DIASTEREOSELECTIVE SYNTHESIS OF α-BUTADIENYL-β-LACTAMS AND SOME STEREOCHEMICAL ASPECTS OF THEIR DIELS-ALDER ADDUCTS‡

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Abstract - An efficient diastereoselective synthesis of α-dienyl-β-lactams *via* [2+2] cycloadditions of imines with butadienyl ketene is reported. The dienyl functionality of α-dienyl-β-lactams was then exploited in Diels-Alder reactions with *N*-phenylmaleimide (NPM), diethyl fumarate (DEF), ethyl acrylate (EA), 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) and stereochemical aspects of their Diels-Alder adducts are reported.

INTRODUCTION

The construction of appropriately substituted β-lactam derivatives continues to be a subject of intense investigations[1] which have resulted in the discovery of various natural, synthetic and biologically active substances containing β-lactam ring.[2,3] Several natural monocyclic β-lactams were shown to exhibit high activity against Gram-negative organisms[4] and the advent of nocardicins,[5] monobactams,[6] sulfazecin[7] as potential drugs suggest that a suitably substituted monocyclic β-lactam ring is perhaps the minimum requirement for biological activity.[8] The bioactivity and pharmaceutical potential of relatively simple structures renewed the interest in chemistry and structure-activity relationship of monocyclic β-lactams. Among the multitude of synthetic methods available for the construction of such compounds,[10] the most popular one is [2+2] imine-ketene cycloaddition, well known as Staudinger reaction.[11] This reaction was extensively studied after the discovery of penicillin, cephalosporin and later the carbapenem antibiotics and is now a well documented and a versatile route to various β-lactam derivatives.[12] We have recently reported the first use of butadienylketene in such reactions leading to diastereoselective synthesis of α-butadienyl-β-lactams.[13] The formation of butadienylketene as an intermediate has been detected in the thermolysis of appropriately substituted cyclobutenones and in the photolysis of substituted phenols *via* transient cyclohexa-2,4-dione intermediates.[14] In continuation of our pursuits in the study of imine-ketene[13] cycloadditions, we have carried out the reactions of various imines with butadienylketene. Here, we

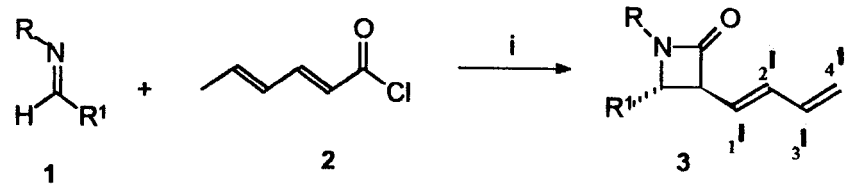
‡Dedicated to Prof. Teruaki Mukaiyama on his 73rd birthday.

disclose different stereo/regiochemical features observed in these cycloaddition reactions and in the Diels-Alder cycloadditions of the resulting α-butadienyl-β-lactam.

RESULTS AND DISCUSSION

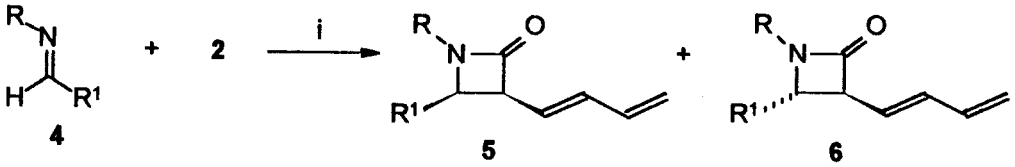
As reported earlier, the treatment of Schiff bases **(1)**, derived from aromatic amines, with butadienylketene, generated *in situ* from sorbyl chloride **(2)** and triethylamine, resulted exclusively in diastereoselective formation of *trans*-3-butadienyl-β-lactams **(3)**[13] (Scheme 1). Similar reactions of butadienylketene with the Schiff bases **(4)** derived from aliphatic amines (*viz.* cyclohexylamine, furfurylamine and *n*-butylamine) and arylaldehydes (benzaldehyde and anisaldehyde[15]) resulted interestingly in either exclusively *cis* or a mixture of *cis*- and *trans*-β-lactams. For example, the reaction of butadienylketene with the Schiff bases derived from cyclohexylamine and arylaldehydes resulted exclusively in the formation of *cis*-β-lactams **(5a** and **5b)** (Scheme 1), which were characterised on the basis of analytical and spectral data.[16] Further, the reactions of Schiff base derived from furfurylamine and benzaldehyde resulted in the exclusive isolation of *cis*-β-lactam **(5c)**. On the other hand, the reactions of Schiff bases, derived from furfurylamine and *p*-anisaldehyde, with butadienylketene resulted in the diastereoselective formation of a *cis/trans* mixture (6.5:1) of β-lactams **(5d/6d)** (Scheme 1).

Several attempts at chromatographic separations of this mixture failed due to their same R_f values. The β-lactams **(5d/6d)** displayed spectroscopic parameters fully compatible with the gross structural features. The relative stereochemistry at C-3 and C-4 in case of **5d/6d** was assigned on the basis of ^{1}H NMR spectrum. The *cis* and *trans* isomers were identified mainly through the observed two signals for H-4 protons; a doublet at δ 4.72 (*J* 5.4 Hz) indicated the formation of *cis*-β-lactam and another doublet at δ 4.26 (*J* 2.2 Hz) showed the presence of *trans* isomer in the mixture. The relative *cis/trans* (6.5:1) ratio was calculated from the integration ratio for the aromatic proton of the two isomers and also from the integration ratio of two signals for one of the protons of the furan ring. Further, the reaction of butadienylketene with Schiff base derived from *n*-butylamine and *p*-anisaldehyde also resulted in the formation of a mixture (4:1) of *cis/trans*-β-lactams **(5e/6e)** (Scheme 1). Thus, unlike the formation exclusively of *trans*-β-lactam in reactions of Schiff base **(1)** with butadienylketene, the reactions with Schiff bases **(4)**, gave either exclusively *cis* or a mixture of *cis*- and *trans*-β-lactams, as was observed in reactions of Schiff bases with vinyl/isopropenylketenes.[17] Further to our studies, we have examined the reactions of various 1-azadienes with butadienylketene which resulted in the exclusive isolation of *cis*-β-lactams **(8)**, irrespective of the nature of alkyl/aryl substituent in **7** (Scheme 1). The products were identified on the basis of IR, MS, ^{1}H and ^{13}C NMR spectra and microanalysis. The β-lactams **(8)** were



1

R = Aryl



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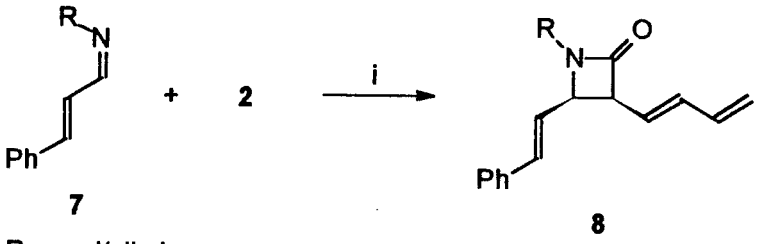
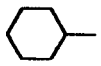
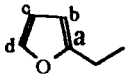
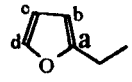
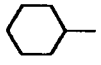
R = alkyl



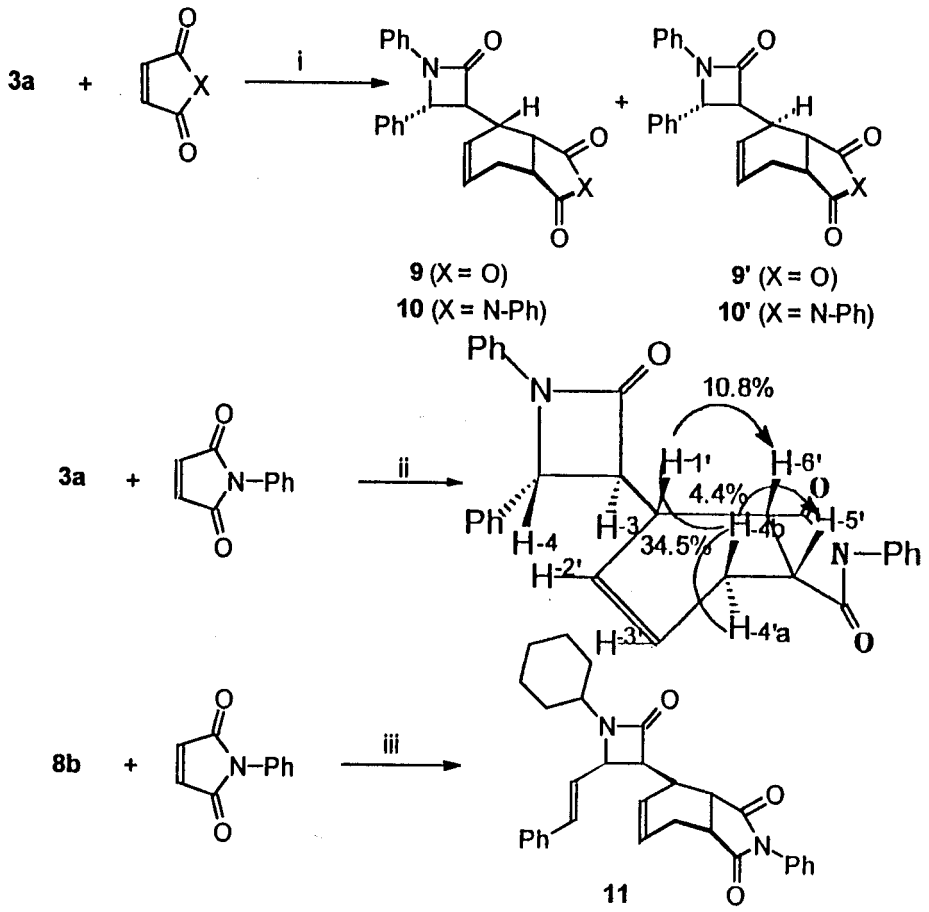
7

R = aryl/alkyl

Entry	Substrate	R	R^1	Product(s)	*cis* : *trans* (%)
1	**1a**	Ph	Ph	**3a**	0 : 100
2	**1b**	Ph	*p*-C_6H_4OMe	**3b**	0 : 100
3	**1c**	*p*-C_6H_4Me	Ph	**3c**	0 : 100
4	**1d**	*p*-C_6H_6Me	*p*-C_6H_4OMe	**3d**	0 : 100
5	**4a**		Ph	**5a**	100 : 0
6	**4b**		*p*-C_6H_4OMe	**5b**	100 : 0
7	**4c**		Ph	**5c**	100 : 0
8	**4d**		*p*-C_6H_4OMe	**5d-6d**	6.5 : 1
9	**4e**	*n*-Bu	*p*-C_6H_4OMe	**5e-6e**	4 : 1
10	**7a**	Ph	-	**8a**	100 : 0
11	**7b**		-	**8b**	100 : 0

cheme 1 *Reagents and conditions:* i, Et_3N, CH_2Cl_2, rt

assigned *cis* stereochemistry on the basis of the observed coupling constant of about 5.5 Hz between H-3 and H-4 protons. It was thought worthwhile to explore the Diels-Alder cycloaddition reactions of α-dienyl-β-lactams so synthesised, especially in view of the earlier interesting stereochemical observations in such cycloadditions.[13] The reactions of **3a** with maleic anhydride(MA) and *N*-phenylmaleimide (NPM) in refluxing toluene were found to yield a mixture (2:1) of diastereoisomers (**9/9'** and **10/10'**), respectively (Scheme 2), but the specific stereochemistry of the individual isomers could not be ascertained earlier. Since the α-position of α-dienyl-β-lactam is a stereocenter one may expect two possible "*endo*" products, (differing in the stereochemical relationship between the centres on the lactam and on the cyclohexene moieties) and two possible "*exo*". However, because of the free rotation possible around C3-C1′ bond both *endo* adducts will have same relative stereochemistry across C3-C1′-C6′-C5′ and same is true for two possible *exo* adducts. Therefore the mixtures (**9/9'** and **10/10'**) may possibly consist of endo-exo



Scheme 2 *Reagents and conditions:* i, Toluene, reflux, 1-2 h; ii, 5M $LiClO_4.Et_2O$, rt, 13-14 h; iii, Toluene, reflux, 1 h

diastereomers. However, a reaction of **3a** with NPM in 5M $LiClO_4$-Et_2O solution at room temperature,resulted in the isolation of a single diastereoisomer as evidenced by its ^1H and ^{13}C NMR spectra. The assignment of "*endo*" configuration for this diastereomer is based on the well established preferential *endo* selectivity in normal Diels-Alder reaction at lower temperatures and NOE studies on **10** (Scheme 2 and Table 1). Irradiation of H-1′ and H-4′a, having very small difference in their chemical shifts resulted in an increment of 10.8% for H-6′ and 11.6% for H-3′ and 34.5% for H-4′b respectively. The enhancement of H-4′b by 34.5% is ascribed mainly to the proximity of geminal H-4′a and partly to H-1′ protons. Irradiation of H-6′ resulted in an increment of 8.1% for H-1′. The NOE results above further support the assigned "*endo*" configuration. The comparison of the ^1H and ^{13}C NMR spectra of this single diastereoisomer with that of ^1H and ^{13}C NMR spectra of the mixture **(10/10')** indicated its identical nature with that of the major isomer **(10).** Therefore, the major isomers in the mixtures **(9/9'** and **10/10')** were assigned the *endo* configuration while the minor isomers were assigned *exo* configuration. Interestingly, the reaction of **8b** with NPM in refluxing toluene, also resulted in the isolation of a single diastereomer **(11)** (Scheme 2), wherein, the *cis* stereochemistry at C-3 and C-4 of the starting β-lactam **(8b)** was retained despite steric constraints.

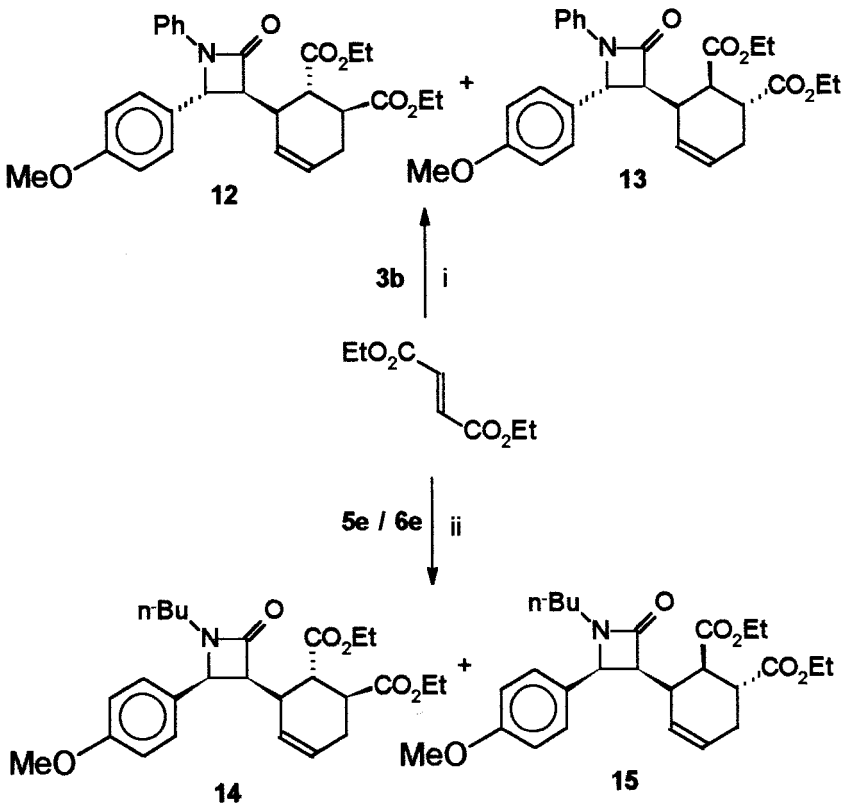
Table:1 NOE data used to prove the stereochemistry of the adduct **(10).**

Peak Irradiated	Enhancement Observed (in %)								
	H-1′	H-2′	H-3′	H-4′a	H-4′b	H-5′	H-6′	H-3	H-4
H-1′/H-4′a	------	2.5	11.6	-------	34.5	-------	10.8	2.9	10.2
H-2′	4.2	-------	-------	-------	-------	-------	-------	7.0	3.6
H-5′	------	------	------	------	4.4	-------	14.5	------	1.1
H-6′	8.1	-------	-------	-------	-------	9.4	------	------	------
H-4	10.7	4.0	-------	-------	------	------	------	------	------

The reactions of β-lactam **(3b)** with Diethyl fumarate in refluxing toluene resulted in the isolation of an inseparable mixture (1:1.5) of diastereomers **(12** and **13)** (Scheme 3). The products in the mixture were assigned the structures **(12** and **13)** on the basis of the ^1H and ^{13}C NMR spectra. The *trans* stereochemistry was assigned to the β-lactam moiety of isomers **(12** and **13)** on the basis of the observed coupling constants of about 2.3 Hz between H-3 and H-4 protons. However, the exact nature of the individual cycloadducts **12** and **13** could not be firmly established due to the presence of a number of unresolved multiplets in the ^1H NMR spectrum. Even the NOE experiments proved to be inconclusive and hence, their specific relative stereochemistry could not be assigned.

Similar treatment of *cis/trans*-α-dienyl-β-lactam mixture **(5e/6e)** with DEF resulted in the isolation of a

mixture of diastereoisomers **(14** and **15)** (Scheme 3). The assignment of *cis* stereochemistry for isomers **(14)** and **(15)** was based on the observed coupling constant of about 5.3 Hz between H-3 and H-4 protons. No trace of *trans* adducts could either be isolated or observed in ^{1}H or ^{13}C NMR spectrum of the mixture. The relative specific stereochemistry could not be assigned even to **14** and **15** with the help of NOE experiments. The attempted isolation of a single specific stereoisomer, by carrying out the reactions

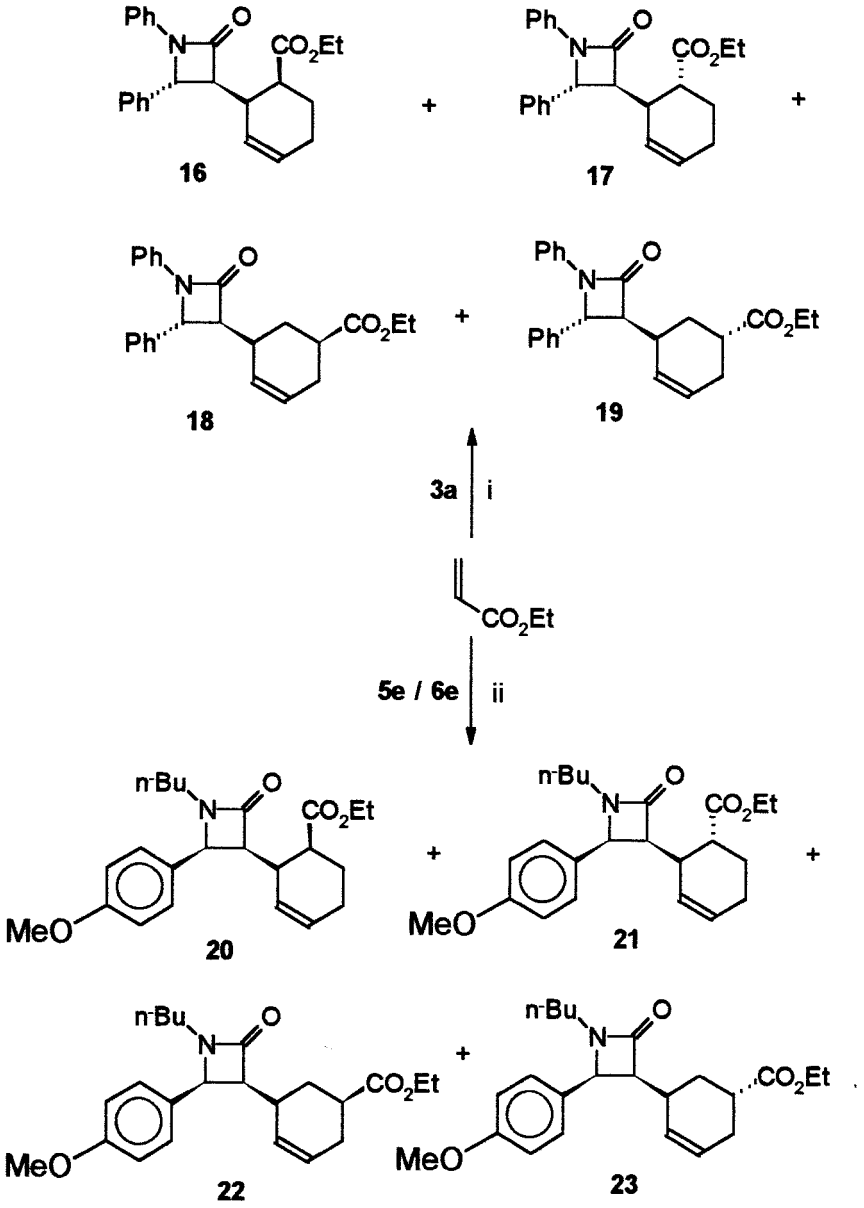


Scheme 3 *Reagents and conditions:* i, Toluene, reflux, 4-5 h; ii, Toluene, reflux, 6-7 h

of α-dienyl-β-lactams with DEF in presence of 5M $LiClO_4$ solution in ether at 0°C, failed and the starting material was recovered unchanged. The reactions of α-dienyl-β-lactams **(3** and **5/6)** with ethyl acrylate (EA) were shown to afford a mixture of stereo as well as regioisomers. For example, the reaction of *trans*-β-lactam **(3a)** with EA afforded an inseparable mixture of products which were characterised mainly on the basis of ^{1}H NMR spectrum and were identified as a mixture (5:4:2:1.2) comprising of **16**, **17**, **18** and **19** (Scheme 4). The formation of these four isomers could be attributed to the four sets of signals observed for H-4 protons and their ratio was based on integration values for these signals in the ^{1}H NMR spectrum of the mixture. The uniform coupling constant value of 1.9-2.5 Hz (between H-3 and H-4 protons) for these four sets of signals for H-4 proton of each isomer further indicated *trans* relative stereochemistry at

C-3 and C-4. Because of the complex nature of ^{1}H and ^{13}C NMR spectra the assignment of exact structure to the individual isomers or the assignment of specific relative regio/stereochemistry is rather difficult.

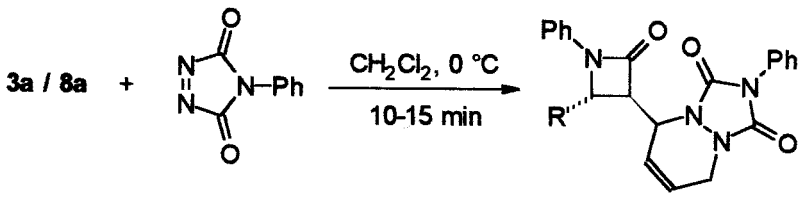
Similarly, the reaction of *cis/ trans*-β-lactam mixture **(5e/6e)** with ethyl acrylate also yielded an inseparable mixture (11:4:2.5 :1) of four stereo/regioisomers **(20, 21, 22** and **23)** (Scheme 4). The formation of these four isomers and their ratio could mainly be inferred from the observed four sets of signals for H-4 proton in its ^{1}H NMR spectrum and from their relative integrations, respectively. The ^{13}C

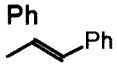


Scheme 4 *Reagents and conditions:* i, Toluene, reflux, 26 h; ii, Toluene, reflux, 30 h

NMR signals also attest to the presence of these four isomers. From the coupling constant value of 5.1-

5.3 Hz between H-3 and H-4 protons in their ^{1}H NMR spectrum it was inferred that all these isomers have *cis* relative stereochemistry at C-3 and C-4. Here again, even traces of *trans* adduct was neither isolated nor observed in ^{1}H NMR spectrum. Because of the complex nature of ^{1}H and ^{13}C NMR spectra, the specific relative regio/stereochemistry for the individual isomers in the mixture could not be assigned even with the help of NOE experiments. In an attempt to simplify the product mixture, the reactions of α-dienyl-β-lactams **(3** and **5/6)** were carried out with EA in 5M $LiClO_4$-Et_2O solution at 0°C. However, these reactions failed and hence the relative regio/stereochemistry of the individual isomers could not be assigned. It was observed that the reaction of *trans*-β-lactam **(3a)** with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD), in methylene chloride at 0 °C, resulted stereospecifically in the corresponding Diels-Alder adduct **(24a)**[13]. However, it is interesting to note that the reaction of *cis*-β-lactam **(8a)**, wtih PTAD under similar conditions also resulted in the synthesis of *trans*-adducts **(24b)** (Scheme 5). In contrast, the earlier mentioned Diels-Alder cycloadditions of *cis*-β-lactams continued to give *cis*-adducts even under much more vigorous conditions of refluxing in toluene. The reversal of stereochemistry observed in reaction of **8a**, with PTAD may possibly due to the stepwise nature of these cycloadditions involving a zwitterionic intermediate which on deprotonation and reprotonation at C-3 possibly leads to the final product **(24b).** This is in broad agreement with the reported literature on similar reactions. [18]



24 a R = Ph
b R = 

Scheme 5 *Reagents and conditions:* i, CH_2Cl_2, 0 °C, 10-15 min

In summary, the reactions of various Schiff bases derived from aromatic amines with butadienylketene gave exclusively *trans*-azetidinones and those derived from aliphatic amines resulted either exclusively in *cis*- or a mixture of *cis*- and *trans*-azetidinones. However, the reaction with 1-azadienes yielded exclusively *cis*-azetidinone irrespective of the amine used. The Diels-Alder cycloaddition reactions of these β-lactams followed interesting stereochemical patterns leading to a convenient route for variety of α-substituted β-lactams.

EXPERIMENTAL

Melting points were determined with a Toshniwal melting point apparatus and are uncorrected. IR spectra

were recorded on a Perkin-Elmer 983 infrared spectrophotometer. ^{1}H NMR spectra were recorded in deuteriochloroform with Bruker AC-F 300 (300 MHz) spectrometer using TMS as internal standard. chemical shift values are expressed as δ (ppm) down field from TMS and J values are in Hz. Splitting patterns are indicated as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br broad. ^{13}C NMR spectra (75.5 MHz) were also recorded on Bruker AC-F 300 spectrometer in deuteriochloroform using TMS as internal standard. MS were obtained by electron impact at 70 eV. Column chromatography was performed on a 60-120 mesh silica gel. Sorbyl chloride was prepared according to the reported procedure.[13]

General Procedure for Azetidinones (3, 5/6 and 8). A solution of sorbyl chloride (0.39 g, 3 mmol) in dry CH_2Cl_2 (30 mL) was added dropwise to a solution of Schiff base (2 mmol) and triethylamine (0.60 g, 6 mmol) in CH_2Cl_2 (30 mL) under stirring at rt. After the addition was complete (*ca.* 1.5 h), the solution was stirred for an additional 15 min, washed with water (5 × 50 mL), and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the crude product thus obtained was purified by column chromatography (silica gel) using a solution of ethyl acetate and hexane (1:9) as eluent.

***cis*-3-(1',3'-Butadienyl)-1-cyclohexyl-4-phenylazetidin-2-one (5a).** Yield 63%; viscous oil. IR ν_{max}/cm^{-1} (KBr) 1746, 1489, 1397 and 1351; δ_H 1.01-1.30 (m, 4H, cyclohexyl), 1.52-2.05 (series of m, 6H, cyclohexyl), 3.38-3.46 (m, 1H, cyclohexyl), 4.08 (dd, *J* 7.5 and 5.6, 1H, H-3), 4.85 (d, *J* 5.6, 1H, H-4), 4.94 (d, *J* 10.0, with fine splitting, 1H, H-4'), 5.08 (d, *J* 17.4, with fine splitting, 1H, H-4'), 5.13 (dd, *J* 15.3 and 7.5, 1H, H-1'), 6.02 (ddd, *J* 17.4, 10.4 and 10.0, 1H, H-3'), 6.25 (dd, *J* 15.3 and 10.4, 1H, H-2'), 7.25-7.38 (m, 5H, ArH); δ_C 25.0, 25.2, 30.5, 31.5, 53.0 (cyclohexyl), 57.2 (C-3), 58.3 (C-4), 117.3 (C-4'), 124.8 (C-1'), 127.5, 128.1, 128.3, 135.4 (C-2'), 136.2 (C-3'), 136.6, 168.1 (C-2); *m/z* 281 (M^+), 156 (M^+-125). *Anal.* Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.49; H, 7.94; N, 5.30.

***cis*-3-(1',3'-Butadienyl)-1-cyclohexyl-4-(*p*-methoxyphenyl)azetidin-2-one (5b).** Yield 69%; viscous oil IR ν_{max}/ cm^{-1} (CCl_4) 1751, 1490, 1391 and 1346; δ_H 1.05-1.31 (m, 4H, cyclohexyl), 1.52-2.03 (series of m, 6H, cyclohexyl), 3.36-3.47 (m, 1H, cyclohexyl), 3.78 (s, 3H, OCH_3), 4.05 (dd, *J* 7.6 and 5.4 , 1H, H-3), 4.81 (d, *J* 5.4, 1H, H-4), 4.95 (d, *J* 9.6, 1H, H-4'), 5.09 (d, *J* 16.4, 1H, H-4'), 5.16 (dd, *J* 15.2 and 7.6, 1H, H-1'), 5.96-6.33 (m, 2H, H-2' and H-3'), 6.88 (d, *J* 8.6, 2H, ArH), 7.18 (d, *J* 8.6, 2H, ArH); δ_C 25.0, 25.2, 30.5, 31.5, 52.9 (cyclohexyl), 55.0 (OCH_3), 57.2 (C-3), 57.9 (C-4), 113.7, 116.9 (C-4'), 124.8 (C-1'), 128.1, 128.5, 134.9 (C-2'), 136.0 (C-3'), 159.2, 168.0 (C-2); *m/z:* 311 (M^+), 186 (M^+-125). *Anal.* Calcd for $C_{20}H_{25}NO_2$: C, 77.14; H, 8.09; 4.50. Found: C, 77.37; H, 8.01; N, 4.44.

***cis*-3-(1',3'-Butadienyl)-1-furfuryl-4-phenylazetidin-2-one (5c).** Yield 57%; viscous oil IR ν_{max}/cm^{-1}

(CCl_4) 1749, 1493, 1397 and 1358; δ_H 4.04 (d, *J* 15.7, 1H, CH_2), 4.17 (dd, *J* 7.0 and 5.3, 1H, H-3), 4.76 (d, *J* 15.7, 1H, CH_2; merged with d, *J* 5.3, 1H, H-4), 4.95 (d, *J* 10.2, 1H, H-4′), 5.07-5.15 (m, 2H, H-4′ and H-1′), 6.01 (ddd, *J* 16.9, 10.3 and 10.2, 1H, H-3′), 6.12 (d, *J* 3.2, 1H, H-b), 6.20-6.29 (m, 2H, H-2′ and H-c), 7.14-7.17 (m, 2H, ArH), 7.27-7.36 (m, 4H, ArH and H-d); δ_C 37.2 (CH_2), 58.4 (C-3), 59.3 (C-4), 108.7 (C-c), 110.4 (C-b), 117.6 (C-4′), 124.3 (C-1′), 127.2, 128.2, 128.6, 135.0, 135.6 (C-2′), 136.1 (C-3′), 142.6 (C-d), 148.8 (C-a), 167.9 (C-2); *m/z:* 279 (M^+), 156 (M^+-123). *Anal.* Calcd for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.48; H, 6.10; N, 5.07.

(*cis*/*trans*,6.5:1)-3-(1',3'-Butadienyl)-1-furfuryl-4-(*p*-methoxyphenyl)azetidin-2-one(5d/6d). Following the general procedure, a mixture consisting in *cis* and *trans* isomers in 6.5:1 ratio was isolated as viscous oil Yield, 59%; IR ν_{max}/ cm^{-1} (CCl_4) 1745, 1491, 1397 and 1356; δ_H 3.73 (s, 3H, OCH_3, *cis* isomer), 3.75 (s, 3H, OCH_3, *trans* isomer), 3.92 (d, *J* 15.7, 1H, CH_2, *trans* isomer), 4.01 (d, *J* 15.7, 1H, *cis* isomer), 4.09-4.14 (m, 2H, H-3, both isomers), 4.26 (d, *J* 2.2, 1H, H-4, *trans* isomer), 4.65 (d, *J* 15.7, 1H, CH_2, *trans* isomer), 4.69 (d, *J* 15.7, 1H, CH_2, *cis* isomer), 4.72 (d, *J* 5.4, 1H, H-4, *cis* isomer), 4.92 (d, *Jcis* = 10.1, with *trans* isomer d merged, 2H, H-4′, both isomers), 5.07 [d, *Jcis* 17.0, with *trans* isomer d merged, 2H, H-4′, both isomer), 5.16 (dd, *Jcis* = 15.3 and 7.7, with *trans* isomer dd merged, 2H, H-1′, both isomers), 6.01 (ddd, *Jcis* = 17.0, 10.3, 10.1, with *trans* isomer ddd merged, 2H, H-3′, both isomers), 6.10 (d, *Jcis* 3.1, with *trans* isomer d merged, 2H, H-b, both isomers), 6.16-6.30 [m, 4H; consisting in at 6.23 (dd, *Jcis* 3.1 and 1.1, with *trans* isomer dd merged, 2H, H-c), 6.26 (dd, *J* 15.7 and 10.3, 1H, H-2′, *cis* isomer) and 6.20 (merged dd, H-2′, *trans* isomer)], 6.85 (d, *J* 8.6, with fine splitting, 2H, ArH, *cis* isomer; merged with d at 6.88, 2H, ArH, *trans* isomer), 7.08 (d, *J* 8.6, with fine splitting, 2H, ArH, *cis* isomer), 7.17 (d, *J* 8.6, with fine splitting, 2H, ArH, *trans* isomer), 7.28 (d, *J* 1.1, with fine splitting, 1H, H-d, *cis* isomer), 7.38 (d, *J* 1.0, 1H, H-d, *trans* isomer); ^{13}C NMR δ 37.0 (CH_2, *cis* isomer) 37.2 (CH_2, *trans* isomer), 55.0 (OCH_3, *cis* isomer), 55.1 (OCH_3, *trans* isomer), 58.3 (C-3, *cis* isomer), 58.9 (C-4, *cis* isomer), 61.4 (C-3, *trans* isomer), 63.4 (C-4, *trans* isomer), 108.46 (C-c, *trans* isomer), 108.54 (C-c, *cis* isomer), 110.4 (C-b, both isomers), 113.9 (ArC, *cis* isomer), 114.3 (ArC, *trans* isomer), 117.4 (C-4′, *cis* isomer), 117.9 (C-4′, *trans* isomer), 124.8 (C-1′, both isomers); 126.3, 127.6, 128.8 (ArC, *trans* isomer); 126.8, 128.5 (ArC, *cis* isomer), 134.7 (C-2′, *trans* isomer), 135.2 (C-2′, *cis* isomer), 136.1 (C-3′, *trans* isomer), 136.2 (C-3′, *cis* isomer), 142.5 (C-d, both isomers), 148.9 (C-a, both isomers), 159.4 (ArC, *cis* isomer), 159.8 (ArC, *trans* isomer), 167.7 (C-2, *trans* isomer), 167.8 (C-2, *cis* isomer); *m/z* 309 (M^+), 186 (M^+- 123). *Anal.* Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.88; H, 6.11; N, 4.46.

(*cis*/*trans*,4:1)-3-(1',3'-Butadienyl)-1-*n*-butyl-4-(*p*-methoxyphenyl)azetidin-2-one(5e/6e). Following

the general procedure a mixture consisting in *cis* and *trans* isomers in the ratio 4:1 was isolated as viscous oil Yield 67%; IR ν_{max}/cm^{-1} (CCl_4) 1747, 1509, 1397 and 1249; δ_H 0.87 (t, *J* 7.3, 3H, CH_3, *cis* isomer), 0.93 (t, *J* 7.3, 3H, CH_3, *trans* isomer), 1.23-1.36 (m, 2H, CH_2, *cis* isomer), 1.39-1.52 (m, 4H, CH_2, both isomers), 1.61-1.68 (m, 2H, CH_2, *trans* isomer), 3.40-3.62 (m, 4H, CH_2-N, both isomers), 3.76 (s, 3H, OCH_3, *cis* isomer), 3.78 (s, 3H, OCH_3, *trans* isomer), 4.10-4.15 (m, 2H, H-3, both isomers), 4.31 (d, *J* 2.1, 1H, H-4, *trans* isomer), 4.80 (d, *J* 5.4, 1H, H-4, *cis* isomer), 4.93 (d, *J* 10.0, with fine splitting, 1H, H-4′, *cis* isomer), 5.05-5.21 [m, 5H; consisting in at 5.08 (d, *J* 16.9, with fine splitting, 1H, H-4′, *cis* isomer), 5.17 (dd, *J* 15.4 and 7.7, 1H, H-1′, *cis* isomer, and merged signals for 2H, H-4′, *trans* isomer and 1H, H-1′, *trans* isomer), 6.04 (ddd, *J* 16.9, 10.3 and 10.0, 1H, H-3′, *cis* isomer), 6.22-6.35 (m, 3H; 2H, H-2′, both isomers and 1H, H-3′, *trans* isomer), 6.87-6.92 [m, 4H; consisting in at 6.89 (d, *J* 8.7, with fine splitting, 2H, ArH, *cis* isomer, with (d, *J* 8.7, 2H, ArH) for *trans* isomer merged], 7.13 (d, *J* 8.7, 2H, ArH, *cis* isomer), 7.19 (d, *J* 8.7, 2H, ArH, *trans* isomer); δ_C 13.6 (CH_3, *cis* isomer), 13.9 (CH_3, *trans* isomer), 20.2 (CH_2, *cis* isomer), 20.4 (CH_2, *trans* isomer), 29.6 (CH_2, *cis* isomer), 29.7 (CH_2, *trans* isomer), 55.1 (NCH_2, *cis* isomer), 55.2 (NCH_2, *trans* isomer), 58.0 (C-3, *cis* isomer), 58.8 (C-4, *cis* isomer), 61.2 (C-3, *trans* isomer), 63.2 (C-4, *trans* isomer), 117.2 (C-4′, *cis* isomer); 117.8 (C-4′, *trans* isomer), 125.1 (C-1′, both isomers), 126.8, 127.7, 129.3 (ArC, *trans* isomer); 127.2, 128.6 (ArC, *cis* isomer), 134.6 (C-2′, *trans* isomer), 135.2 (C-2′, *cis* isomer), 136.2 (C-3′, *trans* isomer), 136.3 (C-3′, *cis* isomer), 159.6 (ArC, *cis* isomer), 159.9 (ArC, *trans* isomer), 168.1 (C-2, *trans* isomer), 168.2 (C-2, *cis* isomer); *m/z* 285 (M^+), 186 (M^+-99). *Anal.* Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91. Found: C, 75.62; H, 8.16; N, 4.79.

***cis*-3-(1',3'-Butadienyl)-1-phenyl-4-(2″-phenylethenyl)azetidin-2-one (8a).** Yield 67%; viscous oil IR ν_{max}/cm^{-1} (CCl_4) 1741, 1598. 1494, 1380 and 1215; δ_H 4.22 (dd, *J* 6.9 and 6.1, 1H, H-3), 4.81 (dd, *J* 8.0 and 6.1, 1H, H-4), 5.09 (d, *J* 9.6, 1H, H-4′), 5.23 (d, *J* 16.0, 1H, H-4′), 5.66 (dd, *J* 14.5 and 6.9, 1H, H-1′), 6.19 (dd, *J* 15.9 and 8.0, 1H, H-1″), 6.25-6.44 (m, 2H, H-2′ and H-3′), 6.76 (d, *J* 15.9, 1H, H-2″), 7.03-7.08 (m, 1H, ArH), 7.22-7.53 (m, 9H, ArH); δ_C 57.0 (C-3), 58.1 (C-4), 114.7, 117.0, 118.4, 124.0, 124.7, 126.6, 126.7, 128.4, 128.5, 128.7, 129.1, 135.4, 135.7, 136.0, 136.3, 137.9, 165.4 (C-2); *m/z* 301 (M^+), 182 (M^+- Ph-N=C=O). *Anal.* Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.60; H, 6.31; N, 4.69.

***cis*-3-(1',3'-Butadienyl)-1-cyclohexyl-4-(2″-phenylethenyl)azetidin-2-one (8b).** Yield 71%; mp 84-85 °C (C_6H_6 : Hexane, 3:1 ratio) IR ν_{max}/cm^{-1} (KBr) 1736 1597, 1491, 1444 and 1393; δ_H 1.04-1.92 (series of m, 10H, cyclohexyl), 3.50 (dddd, *J* 11.7, 11.6, 3.8 and 3.8, 1H, cyclohexyl), 4.01 (dd, *J* 6.7 and 5.6, with fine splitting, 1H, H-3), 4.39 (dd, *J* 9.4 and 5.6, 1H, H-4), 5.07 (d, *J* 9.3, with fine

splitting, 1H, H-4′), 5.19 (d, *J* 16.9, with fine splitting, 1H, H-4′), 5.63 (dd, *J* 14.5 and 6.7, 1H, H-1′), 6.10 (dd, *J* 15.8 and 9.4, 1H, H-1″), 6.23-6.41 (m, 2H, H-2′ and H-3′), 6.64 (d, *J* 15.8, 1H, H-2″), 7.28-7.41 (m, 5H, ArH); δ_C 25.2, 30.6, 32.1, 52.0 (cyclohexyl); 56.4 (C-3), 57.5 (C-4), 117.8, 124.7, 126.6, 126.9, 128.2, 128.7, 134.4, 135.6, 136.0, 136.2, 167.1 (C-2); *m/z* 307 (M^+), 182 (M^+-125). *Anal.* Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 82.17; H, 8.18; N, 4.49.

***trans*-1,4-Diphenyl-3-[(*N*-phenyl)cyclohex-2′-ene-5′,6′-dicarboximido]azetidin-2-one (10).** To a 5M lithium perchlorate-etherate solution (5 mL) were added **3a** (0.3g, 1.10 mmol) and *N*-phenylmalemide (0.19 g, 1.12 mmol). The reaction mixture was stirred at rt for 12 h, the left over solvent was removed and the residue diluted with CH_2Cl_2 (20 mL). The solution was then washed with water (4 × 50 mL), dried over anhydrous sodium sulfate and evaporated under *vacuo*. The crude product thus obtained was purified by column chromatography on silica gel (EtOAc/hexane, 1:3) to give 0.42 g (86%) of adduct **(10)**; mp 250-251 °C (C_6H_6 : Hexane, 3:1 ratio) IR ν_{max}/ cm^{-1} (KBr) 1727, 1702, 1593, 1492 and 1379; δ_H 2.26-2.34 (m, 1H, H-4b), 2.84-2.95 (m, 2H, H-1′ and H-4a), 3.35 (unresolved dd, *J* 8.0 and 8.0, 1H, H-5′), 3.93 (dd, *J* 8.9 and 5.6, 1H, H-6′), 4.18 (dd, *J* 12.1 and 2.4, 1H, H-3), 4.73 (d, *J* 2.4, 1H, H-4), 5.96 (ddd, *J* 9.2, 3.2 and 3.2, 1H, H-2′), 6.11 (dddd, *J* 9.2, 6.7, 3.1 and 3.1, 1H, H-3′), 7.02-7.07 (m, 1H, ArH), 7.15-7.43 (m, 14H, ArH); δ_C 25.1 (C-1′), 37.3 (CH_2), 40.0 (C-5′/6′), 42.0 (C-6′/5′), 59.7 (C-3), 61.4 (C-4), 117.0, 124.0, 126.1, 126.4, 128.6, 128.7, 129.0, 129.1, 129.3, 129.5, 130.5, 131.7, 137.4, 137.5, 166.6 (C-2), 176.7 (NCO), 178.8 (OCN); *m/z* 448 (M^+), 329 (M^+- Ph-N=C=O). *Anal.*Calcd for $C_{29}H_{24}N_2O_3$: C, 77.66; H, 5.39; N, 6.25. Found: C, 77.87; H, 5.45; N, 6.18.

***cis*-1-Cyclohexyl-4-(2″-phenylethenyl)-3-[(*N*-phenyl)cyclohex-2′-ene-5′,6′-dicarboximido]azetidin-2-one (11).** A solution of **8b** (0.30 g, 0.98 mmol) and NPM (0.17 g, 0.98 mmol) in toluene (5 mL) was refluxed for 2 h. The solvent was removed under reduced pressure and the residue purified by chromatography on silica gel column (eluent: mixture of EtOAc/hexane in 1:3 ratio) affording a colorless solid (0.45 g, 96%); mp 154-155 °C (C_6H_6 : Hexane, 3:1 ratio) IR ν_{max}/ cm^{-1} (KBr) 1726, 1700, 1494, 1387 and 1188; δ_H 1.05-1.92 (series of m, 10H, cyclohexyl), 2.12-2.23 (m, 1H, H-1′), 2.70-2.88 (m, 2H, CH_2), 3.16 (ddd, *J* 7.1, 7.1 and 1.6, 1H, H-5′), 3.27 (dd, *J* 9.1 and 7.1, 1H, H-6′), 3.43-3.53 (m, 1H, cyclohexyl), 3.92 (dd, *J* 13.0 and 5.3, 1H, H-3), 4.59 (dd, *J* 9.2 and 5.3, 1H, H-4), 6.05 (dddd, *J* 9.5, 7.1, 3.0 and 3.0, 1H, H-3′), 6.26-6.36 [m, 2H; consisting in at 6.28 (ddd, *J* 9.5, 3.1 and 3.1, 1H, H-2′) and 6.32 (dd, *J* 15.9 and 9.2, 1H, H-1″)], 6.84 (d, *J* 15.9, 1H, H-2″), 7.15-7.16 (m, 1H, ArH), 7.18-7.19 (m, 1H, ArH), 7.32-7.46 (m, 8H, ArH); δ_C 24.0 (C-1′), 25.2, 30.7, 32.1 (cyclohexyl); 40.0 (C-5′/6′, 40.1 (C-6′/5′), 52.0 (cyclohexyl), 54.1 (C-3), 56.4 (C-4), 126.1, 126.4, 126.6, 128.0, 128.5, 128.7, 128.9, 129.1, 131.1, 135.2, 135.9, 168.5 (C-2), 176.6 (OCN), 178.5 (NCO); *m/z* 480 (M^+), 355 (M^+-125). *Anal.*

Calcd for $C_{31}H_{32}N_2O_3$: C, 77.47; H, 6.71; N, 5.83. Found: C, 77.56; H, 6.73; N, 5.79.

Diels-Alder adduct of 3b with DEF (12/13). A solution of **3b** (0.5 g, 1.64 mmol) and DEF (0.28 g, 1.65 mmol) in toluene (6 mL) was refluxed for 4-5 h, whereupon the solvent was removed under reduced pressure and the resulting residue purified by chromatography on 60-120 mesh silica gel (eluent: mixture of AcOEt/hexane in a 1:5 ratio), affording a viscous liquid (0.70 g, 90%) consisting in a mixture of diastereoisomers in 1:1.5 ratio IR ν_{max}/ cm^{-1} (KBr) 1719, 1590, 1493, 1374; δ_H 0.95 (t, *J* 7.1, 3H, CH_3, minor isomer), 1.10 (t, *J* 7.1, 3H, CH_3, major isomer), 1.20-1.28 [m, 6H, consisting in at 1.22 (t, *J* 7.1, 3H, CH_3, major isomer) and 1.25 (t, *J* 7.1, 3H, CH_3, minor isomer)], 2.14-2.55 (series of m, 3H; 2H, minor isomer and 1H, major isomer), 2.90-2.95 (m, 2H, major isomer), 3.08-3.17 (m, 4H, two each for both isomers), 3.26-3.29 (m, 1H, major isomer), 3.35-3.43 (m, 1H, minor isomer), 3.77 (s, 3H, OCH_3, minor isomer), 3.78 (s, 3H, OCH_3, major isomer), 3.77-3.81 (m, merged with -OCH_3 peaks, 1H, minor isomer), 3.95-4.15 (m, 8H, 4 × CH_2, both isomers), 5.76, (br d, 1H, olefinic, major isomer), 5.83-5.91 (m, 2H, olefinic, both isomers), 5.95-6.00 (m, 1H, olefinic, minor isomer), 6.85-6.89 [apparent dd, 4H, consisting in at 6.68 (d, *J* 8.7, 2H, ArH, minor isomers) and 6.87 (d, *J* 8.7, 2H, ArH, major isomer)], 6.99-7.03 (m, 2H, ArH, both isomers), 7.17-7.27 (m, 12H, both isomers); δ_C 13.8, 13.9, 14.1, 14.2 (4 × CH_3, both isomers); 27.8, 37.5, 42.8, 45.6, 55.3, 57.5, 60.8, 61.0, 63.0 (major isomer); 28.3, 35.7, 37.8, 44.6, 55.3, 58.9, 60.61, 60.64, 62.2 (minor isomer); 114.4, 114.5, 117.0, 117.1, 123.8, 124.3, 125.1, 127.4, 127.46, 127.50, 127.9, 129.0, 129.4, 137.4, 159.7 (both isomers); 165.5 (C-2, minor isomer); 165.6 (C-2, major isomer); 173.6, 174.2 (2 × CO_2Et, major isomer); 172.5, 175.3 (2 × CO_2Et, minor isomer); *m/z* 477 (M^+), 358 (M^+- Ph-N=C=O). *Anal.* Calcd for $C_{28}H_{31}NO_6$: C, 70.42; H, 6.54; N, 2.93. Found: C, 70.56; H, 6.44; N, 3.05.

Diels-Alder adducts of 5e/6e with DEF (14/15). A solution of **5d/6d** (0.5 g, 1.75 mmol) and DEF (0.30 g, 1.75 mmol) in toluene (8 mL) was refluxed for 6-7 h. An identical workup as described above afforded 0.69 g (86%) of viscous liquid consisting in a mixture of diastereoisomers 14/15 in 1:1.5 ratio IR ν_{max}/ cm^{-1} (KBr) 1727, 1599, 1501 and 1383; δ_H 0.84-1.41 (series of m, 22H, both isomers), 2.07-2.32 (m, 3H; 2H, major isomer and 1H, minor isomer), 2.38-2.85 (series of m, 8H, both isomers), 2.94-3.07 (m, 3H; 2H, minor isomer and 1H, major isomer), 3.45-3.56 (m, 4H, both isomers), 3.81 (s, 3H, OCH_3, minor isomers), 3.84 (s, 3H, OCH_3, major isomer), 3.89-4.16 (m, 10H, both isomers), 4.64 (d, *J* 5.3, H-4, 1H, major isomer), 4.70 (d, *J* 5.0, 1H, H-4, minor isomer), 5.78-6.01 (series of m, 4H, olefinic, both isomers), 6.91 (d, *J* 8.7, 2H, ArH, minor isomer), 6.94 (d, *J* 8.8, 2H, ArH, major isomer)], 7.16-7.20 [m, 4H, ArH; consisting in at 7.17 (d, *J* 8.8, 2H, major isomer) and 7.18 (d, *J* 8.7, 2H, minor isomer)]; δ_C 13.6, 13.9, 14.1, 14.2, 20.2, 25.6, 27.3, 29.47, 29.50, 31.9, 33.4, 38.4, 39.9, 40.0, 40.6, 43.3, 45.4,

55.26, 55.30, 56.5, 58.1, 58.2, 60.6, 60.8, 114.1, 114.3, 125.8, 126.2, 126.8, 127.0, 127.4, 128.8, 129.1, 159.6 (both isomers); 168.7 (C-2, both isomers), 173.1, 174.6 (CO_2Et, both isomers); *m/z* 457 (M^+), 358 (M^+- 99). Anal. Calcd for $C_{26}H_{35}NO_6$: C, 68.25; H, 7.71; N, 3.06. Found: C, 68.37; H, 7.66; N, 2.99.

Diels-Alder adduct of 3a and EA (16/17/18/19). A solution of **3a** (0.50 g, 1.82 mmol) and EA (0.40 g, 4.0 mmol) in toluene (8 mL) was refluxed for 26 h. The solvent was removed under *vacuo* and the residue purified by column chromatography on silica gel (eluent: EtOAc/hexane, in a 1:4 ratio) affording a viscous liquid consisting in a mixture of *trans* diastereo/regioisomers in 5:4:2:1.2 ratio IR ν_{max}/ cm^{-1} (CCl_4) 1721(br), 1590, 1493 and 1380 cm^{-1}; δ_H 0.87-1.07 (m, 9H, 3 × CH_3, three isomers), 1.96 (t, *J* 7.1, 3H, CH_3, one isomer) 1.22-1.30 (m, 4H, all isomers), 1.76-2.25 (series of m, 16H, all isomers), 2.59-4.22 (series of m, 16H, all isomers), 4.77 (d, *J* 2.3, 1H, H-4, one isomer), 4.80 (d, *J* 2.5, 1H, H-4, one isomer), 4.85 (d, *J* 1.9, 1H, H-4, one isomer), 4.88 (d, *J* 2.2, 1H, H-4, one isomer), 5.86-6.03 (series of m, 8H, olefinic, all isomers), 7.00-7.04 (m, 4H, ArH, all isomers), 7.22-7.35 (m, 36H, ArH, all isomers); δ_C 13.9, 14.0, 14.1, 14.2, 22.1, 22.3, 23.7, 24.0, 25.3, 27.8, 29.7, 35.3, 36.0, 36.4, 36.5, 37.1, 42.1, 42.3, 43.5, 43.6, 58.5, 59.5, 60.2, 60.6, 60.7, 61.4, 61.7, 62.2, 63.1, 64.0, 64.3, 116.9, 117.0, 117.1, 118.5, 123.7, 123.8, 124.0, 124.9, 125.1, 125.2, 125.5, 125.8, 126.0, 126.2, 126.5, 127.4, 128.4, 128.6, 128.9, 129.0, 129.1, 129.2, 130.0, 135.5, 135.9, 137.5, 137.6, 137.7, 137.8; 166.1, 166.2, 166.38, 166.42 (C-2, all isomers); 173.0, 173.1, 174.4, 175.2 (CO_2Et, all isomers); *m/z* 375 (M^+), 256 (M^+- Ph-N=C=O). *Anal.* Calcd for $C_{24}H_{25}NO_3$: C, 76.77; H, 6.71; N, 3.73. Found: C, 76.60; H, 6.78; N, 3.66.

Diels-Alder adduct of 5e/6e with EA (20/21/22/23). A solution of **5/6e** (0.3 g, 1.06 mmol) and EA (0.25 g, 2.50 mmol) in toluene (5 mL) was refluxed for 30 h. An identical workup as employed above afforded 0.35 g (86%) of a viscous liquid consisting in a mixture of four *cis* diastereo/regioisomers in 11:4:2.5:1 ratio IR ν_{max}/ cm^{-1} (CCl_4) 1725 (br), 1589, 1489 and 1381 cm^{-1}; δ_H 0.85-1.47 (series of m, 40H, all isomers), 1.71-2.32 (series of m, 16H, all isomers), 2.49-2.90 (series of m, 10H), 3.35-3.57 (m, 7H, all isomers), 3.61 (dd, *J* 10.6 and 5.2, 1H, H-3, one isomer), 3.79-3.90 (m, 14H; consisting in 12H for four OCH_3 signals at δ 3.81, 3.82, 3.84, and 3.86 as singlets), 4.02-4.27 (series of m, 8H, all isomers), 4.68 (d, *J* 5.2, 1H, H-4, one isomer), 4.72 (d, *J* 5.1, 1H, H-4, one isomer), 4.77 (d, *J* 5.2, 1H, H-4, one isomer), 4.79 (d, *J* 5.3, 1H, H-4, one isomer), 5.70-5.75 (m, 4H, olefinic), 5.85-5.95 (m, 4H, olefinic), 6.89-6.94 (m, 8H, ArH, merged doublets for all isomers, *J* ~ 8.7), 7.20-7.24 (m, 8H, ArH; merged doublets for all isomers, *J* ~ 8.7); δ_C 13.6, 14.0, 14.1, 14.2, 14.3, 20.1, 20.2, 20.9, 21.7, 21.9, 22.8, 23.2, 24.1, 29.51, 29.55, 29.64, 29.7, 32.1, 33.5, 39.5, 39.6, 39.8, 40.7, 55.2, 55.3, 56.6, 57.5, 57.6, 57.9, 58.0, 58.6, 58.8, 60.0, 60.1, 60.6, 61.3, 113.9, 114.0, 114.1, 114.2, 114.29, 114.34, 117.4, 126.0, 126.3, 127.0, 127.1, 127.4, 127.5, 127.7, 128.1, 128.3, 128.6, 128.9, 132.0, 133.6, 135.4, 136.3,

159.6, 159.7; 169.3, 169.6 (C-2, all isomers); 173.7, 174.5, 174.9 (CO_2Et, all isomers); *m/z* 385 (M^+), 286 (M^+- *n*-Bu-N=C=O). *Anal.*Calcd for $C_{23}H_{31}NO_4$: C, 71.66; H, 8.11; N, 3.63. Found: C, 71.57; H, 8.20; N, 3.74.

***trans*-1-Phenyl-4-(2″-phenylethenyl)-7',9'-dioxo-3-[8'-phenyl1',6',8'triaza[4.3.0]bicyclonon-3'-enyl] azetidin-2-one (24b).** To a stirred solution of PTAD (0.58 g, 3.32 mmol) in CH_2Cl_2 (25 mL) at 0 °C was added **8a** (1.0 g, 3.32 mmol) in portions over a period of 5 min. The solution was stirred at rt for an additional 10 min. The crude product obtained after removal of the solvent was purified by recrystallisation from EtOAc to yield 1.50 g (95%) of the adduct **(24b)**; mp 186-187 °C IR ν_{max}/ cm^{-1} (KBr) 1741, 1704, 1596, 1499 and 1418; δ_H 3.49 (dd, *J* 10.3 and 2.3, 1H, H-3), 3.98 (dq, *J* 16.8 and 2.3, 1H, CH_2), 4.35 (m, 1H, CH_2), 5.01-5.07 (m, 1H, H-1′), 5.19 (dd, *J* 9.0 and 2.3, 1H, H-4), 6.04 (dddd, *J* 10.0, 4.1, 2.0 and 2.0, 1H, olefinic), 6.15 (dd, *J* 15.9 and 9.0, 1H, H-1″), 6.41 (dddd, *J* 10.0, 4.7, 2.3 and 2.3, 1H, olefinic), 6.77 (d, *J* 15.9, 1H, H-2″), 7.03-7.09 (m, 1H, ArH), 7.15-7.19 (m, 2H, ArH), 7.23-7.24 (m, 10H, ArH), 7.42 (d, *J* 8.5, with fine splitting, 2H, ArH); δ_C 44.4 (C-1′), 52.8 (CH_2), 58.7 (C-3), 60.6 (C-4), 116.9, 121.8, 123.5, 124.3, 125.4, 125.9, 126.7, 128.4, 128.5, 128.6, 129.1, 130.5, 135.1, 135.6, 137.6, 151.7, 153.5, 162.5 (C-2); *m/z* 476 (M^+), 357 (M^+- Ph-N=C=O). *Anal.* Calcd for $C_{29}H_{24}N_4O_3$: C, 73.09; H, 5.08; N, 11.76. Found: C, 73.23; H, 4.99; N, 11.68.

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15. These aldehydes were particularly chosen because of the reported *in vivo* activity of monocyclic

β-lactams, having an aryl, especially p-methoxyphenyl group at 4-position alongwith an extended carbon chain at 3-position, in cholesterol-fed hamster model.[9]

16. The assignment of the *cis* stereochemistry to the β-lactam **(5a)** and **(5b)** was based on the observed coupling constant of about 5.6 Hz for methine protons H-3 and H-4.

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