$ 3.5, $J_{3,8'}$ 7.6, $J_{3,5}$ 1.6, 1H, H-3), 2.43 (td, $J_{1,2'} = J_{1,6} = 13.0$, $J_{1,2}$ 2.8, 1H, H-1), 2.36 (dd, $J_{2,1}$ 2.8, $J_{2,2'} = 13.0$, 1H, H-2), 1.94 (td, $J_{2',1} = J_{2',2} = 13.0$, $J_{2',3}$ 2.8, 1H, H′-2), 2.19 (s, 3H, 4-OAc), 2.10 (s, 3H, 8-OAc); δ_C 175.3 (C=O lactone), 170.8 (O*C*OCH$_3$), 169.0 (4-O*C*OCH$_3$), 149.4 (C-4), 114.9 (C-5), 70.3 (C-7), 64.5 (C-8), 40.5, 40.0, 36.9 (C-1, -3, -6), 23.9 (C-2), 21.0, 20.9 (2 × OCO*C*H$_3$); *m*/*z*(CI) 209 (M − OAc, 24%), 166 (M − OAc − OAc, 100) (Found: [M − OAc]$^+$, 209.0798. $C_{11}H_{13}O_4$ requires *m*/*z*, 209.0813).

Data for compound **13**: ν_{max}(film)/cm^{-1} 2925 (C–H aliphatic), 1760 (C=O vinyl ester), 1740 (C=O ester), 1730 (C=O lactone), 1680 (C=C) and 1250 (C–O–C); δ_H 5.47 (dd, $J_{5,3}$ 1.6, $J_{5,6}$ 3.9, 1H, H-5), 4.47 (dd, $J_{7,6}$ 7.7, $J_{7,7'}$ 9.0, 1H, H-7), 4.13 (dd, $J_{8,3}$ 4.5, $J_{8,8'}$ 11.2, 1H, H-8), 4.07 (dd, $J_{7',6}$ 5.6, $J_{7',7}$ 9.0, 1H, H′-7), 4.04 (dd, $J_{8',3}$ 7.1, $J_{8',8}$ 11.2, 1H, H′-8), 3.33 (m, $J_{6,7}$ 7.7, $J_{6,7'}$ 5.6, $J_{6,5}$ 3.9, 1H, H-6), 2.83 (q, $J_{1,6}$ 8.1, $J_{1,2'} = J_{1,2} = 8.0$, 1H, H-1), 2.80 (m, $J_{3,5}$ 1.6, $J_{3,8'}$ 7.1, $J_{3,8}$ 4.5, $J_{3,2}$ 6.1, 1H, H-3), 2.21 (ddd, $J_{2,2'}$ 14.1, $J_{2,3}$ 6.1, $J_{2,1}$ 8.0, 1H, H-2), 2.16 (m, $J_{2',2}$ 14.1, $J_{2',1}$ 8.0, 1H, H′-2), 2.18 (s, 3H, 4-OAc), 2.04 (s, 3H, 8-OAc); δ_C 178.1 (C=O lactone), 170.7 (O*C*OCH$_3$), 169.1 (4-O*C*OCH$_3$), 149.5 (C-4), 114.5 (C-5), 71.3 (C-7), 64.1 (C-8), 36.3, 34.8, 34.7 (C-1, -3, -6),

24.0 (C-2), 20.9 (2 × OCO*C*H$_3$); *m*/*z*(CI) 269 (M + H, 28%), 209 (M − OAc, 62), 166 (M − OAc − OAc, 100) (Found: [M + H]$^+$, 269.1007. $C_{13}H_{17}O_6$ requires *m*/*z*, 269.1025).

Intramolecular Diels–Alder reaction of (2*E*,4*Z*)-4,6-diacetoxyhexa-2,4-dienyl cinnamate 6

To a solution of a 15 : 1 mixture of compound **6** and its 2*E*,4*E*-isomer (0.085 g, 0.25 mmol) in benzonitrile (4 mL) was added hydroquinone (catalytic amount). After reflux for 24 h, TLC (hexane–ethyl acetate 1 : 1) showed absence of the starting material and the appearance of two new products with R_f 0.46 (**15**) and R_f 0.36 (**14**) (ratio 1 : 1.6, respectively, ^{1}H NMR). Then, the solvent was evaporated off to leave an oil, which was subjected to column chromatography (hexane–ethyl acetate 2 : 1) to afford pure isobenzofuranones **14** and **15** (total yield 60 mg, 70%).

Data for compound **15**: colourless oil, ν_{max}(KBr)/cm^{-1} 2900 (C–H aliphatic), 1755 (C=O ester), 1730 (C=O lactone), 1680 (C=C), 1600, 1490 (C=Carom) and 1230 (C–O–C); δ_H 7.4–7.2 (m, 5H, ArH), 5.62 (dd, $J_{5,3}$ 1.6, $J_{5,6}$ 3.3, 1H, H-5), 4.38 (dd, $J_{7,6}$ 6.6, $J_{7,7'}$ 8.9, 1H, H-7), 4.17 (dd, $J_{8,3}$ 3.6, $J_{8,8'}$ 11.3, 1H, H-8), 4.16 (dd, $J_{7',6}$ 3.3, $J_{7',7}$ 8.9, 1H, H′-7), 4.08 (dd, $J_{8',3}$ 7.1, $J_{8',8}$ 11.3, 1H, H′-8), 3.70 (dd, $J_{2,1}$ 4.7, $J_{2,3}$ 4.0, 1H, H-2), 3.27 (m, $J_{6,7}$ 6.6, $J_{6,5}$ 3.3, $J_{6,7'}$ 3.3, $J_{6,1}$ 7.7, 1H, H-6), 2.93 (m, $J_{3,5}$ 1.6, $J_{3,2}$ 4.0, $J_{3,8'}$ 7.1, $J_{3,8}$ 3.6, 1H, H-3), 2.86 (dd, $J_{1,2}$ 4.7, $J_{1,6}$ 7.7, 1H, H-1), 2.18 (s, 3H, 4-OAc), 2.04 (s, 3H, 8-OAc); δ_C 176.3 (C=O lactone), 170.7 (8-O*C*OCH$_3$), 169.1 (4-O*C*OCH$_3$), 149.1 (C-4), 142.9 (C-1arom), 129.1, 127.2 (C-2arom, -3arom, -5arom, -6arom), 127.3 (C-4arom), 115.9 (C-5), 71.7 (C-7), 63.6 (C-8), 43.7 (C-1), 41.0 (C-3), 40.6 (C-2), 34.2 (C-6), 20.9 (2 × OCO*C*H$_3$); *m*/*z*(CI) 345 (M + H, 15%), 285 (M − OAc, 60), 243 (M − OAc − ketene, 100) (Found: [M + H]$^+$ 345.1336. $C_{19}H_{20}O_6$ requires *m*/*z*, 345.1338).

Data for compound **14**: mp 148–149 °C (from ethanol) (Found: C, 66.28; H, 5.85. $C_{19}H_{20}O_6$ requires C, 66.27; H, 5.85%); ν_{max}(KBr)/cm^{-1} 2900 (C–H aliphatic), 1780 (C=O vinyl ester), 1750 (C=O ester), 1730 (C=O lactone), 1670 (C=C), 1600, 1490 (C=Carom) and 1250 (C–O–C); δ_H 7.35–7.20 (m, 5H ArH), 5.81 (br s, 1H, H-5), 4.47 (dd, $J_{7,6}$ 5.9, $J_{7,7'}$ 8.1, 1H, H-7), 4.14 (dd, $J_{8,3}$ 3.9, $J_{8,8'}$ 11.8, 1H, H-8), 3.98 (dd, $J_{7',6}$ 10.7, $J_{7',7}$ 8.1, 1H, H′-7), 3.59 (dd, $J_{2,1}$ 10.8, $J_{2,3}$ 7.0, 1H, H-2), 3.39 (dd, $J_{8',3}$ 2.5, $J_{8',8}$ 11.8, 1H, H′-8), 3.20 (m, $J_{6,1}$ 12.9, $J_{6,7'}$ 10.7, $J_{6,7}$ 5.9, 1H, H-6), 3.15 (dd, $J_{1,2}$ 10.8, $J_{1,6}$ 12.9, 1H, H-1), 2.91 (m, $J_{3,8}$ 3.9, $J_{3,2}$ 7.0, $J_{3,8'}$ 2.5, 1H, H-3), 2.15 (s, 3H, 4-OAc), 1.96 (s, 3H, 8-OAc); δ_C 173.2 (C=O lactone), 170.0 (8-O*C*OCH$_3$), 169.0 (4-O*C*OCH$_3$), 149.0 (C-4), 136.2 (C-1arom), 128.4, 128.2 (C-2arom, -3arom, -5arom, -6arom), 127.4 (C-4arom), 114.2 (C-5), 69.5 (C-7), 61.1 (C-8), 43.6 (C-3), 43.1 (C-2), 41.7 (C-1), 41.2 (C-6), 21.0, 20.8 (2 × OCO*C*H$_3$).

Intramolecular Diels–Alder reaction of (2*E*,4*Z*)-4,6-diacetoxy-*N*-acetyl-*N*-allylhexa-2,4-dienamine 8

A solution of triene **8**[11] (0.07 g, 0.24 mmol) and hydroquinone (catalytic amount) in benzonitrile (3 mL) was heated at 140 °C for 4.5 h. The solvent was evaporated off and the residue was found to be an inseparable mixture of adducts *cis*-**16** and *trans*-**17** (ratio 1 : 1, quant. yield); spectral data for the mixture **16** + **17**: δ_H 5.72 br s, 5.68 br s (1H, H-7 for **17** *Z*/*E*-isomers), 5.53 dd, 5.50 dd ($J_{5,7}$ 2.2, $J_{7,7a}$ 5.1, 1H, H-7 for **16** *Z*/*E*-isomers), 4.20–2.80 (methylene groups on C-1, -3, -4 and -8), 3.00–2.80 (2H, H-5 and -7a), 2.42–2.29 (1H, H-3a), 1.90–1.80 (1H, H-4), 1.70–1.40 (1H, H′-4), 2.17, 2.16, 2.15, 2.07, 2.06, 2.05, 2.00 (18H, 4 × OAc and 2 × NAc); δ_C for the mixture **16** + **17**: 170.7 (C=O amide), 169.2, 169.1 (C=O ester), 149.3, 148.7, 148.4, 148.0 (C-6), 116.5, 115.8, 115.2, 114.7 (C-7), 64.6, 64.1, 63.8 (C-8), 52.8, 51.7, 51.0, 50.8, 49.9, 49.1, 48.9 (C-1, -3), 42.2, 40.8, 38.4, 37.7, 37.1, 36.7, 36.6, 36.1, 36.0, 35.9, 34.2 (C-3a, -5, -7a), 28.9, 28.8, 26.9, 26.8 (C-4), 22.3, 22.1, 22.0 (NCO*C*H$_3$), 20.9, 20.8, 20.7 (OCO*C*H$_3$).

3,4,5,6,7-Penta-*O*-acetyl-1,2-dideoxy-1-nitro-D-*galacto*-heptitol 19

A stirred suspension of a 2 : 1 mixture of 2,3,4,5,6,7-hexa-*O*-acetyl-1-deoxy-1-nitro-D-*glycero*-L-*manno*-(and -L-*gluco*)-heptitol[18] **18** (9.01 g, 18.27 mmol) in 3 : 2 ethanol–1,4-dioxane (264 mL) was treated with sodium borohydride (2.76 g, 72.64 mmol) at room temperature. After 25 min, the reaction mixture was acidified to pH 6 with acetic acid, and stirring was continued for 45 min, until cessation of evolution of hydrogen. Then, the solid was removed by filtration, the mixture was evaporated, and the residue was treated with methylene dichloride (3 × 100 mL) and filtered again. The solution was successively washed with saturated aq. sodium hydrogen carbonate (2 × 100 mL), water, and brine. The organic layer was dried and concentrated to give the title compound **19** as a solid (5.4 g, 68%), mp 158–159 °C (from ethanol) lit.[19b] mp 158 °C.

3,4,5,6,7-Penta-*O*-acetyl-2-deoxy-*aldehydo*-D-*galacto*-heptose 20

To a stirred solution of **19** (5.63 g, 12.8 mmol) in 1 : 1 acetone–methanol (245 mL) at −5 °C was added dropwise 0.1 M aq. potassium hydroxide (128 mL, 12.8 mmol) followed by 0.05 M potassium permanganate (168 mL, 8.4 mmol) containing magnesium sulfate (2.32 g, 9.4 mmol). The temperature was kept below 0 °C during the addition, and stirring was continued at 0 °C for 1 h and for an additional 1 h at room temperature. The reaction mixture was filtered on Celite and washed on the filter with 1 : 1 methanol–water. The filtrate was treated with sodium chloride until saturation and the solution was extracted with methylene dichloride (4 × 100 mL). The organic extract was washed with water (100 mL), dried, and evaporated, to yield the title compound **20** (3.9 g, 75%) as an unstable white solid; ν_{max}(KBr)/cm^{-1} 2820 and 2720 (C–H aldehyde), 1750 (C=O ester), 1715 (C=O aldehyde) and 1245 (C–O–C); δ_H 9.65 (d, $J_{1,2'}$ 2.3, 1H, CHO), 5.49 (td, $J_{3,4}$ 1.8, $J_{3,2}$ 6.9, $J_{3,2'}$ 6.6, 1H, H-3), 5.37 (dd, $J_{5,6}$ 1.8, $J_{5,4}$ 10.0, 1H, H-5), 5.32 (m, $J_{6,7}$ 4.8, $J_{6,7'}$ 7.7, $J_{6,5}$ 1.8, 1H, H-6), 5.27 (dd, $J_{4,5}$ 10.0, $J_{4,3}$ 1.8, 1H, H-4), 4.29 (dd, $J_{7,6}$ 4.8, $J_{7,7'}$ 11.7, 1H, H-7), 3.84 (dd, $J_{7',6}$ 7.7, $J_{7',7}$ 11.7, 1H, H′-7), 2.63 (dd, $J_{2,2'}$ 17.1, $J_{2,3}$ 6.9, 1H, H-2), 2.58 (ddd, $J_{2',2}$ 17.1, $J_{2',1}$ 2.3, $J_{2',3}$ 6.6, 1H, H′-2), 2.14 (s, 3H, OAc), 2.13 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.02 (s, 3H, OAc); δ_C 197.8 (CHO), 170.4, 170.3, 170.2, 169.8 (5 × O*C*OCH$_3$), 69.3, 67.7, 67.6, 65.4 (C-3, -4, -5, -6), 62.2 (C-7), 44.7 (C-2), 20.6 (5 × OCO*C*H$_3$).

The 2,4-dinitrophenylhydrazone of **20** showed mp 140–142 °C (from benzene–diethyl ether); ν_{max}(KBr)/cm^{-1} 3300 (NH), 1740 (C=O ester), 1675 (C=N), 1515, 1370 (NO_2) and 1220 (C–O–C); δ_H 11.04 (s, 1H, NH), 9.11 (d, $J_{3arom,5arom}$ 2.5, 1H, H-3arom), 8.31 (dd, $J_{5arom,6arom}$ 9.6, $J_{5arom,3arom}$ 2.5, 1H, H-5arom), 7.92 (d, $J_{5arom,6arom}$ 9.6, 1H, H-6arom), 7.44 (t, $J_{1,2}$ 3.0, 1H, CHN), 5.35 (m, 4H, H-3, -4, -5, -6), 4.31 (dd, $J_{7,6}$ 4.8, $J_{7,7'}$ 11.6, 1H, H-7), 3.38 (dd, $J_{7',6}$ 7.7, $J_{7',7}$ 11.6, 1H, H′-7), 2.62 (m, $J_{2,1}$ 3.0, 2H, H_2-2), 2.15 (s, 3H, OAc), 2.13 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.03 (s, 3H, OAc); δ_C 170.5, 170.4, 170.2, 170.1 (5 × O*C*OCH$_3$), 146.6 (C-1arom), 144.9 (C=N), 138.2 (C-4arom), 129.8 (C-5arom), 129.2 (C-2arom), 123.4 (C-3arom), 116.4 (C-6arom), 69.2, 67.7, 67.4 (C-3, -4, -5, -6), 62.2 (C-7), 34.5 (C-2), 20.9, 20.7, 20.6 (5 × OCO*C*H$_3$); *m*/*z*(CI) 585 (M + H, 5%), 525 (M + H − AcOH, 7), 465 (M + H − 2AcOH, 13), 405 (M + H − 3AcOH, 8), 345 (M + H − 4AcOH, 37), 303 (100), 247 (70), 225 (25), 183 (42), 123 (54) (Found: [M + H]$^+$, 585.1658. $C_{23}H_{29}N_4O_{14}$ requires *m*/*z*, 585.1680).

(2*E*,4*Z*,6*S*)-4,6,7-Triacetoxyhepta-2,4-dienal 21

To a stirred solution of *aldehydo*-heptose **20** (3.38 g, 8.36 mmol) in dry methylene dichloride (35 mL) was added DBU (1.2 mL, 8.36 mmol). After being stirred for 16 h at room temperature,

the reaction mixture was washed successively with water (50 mL), 0.1 M hydrochloric acid (2 × 50 mL), saturated aq. sodium hydrogen carbonate (50 mL), and again with water (50 mL). The organic layer was dried and concentrated to give an oil, which was trituated in diethyl ether (3 × 50 mL). The resulting dark-coloured residue was removed by filtration and the filtrate was evaporated to leave an oil, shown to be a 9 : 1 mixture (1.51 g, 64%) of **21** and its 2*E*,4*E*-isomer. Analytical data for this mixture were in agreement with those reported earlier.[9a]

(2*E*,4*Z*,6*S*)-4,6,7-Triacetoxyhepta-2,4-dien-1-ol 22

To a stirred solution of a 9 : 1 mixture of compound **21** and its 2*E*,4*E*-isomer (1.8 g, 6.3 mmol) in methanol (9 mL) at 0 °C was added sodium borohydride (0.23 g, 6 mmol). After being stirred for 20 min at 0 °C, the reaction mixture was diluted with water (20 mL), extracted with methylene dichloride (4 × 10 mL), and the extract was dried and concentrated to leave an oil, shown to be a 15 : 1 mixture of the title compound **22** and its 2*E*,4*E*-isomer (1.4 g, 77%); ν_{max}(film)/cm^{-1} 3500–3300 (OH), 1755 (C=O vinyl ester), 1730 (C=O ester) and 1660 (C=C diene); δ_H 6.19 (dt, $J_{3,1}$ 1.6, $J_{3,2}$ 15.7, 1H, H-3), 5.90 (dt, $J_{2,3}$ 15.7, $J_{2,1}$ 4.9, 1H, H-2), 5.76 (m, $J_{6,7}$ 3.6, $J_{6,5}$ 9.0, $J_{6,7'}$ 7.2, 1H, H-6), 5.35 (d, $J_{5,6}$ 9.0, 1H, H-5), 4.25 (dd, $J_{7,6}$ 3.6, $J_{7,7'}$ 11.7, 1H, H-7), 4.24 (dd, $J_{1,2}$ 4.9, $J_{1,3}$ 1.6, 2H, H_2-1), 4.04 (dd, $J_{7',6}$ 7.2, $J_{7',7}$ 11.7, 1H, H′-7), 2.30 (s, 3H, 4-OCO*CH*$_3$), 2.07 (s, 3H, OAc), 2.05 (s, 3H, OAc); δ_C 170.7, 170.0 (2 × O*C*OCH$_3$), 168.6 (4-O*C*OCH$_3$), 148.8 (C-4), 132.1 (C-3), 123.6 (C-2), 114.9 (C-5), 66.3 (C-6), 64.4 (C-7), 62.3 (C-1), 20.9, 20.7, 20.5 (3 × OCO*C*H$_3$).

(2*E*,4*Z*,6*S*)-1,4,6,7-Tetraacetoxyhepta-2,4-diene 9

A solution of a 15 : 1 mixture of **22** and its 2*E*,4*E*-isomer (0.93 g, 3.25 mmol) in pyridine (11 mL) was treated with acetic anhydride (11 mL). After 4 h at room temperature, the reaction mixture was poured into 2 M hydrochloric acid (80 mL) at 0 °C, extracted with methylene dichloride (4 × 20 mL), and the extract was washed successively with 2 M hydrochloric acid (2 × 60 mL), saturated aq. sodium hydrogen carbonate (3 × 60 mL), and water (2 × 60 mL). The organic layer was dried and evaporated to give an oil, which was purified by column chromatography (hexane–ethyl acetate 24 : 10). A 15 : 1 mixture of the title compound **9** and its 2*E*,4*E*-isomer was obtained as a colourless oil (0.74 g, 70%); ν_{max}(film)/cm^{-1} 2930 (C–H aliphatic), 1755 (C=O vinyl ester), 1730 (C=O ester), 1660 (C=C diene) and 1210 (C–O–C); δ_H 6.18 (dt, $J_{3,2}$ 15.7, $J_{3,1}$ 1.0, 1H, H-3), 5.82 (dt, $J_{2,3}$ 15.7, $J_{2,1}$ 5.9, 1H, H-2), 5.74 (ddd, $J_{6,5}$ 9.0, $J_{6,7'}$ 7.2, $J_{6,7}$ 3.6, 1H, H-6), 5.39 (d, $J_{5,6}$ 9.0, 1H, H-5), 4.62 (dd, $J_{1,2}$ 5.9, $J_{1,3}$ 1.0, 2H, H_2-1), 4.25 (dd, $J_{7,6}$ 3.6, $J_{7,7'}$ 11.8, 1H, H-7), 4.03 (dd, $J_{7',6}$ 7.2, $J_{7',7}$ 11.8, 1H, H′-7), 2.30 (s, 3H, 4-OAc), 2.07 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.04 (s, 3H, OAc); δ_C 170.6, 169.9 (3 × O*C*OCH$_3$), 168.3 (4-O*C*OCH$_3$), 148.3 (C-4), 126.8 (C-3), 126.5 (C-2), 116.1 (C-5), 66.3 (C-6), 64.3 (C-7), 63.5 (C-1), 20.9, 20.7, 20.5 (4 × OCO*C*H$_3$); *m*/*z*(CI) 329 (M + H, 23%), 269 (M + H − AcOH, 22), 227 (50), 209 (M + H − 2AcOH, 15), 167 (100), 149 (M + H − 3AcOH), 124 (54), 107 (79) (Found: $[M + H]^+$, 329.1250. $C_{15}H_{21}O_8$ requires *m*/*z*, 329.1236).

Diels–Alder reaction of (2*E*,4*Z*,6*S*)-1,4,6,7-tetraacetoxyhepta-2,4-diene 9 with *N*-phenylmaleimide

A solution of a 15 : 1 mixture of diene **9**[11] (0.76 g, 2.3 mmol) in dry toluene (12 mL) was treated with *N*-phenylmaleimide (0.4 g, 2.3 mmol) and hydroquinone (catalytic amount). After heating at 105 °C for 5 days, the mixture was evaporated, yielding a mixture of adducts **23** and **24** (ratio 1.7 : 1). Column chromatography of this mixture (hexane–ethyl acetate 15 : 10) yielded pure compounds **24** (R_f 0.15, mp 78–80 °C) and **23** (R_f 0.14; mp 73–75 °C) (total yield: 0.68 g, 60%).

Analytical data for isoindolinedione **24** (Found: C, 59.94; H, 5.50; N, 2.70. $C_{25}H_{27}NO_{10}$ requires C, 59.88; H, 5.43; N, 2.79%); ν_{max}(KBr)/cm^{-1} 2960 (C–H aliphatic), 1740 (C=O ester), 1705 (C=O amide), 1655 (C=C), 1595, 1495 (C=Carom), 1230 (C–O–C); δ_H§ 7.46–7.31 (m, 5H, ArH), 5.65 (dt, $J_{8,3}$ 10.5, $J_{8,9} = J_{8,9'} = 2.5$, 1H, H-8), 5.55 (dd, $J_{5,3}$ 2.3, $J_{5,6}$ 3.3, 1H, H-5), 4.76 (dd, $J_{7,6}$ 6.4, $J_{7,7'}$ 11.3, 1H, H-7), 4.75 (dd, $J_{9,9'}$ 12.9, $J_{9,8}$ 2.5, 1H, H-9), 4.61 (dd, $J_{9',9}$ 12.9, $J_{9',8}$ 2.5, 1H, H′-9), 4.51 (dd, $J_{7',6}$ 8.7, $J_{7',7}$ 11.3, 1H, H′-7), 3.55 (dd, $J_{2,1}$ 8.9, $J_{2,3}$ 5.6, 1H, H-2), 3.50 (dd, $J_{1,2}$ 8.9, $J_{1,6}$ 5.5, 1H, H-1), 3.00 (ddd, $J_{3,8}$ 10.5, $J_{3,5}$ 2.3, $J_{3,2}$ 5.6, 1H, H-3), 2.82 (m, $J_{6,5}$ 3.3, $J_{6,7}$ 6.4, $J_{6,7'}$ 8.7, $J_{6,1}$ 5.5, 1H, H-6), 2.12 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.05 (s, 3H, OAc); δ_C§ 175.3, 175.1 (2 × C=O amide), 170.8, 170.5, 169.8, 168.8 (4 × O*C*OCH$_3$), 147.0 (C-4), 131.6 (C-1arom), 129.0 (C-3arom, -5arom), 128.8 (C-4arom), 126.8 (C-2arom, -6arom), 116.5 (C-5), 68.6 (C-8), 63.9 (C-7), 63.3 (C-9), 42.4 (C-1), 41.8 (C-2), 39.2 (C-3), 36.1 (C-6), 21.0, 20.9, 20.4 (4 × OCO*C*H$_3$).

Analytical data for compound **23** (Found: C, 59.90; H, 5.38; N, 2.73. $C_{25}H_{27}NO_{10}$ requires C, 59.88; H, 5.43; N, 2.79%); ν_{max}(KBr)/cm^{-1} 2960 (C–H aliphatic), 1740 (C=O ester), 1705 (C=O amide), 1655 (C=C), 1595, 1495 (C=Carom), 1230 (C–O–C); δ_H§ 7.43–7.28 (m, 5H, ArH), 5.62 (dd, $J_{5,3}$ 2.7, $J_{5,6}$ 3.6, 1H, H-5), 5.55 (ddd, $J_{8,3}$ 11.4, $J_{8,9}$ 2.3, $J_{8,9'}$ 4.9, 1H, H-8), 4.77 (dd, $J_{9,8}$ 2.3, $J_{9,9'}$ 12.3, 1H, H-9), 4.74 (dd, $J_{7,7'}$ 11.3, $J_{7,6}$ 6.8, 1H, H-7), 4.52 (dd, $J_{7',6}$ 8.4, $J_{7',7}$ 11.3, 1H, H′-7), 4.03 (dd, $J_{9',8}$ 4.9, $J_{9',9}$ 12.3, 1H, H′-9), 3.69 (dd, $J_{2,3}$ 5.9, $J_{2,1}$ 9.0, 1H, H-2), 3.47 (dd, $J_{1,2}$ 9.0, $J_{1,6}$ 6.2, 1H, H-1), 2.96 (ddd, $J_{3,5}$ 2.7, $J_{3,8}$ 11.4, $J_{3,2}$ 5.9, 1H, H-3), 2.78 (m, $J_{6,5}$ 3.6, $J_{6,7}$ 6.8, $J_{6,7'}$ 8.4, $J_{6,1}$ 6.2, 1H, H-6), 2.23 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.07 (s, 3H, OAc); δ_C§ 175.4, 174.8 (2 × C=O amide), 170.7, 170.6, 169.2, 168.2 (4 × O*C*OCH$_3$), 145.5 (C-4), 131.6 (C-1arom), 129.0 (C-3arom, -5arom), 128.7 (C-4arom), 126.8 (C-2arom, -6arom), 116.4 (C-5), 68.2 (C-8), 64.8 (C-9), 63.9 (C-7), 41.6 (C-1), 41.3 (C-2), 38.5 (C-3), 36.4 (C-6), 21.0, 20.9, 20.8, 20.7 (4 × OCO*C*H$_3$).

Acknowledgements

We thank the CICYT (Ministerio de Educación y Ciencia) through grant PB98-0997, the Junta de Extremadura (Consejería de Educación) and the Fondo Social Europeo through grants IPR99C032 and IPR98A066, and the Servicio de Espectrometría de Masas de la Universidad de Córdoba for mass spectra.

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