90. The Asymmetric Synthesis of Fused Cyclopentenone Ring Systems: A Formal Asymmetric Total Synthesis of (−)-Isocomene

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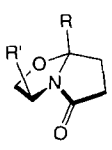
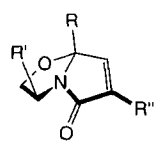
Optically active tricyclic oxazolidine lactams **10** have been prepared using two different routes (*Scheme 1*). They can be obtained by acid-mediated intramolecular cyclization of bicyclic lactams **13** *via* their acyliminium intermediates producing appended five-, six-, and seven-membered tricyclic systems. Alternatively, **10** can be prepared by cyclocondensation of chiral amino alcohols with cyclopentane-1,2-dicarboxylic acids **12** to give the imide which is reduced or alkylated to the amino alcohols and cyclized to a diastereoisomer mixture of **10**. Alkylation of **10** (R″ = H) *via* its enolate gives stereospecifically α-quaternary products **10** (R″ = alkyl). Degradation of the latter with MeLi or *Red-Al*® followed by mild acid hydrolysis and aldol cyclization produces the bicyclic ketones **14** and **15** as 1:1 mixtures, readily separated and isolated in > 99% ee. This sequence produced a known non-racemic intermediate **69** for the synthesis of (−)-isocomene.

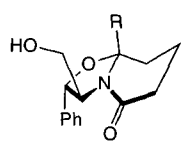
1. Introduction. – Over the past several years, we have reported the synthesis of a number of chiral, non-racemic compounds containing quaternary C-atoms that have been produced from bicyclic lactams of the type **1–3** [1]. These oxazolidine lactams were prepared by one of two methods: *a*) by the reaction of a keto acid and an amino alcohol [2] or *b*) from an amino-alcohol-derived succinimide which is reductively alkylated [3]. Elaboration of the bicyclic lactams was performed either by alkylation of the lactam



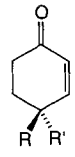
1 R = H, Me
R' = i-Pr, *t*-Bu



2 R = H, Me
R' = i-Pr, *t*-Bu
R'' = H, Me, CO_2Me



3 R = H, Me



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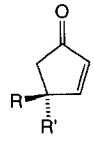

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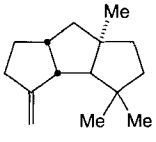

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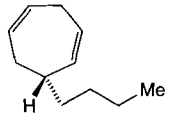

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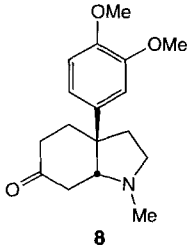

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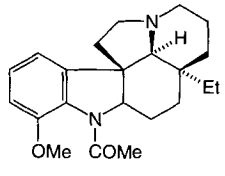

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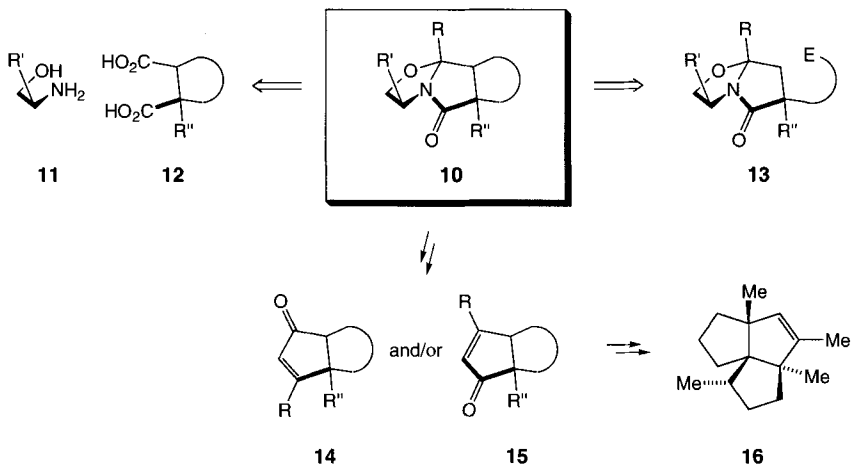
enolates of the saturated compounds **1** and **3** or by cycloaddition reactions to the C=C bond of **2**. Examples of enantiomerically pure carbocycles which were prepared by this route include cyclohexenones **4** [4], cyclopentenones **5** [5], and the natural products (+)-$\Delta^{9(12)}$-capnellene (**6**) [6], (−)-dyctopterene C′ (**7**) [7], (+)-mesembrine (**8**) [8], and (+)-aspidospermine (**9**) [9a] (more recently, we have extended this work to chiral piperidines, pyrrolidines, and related natural products [9b]).

Scheme 1



To extend the synthetic versatility of these bicyclic lactams, we began a study aiming at the synthesis of tricyclic compounds of type **10** (*Scheme 1*). Such compounds should be accessible by two paths: either by the condensation of amino alcohols **11** with cycloalkane-1,2-dicarboxylic acids **12** (succinimide path [3]) or by the novel acid-catalyzed annulation reaction of bicyclic lactam derivatives of type **13**, as described in our preliminary communication [10]. We now report the synthesis of tricyclic lactams of type **10** using both strategies, and also the subsequent transformations of such compounds **10** into fused cyclopentenone ring systems of type **14** and **15**. Included is the preparation of a key intermediate for the enantiospecific synthesis of (−)-isocomene ((−)-**16**).

2. Synthesis of Tricyclic Lactams of Type 10. – 2.1. *Intramolecular Acid-Catalyzed Annulation.* Oxazolidine derivatives of type **13**, tethered to carbonyl functions as the electrophilic groups (E) on the side chain, were obtained in several steps from the simple precursors **17**–**19** (*Scheme 2*). Deprotonation at C(α) of the lactams **17**–**19** with lithium diisopropylamide (LDA) in THF at −78° and reaction of the corresponding enolates with ω-halogenoalkenes or 2-(2-iodoethyl)-1,3-dioxolane in the presence of *N*,*N*′-dimethylpropyleneurea (= 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one; DMPU) afforded the α-monosubstituted derivatives **20a**,**b**–**26a**,**b** (*Table 1*). In addition, a small quantity of the doubly alkylated compounds **22c**, **23c**, **25c**, and **26c** was frequently

Table 1. *α-Alkylations of Bicyclic Lactams* **17–19** *with Organic Halides* (see *Scheme 2*)

Substrate	Products							
		R	R′	R″	R‴	Yield [%]	dr
17[a])	**20a**	Me	i-Pr	H	CH_2=C(Me)CH_2CH_2	46	1.4:1
	20b	Me	i-Pr	CH_2=C(Me)CH_2CH_2	H	33	
17[a])	**21a**	Me	i-Pr	H	$OCH_2CH_2OCHCH_2CH_2$	44	1.5:1
	21b	Me	i-Pr	$OCH_2CH_2OCHCH_2CH_2$	H	30	
17[a])	**22a**	Me	i-Pr	H	CH_2=$CHCH_2CH_2CH_2$	38	1.5:1
	22b	Me	i-Pr	CH_2=$CHCH_2CH_2CH_2$	H	25	
	22c	Me	i-Pr	CH_2=$CHCH_2CH_2CH_2$	CH_2=$CHCH_2CH_2CH_2$	13	
17[a])	**23a**	Me	i-Pr	H	CH_2=$CHCH_2CH_2CH_2CH_2$	49	1.8:1
	23b	Me	i-Pr	CH_2=$CHCH_2CH_2CH_2CH_2$	H	27	
	23c	Me	i-Pr	CH_2=$CHCH_2CH_2CH_2CH_2$	CH_2=$CHCH_2CH_2CH_2CH_2$	7	
18[a])	**24a**	H	i-Pr	H	CH_2=C(Me)CH_2CH_2	32	1.7:1
	24b	H	i-Pr	CH_2=C(Me)CH_2CH_2	H	19	
19[a])	**25a**	H	*t*-Bu	H	CH_2=$CHCH_2CH_2CH_2$	47	1.8:1
	25b	H	*t*-Bu	CH_2=$CHCH_2CH_2CH_2$	H	27	
	25c	H	*t*-Bu	CH_2=$CHCH_2CH_2CH_2$	CH_2=$CHCH_2CH_2CH_2$	7	
19[a])	**26a**	H	*t*-Bu	H	CH_2=$CHCH_2CH_2CH_2CH_2$	42	2.0:1
	26b	H	*t*-Bu	CH_2=$CHCH_2CH_2CH_2CH_2$	H	21	
	26c	H	*t*-Bu	CH_2=$CHCH_2CH_2CH_2CH_2$	CH_2=$CHCH_2CH_2CH_2CH_2$	13	
20a/20b	**27a**	Me	i-Pr	Me	CH_2=C(Me)CH_2CH_2	9	1:10.6
	27b	Me	i-Pr	CH_2=C(Me)CH_2CH_2	Me	84	
21a/21b	**28a**	Me	i-Pr	Me	$OCH_2CH_2OCHCH_2CH_2$	7	1:9.3
	28b	Me	i-Pr	$OCH_2CH_2OCHCH_2CH_2$	Me	74	
22a/22b	**29a**	Me	i-Pr	Me	CH_2=$CHCH_2CH_2CH_2$	8	1:10.0
	29b	Me	i-Pr	CH_2=$CHCH_2CH_2CH_2$	Me	80	
23a/23b	**30a**	Me	i-Pr	Me	CH_2=$CHCH_2CH_2CH_2CH_2$	11	1:7.5
	30b	Me	i-Pr	CH_2=$CHCH_2CH_2CH_2CH_2$	Me	83	
25a/25b	**31a**	H	*t*-Bu	Me	CH_2=$CHCH_2CH_2CH_2$	5	1:18.4
	31b	H	*t*-Bu	CH_2=$CHCH_2CH_2CH_2$	Me	92	
26a/26b	**32a**	H	*t*-Bu	Me	CH_2=$CHCH_2CH_2CH_2CH_2$	6	1:16
	32b	H	*t*-Bu	CH_2=$CHCH_2CH_2CH_2CH_2$	Me	94	

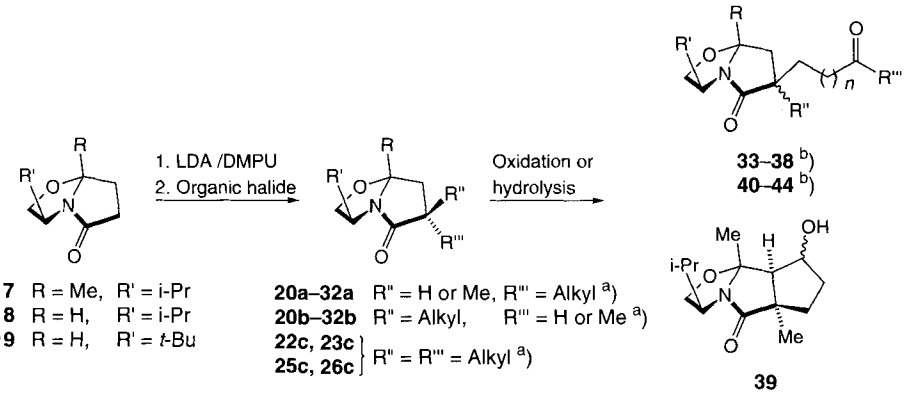
[a]) See [1b] for the synthesis of these chiral lactams.

Table 2. *Conversion of the α-Alkylated Bicyclic Lactams* **20a, b**, **24a, b**, **27a, b**, *and* **29b–32b** *to the Annulation Precursors* **33–38** *and* **40** **44** *and of* **28b** *to* **39** (see *Scheme 2*)

Substrate	Conditions	Products						
			R	R′	R″	R‴	*n*	Yield [%]
20a	O_3, Me_2S	**33**	Me	i-Pr	H (*'exo'*)	Me	1	89
20b	O_3, Me_2S	**34**	Me	i-Pr	H (*'endo'*)	Me	1	91
24a	O_3, Me_2S	**35**	H	i-Pr	H (*'exo'*)	Me	1	71
24b	O_3, Me_2S	**36**	H	i-Pr	H (*'endo'*)	Me	1	93
27a	O_3,Me_2S	**37**	Me	i-Pr	Me (*'exo'*)	Me	1	95
27b	O_3, Me_2S	**38**	Me	i-Pr	Me (*'endo'*)	Me	1	98
28b	HCl/H_2O[a])	**39**[a])	Me	i-Pr	Me (*'endo'*)	H[a])	1	77[a])
29b	O_3, Me_2S	**40**	Me	i-Pr	Me (*'endo'*)	H	2	90
29b	$CuCl_2/PdCl_2$, O_2	**41**	Me	i-Pr	Me (*'endo'*)	Me	2	35
30b	O_3, Me_2S	**42**	Me	i-Pr	Me (*'endo'*)	H	3	97
31b	O_3, Me_2S	**43**	H	*t*-Bu	Me (*'endo'*)	H	2	94
32b	O_3, Me_2S	**44**	H	*t*-Bu	Me (*'endo'*)	H	3	98

[a]) These conditions led to an annulated product directly (see *Exper. Part*).

Scheme 2



17 R = Me, R' = i-Pr
18 R = H, R' = i-Pr
19 R = H, R' = *t*-Bu

20a–32a R" = H or Me, R"' = Alkyl a)
20b–32b R" = Alkyl, R"' = H or Me a)
22c, 23c, **25c, 26c** R" = R"' = Alkyl a)

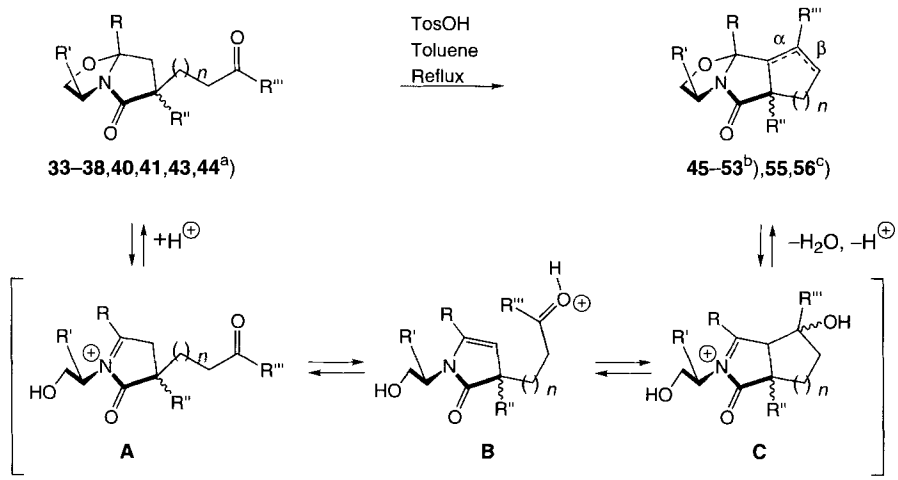
a) See *Table 1* for R, R', R", and R"'. b) See *Table 2* for R, R', R", R"', and *n*.

isolated. The monosubstituted compounds were resubjected to the procedure of deprotonation and alkylation and gave, almost quantitatively, the α,α-disubstituted products **27a,b–32a,b**. On the second alkylation process, the '*endo*' entry always exceeded the '*exo*' entry by a ratio of *ca.* 8:1 to 20:1 (*Table 1*) [1]. Ozonolysis of the olefinic bond in **20a,b**, **24a,b**, **27a**, **b**, and **29b–32b** followed by reductive workup or *Wacker* oxidation of **29b** produced **33–38** and **40–44** possessing the electrophilic carbonyl function which was required for the annulation process (*Table 2*). Hydrolysis of **28b** led directly to the annulated product **39**.

The configurational assignments of the '*endo*'/'*exo*' products are mainly based on ^{1}H-NMR data whereby the chemical shifts of the signals derived from '*exo*'-positioned H–C(α) or Me–C(α) are characteristically shifted downfield by *ca.* 0.25 and 0.15 ppm as compared to the corresponding signals arising from '*endo*' groups. *E.g.*, the resonances of the H–C(α) of **20a** and **20b** appear at δ 2.80 ($H_{'exo'}$) and 2.67 ($H_{'endo'}$), respectively, whereas the resonances for Me–C(α) of **27a** and **27b** were found at δ 1.30 ($Me_{'exo'}$) and 1.17 ($Me_{'endo'}$). The assignments are further supported by ^{1}H-NOE (nuclear *Overhauser* effect) experiments performed with the cyclized products and by chemical correlations (see below). A tentative assignment of the '*endo*'/'*exo*' configuration is also possible from the relative chromatographic behavior and the optical rotations of the corresponding products. The compounds with the (larger) alkyl group positioned '*endo*' showed in all cases higher R_f values on TLC and lower (positive) $[\alpha]_D^{23}$ values than the corresponding '*exo*' products.

The cyclizations were performed [10] by treatment of the aldehydes or ketones **33–38**, **40**, **41**, **43**, and **44** with toluene-4-sulfonic acid (TosOH) in toluene at reflux. This furnished the tricyclic products **45–53** (**51** from **39** by H_2O elimination) and **55** (n = 1, 2; C=C bond in β-position) or **56** (n = 3; C=C bond in α-position, from **44**) (*Scheme 3*, *Table 3*). The formation of the tricyclic compounds may be envisioned as proceeding through the series of intermediates as shown in *Scheme 3*. Acid-catalyzed fragmentation of the oxazolidine ring of the chiral lactam would afford *N*-acyliminium ions **A**, which may be in equilibrium with enamides **B** [11–15]. Nucleophilic attack of the enamide π-system at the electrophilic ketone or aldehyde group of the side chain, activated by protonation, could afford **C**, which upon loss of H_2O and recyclization would furnish the tricyclic products **45–53**, **55**, and **56**.

Scheme 3



a) See *Table 2* for R, R′, R″, R‴, and *n*. b) **51** from **39** by H_2O elimination. c) See *Table 3* for R, R′, R″, R‴, ring size (*n*), and C=C bond position.

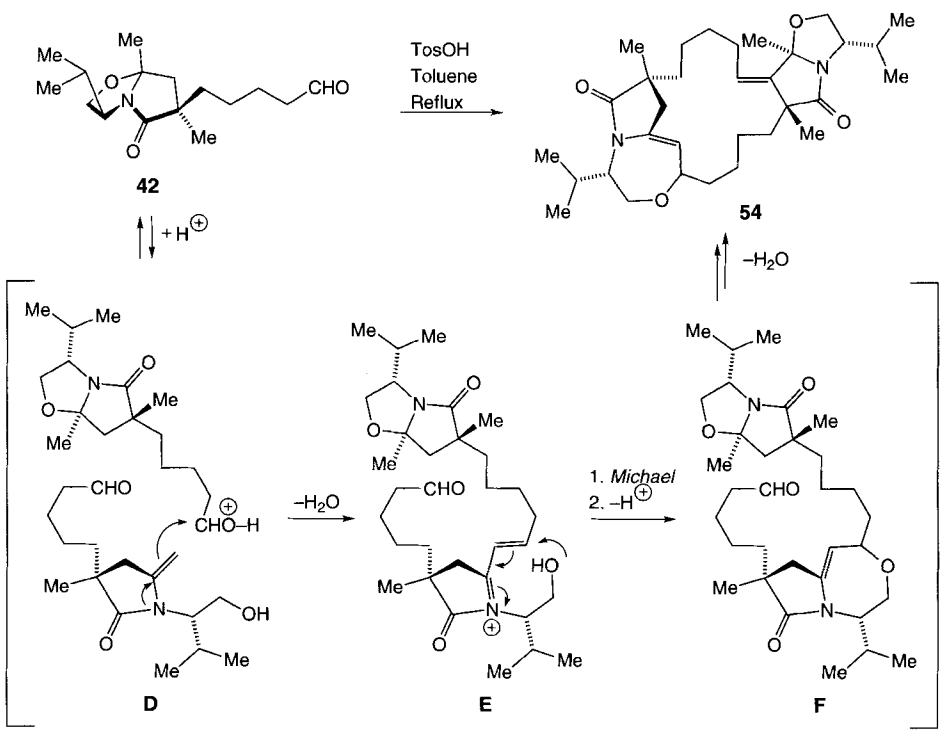
Based on the above, the annulation of a five- or six-membered ring ($n = 1, 2$) onto a bicyclic system of type **17–19** appears to proceed rather smoothly. The entropically favored intramolecular attack of the postulated enamide **B** to the carbonyl groups of the side chains seems sufficiently facile to preclude any intermolecular reactions from becoming competitive. When larger rings were attempted in this annulation, however, the

Table 3. *Annulation Reaction of Bicyclic Oxazolidines* **33–38** *and* **40–44**, *and of Tricyclic Oxazolidine* **39** *to the Tricyclic Derivatives* **45–56** (see *Scheme 3*)

Substrate	Reaction time[a] [min]	Products	R	R′	R″	R‴	Ring size	Double bond	Yield [%]
33/34	240	**45**	Me	i-Pr	H (*'exo'*)	Me	5	β	57
		46	Me	i-Pr	H (*'endo'*)	Me	5	β	0 (57, total)
35/36	90	**47**	H	i-Pr	H (*'exo'*)	Me	5	β	23
		48	H	i-Pr	H (*'endo'*)	Me	5	β	38 (61, total)
37	45	**49**	Me	i-Pr	Me (*'exo'*)	Me	5	β	80
38	30	**50**	Me	i-Pr	Me (*'endo'*)	Me	5	β	80
39	15	**51**	Me	i-Pr	Me (*'endo'*)	H	5	β	84
40	10	**52**	Me	i-Pr	Me (*'endo'*)	H	6	β	90
41	30	**53**	Me	i-Pr	Me (*'endo'*)	Me	6	β	89
42	480	**54**[b]	–	–	–	–	(7)	–	25
43	30	**55**	H	*t*-Bu	Me (*'endo'*)	H	6	β	87
44	240	**56**	H	*t*-Bu	Me (*'endo'*)	H	7	α	24

a) In refluxing toluene in the presence of TosOH (cat.) until starting material was consumed.
b) The 'dimer' **54** was isolated (*Scheme 4*).

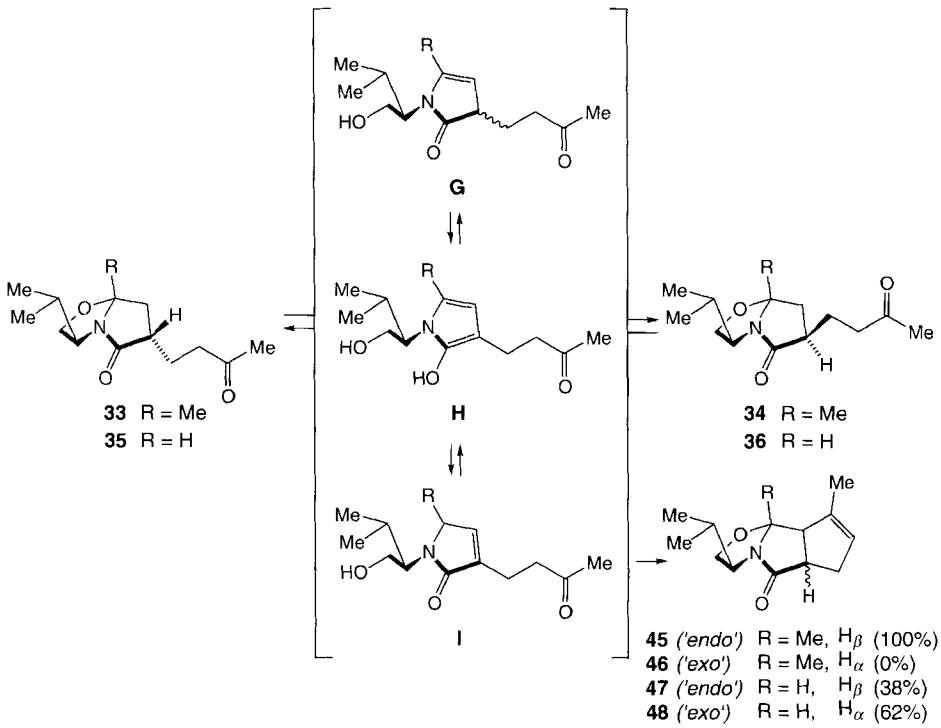
Scheme 4



cyclization step became more sluggish. Only after prolonged heating did lactam **44** ($n = 3$, annulation of a seven-membered ring) produce any cyclized product **56**, although in low yield (24%). However, aldehyde **42** did not afford the annulation product but only the 'dimeric' compound **54** (25%; *Scheme 4*). Not surprisingly, its formation can be explained by invoking enamide condensations. Thus, the intermolecular reaction of enamide **D** with the aldehyde group of a second molecule **42** could give **E**, which should furnish **F** after *Michael* addition of the valinol OH group to the α,β-unsaturated acyliminium system. Subsequent condensation of the second aldehyde group and the second bicyclic lactam portion would account for the observed product **54**.

It was also observed that the stereochemistry of the annulations appears to be thermodynamically controlled (*Scheme 5*). In all cases, the expected, more stable, *cis*-fused polycycles were formed. The epimeric monosubstituted precursors **33** and **34** (R = Me) or **35** and **36** (R = H) afforded, regardless of the configuration at C(α) in the starting material, the same product or mixture of products. Thus, **45** was obtained from **33** and **34**, and **35** and **36** gave both the mixture **47**/**48** 38:62. Furthermore, cyclization of the α-substituted bicyclic lactams (R″ = H) proceeded with much lower rates than that of the α,α-disubstituted ones (R″ = H; 90–240 *vs.* R″ = Me; 10–45 min for complete conversion), and the yields of the tricyclic products **45**–**48** with R″ = H were comparatively lower than that of the tricyclic products **49**–**53** with R″ = Me (57–61 *vs.* 80–90%).

Scheme 5



GC Analysis revealed that, prior to cyclization, a fast acid-catalyzed epimerization at C(α) of the starting lactams **33** and **35** occurred (H_β preference *ca.* 4:1). The annulation products **45** or the mixture **47**/**48** were detected later. The rapid equilibration and the slow ring formation can be explained assuming that intermediates of type **G**–**I** (*Scheme 5*) are present in the equilibrium mixture. The relative population of these species has been shown to depend on the nature of the substituents on the five-membered ring [16] [17]. In most cases, the α,β-unsaturated lactam **I** is the most stable form, followed by the β,γ-unsaturated lactam **G**. The aromatic system **H** is proposed as intermediate in the conversion **G**⇆**I**. With the ready formation and a high population of **I** (or **H**), one could then rationalize the slow ring closure.

The final ratio of '*endo*' and '*exo*' products **45**–**48** does not reflect the relative stabilities of the '*endo*'- and '*exo*'-alkylated annulation precursors **33**–**36**. We think that the ratio of products are thermodynamically controlled, *i.e.*, by the relative stabilities of the annulation products **45**–**48**. The assumption is based on two facts: *i*) no preference of either '*endo*' or '*exo*' attack was observed for the α,α-disubstituted bicyclic lactams and *ii*) under the acidic reaction conditions, the '*endo*' and '*exo*' products (**45**/**46**, **47**/**48**) should be in equilibrium with each other *via* intermediates similar to **G**–**I**. The exclusive formation of the '*endo*'-annulated product **45** from **33** and **34** as compared to the formation of a mixture **47**/**48** 38:62 ('*endo*'-annulated/'*exo*'-annulated) from **35** and **36**

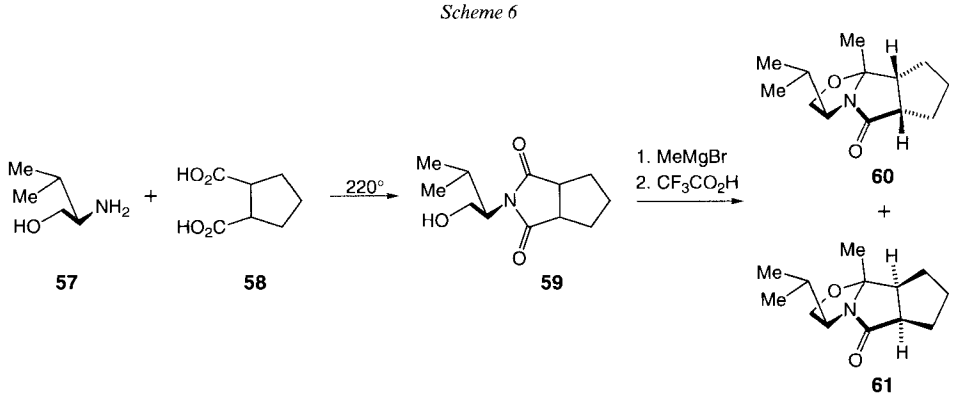
can be explained by invoking an unfavorable steric interaction. In the '*endo*'-annulated **46**, the Me group at the cyclopentene moiety may be too close to the angular Me group at the lactam ring, an interaction which is absent in **45**. In the case of **47** and **48**, no such steric interaction between the Me group and the angular H-atom occurs, and the '*exo*'-annulated product **48** is more favored.

The configurational assignments for **45**–**48** were established by ^{1}H-NOE experiments. Since only one of the two possible isomers **45** and **46** was formed, and the signals for H–C(α) of **47** and **48** could not be assigned unambiguously, the relative chemical shifts of H–C(α) could not be used as evidence. By irradiation at the absorption frequencies of the angular substituents of **45** (Me) and **47** (H), distinct NOE enhancements were observed for the signals of the *cis*-positioned protons, confirming the '*endo*'-annulation of the cyclopentene ring (see *Exper. Part*). The configurations of the chiral centers of **45** were additionally secured by chemical correlation. Thus, deprotonation of **45** with LDA, followed by trapping of the enolate with MeI in presence of DMPU, furnished the '*endo*'-annulated product **49** in 70% yield which was identical in every respect with **49** obtained from **37** by the annulation reaction. The configuration of **37** was assigned from its precursor **27a**.

2.2. *Condensation of Cycloalkane-1,2-dicarboxylic Acids.* Tricyclic lactams were also readily accessible from cycloalkane-1,2-dicarboxylic acids. *E.g.*, condensation of neat (+)-(*S*)-valinol (**57**) with dicarboxylic acid **58** at 220° for 2.5 h afforded imide **59** (99%). Addition of MeMgBr to either one of the carboxy groups followed by acid cyclization of the intermediate with CF_3CO_2H produced pure tricyclic lactams **60** and **61** in 17.5 and 26.5% yield, respectively, after isolation (*Scheme 6*). The ratio of products most probably reflects their relative stabilities rather than the regioselectivity of the addition of MeMgBr to **59**. The tricyclic lactams **60** and **61** can, as previously mentioned for **33**–**36**, undergo epimerization in an acid-catalyzed equilibrium of intermediates such as **G**–**I** (*Scheme 5*). Despite the low chemical as well as stereochemical efficiency, the preparation of tricyclic oxazolidines **60** and **61** is still convenient, due to the low number of synthetic steps and the simple procedures involved.

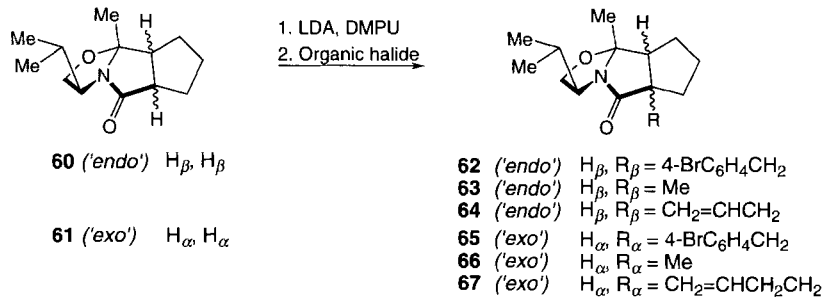
The tricyclic oxazolidine derivatives **60** and **61** can be readily alkylated at C(α) by deprotonation and quenching of the resulting enolate with alkyl halides (*Scheme 7*). Thus, enolization of **60** with LDA, followed by treatment with 4-bromobenzyl bromide, allyl bromide, or MeI, afforded **62**–**64** as single diastereoisomers. Likewise, **61** gave rise to **65**–**67** by sequential treatment with base and electrophiles. The products **62** and **65** allowed the relative configuration of the annulated rings to be readily assigned. The

Scheme 6



57 **58** **59**

Scheme 7



60 *('endo')* H_β, H_β

61 *('exo')* H_α, H_α

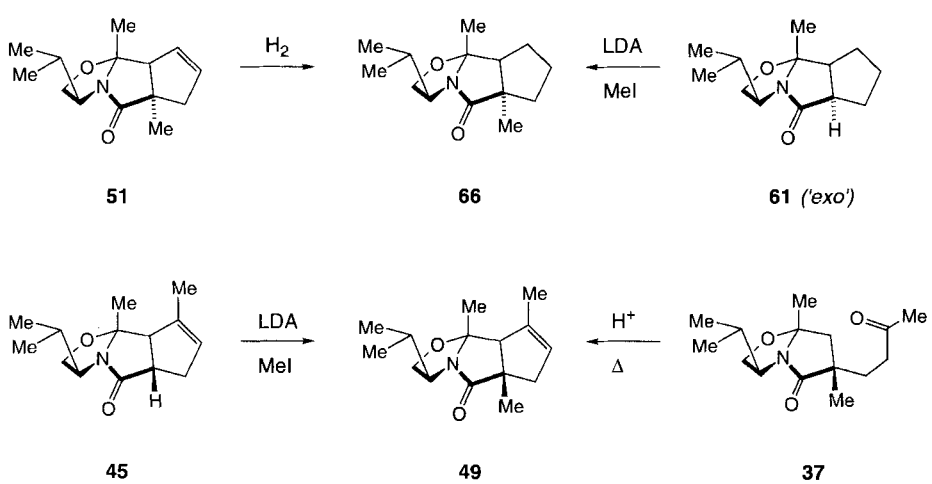
62 *('endo')* H_β, R_β = 4-$BrC_6H_4CH_2$
63 *('endo')* H_β, R_β = Me
64 *('endo')* H_β, R_β = CH_2=$CHCH_2$
65 *('exo')* H_α, R_α = 4-$BrC_6H_4CH_2$
66 *('exo')* H_α, R_α = Me
67 *('exo')* H_α, R_α = CH_2=$CHCH_2CH_2$

angular Me group of **62** suffers a significant upfield shielding effect (δ 0.69), due to the anisotropy of the aromatic ring of the *cis*-positioned 4-bromobenzyl substituent [18], an effect that is not observed for **62** (δ 1.14).

It is of interest that the alkylations of oxazolidine derivatives **60** and **61** proceeded from the face of the enolate so as to retain the original '*exo*'- or '*endo*'-*cis*-fusion of the 5,5-bicyclic system. This was confirmed by catalytic hydrogenation of the cyclopentene derivative **51**, obtained by the annulation process described above. Compound **66** obtained by hydrogenation of **51** was identical with **66** derived from metalation/alkylation of **61** (*Scheme 8*). Additionally, when the tricyclic lactam **45** was treated with LDA and MeI, it gave **49**, identical to the product obtained from keto lactam **37** under annulation conditions.

2.3. *Conversion to Fused Chiral Cyclopentenones.* The saturated tricyclic systems **63**, **64**, and **67** were readily converted to *ca.* 1:1 mixtures of isomeric bicyclo[3.3.0]octenones **68**–**73** by successive treatment with MeLi, aqueous $(Bu_4N)H_2PO_4$ solution, and EtONa

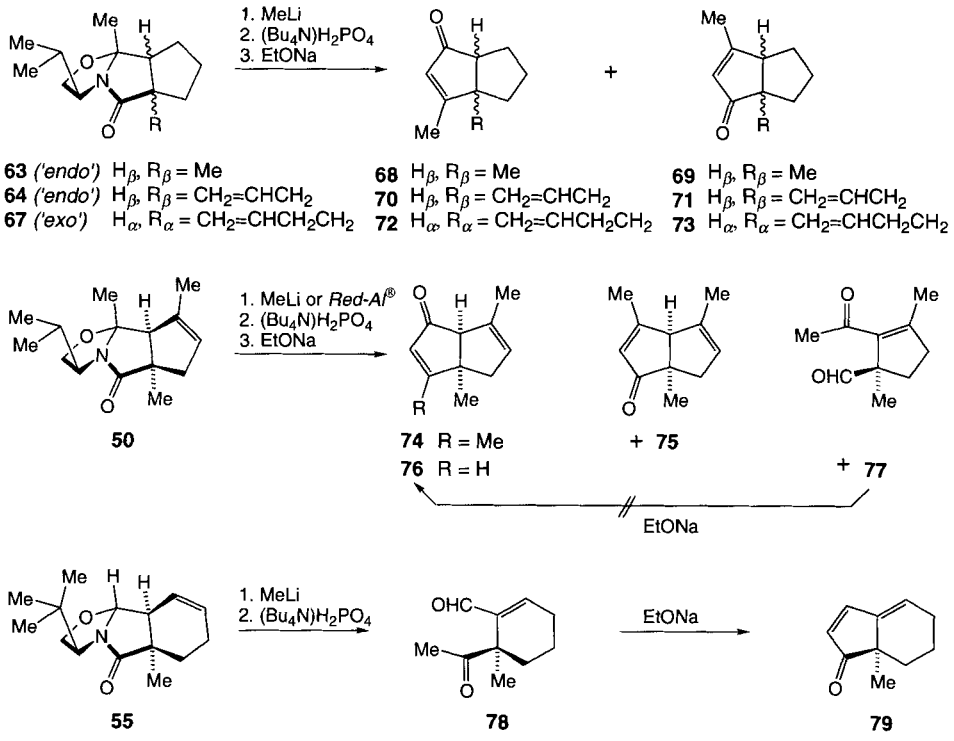
Scheme 8



51 **66** **61** *('exo')*

45 **49** **37**

Scheme 9



63 *('endo')* H_β, R_β = Me **68** H_β, R_β = Me **69** H_β, R_β = Me
64 *('endo')* H_β, R_β = CH_2=$CHCH_2$ **70** H_β, R_β = CH_2=$CHCH_2$ **71** H_β, R_β = CH_2=$CHCH_2$
67 *('exo')* H_α, R_α = CH_2=$CHCH_2CH_2$ **72** H_α, R_α = CH_2=$CHCH_2CH_2$ **73** H_α, R_α = CH_2=$CHCH_2CH_2$

50 **74** R = Me + **75** + **77**
76 R = H

55 **78** **79**

(*Scheme 9*). Similar bicyclic ketones **74**, **75**, and **79** were obtained from the unsaturated tricycles **50** and **55** by addition of MeLi, followed by acidic hydrolysis and aldol-like cyclizations. The reduction of **50** with sodium dihydridobis(methoxyethoxy)aluminate (*Red-Al*®), however, gave mainly keto aldehyde **77** along with traces of bicyclic ketone **76**. In contrast to the ready cyclization of keto aldehyde **78** to **79**, the related system **77** could not be induced to cyclize to the corresponding fused cyclopentenone **76**. Various base treatments led to complete decomposition of **77**. All isomeric pairs of bicyclic ketones formed above were readily separated and characterized as single enantiomerically pure products. Attempts to drive the aldol cyclizations leading to **68**–**73** to a single regioisomer (*e.g.* **68** *vs.* **69**) failed under a variety of cyclization conditions. This problem was observed earlier in our laboratory and by others [19] and is due to the various rates of ring closure and the amount of H_2O present. Aldol cyclizations to cyclohexenones may, on the other hand, be regiochemically controlled by adjusting cyclization conditions.

Support for the structural assignments of the bicycles **68**–**75** was obtained from the spectral properties of the purified compounds. *E.g.*, **74**, in contrast to **75**, shows ^{1}H-NMR chemical shifts very similar to **76**. Since the precursor of **76** is keto aldehyde **77**, it can only cyclize in the manner shown. Likewise, distinct chemical shifts are observed for the respective pairs of products obtained from **63**, **64**, and **67**. Particularly informative are the

relative chemical shifts of the angular H-atoms, the signals of which appear at *ca.* 0.3 ppm upfield for compounds of type **74**. The assignments are additionally supported for some compounds by NOE experiments (see *Exper. Part*) and, for the known compound **68** [20] [21], **69** [22], and **79** [23], by comparison of the spectra with reported data. The latter have been prepared in racemic form using various synthetic routes. Interestingly, racemic **69** has been employed for the stereoselective preparation of (±)-isocomene ((±)-**16**) by *Dreiding* and coworkers [22], thus making the enantiospecific preparation of (+)-**69** a formal asymmetric total synthesis of (−)-isocomene ((−)-**16**). Further application of the chiral bicyclic lactam methodology towards natural and unnatural C-frameworks are currently underway and will be reported in the future.

We are grateful to the *National Institutes of Health* and the *National Science Foundation* for financial support of this work. Postdoctoral fellowships to *St. B.* from the *Swiss National Science Foundation* and to *R. H. W.* from *Merck* are also gratefully acknowledged.

Experimental Part

General. Unless otherwise stated, all solvents were distilled prior to use. THF and Et_2O were dried over Na-benzophenone-ketyl. All reactions were carried out under Ar. Soln. of salts and acids for workup procedures were prepared in deionized H_2O. Extracts were dried (Na_2SO_4) and evaporated *in vacuo*. Chromatography: silica gel *Merck 60* (40–63 μm). IR Spectra: relevant signals only, data in cm^{-1}. ^{1}H-NMR: at 300 MHz in $CDCl_3$; *Bruker AC-300*; δ in ppm rel. to $CHCl_3$ (7.26 ppm), J in Hz. ^{13}C-NMR: at 75.6 MHz in $CDCl_3$ unless otherwise stated; *Bruker AC-300*; δ in ppm rel. to $CDCl_3$ (77.0 ppm); multiplicities from DEPT experiments. Microanalyses were determined by *Desert Analytics*, Tucson, Arizona.

1. *Alkylation of Bicyclic Oxazolidine Derivatives.* 1.1. *(3S,6S,7aR)- and (3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-7a-methyl-6-(3-methylbut-3-enyl)pyrrolo[2,1-b]oxazol-5-one* (**20a** and **20b**, resp.). To a soln. of freshly prepared LDA (3.27 mmol) and *N,N'*-dimethylpropyleneurea (DMPU, 3.27 mmol) in THF (10 ml) was added dropwise neat (3*S*,7a*R*)-2,3,5,6,7,7a-hexahydro-3-isopropyl-7a-methylpyrrolo[2,1-*b*]oxazol-5-one (**17**, 500 mg, 2.73 mmol) at −78°. The soln. was allowed to warm slowly to 0° and then stirred at 0° for 30 min. After recooling to −78°, 4-iodo-2-methylbut-1-ene (614 mg, 3.27 mmol) was added slowly. The mixture was kept at −78° for 30 min, allowed to warm to 0° for an additional 30 min, cooled again to −78°, and quenched with AcOH. H_2O was added and the mixture extracted with Et_2O. The extracts were washed with sat. $NaHCO_3$ soln., H_2O, and brine to give, after chromatography (Et_2O/hexane 1:10), 318 mg (46%) of **20a** and 223 mg (33%) of **20b**.

Data of **20**: $[\alpha]_D^{23} = +70.6$ ($c = 0.50$, $CHCl_3$). IR (neat): 3070, 1710, 1645. ^{1}H-NMR: 4.74–4.70 (*m*, 2 H); 4.15, 3.86 (*AB* of *ABX*, $J_{AB} = 8.7$, $J_{AX} = 7.4$, $J_{BX} = 6.3$, 2 H); 3.66–3.54 (*m*, 1 H); 2.85–2.75 (*m*, 1 H); 2.38, 1.79 (*AB* of *ABX*, $J_{AB} = 12.5$, $J_{AX} = 8.3$, $J_{BX} = 12.0$, 2 H); 2.11–2.02 (*m*, 3 H); 1.72 (*s*, 3 H); 1.68–1.60 (*m*, 1 H); 1.49–1.40 (*m*, 4 H, therein 1.47 (*s*, 3 H)); 1.02 (*d*, $J = 6.6$, 3 H); 0.89 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 179.5, 144.9 (2*s*); 110.4 (*t*); 97.4 (*s*); 70.8 (*t*); 61.1, 43.5 (2*d*); 41.9, 35.2 (2*t*); 33.4 (*d*); 28.4 (*t*); 24.8, 22.2, 20.4, 18.6 (4*q*). Anal. calc. for $C_{15}H_{25}NO_2$ (251.372): C 71.67, H 10.02, N 5.57; found: C 71.56, H 9.96, N 5.77.

Data of **20b**: $[\alpha]_D^{23} = +32.7$ ($c = 0.71$, $CHCl_3$). IR (neat): 3070, 1710, 1650. ^{1}H-NMR: 4.74–4.71 (*m*, 2 H); 4.17, 3.78 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.8$, $J_{BX} = 6.9$, 2 H); 3.65–3.52 (*m*, 1 H); 2.61–2.52 (*m*, 1 H); 2.42, 1.85 (*AB* of *ABX*, $J_{AB} = 13.6$, $J_{AX} = 10.2$, $J_{BX} = 4.0$, 2 H); 2.15–1.96 (*m*, 3 H); 1.77–1.41 (*m*, 8 H, therein 1.73 (*s*, 3 H), and 1.48 (*s*, 3 H)); 1.05 (*d*, $J = 6.4$, 3 H); 0.88 (*d*, $J = 6.5$, 3 H). ^{13}C-NMR: 182.9, 144.6 (2*s*); 110.5 (*t*); 98.7 (*s*); 70.3 (*t*); 62.5, 43.6 (2*d*); 38.3, 35.3 (2*t*); 33.9 (*d*); 31.0 (*t*); 25.7, 22.3, 20.7, 18.8 (4*q*). Anal. calc. for $C_{15}H_{25}NO_2$ (251.372): C 71.67, H 10.02, N 5.57; found: C 71.58, H 10.02, N 5.38.

1.2. *(3S,6S,7aR)- and (3S,6R,7aR)-6-[2-(1,3-Dioxolan-2-yl)ethyl]-2,3,5,6,7,7a-hexahydro-3-isopropyl-7a-methylpyrrolo[2,1-b]oxazol-5-one* (**21a** and **21b**, resp.). Analogously to *1.1* with **17** (500 mg, 2.73 mmol), LDA (3.3 mmol), DMPU (3.3 mmol), and 2-(2-bromoethyl)-1,3-dioxolane (1.48 g, 8.20 mmol). Chromatography (Et_2O/hexane 1:3) gave 543 mg (74%) of **21a**/**21b** (3:2). IR (neat, mixture): 1715. ^{1}H-NMR (mixture): 4.91–4.85 (*m*, 1 H); 4.21–4.10 (*m*, 1 H); 4.01–3.73 (*m*, 5 H); 3.65–3.46 (*m*, 1 H); 2.93–2.79, 2.67–2.55 (2*m*, 1 H); 2.49–2.33 (*m*, 1 H); 2.08–1.51 (*m*, 6 H); 1.48, 1.47 (2*s*, 3 H); 1.04, 1.02 (2*d*, $J = 6.6$, 3 H); 0.89, 0.88 (2*d*, $J = 6.7$, 3 H).

1.3. *(3S,6S,7aR)- and (3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-7a-methyl-6-(pent-4-enyl)pyrrolo[2,1-b]oxazol-5-one* (**22a** and **22b**, resp.) *and (3S,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-7a-methyl-6,6-di(pent-4-enyl)pyrrolo[2,1-b]oxazol-5-one* (**22c**). Analogously to *1.1* with **17** (3.00 g, 16.4 mmol), LDA (19.6 mmol), DMPU (2.8 ml), and 5-bromopent-1-ene (2.93 g, 19.7 mmol). Chromatography (Et_2O/hexane 1:10) gave 682 mg (13%) of **22c**, 1.55 g (38%) of **22a**, and 1.01 g (25%) of **22b**.

Data of **22a**: $[\alpha]_D^{23} = +68.5$ ($c = 1.40$, $CHCl_3$). IR (neat): 3075, 1710, 1640. ^{1}H-NMR: 5.78–5.72 (*m*, 1 H); 5.05–4.92 (*m*, 2 H); 4.14, 3.85 (*AB* of *ABX*, $J_{AB} = 8.7$, $J_{AX} = 7.4$, $J_{BX} = 6.2$, 2 H); 3.64–3.55 (*m*, 1 H); 2.84–2.76 (*m*, 1 H); 2.37 (*dd*, $J = 12.6$, 8.4, 1 H); 2.12–2.03 (*m*, 2 H); 1.92–1.29 (*m*, 9 H, therein 1.47 (*s*, 3 H)); 1.02 (*d*, $J = 6.7$, 3 H); 0.89 (*d*, $J = 6.7$, 3 H). ^{13}C-NMR: 179.5 (*s*); 138.4 (*d*); 114.7 (*t*); 97.4 (*s*); 70.9 (*t*); 61.1, 44.0 (2*d*); 42.0, 35.6 (2*t*); 33.4 (*d*); 30.0, 26.8 (2*t*); 24.8, 22.5, 19.0 (3*q*).

Data of **22b**: $[\alpha]_D^{23} = +33.2$ ($c = 1.95$, $CHCl_3$). IR (neat): 3075, 1710, 1640. ^{1}H-NMR: 5.85–5.72 (*m*, 1 H); 5.06–4.94 (*m*, 2 H); 4.17, 3.77 (*AB* of *ABX*, $J_{AB} = 8.7$, $J_{AX} = 7.7$, $J_{BX} = 6.9$, 2 H); 3.63–3.54 (*m*, 1 H); 2.63–2.54 (*m*, 1 H); 2.41, 1.86 (*AB* of *ABX*, $J_{AB} = 13.8$, $J_{AX} = 10.3$, $J_{BX} = 4.2$, 2 H); 2.13–2.05 (*m*, 2 H); 1.85–1.79 (*m*, 1 H); 1.68–1.41 (*m*, 7 H, therein 1.48 (*s*, 3 H)); 1.05 (*d*, $J = 6.7$, 3 H); 0.88 (*d*, $J = 6.7$, 3 H). ^{13}C-NMR: 182.9 (*s*); 138.2 (*d*); 114.8 (*t*); 98.8 (*s*); 70.4 (*t*); 62.5, 44.1 (2*d*); 38.5 (*t*); 34.0 (*d*); 33.5, 32.5, 26.6 (3*t*); 25.7, 20.8, 18.9 (3*q*).

Data of **22c**: $[\alpha]_D^{23} = +37.6$ ($c = 1.43$, $CHCl_3$). IR (neat): 3075, 1710, 1640. ^{1}H-NMR: 5.86–5.69 (*m*, 2 H); 5.04–4.90 (*m*, 4 H); 4.16, 3.74 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 8.0$, $J_{BX} = 7.0$, 2 H); 3.63–3.47 (*m*, 1 H); 2.20, 1.96 (*AB*, $J = 14.2$, 2 H); 2.09–1.97 (*m*, 4 H); 1.68–1.09 (*m*, 12 H, therein 1.47 (*s*, 3 H)); 1.05 (*d*, $J = 6.7$, 3 H); 0.87 (*d*, $J = 6.5$, 3 H). ^{13}C-NMR: 184.0 (*s*); 138.5, 138.3 (2*d*); 114.8, 114.6 (2*t*); 96.8 (*s*); 70.1 (*t*); 62.3 (*d*); 51.1 (*s*); 43.0, 38.1, 36.8 (3*t*); 34.2 (*d*); 34.1, 33.9 (2*t*); 25.4 (*q*); 23.9, 23.6 (2*t*); 20.9, 18.9 (2*q*).

1.4. *(3S,6S,7aR)- and (3S,6R,7aR)-6-(Hex-5-enyl)-2,3,5,6,7,7a-hexahydro-3-isopropyl-7a-methylpyrrolo[2,1-b]oxazol-5-one* (**23a** and **23b**, resp.) *and (3S,7aR)-6,6-Di(hex-5-enyl)-2,3,5,6,7,7a-hexahydro-3-isopropyl-7a-methylpyrrolo[2,1-b]oxazol-5-one* (**23c**). Analogously to *1.1* with **17** (300 mg, 1.64 mmol), LDA (1.64 mmol), DMPU (0.15 ml), and 6-iodohex-1-ene (344 mg, 1.64 mmol). Chromatography (Et_2O/hexane 1:10) gave 40 mg (7%) of **23c**, 212 mg (49%) of **23a**, and 118 mg (27%) of **23b**.

Data of **23a**: $[\alpha]_D^{23} = +68.0$ ($c = 1.60$, $CHCl_3$). IR (neat): 3075, 1715, 1640. ^{1}H-NMR: 5.86–5.73 (*m*, 1 H); 5.03–4.92 (*m*, 2 H); 4.14, 3.85 (*AB* of *ABX*, $J_{AB} = 8.8$, $J_{AX} = 7.5$, $J_{BX} = 6.2$, 2 H); 3.63–3.55 (*m*, 1 H); 2.82–2.75 (*m*, 1 H); 2.36, 1.78 (*AB* of *ABX*, $J_{AB} = 12.6$, $J_{AX} = 8.4$, $J_{BX} = 11.2$, 2 H); 2.09–2.02 (*m*, 2 H); 1.90–1.83 (*m*, 1 H); 1.69–1.55 (*m*, 1 H); 1.46 (*s*, 3 H); 1.44–1.26 (*m*, 5 H); 1.02 (*d*, $J = 6.7$, 3 H); 0.89 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 179.5 (*s*); 138.7 (*d*); 114.3 (*t*); 97.4 (*s*); 70.8 (*t*); 61.0, 44.1 (2*d*); 41.9, 33.5 (2*t*); 33.3 (*d*); 30.2, 28.6, 26.6 (3*t*); 24.8, 20.4, 19.0 (3*q*).

Data of **23b**: $[\alpha]_D^{23} = +31.7$ ($c = 1.32$, $CHCl_3$). IR (neat): 3075, 1715, 1640. ^{1}H-NMR: 5.84–5.75 (*m*, 1 H); 5.04–4.92 (*m*, 2 H); 4.18, 3.77 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.8$, $J_{BX} = 6.9$, 2 H); 3.63–3.54 (*m*, 1 H); 2.60–2.57 (*m*, 1 H); 2.40, 1.85 (*AB* of *ABX*, $J_{AB} = 13.9$, $J_{AX} = 10.2$, $J_{BX} = 4.1$, 2 H); 2.07–2.03 (*m*, 2 H); 1.87–1.79 (*m*, 1 H); 1.70–1.40 (*m*, 9 H, therein 1.48 (*s*, 3 H)); 1.05 (*d*, $J = 6.6$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 183.0 (*s*); 138.7 (*d*); 114.5 (*t*); 98.8 (*s*); 70.4 (*t*); 62.4, 44.3 (2*d*); 38.5 (*t*); 34.0 (*d*); 33.5, 32.9, 28.6, 26.8 (4*t*); 25.7, 20.8, 18.9 (3*q*).

Data of **23c**: $[\alpha]_D^{23} = +35.2$ ($c = 1.20$, $CHCl_3$). IR (neat): 3075, 1710, 1640. ^{1}H-NMR: 5.83–5.71 (*m*, 2 H); 5.03–4.89 (*m*, 4 H); 4.15, 3.74 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.9$, $J_{BX} = 7.0$, 2 H); 3.62–3.53 (*m*, 1 H); 2.19, 1.95 (*AB*, $J = 14.2$, 2 H); 2.09–1.99 (*m*, 4 H); 1.67–1.22 (*m*, 16 H, therein 1.47 (*s*, 3 H)); 1.04 (*d*, $J = 6.6$, 3 H); 0.87 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 184.2 (*s*); 138.9, 138.7 (2*d*); 114.5, 114.3 (2*t*); 96.8 (*s*); 70.1 (*t*); 62.2 (*d*); 51.2 (*s*); 43.0, 38.5, 37.2 (3*t*); 34.2 (*d*); 33.6, 33.5, 29.3, 29.1 (4*t*); 25.3 (*q*); 24.1, 23.7 (2*t*); 20.8, 18.9 (2*q*).

1.5. *(3S,6S,7aR)- and (3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6-(3-methylbut-3-enyl)pyrrolo[2,1-b]oxazol-5-one* (**24a** and **24b**, resp.). Analogously to *1.1* with (3*S*,7a*R*)-2,3,5,6,7,7a-hexahydro-3-isopropylpyrrolo[2,1-*b*]oxazol-5-one (**18**, 1.00 g, 5.40 mmol), LDA (6.49 mmol), DMPU (6.5 mmol), and 4-iodo-2-methylbut-1-ene (1.27 g, 6.48 mmol). Chromatography (Et_2O/hexane 1:10) gave 411 mg (32%) of **24a** and 248 mg (19%) of **24b**.

Data of **24a**: $[\alpha]_D^{23} = +75.8$ ($c = 1.05$, $CHCl_3$). IR (neat): 3075, 1715, 1650. ^{1}H-NMR: 5.05 (*dd*, $J = 6.0$, 3.5, 1 H); 4.71 (*m* ('*d*'), 2 H); 4.23–4.12 (*m*, 1 H); 3.79–3.61 (*m*, 2 H); 2.82–2.53 (*m*, 2 H); 2.15–2.05 (*m*, 4 H); 1.72 (*s*, 3 H); 1.73–1.62 (*m*, 1 H); 1.58–1.42 (*m*, 1 H); 0.99 (*d*, $J = 6.7$, 3 H); 0.90 (*d*, $J = 6.7$, 3 H). ^{13}C-NMR: 180.2, 144.9 (2*s*); 110.6 (*t*); 90.2 (*d*); 71.1 (*t*); 60.5, 42.8 (2*d*); 35.2, 32.4 (2*t*); 32.0 (*d*); 29.4 (*t*); 22.2, 19.6, 18.5 (3*q*).

Data of **24b**: $[\alpha]_D^{23} = +32.9$ ($c = 1.39$, $CHCl_3$). IR (neat): 3075, 1715, 1650. ^{1}H-NMR: 4.98 (*dd*, $J = 6.0$, 1.5, 1 H); 4.74–4.71 (*m*, 2 H); 4.14, 3.58 (*AB* of *ABX*, $J_{AB} = 7.7$, $J_{AX} = 6.8$, $J_{BX} = 7.1$, 2 H); 3.75–3.41 (*m*, 1 H); 2.68–2.53 (*m*, 1 H); 2.34–2.21 (*m*, 1 H); 2.14–1.93 (*m*, 4 H); 1.74 (*s*, 3 H); 1.71–1.57 (*m*, 2 H); 1.01 (*d*, $J = 6.6$, 3 H); 0.91 (*d*, $J = 6.7$, 3 H). ^{13}C-NMR: 182.9, 144.7 (2*s*); 110.6 (*t*); 90.8 (*d*); 70.8 (*t*); 61.7, 42.5 (2*d*); 35.1 (*t*); 32.0 (*d*); 30.8, 30.3 (2*t*); 22.3, 19.8, 18.5 (3*q*).

1.6. *(3S,6S,7aR)- and (3S,6R,7aR)-3-(*tert*-Butyl)-2,3,5,6,7,7a-hexahydro-6-(pent-4-enyl)pyrrolo[2,1-b]oxazol-5-one* (**25a** and **25b**, resp.) *and (3S,7aR)-3-(*tert*-Butyl)-2,3,5,6,7,7a-hexahydro-6,6-di(pent-4-enyl)pyrrolo[2,1-b]oxazol-5-one* (**25c**). Analogously to *1.1* with (3*S*,7a*R*)-3-*tert*-butyl-2,3,5,6,7,7a-hexahydropyrrolo[2,1-*b*]-oxazol-5-one (**19**, 376 mg, 2.0 mmol), LDA (2.2 mmol), DMPU (2.2 mmol), and 5-bromopent-1-ene (372 mg, 2.5 mmol). Chromatography (AcOEt/hexane 1:10) gave 45 mg (7%) of **25c** (not characterized) and 374 mg (74%) of **25a**/**25b** (1.8:1), which were separated and characterized.

Data of **25a**: $[\alpha]_D^{23} = +64.7$ ($c = 2.9$, $CHCl_3$). IR (neat): 2960, 1715, 1640. ^{1}H-NMR: 5.70 (*m*, 1 H); 4.98 (*m*, 1 H); 4.93 (*m*, 1 H); 4.66 (*dd*, $J = 6.2, 3.1$, 1 H); 3.77 (*m*, 2 H); 3.46 (*dd*, $J = 7.6, 6.1$, 1 H); 2.26 (*m*, 1 H); 2.05–1.80 (*m*, 4 H); 1.56–1.17 (*m*, 4 H); 0.79 (*s*, 9 H). ^{13}C-NMR (C_6D_6): 180.4 (*s*); 138.7 (*d*); 114.8 (*t*); 91.1 (*d*); 68.0 (*t*); 64.0, 42.6 (2*d*); 33.9 (*s*); 33.8, 32.3, 31.4 (3*t*); 26.7 (*q*, 3 C); 26.2 (*t*). Anal. calc. for $C_{15}H_{25}NO_2$ (251.372): C 71.67, H 10.02, N 5.57; found: C 71.41, H 9.96, N 5.49.

Data of **25b**: $[\alpha]_D^{23} = +18.4$ ($c = 2.8$, $CHCl_3$). IR (neat): 2960, 1715, 1640. ^{1}H-NMR: 5.66 (*tdd*, $J = 6.7, 17.0, 10.2$, 1 H); 4.96 (*md*, $J = 17$, 1 H); 4.94 (*md*, $J = 10.2$, 1 H); 4.64 (*dd*, $J = 6.0, 1.5$, 1 H); 3.74 (*m*, 2 H); 3.42 (*dd*, $J = 7.9, 6.7$, 1 H); 2.39 (*m*, 1 H); 1.99 (*ddd*, $J = 14.3, 9.9, 1.5$, 1 H); 1.85 (*m*, 2 H); 1.65 (*m*, 2 H); 1.47 (*td*, $J = 6.0, 14.3$, 1 H); 1.26 (*m*, 3 H); 0.78 (*s*, 9 H). ^{13}C-NMR (C_6D_6): 182.7 (*s*); 138.6 (*d*); 114.8 (*t*); 91.9 (*d*); 67.8 (*t*); 65.2, 42.4 (2*d*); 33.8 (*s*); 33.7, 32.5, 30.5 (3*t*); 26.6 (*q*, 3 C); 26.5 (*t*).

1.7. *(3S,6S,7aR)- and (3S,6R,7aR)-3-(*tert*-Butyl)-6-(hex-5-enyl)-2,3,5,6,7,7a-hexahydropyrrolo[2,1-b]oxazol-5-one* (**26a** and **26b**, resp.) *and (3S,7aR)-3-(*tert*-Butyl)-6,6-di(hex-5-enyl)-2,3,5,6,7,7a-hexahydropyrrolo[2,1-b]oxazol-5-one* (**26c**). Analogously to *1.1* with **19** (376 mg, 2.0 mmol), LDA (2.1 mmol), DMPU (2.2 mmol), and 6-bromohex-1-ene (408 mg, 2.5 mmol). Chromatography (AcOEt/hexane 1:10) gave 90 mg (13%) of **26c** (not characterized), 223 mg (42%) of **26a**, and 112 mg (21%) of **26b** (not characterized). **26a**: $[\alpha]_D^{23} = +45.3$ ($c = 0.40$, $CHCl_3$). IR (neat): 2930, 1715. ^{1}H-NMR: 5.78 (*tdd*, $J = 6.7, 17.0, 10.2$, 1 H); 5.03 (*dd*, $J = 6.2, 3.4$, 1 H); 4.98 (*md*, $J = 17.0$, 1 H); 4.92 (*md*, $J = 10.2$, 1 H); 4.08 (*dd*, $J = 6.7, 7.4$, 1 H); 3.79 (*dd*, $J = 7.0, 6.7$, 1 H); 3.76 (*dd*, $J = 7.4, 7.0$, 1 H); 2.72 (*m*, 1 H); 2.55 (*ddd*, $J = 13.5, 9.5, 6.2$, 1 H); 2.05 (*m*, 2 H); 1.86 (*m*, 1 H); 1.63 (*ddd*, $J = 13.5, 8.5, 3.4$, 1 H); 1.32 (*m*, 5 H); 0.91 (*s*, 9 H). ^{13}C-NMR: 180.8 (*s*); 138.8 (*d*); 114.4 (*t*); 90.9 (*d*); 68.3 (*t*); 63.5, 43.1 (2*d*); 33.9 (*s*); 33.5, 32.4, 31.2, 28.7 (4*t*); 26.6 (*q*, 3 C); 26.1 (*t*). Anal. calc. for $C_{16}H_{27}NO_2$ (265.399): C 72.41, H 10.25, N 5.28; found: C 72.29, H 10.30, N 5.18.

1.8. *(3S,6S,7aR)- and (3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6,7a-dimethyl-6-(3-methylbut-3-enyl)pyrrolo[2,1-b]oxazol-5-one* (**27a** and **27b**, resp.). Analogously to *1.1* with **20a**/**20b** (1.00 g, 4.00 mmol), LDA (6.0 mmol), DMPU (6.0 mmol), and MeI (0.76 ml, 12.0 mmol). Chromatography (Et_2O/hexane 1:10) gave 83 mg (9%) of **27a** and 893 mg (84%) of **27b**.

Data of **27a**: $[\alpha]_D^{23} = +66.0$ ($c = 1.38$, $CHCl_3$). IR (neat): 3070, 1710, 1650. ^{1}H-NMR: 4.67 (*m* ('*d*'), 2 H); 4.17, 3.77 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.8$, $J_{BX} = 6.9$, 2 H); 3.64–3.51 (*m*, 1 H); 2.24, 1.94 (*AB*, $J = 13.5$, 2 H), 2.14–1.52 (*m*, 9 H, therein *B* portion of *AB* and 1.71 (*s*, 3 H)); 1.49 (*s*, 3 H); 1.30 (*s*, 3 H); 1.04 (*d*, $J = 6.6$, 3 H); 0.87 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 183.9, 145.6 (2*s*); 109.8 (*t*); 96.7 (*s*); 70.5 (*t*); 61.7 (*d*); 47.4 (*s*); 46.0, 36.5 (2*t*); 34.1 (*d*); 32.5 (*t*); 25.9 (*q*, 2 C); 22.5, 20.7, 18.8 (3*q*). CI-MS (isobutane): 266 ($[M + H]^+$). Anal. calc. for $C_{16}H_{27}NO_2$ (265.399): C 72.41, H 10.25, N 5.28; found: C 72.35, H 10.01, N 5.40.

Data of **27b**: $[\alpha]_D^{23} = +17.4$ ($c = 0.92$, $CHCl_3$). IR (neat): 3075, 1715, 1650. ^{1}H-NMR: 4.71–4.69 (*m*, 2 H); 4.19, 3.76 (*AB* of *ABX*, $J_{AB} = 8.5$, $J_{AX} = 7.7$, $J_{BX} = 7.1$, 2 H); 3.66–3.58 (*m*, 1 H); 2.16, 2.06 (*AB*, $J = 13.7$, 2 H), 2.09–1.97 (*m*, 3 H, therein *B* portion of *AB*); 1.74–1.62 (*m*, 6 H, therein 1.73 (*s*, 3 H)); 1.49 (*s*, 3 H); 1.17 (*s*, 3 H); 1.05 (*d*, $J = 6.4$, 3 H); 0.88 (*d*, $J = 6.4$, 3 H). ^{13}C-NMR: 184.3, 145.1 (2*s*); 109.9 (*t*); 96.5 (*s*); 70.1 (*t*); 62.2 (*d*); 47.0 (*s*); 46.0, 37.7 (2*t*); 34.0 (*d*); 32.7 (*t*); 25.2, 24.4, 22.5, 20.7, 18.8 (5*q*). CI-MS (isobutane): 266 ($[M + H]^+$). Anal. calc. for $C_{16}H_{27}NO_2$ (265.399): C 72.41, H 10.25, N 5.28; found: C 72.14, H 9.99, N 5.21.

1.9. *(3S,6S,7aR)- and (3S,6R,7aR)-6-[2-(1,3-Dioxolan-2-yl)ethyl]-2,3,5,6,7,7a-hexahydro-3-isopropyl-6,7a-dimethylpyrrolo[2,1-b]oxazol-5-one* (**28a** and **28b**, resp.). Analogously to *1.1* with **21a**/**21b** (540 mg, 2.02 mmol), LDA (2.42 mmol), DMPU (2.42 mmol), and MeI (0.64 ml, 10.1 mmol). Chromatography (Et_2O/hexane 1:3) gave 58 mg (10%) of **28a**/**28b** 3:7 (**28a** was not characterized) and 405 mg (71%) of pure **28b**. **28b**: $[\alpha]_D^{23} = +20.6$ ($c = 1.05$, $CHCl_3$). IR (neat): 1715. ^{1}H-NMR: 4.86 (br. *s*, 1 H); 4.19 (*t*, $J = 8.1$, 1 H); 4.01–3.43 (*m*, 6 H); 2.13, 2.07 (*AB*, $J = 13.9$, 2 H); 1.70–1.57 (*m*, 5 H); 1.48 (*s*, 3 H); 1.15 (*s*, 3 H); 1.04 (*d*, $J = 6.6$, 3 H); 0.87 (*d*, $J = 6.5$, 3 H). ^{13}C-NMR: 184.4 (*s*); 104.3 (*d*); 96.6 (*s*); 70.2 (*t*); 64.9 (*t*, 2 C); 62.5 (*d*); 46.8 (*s*); 46.2 (*t*); 34.0 (*d*); 33.5, 29.3 (2*t*); 25.3, 24.5, 20.7, 18.9 (4*q*).

1.10. *(3S,6S,7aR)- and (3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6,7a-dimethyl-6-(pent-4-enyl)-pyrrolo[2,1-b]oxazol-5-one* (**29a** and **29b**, resp.). Analogously to *1.1* with **22a**/**22b** (2.48 g, 9.88 mmol), LDA (13.2 mmol), DMPU (13.2 mmol), and MeI (1.6 ml, 25 mmol). Chromatography (Et_2O/hexane 1:10) gave 215 mg (8%) of **29a** and 2.09 g (80%) of **29b**.

Data of **29a**: $[\alpha]_D^{23} = +59.4$ ($c = 1.23$, $CHCl_3$). IR (neat): 3075, 1715, 1640. ^{1}H-NMR: 5.85–5.68 (*m*, 1 H); 5.03–4.91 (*m*, 2 H); 4.18, 3.77 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.8$, $J_{BX} = 7.1$, 2 H); 3.63–3.51 (*m*, 1 H); 2.23, 1.93 (*AB*, $J = 13.7$, 2 H), 2.08–1.99 (*m*, 3 H, therein *B* portion of *AB*); 1.74–1.13 (*m*, 11 H, therein 1.49, 1.28 (2*s*, 3 H each)); 1.05 (*d*, $J = 6.6$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 184.1 (*s*); 138.5 (*d*); 114.6 (*t*); 96.7 (*s*); 70.5 (*t*); 61.7 (*d*); 47.6 (*s*); 46.1, 37.9 (2*t*); 34.13 (*d*); 34.06 (*t*); 25.9 (*q*, 2 C); 23.8 (*t*); 20.7, 18.9 (2*q*).

Data of **29b**: $[\alpha]_D^{23} = +21.1$ ($c = 1.49$, $CHCl_3$). IR (neat): 3075, 1715, 1640. ^{1}H-NMR: 5.84–5.75 (*m*, 1 H); 5.02–4.91 (*m*, 2 H); 4.18, 3.57 (*AB* of *ABX*, $J_{AB} = 8.5$, $J_{AX} = 7.9$, $J_{BX} = 7.3$, 2 H); 3.63–3.54 (*m*, 1 H); 2.15–2.01 (*m*, 4 H); 1.72–1.23 (*m*, 8 H, therein 1.47 (*s*, 3 H)); 1.14 (*s*, 3 H); 1.04 (*d*, $J = 6.5$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 184.7 (*s*); 138.3 (*d*); 114.8 (*t*); 96.7 (*s*); 70.3 (*t*); 62.3 (*d*); 47.3 (*s*); 46.1, 39.1 (2*t*); 34.2 (*d*); 33.9 (*t*); 25.3, 24.7 (2*q*); 24.0 (*t*); 20.8, 18.9 (2*q*).

1.11. *(3S,6S,7aR)- and (3S,6R,7aR)-6-(Hex-5-enyl)-2,3,5,6,7,7a-hexahydro-3-isopropyl-6,7a-dimethylpyrrolo[2,1-b]oxazol-5-one* (**30a** and **30b**, resp.). Analogously to *1.1* with **23a**/**23b** (834 mg, 3.15 mmol), LDA (5.46 mmol), DMPU (5.46 mmol), and MeI (0.70 ml, 11 mmol). Chromatography (Et_2O/hexane 1:10) gave 94 mg (11%) of **30a** and 730 g (83%) of **30b**.

Data of **30a**: $[\alpha]_D^{23} = +55.8$ ($c = 1.20$, $CHCl_3$). IR (neat): 3075, 1715, 1640. ^{1}H-NMR: 5.83–5.71 (*m*, 1 H); 5.01–4.90 (*m*, 2 H); 4.17, 3.77 (*AB* of *ABX*, $J_{AB} = 8.7$, $J_{AX} = 7.8$, $J_{BX} = 7.0$, 2 H); 3.61–3.53 (*m*, 1 H); 2.22, 1.93 (*AB*, $J = 13.6$, 2 H), 2.07–2.00 (*m*, 3 H, therein *B* portion of *AB*); 1.68–1.52 (*m*, 1 H); 1.49 (*s*, 3 H); 1.48–1.32 (*m*, 5 H); 1.28 (*s*, 3 H); 1.14–1.07 (*m*, 1 H); 1.05 (*d*, $J = 6.6$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 184.1 (*s*); 138.8 (*d*); 114.3 (*t*); 96.7 (*s*); 70.4 (*t*); 61.7 (*d*); 47.6 (*s*); 46.0, 38.1 (2*t*); 34.1 (*d*); 33.5, 29.2 (2*t*); 25.9, 25.8 (2*q*); 23.8 (*t*); 20.7, 18.9 (2*q*).

Data of **30b**: $[\alpha]_D^{23} = +20.3$ ($c = 2.09$, $CHCl_3$). IR (neat): 3075, 1715, 1640. ^{1}H-NMR: 5.83–5.74 (*m*, 1 H); 5.02–4.92 (*m*, 2 H); 4.18, 3.57 (*AB* of *ABX*, $J_{AB} = 8.5$, $J_{AX} = 8.5$, $J_{BX} = 7.3$, 2 H); 3.63–3.55 (*m*, 1 H); 2.15–2.01 (*m*, 4 H); 1.68–1.26 (*m*, 10 H, therein 1.47 (*s*, 3 H)); 1.14 (*s*, 3 H); 1.04 (*d*, $J = 6.5$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 184.7 (*s*); 138.6 (*d*); 114.4 (*t*); 96.6 (*s*); 70.2 (*t*); 62.2 (*d*); 47.2 (*s*); 46.0, 39.4 (2*t*); 34.1 (*d*); 33.4, 29.0 (2*t*); 25.1, 24.7 (2*q*); 24.1 (*t*); 20.7, 18.9 (2*q*).

1.12. *(3S,6S,7aR)- and (3S,6R,7aR)-3-(*tert*-Butyl)-2,3,5,6,7,7a-hexahydro-6-methyl-6-(pent-4-enyl)pyrrolo[2,1-b]oxazol-5-one* (**31a** and **31b**, resp.). Analogously to *1.1* with **25a**/**25b** (503 mg, 2.0 mmol), LDA (2.5 mmol), DMPU (2.5 mmol), and MeI (426 mg, 3.0 mmol). Chromatography (Et_2O/hexane 1:10) gave 26 mg (5%) of **31a** (not characterized) and 489 mg (92%) of **31b**. **31b**: $[\alpha]_D^{23} = +12.0$ ($c = 0.33$, $CHCl_3$). IR (neat): 3075, 1715, 1640. ^{1}H-NMR (C_6D_6): 5.70 (*tdd*, $J = 6.6$, 17.0, 10.2, 1 H); 4.98 (*tdd*, $J = 1.5$, 17.0, 2.1, 1 H); 4.93 (*tdd*, $J = 1.2$, 10.2, 2.1, 1 H); 4.65 (*dd*, $J = 2.5$, 6.1, 1 H); 3.73–3.58 (*m*, 2 H); 3.47–3.32 (*m*, 1 H); 1.90–1.67 (*m*, 4 H); 1.50–1.20 (*m*, 4 H); 1.17 (*s*, 3 H); 0.77 (*s*, 9 H). ^{13}C-NMR (C_6D_6): 183.5 (*s*); 138.6 (*d*); 114.9 (*t*); 90.3 (*d*); 67.9 (*t*); 64.5 (*d*); 46.6 (*s*); 39.7, 38.7 (2*t*); 34.1 (*s*); 33.8 (*t*); 26.3 (*q*, 3 C); 25.6 (*q*); 24.5 (*t*). Anal. calc. for $C_{16}H_{27}NO_2$ (265.399): C 72.41, H 10.25, N 5.28; found: C 72.65, H 10.24, N 5.31.

1.13. *(3S,6S,7aR)- and (3S,6R,7aR)-3-(*tert*-Butyl)-6-(hex-5-enyl)-2,3,5,6,7,7a-hexahydro-6-methylpyrrolo[2,1-b]oxazol-5-one* (**32a** and **32b**, resp.). Analogously to *1.1* with **26a**/**26b** (530 mg, 2.0 mmol), LDA (2.4 mmol), DMPU (2.3 mmol), and MeI (426 mg, 3.0 mmol). Chromatography (Et_2O/hexane 1:10) gave 32 mg (6%) of **32a** (not characterized) and 530 mg (94%) of **32b**. **32b**: $[\alpha]_D^{23} = +5.2$ ($c = 0.25$, $CHCl_3$). IR (neat): 2965, 1715, 1640. ^{1}H-NMR: 5.78 (*tdd*, $J = 6.7$, 17.0, 10.2, 1 H); 5.01–4.88 (*m*, 3 H); 4.07 (*m*, 1 H); 3.75 (*m*, 2 H); 2.72 (*m*, 1 H); 2.56 (*dd*, $J = 14.1$, 6.3, 1 H); 2.04 (*m*, 2 H); 1.80 (*dd*, $J = 14.1$, 2.8, 1 H); 1.20–1.65 (*m*, 6 H); 1.17 (*s*, 3 H); 0.91 (*s*, 9 H). ^{13}C-NMR: 183.6 (*s*); 138.6 (*d*); 114.6 (*t*); 90.1 (*d*); 68.2 (*t*); 63.8 (*d*); 47.3 (*s*); 39.9, 38.8 (2*t*); 33.9 (*s*); 33.5, 28.9 (2*t*); 26.2 (*q*, 3 C); 25.2 (*q*); 24.4 (*t*). Anal. calc. for $C_{17}H_{29}NO_2$ (279.426): C 73.07, H 10.46, N 5.01; found: C 72.90, H 10.55, N 4.83.

2. *Conversion of α-Alkylated Bicyclic Oxazolidine Derivatives to Annulation Precursors.* 2.1. *(3S,6S,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-7a-methyl-6-(3-oxobutyl)pyrrolo[2,1-b]oxazol-5-one* (**33**). Through a soln. of **20a** (643 mg, 2.56 mmol) in CH_2Cl_2/MeOH 2:1 (5 ml) at −78° was passed O_3 until the blue color persisted. Excess O_3 was removed with a stream of Ar. To reduce the peroxide, Me_2S (6 ml), and after 1 h, H_2O (1 ml) were added. The mixture was allowed to warm to 23° and stirred 3–4 h at 23° (TLC control). After evaporation, the residue was diluted with H_2O and extracted with CH_2Cl_2. The combined org. layers were washed with H_2O and brine to give, after chromatography (Et_2O/hexane 1:2), 578 mg (89%) of **33.** $[\alpha]_D^{23} = +39.7$ ($c = 1.61$, $CHCl_3$). IR (neat): 1720, 1705. ^{1}H-NMR: 4.16, 3.86 (*AB* of *ABX*, $J_{AB} = 9.0$, $J_{AX} = 7.4$, $J_{BX} = 6.2$, 2 H); 3.64–3.53 (*m*, 1 H); 2.95–2.78 (*m*, 1 H); 2.65 (*t*, $J = 6.9$, 2 H); 2.37 (*dd*, $J = 12.5$, 8.4, 1 H); 2.15 (*s*, 3 H); 2.14–1.55 (*m*, 4 H); 1.47 (*s*, 3 H); 1.02 (*d*, $J = 6.7$, 3 H); 0.89 (*d*, $J = 6.5$, 3 H). ^{13}C-NMR: 207.5, 178.9, 97.0 (3*s*); 70.5 (*t*); 61.0, 42.8 (2*d*); 41.7, 40.5 (2*t*); 33.0 (*d*); 29.4, 24.5 (2*q*); 24.4 (*t*); 20.1, 18.7 (2*q*).

2.2. *(3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-7a-methyl-6-(3-oxobutyl)pyrrolo[2,1-b]oxazol-5-one* (**34**). Analogously to *2.1* with **20b** (366 mg, 1.46 mmol). Chromatography (Et_2O/hexane 1:2) gave 337 mg (91%) of **34**. $[\alpha]_D^{23} = +54.7$ ($c = 0.95$, $CHCl_3$). IR (neat): 1725, 1710. ^{1}H-NMR: 4.18, 3.78 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.9$, $J_{BX} = 6.8$, 2 H); 3.62–3.49 (*m*, 1 H); 2.71–2.39 (*m*, 4 H); 2.17 (*s*, 3 H); 1.99–1.59 (*m*, 4 H); 1.49 (*s*, 3 H); 1.04 (*d*, $J = 6.6$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 207.0, 181.6, 98.3 (3*s*); 70.0 (*t*); 62.4, 43.0 (2*d*); 40.5, 38.9 (2*t*); 33.4 (*d*); 29.4 (*q*); 26.8 (*t*); 25.4, 20.2, 18.5 (3*q*).

2.3. *(3S,6S,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6-(3-oxobutyl)pyrrolo[2,1-b]oxazol-5-one* (**35**). Analogously to *2.1* with **24a** (405 mg, 1.71 mmol). Chromatography (Et_2O/hexane 1:2) gave 380 mg (93%) of **35**. $[\alpha]_D^{23} = +75.8$ ($c = 1.05$, $CHCl_3$). IR (neat): 1715. ^{1}H-NMR: 5.04 (*dd*, $J = 6.1$, 3.4, 1 H); 4.21–4.16 (*m*, 1 H); 3.73–3.62 (*m*, 2 H); 2.82–2.74 (*m*, 1 H); 2.66–2.54 (*m*, 3 H); 2.15 (*s*, 3 H); 2.01–1.91 (*m*, 1 H); 1.81–1.61 (*m*, 3 H); 0.99 (*d*, $J = 6.7$, 3 H); 0.90 (*d*, $J = 6.7$, 3 H). ^{13}C-NMR: 208.1, 179.7 (2*s*); 89.8 (*d*); 71.0 (*t*); 60.4, 42.0 (2*d*); 40.5, 33.3 (2*t*); 31.9 (*d*); 29.8 (*q*); 25.3 (*t*); 19.5, 18.4 (2*q*).

2.4. *(3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6-(3-oxobutyl)pyrrolo[2,1-b]oxazol-5-one* (**36**). Analogously to *2.1* with **24b** (240 mg, 1.01 mmol). Chromatography (Et_2O/hexane 1:2) gave 172 mg (71%) of **36**. $[\alpha]_D^{23} = +49.6$ ($c = 1.17$, $CHCl_3$). IR (neat): 1715. ^{1}H-NMR: 4.99 (*dd*, $J = 6.1$, 1.8, 1 H); 4.14, 3.59 (*AB* of *ABX*, $J_{AB} = 8.0$, $J_{AX} = 6.9$, $J_{BX} = 6.9$, 2 H); 3.65–3.63 (*m*, 1 H); 2.68–2.56 (*m*, 3 H); 2.32–2.24 (*m*, 1 H); 2.17 (*s*, 3 H); 2.04–1.87 (*m*, 3 H); 1.68–1.61 (*m*, 1 H); 1.00 (*d*, $J = 6.7$, 3 H); 0.90 (*d*, $J = 6.7$, 3 H). ^{13}C-NMR: 208.0, 182.1 (2*s*); 90.7 (*d*); 70.9 (*t*); 61.6, 42.0 (2*d*); 40.7 (*t*); 32.0 (*d*); 31.0 (*t*); 30.0 (*q*); 26.9 (*t*); 19.8, 18.5 (2*q*).

2.5. *(3S,6S,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6,7a-dimethyl-6-(3-oxobutyl)pyrrolo[2,1-b]oxazol-5-one* (**37**). Analogously to *2.1* with **27a** (240 mg, 0.91 mmol). Chromatography (Et_2O/hexane 1:4) gave 230 mg (95%) of **37**. $[\alpha]_D^{23} = +60.4$ ($c = 0.91$, $CHCl_3$). IR (neat): 1715, 1705. ^{1}H-NMR: 4.21, 3.78 (*AB* of *ABX*, $J_{AB} = 8.8$, $J_{AX} = 8.8$, $J_{BX} = 7.1$, 2 H); 3.64–3.51 (*m*, 1 H); 2.56–2.26 (*m*, 2 H); 2.16, 1.95 (*AB*, $J = 13.9$, 2 H); 2.13 (*s*, 3 H); 1.86–1.64 (*m*, 3 H); 1.50 (*s*, 3 H); 1.31 (*s*, 3 H); 1.13 (*d*, $J = 6.5$, 3 H); 0.88 (*d*, $J = 6.5$, 3 H). ^{13}C-NMR: 208.2, 183.5, 96.6 (3*s*); 70.4 (*t*); 61.8 (*d*); 46.8 (*s*); 46.0, 39.0 (2*t*); 34.1 (*d*); 31.9 (*t*); 29.9, 26.2, 25.7, 20.7, 18.9 (5*q*).

2.6. *(3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6,7a-dimethyl-6-(3-oxobutyl)pyrrolo[2,1-b]oxazol-5-one* (**38**). Analogously to *2.1* with **27b** (200 mg, 0.75 mmol). Chromatography (Et_2O/hexane 1:2) gave 197 mg (98%) of **38**. $[\alpha]_D^{23} = +25.7$ ($c = 0.98$, $CHCl_3$). IR (neat): 1710. ^{1}H-NMR: 4.20, 3.77 (*AB* of *ABX*, $J_{AB} = 8.7$, $J_{AX} = 7.7$, $J_{BX} = 7.0$, 2 H); 3.63–3.51 (*m*, 1 H); 2.59–2.49 (*m*, 2 H); 2.16 (*s*, 3 H); 2.10 (*s*, 2 H); 2.03–1.58 (*m*, 3 H); 1.50 (*s*, 3 H); 1.14 (*s*, 3 H); 1.03 (*d*, $J = 6.4$, 3 H); 0.88 (*d*, $J = 6.7$, 3 H). ^{13}C-NMR: 207.5, 184.3, 96.5 (3*s*); 70.1 (*t*); 61.8 (*d*); 47.2 (*t*); 46.1 (*s*); 38.6 (*t*); 33.8 (*d*); 33.1 (*t*); 29.8, 25.2, 23.6, 20.5, 18.6 (5*q*).

2.7. *(3S,5aR,8R,8aR,8bR)- and (3S,5aR,8S,8aR,8bR)-2,3,5a,6,7,8,8a,8b-Octahydro-8-hydroxy-3-isopropyl-5a,8a-dimethyl-5H-cyclopenta[3,4]pyrrolo[2,1-b]oxazol-5-one* (**39**). A soln. of **28b** (210 mg, 0.68 mmol) in acetone (5.0 ml), H_2O (0.5 ml), and conc. aq. HCl soln. (3 drops) was stirred at 23° for 20 h. Acetone was evaporated, H_2O added, and the mixture extracted with Et_2O. The extracts were washed with 5% $NaHCO_3$ soln., H_2O, and brine to give, after chromatography (Et_2O/hexane 1:1), 132 mg (77%) of **39**. $[\alpha]_D^{23} = +4.1$ ($c = 1.00$, $CHCl_3$). IR (neat): 3400 (br.), 1710. ^{1}H-NMR: 4.48–4.44 (*m*, 1 H); 4.13 (*t*, $J = 8.0$, 1 H); 3.75–3.54 (*m*, 2 H); 2.38 (br. *s*, 1 H); 2.10–1.43 (*m*, 5 H); 1.40 (*s*, 3 H); 1.36 (*s*, 3 H); 1.26 (br. *s*, 1 H, exchange with D_2O); 1.04 (*d*, $J = 6.5$, 3 H); 0.87 (*d*, $J = 6.5$, 3 H). ^{13}C-NMR: 187.4, 98.3 (2*s*); 75.3 (*d*); 68.8 (*t*); 64.3, 62.1 (2*d*); 53.0 (*s*); 35.3, 34.5 (2*t*); 33.8 (*d*); 26.0, 20.7, 19.9, 18.8 (4*q*).

2.8. *(3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6,7a-dimethyl-6-(4-oxobutyl)pyrrolo[2,1-b]oxazol-5-one* (**40**). Analogously to *2.1* with **29b** (493 mg, 1.86 mmol). Chromatography (Et_2O/hexane 1:4) gave 445 mg (90%) of **40**. $[\alpha]_D^{23} = +30.6$ ($c = 1.44$, $CHCl_3$). IR (neat): 2725, 1710. ^{1}H-NMR: 9.77 (*t*, $J = 1.3$, 1 H); 4.19, 3.76 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.8$, $J_{BX} = 7.0$, 2 H); 3.64–3.47 (*m*, 1 H); 2.49–2.45 (*m*, 2 H); 2.17, 2.07 (*AB*, $J = 14.0$, 2 H); 1.73–1.50 (*m*, 5 H); 1.48 (*s*, 3 H); 1.16 (*s*, 3 H); 1.04 (*d*, $J = 6.6$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 201.9 (*d*); 184.5, 96.7 (2*s*); 70.3 (*t*); 62.4 (*d*); 47.2 (*s*); 45.9, 43.8, 38.9 (3*t*); 34.1 (*d*); 25.3, 24.6, 20.8, 18.9 (4*q*); 17.4 (*t*).

2.9. *(3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6,7a-dimethyl-6-(4-oxopentyl)pyrrolo[2,1-b]oxazol-5-one* (**41**). Through a suspension of CuCl (370 mg, 3.78 mmol) and $PdCl_2(MeCN)_2$ (39 mg, 0.15 mmol) in MeOH (5 ml) at 23° was passed O_2 for 2 h, and after addition of **29b** (200 mg, 0.76 mmol), for another 48 h. It was quenched with sat. NH_4OH soln., evaporated, diluted with H_2O, and extracted with Et_2O to give, after chromatography (Et_2O/hexane 1:4), 75 mg (35%) of **41** along with 59 mg (29%) of C=C bond isomers of **29a**. **41**: $[\alpha]_D^{23} = +15.8$ ($c = 0.96$, $CHCl_3$). IR (neat): 1710. ^{1}H-NMR: 4.18, 3.76 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 8.0$, $J_{BX} = 7.0$, 2 H); 3.63–3.54 (*m*, 1 H); 2.47–2.42 (*m*, 2 H); 2.19, 2.05 (*AB*, $J = 14.0$, 2 H); 2.13 (*s*, 3 H); 1.69–1.42 (*m*, 8 H, therein 1.48 (*s*, 3 H)); 1.15 (*s*, 3 H); 1.04 (*d*, $J = 6.6$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 208.3, 184.6, 96.8 (3*s*); 70.2 (*t*); 62.4 (*d*); 47.2 (*s*); 45.7, 43.4, 38.8 (3*t*); 34.1 (*d*); 29.9, 25.2, 24.7, 20.8 (4*q*); 18.9 (*t* and *q*).

2.10. *(3S,6R,7aR)-2,3,5,6,7,7a-Hexahydro-3-isopropyl-6,7a-dimethyl-6-(5-oxopentyl)pyrrolo[2,1-b]oxazol-5-one* (**42**). Analogously to *2.1* with **30b** (707 mg, 2.53 mmol). Chromatography (Et_2O/hexane 1:4) gave 693 mg

(97%) of **42**. $[\alpha]_D^{23} = +18.6$ ($c = 2.76$, $CHCl_3$). IR (neat): 2720, 1710. ^{1}H-NMR: 9.75 (t, $J = 1.5$, 1 H); 4.17, 3.74 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.9$, $J_{BX} = 7.1$, 2 H); 3.61–3.52 (m, 1 H); 2.61–2.42 (m, 2 H); 2.09, 2.02 (*AB*, $J = 14.0$, 2 H); 1.67–1.52 (m, 5 H); 1.45 (s, 3 H); 1.42–1.14 (m, 2 H); 1.13 (s, 3 H); 1.02 (d, $J = 6.6$, 3 H); 0.86 (d, $J = 6.6$, 3 H). ^{13}C-NMR: 202.3 (d); 184.6, 96.7 (2s); 70.2 (t); 62.3 (d); 47.1 (s); 46.1, 43.7, 39.5 (3t); 34.1 (d); 25.2, 24.7 (2q); 24.3, 22.3 (2t); 20.8, 18.9 (2q).

2.11. *(3S,6*R*,7a*R*)-3-(*tert*-Butyl)-2,3,5,6,7,7a-hexahydro-6-methyl-6-(4-oxobutyl)pyrrolo[2,1-*b*]oxazol-5-one* (**43**). Analogously to *2.1* with **31b** (265 mg, 1.0 mmol). Chromatography (Et_2O/hexane 1:4) gave 250 mg (94%) of **43**. $[\alpha]_D^{23} = +9.1$ ($c = 0.30$, $CHCl_3$). IR (neat): 2720, 1710. ^{1}H-NMR: 9.75 (t, $J = 1.4$, 1 H); 4.94 (dd, $J = 6.3$, 2.4, 1 H); 4.02 (m, 1 H); 3.75 (m, 2 H); 2.45 (m, 2 H); 2.29 (dd, $J = 14.3$, 6.3, 1 H); 1.83 (dd, $J = 14.3$, 2.4, 1 H); 1.45–1.75 (m, 4 H); 1.16 (s, 3 H); 0.90 (s, 9 H). ^{13}C-NMR: 201.7 (d); 183.5 (s); 90.1 (d); 68.1 (t); 64.1 (d); 46.9 (s); 43.7, 39.2, 38.3 (3t); 33.8 (s); 26.2 (q, 3 C); 25.1 (t); 17.4 (q). Anal. calc. for $C_{15}H_{25}NO_3$ (267.371): C 67.38, H 9.42, N 5.24; found: C 67.22, H 9.23, N 5.55.

2.12. *(3S,6*R*,7a*R*)-3-(*tert*-Butyl)-2,3,5,6,7,7a-hexahydro-6-methyl-6-(5-oxopentyl)pyrrolo[2,1-*b*]oxazol-5-one* (**44**). Analogously to *2.1* with **32b** (410 mg, 1.47 mmol). Chromatography (Et_2O/hexane 1:4) gave 412 mg (99%) of crude **44**. IR (neat): 2720, 1710. ^{1}H-NMR: 9.76 (t, $J = 1.6$, 1 H); 4.94 (dd, $J = 6.3$, 2.6, 1 H); 4.42–4.10 (m, 1 H); 3.85–3.71 (m, 2 H); 2.45 (dt, $J = 1.6$, 7.2, 2 H); 2.26 (dd, $J = 14.1$, 6.3, 1 H); 1.83 (dd, $J = 14.1$, 2.6, 1 H); 1.70–1.20 (m, 6 H); 1.17 (s, 3 H); 0.92 (s, 9 H). This material was used without any further purification.

3. *Annulation Reaction.* 3.1. *(3S,5a*S*,8a*S*,8b*R*)-2,3,5a,6,8a,8b-Hexahydro-3-isopropyl-8,8b-dimethyl-5*H*-cyclopenta[3,4]pyrrolo[2,1-*b*]oxazol-5-one* (**45**). A soln. of **33** and/or **34** (146 mg, 0.58 mmol) and TosOH (20 mg, 0.06 mmol) in toluene (10 ml) was heated to reflux for 4 h while the condensates were dried by passing over 3-Å molecular sieves (GC: fast equilibration of the starting materials to **33**/**34** *ca.* 4:1). After cooling to 23°, the mixture was poured into H_2O and extracted with Et_2O. The org. layers were washed with sat. $NaHCO_3$ soln., H_2O, and brine to give, after chromatography (Et_2O/hexane 1:9), 78 mg (57%) of **45**. $[\alpha]_D^{23} = +93.8$ ($c = 0.69$, $CHCl_3$). IR (neat): 3040, 1710. ^{1}H-NMR: 5.40–5.39 (m, 1 H); 4.01, 3.83 (*AB* of *ABX*, $J_{AB} = 8.5$, $J_{AX} = 7.3$, $J_{BX} = 5.5$, 2 H); 3.60–3.48 (m, 1 H); 3.45–3.36 (m, 2 H); 3.18 (br. d, $J = 7.8$, 1 H); 2.76–2.65 (m, 1 H); 2.53–2.39 (m, 1 H); 1.84–1.82 (m, 3 H); 1.74–1.59 (m, 1 H); 1.56 (s, 3 H); 1.04 (d, $J = 6.6$, 3 H); 0.88 (d, $J = 6.5$, 3 H). ^{1}H-NOE: irrad. at 1.56 → NOE at 3.45–3.36 (1.3%) and 3.18 (3.3%). ^{13}C-NMR: 181.2, 137.8 (2s); 127.6 (d); 100.7 (s); 70.8 (t); 61.4, 58.9, 48.1 (3d); 34.4 (t); 33.0 (d); 27.6, 20.3, 19.1, 16.5 (4q). EI-MS: 235 (10, M^+), 215 (5, $[M - 20]^+$), 200 (17, $[M - 35]^+$), 128 (100), 80 (62), 79 (15), 44 (17), 41 (8).

3.2. *(3S,5a*S*,8a*S*,8b*R*)- and (3S,5a*R*,8a*R*,8b*R*)-2,3,5a,6,8a,8b-Hexahydro-3-isopropyl-8-methyl-5*H*-cyclopenta[3,4]pyrrolo[2,1-*b*]oxazol-5-one* (**47** and **48**, resp.). Analogously to *3.1*, **35** and/or **36** (379 mg, 1.66 mmol) was reacted for 1.5 h. Chromatography (Et_2O/hexane 1:4) gave 84 mg (23%) of **47** and 140 mg (38%) of **48**.

Data of **47**: M.p. 61–62° (EtOH/hexane). $[\alpha]_D^{23} = +142.9$ ($c = 1.20$, $CHCl_3$). IR (neat): 3040, 1710, 1660. ^{1}H-NMR: 5.42–5.41 (m, 1 H); 5.21 (d, $J = 6.1$, 1 H); 4.16–4.07 (m, 1 H); 3.72–3.58 (m, 2 H); 3.46–3.35 (m, 2 H); 2.72–2.45 (m, 2 H); 1.83–1.82 (m, 3 H); 1.73–1.60 (m, 1 H); 1.00 (d, $J = 6.7$, 3 H); 0.90 (d, $J = 6.7$, 3 H). ^{1}H-NOE: irrad. at 5.21 → NOE at 3.72–3.58 (2.9%), 3.46–3.35 (11.8%), and 1.73–1.60 (1.7%). ^{13}C-NMR: 181.4, 137.0 (2s); 127.5, 93.0 (2d); 71.1 (t); 60.0, 50.5, 47.8 (3d); 34.8 (t); 31.2 (d); 19.6, 18.5, 16.6 (3q).

Data of **48** (oil): $[\alpha]_D^{23} = -72.9$ ($c = 1.22$, $CHCl_3$). IR (neat): 3045, 1715. ^{1}H-NMR: 5.39–5.35 (m, 1 H); 4.73 (s, 1 H); 4.16, 3.58 (*AB* of *ABX*, $J_{AB} = 7.9$, $J_{AX} = 6.8$, $J_{BX} = 6.8$, 2 H); 3.75–3.64 (m, 1 H); 3.33–3.25 (m, 2 H); 2.86–2.72 (m, 1 H); 2.65–2.53 (m, 1 H); 1.84–1.82 (m, 3 H); 1.71–1.55 (m, 1 H); 1.00 (d, $J = 6.7$, 3 H); 0.89 (d, $J = 6.7$, 3 H). ^{13}C-NMR: 184.1, 137.3 (2s); 126.1, 94.1 (2d); 70.6 (t); 61.6, 52.8, 46.0 (3d); 36.3 (t); 32.1 (d); 19.9, 18.4, 14.5 (3q).

3.3. *(3S,5a*S*,8a*R*,8b*R*)-2,3,5a,6,8a,8b-Hexahydro-3-isopropyl-5a,8,8b-trimethyl-5*H*-cyclopenta[3,4]pyrrolo-[2,1-*b*]oxazol-5-one* (**49**). Analogously to *3.1*, **37** (100 mg, 0.41 mmol) was reacted for 45 min. Chromatography (Et_2O/hexane 1:4) gave 83 mg (80%) of **49**.

Analogously to *1.1* with **45** (50 mg, 0.21 mmol), LDA (0.26 mmol), DMPU (0.26 mmol), and MeI (0.04 ml, 0.63 mmol). Chromatography (Et_2O/hexane 1:9) gave 36.9 mg (70%) of **49**. $[\alpha]_D^{23} = +97.2$ ($c = 0.86$, $CHCl_3$). IR (neat): 3010, 1700. ^{1}H-NMR: 5.30 (br. s, 1 H); 4.06, 3.79 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.5$, $J_{BX} = 6.3$, 2 H); 3.60–3.48 (m, 1 H); 2.86–2.77 (m, 2 H); 2.16–2.06 (m, 1 H); 1.89 (br. s, 3 H); 1.73–1.58 (m, 1 H); 1.55 (s, 3 H); 1.42 (s, 3 H); 1.05 (d, $J = 6.6$, 3 H); 0.88 (d, $J = 6.6$, 3 H). ^{13}C-NMR: 184.4, 137.5 (2s); 126.3 (d); 99.5 (s); 70.5 (t); 65.8, 61.3 (2d); 55.5 (s); 43.5 (t); 33.4 (d); 27.7, 24.6, 20.4, 19.0, 16.7 (5q). EI-MS: 249 (12, M^+), 229 (4, $[M - 20]^+$), 214 (11, $[M - 35]^+$), 186 (6), 128 (76), 94 (100), 79 (28), 77 (6), 41 (5).

3.4. *(3S,5a*R*,8a*S*,8b*R*)-2,3,5a,6,8a,8b-Hexahydro-3-isopropyl-5a,8,8b-trimethyl-5*H*-cyclopenta[3,4]pyrrolo-[2,1-*b*]oxazol-5-one* (**50**). Analogously to *3.1*, **38** (170 mg, 0.64 mmol) was reacted for 30 min. Chromatography (Et_2O/hexane 1:4) gave 126 mg (80%) of **50**. $[\alpha]_D^{23} = -75.0$ ($c = 1.28$, $CHCl_3$). IR (neat): 3010, 1710. ^{1}H-NMR: 5.45–5.44 (m, 1 H); 4.24, 3.78 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.8$, $J_{BX} = 7.2$, 2 H); 3.66–3.53 (m, 1 H); 2.75–2.74

(*m*, 1 H); 2.69–2.57 (*m*, 1 H); 2.23–2.12 (*m*, 1 H); 1.86–1.84 (*m*, 3 H); 1.77–1.59 (*m*, 1 H); 1.33 (*s*, 3 H); 1.23 (*s*, 3 H); 1.09 (*d*, J = 6.6, 3 H); 0.88 (*d*, J = 6.6, 3 H). ^{13}C-NMR: 182.8, 137.7 (2*s*); 126.6 (*d*); 99.1 (*s*); 70.5 (*t*); 67.2, 61.6 (2*d*); 55.3 (*s*); 44.3 (*t*); 33.5 (*d*); 23.9, 21.0, 20.7, 18.9, 17.2 (5*q*). CI-MS: 250 ([M + H]$^+$).

3.5. *(3S,5aR,8aS,8bR)-2,3,5a,6,8a,8b-Hexahydro-3-isopropyl-5a,8b-dimethyl-5*H*-cyclopenta[3,4]pyrrolo-[2,1-b]oxazol-5-one* (**51**). Analogously to *3.1*, **39** (21.2 mg, 0.084 mmol) was reacted for 15 min. Chromatography (Et_2O/hexane 1:4) gave 16.8 mg (84%) of **51**. M.p. 93.0–95.0° (MeOH/H_2O). $[\alpha]_D^{23} = -14.8$ (c = 1.03, $CHCl_3$). IR (neat): 3015, 1705, 1620. ^{1}H-NMR: 5.75–5.72 (*m*, 2 H); 4.20, 3.76 (*AB* of *ABX*, J_{AB} = 8.5, J_{AX} = 7.9, J_{BX} = 7.0, 2 H); 3.67–3.57 (*m*, 1 H); 3.07 (br. *s*, 1 H); 2.82–2.73 (*m*, 1 H); 2.34–2.24 (*m*, 1 H); 1.72–1.56 (*m*, 1 H); 1.31 (*s*, 3 H); 1.30 (*s*, 3 H); 1.04 (*d*, J = 6.7, 3 H); 0.87 (*d*, J = 6.6, 3 H). ^{13}C-NMR: 185.9 (*s*); 131.6, 128.6 (2*d*); 99.7 (*s*); 69.7 (*t*); 63.2, 61.9 (2*d*); 55.4 (*s*); 45.1 (*t*); 34.2 (*d*); 25.2, 21.2, 20.9, 19.0 (4*q*).

3.6. *(3S,5aR,9aS,9bR)-2,3,5,5a,6,7,9a,9b-Octahydro-3-isopropyl-5a,9b-dimethyloxazolo[2,3-a]isoindol-5-one* (**52**). Analogously to *3.1*, **40** (109 mg, 0.41 mmol) was reacted for 10 min. Chromatography (Et_2O/hexane 1:6) gave 91 mg (90%) of **52**. $[\alpha]_D^{23} = -12.5$ (c = 0.98, $CHCl_3$). IR (neat): 3015, 1695. ^{1}H-NMR: 5.99–5.91 (*m*, 1 H); 5.81–5.73 (*m*, 1 H); 4.24, 3.83 (*AB* of *ABX*, J_{AB} = 8.7, J_{AX} = 7.5, J_{BX} = 6.8, 2 H); 3.67–3.59 (*m*, 1 H); 2.46–2.44 (*m*, 1 H); 2.13–2.07 (*m*, 2 H); 1.76–1.57 (*m*, 3 H); 1.34 (*s*, 3 H); 1.13 (*s*, 3 H); 1.03 (*d*, J = 6.6, 3 H); 0.89 (*d*, J = 6.6, 3 H). ^{1}H-NOE: irrad. at 2.46–2.44 → NOE at 5.81–5.73 (7.7%) and 1.03 (3.6%); irrad. at 1.34 → NOE at 5.81–5.73 (2.4%), 3.83 (2.0%), and 1.76–1.57 (1.8%); irrad. at 1.13 → NOE at 2.46–2.44 (4.4%), 2.13–2.07 (2.3%), and 1.76–1.57 (1.5%). ^{13}C-NMR: 182.8 (*s*); 129.0, 122.8 (2*d*); 98.6 (*s*); 71.1 (*t*); 61.0, 52.1 (2*d*); 45.6 (*s*); 34.1 (*d*); 28.8 (*t*); 22.9 (*q*); 21.1 (*t*); 20.6, 20.5, 19.0 (3*q*).

3.7. *(3S,5aR,9aS,9bR)-2,3,5,5a,6,7,9a,9b-Octahydro-3-isopropyl-5a,9,9b-trimethyloxazolo[2,3-a]isoindol-5-one* (**53**). Analogously to *3.1*, **41** (72 mg, 0.26 mmol) was reacted for 30 min. Chromatography (Et_2O/hexane 1:8) gave 60 mg (89%) of **53**. $[\alpha]_D^{23} = -28.7$ (c = 0.87, $CHCl_3$). IR (neat): 3015, 1710. ^{1}H-NMR: 5.65–5.64 (*m*, 1 H); 4.26, 3.87 (*AB* of *ABX*, J_{AB} = 8.8, J_{AX} = 7.5, J_{BX} = 6.6, 2 H); 3.66–3.57 (*m*, 1 H); 2.26 (*s*, 1 H); 2.13–2.09 (*m*, 2 H); 1.78–1.77 (*m*, 3 H); 1.70–1.61 (*m*, 3 H); 1.37 (*s*, 3 H); 1.08 (*s*, 3 H); 1.03 (*d*, J = 6.7, 3 H); 0.89 (*d*, J = 6.6, 3 H). ^{13}C-NMR: 182.3, 129.1 (2*s*); 123.9 (*d*); 98.6 (*s*); 71.5 (*t*); 60.5, 57.3 (2*d*); 46.4 (*s*); 34.0 (*d*); 28.0 (*t*); 23.4, 21.9 (2*q*); 21.7 (*t*); 20.6, 20.1, 19.0 (3*q*).

3.8. *(1R or 1S,6R,9S,12R,19R,22S,13E or 13Z,25Z)-9,22-Diisopropyl-6,12,19-trimethyl-11,24-dioxa-8,21-diazapentacyclo[17.5.3.0^{6,13}.0^{8,12}.0^{21,26}]heptacosa-13,25-diene-7,20-dione* (**54**). Analogously to *3.1*, **42** (211 mg, 0.75 mmol) was reacted for 8 h. Chromatography (Et_2O/hexane 1:1) gave 50 mg (25%) of **54**. ^{1}H-NMR: 6.00 (*dd*, J = 8.5, 1.9, 1 H); 5.71–5.64 (*m*, 1 H); 4.27 (*dd*, J = 13.4, 3.1, 1 H); 4.19 (*t*, J = 8.2, 1 H); 3.86 (*dd*, J = 10.9, 2.1, 1 H); 3.76 (*dd*, J = 8.6, 7.1, 1 H); 3.63–3.55 (*m*, 1 H); 3.31 (*d*, J = 12.9, 1 H); 3.27–3.22 (*m*, 1 H); 2.73 (*d*, J = 16.0, 1 H); 2.45–1.98 (*m*, 7 H); 1.90–1.24 (*m*, 15 H, therein 1.47 (*s*, 3 H)); 1.20 (*s*, 3 H); 1.15 (*s*, 3 H); 1.05 (*d*, J = 6.3, 3 H); 1.04 (*d*, J = 6.5, 3 H); 0.88 (*d*, J = 6.6, 3 H); 0.83 (*d*, J = 6.8, 3 H). ^{13}C-NMR: 184.6, 182.7, 135.5 (3*s*); 130.2 (*d*); 122.3 (*s*); 121.0 (*d*); 98.7 (*s*); 80.9 (*d*); 71.4, 70.3 (2*t*); 66.2, 59.0 (2*d*); 49.3, 47.3 (2*s*); 46.2, 39.7, 36.7, 35.7 (4*t*); 34.1 (*d*); 33.4, 30.1 (2*t*); 29.1 (*d*); 26.1 (*t*); 25.3 (*q*); 24.7 (*t*); 24.6 (*q*); 23.1 (*t*); 22.8, 20.8, 20.0, 19.3, 18.9 (5*q*).

3.9. *(3S,5aR,9aS,9bR)-3-(*tert*-Butyl)-2,3,5,5a,6,7,9a,9b-octahydro-5a-methyloxazolo[2,3-a]isoindol-5-one* (**55**). Analogously to *3.1*, **43** (315 mg, 1.17 mmol) was reacted for 5 h. Chromatography (Et_2O/hexane 1:6) gave 255 mg (87%) of **55**. $[\alpha]_D^{23} = +4.3$ (c = 1.50, hexane). IR (neat): 3025, 1715. ^{1}H-NMR: 5.97–5.79 (*m*, 2 H); 4.76 (*d*, J = 3.8, 1 H); 4.09, 3.82 (*AB* of *ABX*, J_{AB} = 8.2, J_{AX} = 7.0, J_{BX} = 6.7, 2 H); 3.78 (*dd*, J = 7.0, 6.7, 1 H); 2.36–2.30 (*m*, 1 H); 2.08–2.02 (*m*, 2 H); 1.73–1.66 (*m*, 2 H); 1.15 (*s*, 3 H); 0.91 (*s*, 9 H). ^{13}C-NMR: 183.7 (*s*); 129.1, 124.4, 95.6 (3*d*); 68.6 (*t*); 63.1, 47.2 (2*d*); 46.0, 34.1 (2*s*); 30.7 (*t*); 26.2 (*q*, 3 C); 21.4 (*t*); 21.2 (*q*). Anal. calc. for $C_{15}H_{23}NO_2$ (249.356): C 72.25, H 9.30, N 5.62; found: C 72.54, H 9.45, N 5.37.

3.10. *(3S,5aR,10bR)-3-(*tert*-Butyl)-2,3,5a,6,7,8,9,10b-octahydro-5a-methyl-5*H*-cyclohepta[3,4]pyrrolo-[1,2-b]oxazol-5-one* (**56**). Analogously to *3.1*, **44** (420 mg, 1.47 mmol) was reacted for 30 min. Chromatography (Et_2O/hexane 1:6) gave 95 mg (24%) of **56**. $[\alpha]_D^{23} = +11.5$ (c = 0.013, $CHCl_3$). IR (neat): 3025, 1715. ^{1}H-NMR: 6.19 (*t*, J = 6.4, 1 H); 5.04 (*s*, 1 H); 4.08–4.00 (*m*, 1 H); 3.84–3.72 (*m*, 2 H); 2.30–2.22 (*m*, 2 H); 1.97–1.78 (*m*, 4 H); 1.50–1.20 (*m*, 2 H); 1.28 (*s*, 3 H); 0.95 (*s*, 9 H). ^{13}C-NMR: 187.2, 140.7 (2*s*); 132.3, 92.8 (2*d*); 67.4 (*t*); 66.2, 48.8 (2*d*); 34.9, 33.6 (2*s*); 27.8, 27.5 (2*t*); 26.2 (*q*, 3 C); 25.6 (*q*); 21.0 (*t*).

4. *Preparation and Alkylation of* **60** *and* **61**. 4.1. *(R)-N-[1-(Hydroxymethyl)-2-methylpropyl]cyclopentane-1,2-dicarboximide* (**59**). A mixture of (+)-(*S*)-valinol (**57**, 1.95 g, 18.9 mmol) and cyclopentane-1,2-dicarboxylic acid (**58**, 3.00 g, 18.9 mmol) was heated with a heating gun to give a homogeneous liquid. The mixture was heated to 220° while a stream of Ar was passed over the liquid. Cooling to 23° resulted in 4.20 g (99%) of **59** as a glassy brown product, which was used for further transformation without purification. A sample of pure **59** was obtained by bulb-to-bulb distillation (250°/0.1 Torr) and recrystallization. M.p. 89.0–90.0° (pentane/Et_2O). $[\alpha]_D^{23} = +11.2$ (c = 1.05, EtOH). IR (neat): 3480, 1695. ^{1}H-NMR: 4.03–3.93 (*m*, 1 H); 3.82–3.68 (*m*, 2 H); 3.16–3.11 (*m*, 2 H); 2.83

(br. *s*, 1 H); 2.40–2.34 (*m*, 1 H); 2.18–2.07 (*m*, 2 H); 1.93–1.71 (*m*, 3 H); 1.38–1.30 (*m*, 1 H); 1.00 (*d*, *J* = 6.7, 3 H); 0.76 (*d*, *J* = 6.7, 3 H). ^{13}C-NMR: 181.4 (*s*, 2 C); 61.3 (*t*); 60.5 (*d*); 44.9 (*d*, 2 C); 34.7 (*d*); 30.4 (*t*, 2 C); 26.0 (*t*); 24.6, 19.7 (2*q*). Anal. calc. for $C_{12}H_{19}NO_3$ (225.290): C 63.98, H 8.50; found: C 64.22, H 8.44.

4.2. *(3*S*,5a*S*,8a*R*,8b*R*)- and (3*S*,5a*R*,8a*S*,8b*R)-2,3,5a,6,7,8,8a,8b-Octahydro-3-isopropyl-8b-methyl-5*H*-cyclopenta[3,4]pyrrolo[2,1-*b*]oxazol-5-one* (**60** and **61**, resp.). To a soln. of **59** (730 mg, 3.20 mmol) in THF (25 ml) was added 3M MeMgBr in Et_2O (3.3 ml, 9.9 mmol) at 23°. The mixture was stirred for 3 h, then poured into 25 ml of sat. NH_4Cl soln., and extracted with Et_2O. The extracts were washed with brine, dried (K_2CO_3), and evaporated. The residue was dissolved in CH_2Cl_2 (20 ml) and added to a soln. of CF_3CO_2H (2.5 ml, 32 mmol) in CH_2Cl_2 (50 ml) at 0°. The mixture was warmed to 23°, stirred for another 1.5 h, and then poured on sat. $NaHCO_3$ soln. (50 ml). Extraction with CH_2Cl_2 and chromatography (AcOEt/hexane 15:85) gave 118 mg (17%) of **60** and 196 mg (27%) of **61**.

Data of **60**: M.p. 62.0–63.0 (hexane/AcOEt). $[\alpha]_D^{23} = +81.7$ (*c* = 1.48, EtOH). IR (neat): 1710. ^{1}H-NMR: 4.09 (*t*, *J* = 7.8, 1 H); 3.81 (*t*, *J* = 7.8, 1 H); 3.54–3.45 (*m*, 1 H); 3.22–3.15 (*m*, 1 H); 2.56–2.50 (*m*, 1 H); 2.04–1.99 (*m*, 1 H); 1.78–1.33 (*m*, 6 H); 1.43 (*s*, 3 H); 0.96 (*d*, *J* = 6.6, 3 H); 0.81 (*d*, *J* = 6.6, 3 H). ^{13}C-NMR: 180.7, 98.7 (2*s*); 71.3 (*t*); 61.2, 50.6, 49.3, 33.5 (4*d*); 28.9, 27.2, 26.8 (3*t*); 26.1, 20.3, 18.9 (3*q*). EI-MS: 223 (17, $M^{+\cdot}$), 208 (43), 180 (31), 140 (37), 128 (100), 84 (36). Anal. calc. for $C_{13}H_{21}NO_2$ (223.318): C 69.92, H 9.48; found: C 70.02, H 9.44.

Data of **61**: $[\alpha]_D^{23} = +27.4$ (*c* = 1.20, EtOH). IR (neat): 1715. ^{1}H-NMR: 4.06 (*t*, *J* = 8.2, 1 H); 3.64 (*t*, *J* = 8.2, 1 H); 3.55–3.51 (*m*, 1 H); 2.99–2.92 (*m*, 1 H); 2.75–2.68 (*m*, 1 H); 1.92–1.29 (*m*, 7 H); 1.29 (*s*, 3 H); 0.97 (*d*, *J* = 6.6, 3 H); 0.80 (*d*, *J* = 6.6, 3 H). ^{13}C-NMR: 184.6, 101.2 (2*s*); 69.2 (*t*); 64.0, 48.5, 46.7, 33.9 (4*d*); 30.7, 29.4, 26.0 (3*t*); 20.7, 19.9, 18.9 (3*q*). EI-MS: 223 (6, $M^{+\cdot}$), 208 (34), 188 (38), 139 (40), 138 (90), 128 (60), 55 (100). Anal. calc. for $C_{13}H_{21}NO_2$ (223.318): C 69.92, H 9.48; found: C 69.63, H 9.81.

4.3. *(3*S*,5a*S*,8a*R*,8b*R)-5a-(4-Bromobenzyl)-2,3,5a,6,7,8,8a,8b-octahydro-3-isopropyl-8b-methyl-5*H*-cyclopenta[3,4]pyrrolo[2,1-*b*]oxazol-5-one* (**62**). Analogously to *1.1* with **60** (176 mg, 0.79 mmol), LDA (1.2 mmol), DMPU (2 ml), and 4-bromobenzyl bromide (650 mg, 2.6 mmol). Chromatography (AcOEt/hexane 1:9) gave 263 mg (85%) of **62**. $[\alpha]_D^{23} = -26.6$ (*c* = 0.67, EtOH). IR (neat): 1700. ^{1}H-NMR: 7.38 (*d*, *J* = 8.3, 2 H); 7.06 (*d*, *J* = 8.3, 2 H); 4.08 (*t*, *J* = 8.1, 1 H); 3.64 (*dd*, *J* = 8.4, 6.7, 1 H); 3.57–3.49 (*m*, 1 H); 3.24 (*d*, *J* = 13.3, 1 H); 2.52 (*d*, *J* = 13.3, 1 H); 2.29–2.09 (*m*, 3 H); 1.58–1.22 (*m*, 5 H); 0.96 (*d*, *J* = 6.6, 3 H); 0.80 (*d*, *J* = 6.6, 3 H); 0.69 (*s*, 3 H). ^{13}C-NMR: 183.0, 137.3 (2*s*); 131.9, 131.2 (2*d*, 2 C each); 120.7, 97.8 (2*s*); 70.3 (*t*); 63.1, 61.7 (2*d*); 49.8 (*s*); 42.8, 39.8 (2*t*); 34.3 (*d*); 28.5, 26.5 (2*t*); 25.3, 20.6, 19.0 (3*q*). Anal. calc. for $C_{20}H_{26}BrNO_2$ (392.345): C 61.23, H 6.68; found: C 61.65, H 6.76.

4.4. *(3*S*,5a*S*,8a*R*,8b*R)-2,3,5a,6,7,8,8a,8b-Octahydro-3-isopropyl-5a,8b-dimethyl-5*H*-cyclopenta[3,4]pyrrolo-[2,1-*b*]oxazol-5-one* (**63**). Analogously to *1.1* with **60** (176 mg, 0.79 mmol), LDA (1.2 mmol), DMPU (2 ml), and MeI (439 mg, 2.6 mmol). Chromatography (AcOEt/hexane 3:7) gave 185 mg (100%) of **63**. $[\alpha]_D^{23} = +77.0$ (*c* = 1.14, EtOH). IR (neat): 1710. ^{1}H-NMR: 4.13 (*t*, *J* = 7.8, 1 H); 3.81 (*dd*, *J* = 8.7, 6.5, 1 H); 3.59–3.51 (*m*, 1 H); 2.23–1.97 (*m*, 2 H); 1.68–1.23 (*m*, 6 H); 1.46 (*s*, 3 H); 1.37 (*s*, 3 H); 1.10 (*d*, *J* = 6.6, 3 H); 0.86 (*d*, *J* = 6.6, 3 H). ^{13}C-NMR: 184.1, 97.7 (2*s*); 70.7 (*t*); 61.1, 57.3 (2*d*); 55.2 (*s*); 38.5 (*t*); 33.8 (*d*); 28.0, 27.4 (2*t*); 26.5, 24.4, 20.4, 18.9 (4*q*). Anal. calc. for $C_{14}H_{23}NO_2$ (237.345): C 70.85, H 9.77; found: C 70.92, H 9.70.

4.5. *(3*S*,5a*R*,8a*R*,8b*R)-5a-Allyl-2,3,5a,6,7,8,8a,8b-octahydro-3-isopropyl-8b-methyl-5*H*-cyclopenta[3,4]-pyrrolo[2,1-*b*]oxazol-5-one* (**64**). Analogously to *1.1* with **60** (176 mg, 0.79 mmol), LDA (1.2 mmol), DMPU (2 ml), and allyl bromide (315 mg, 2.6 mmol). Chromatography (AcOEt/hexane 3:7) gave 206 mg (99%) of **64**. $[\alpha]_D^{23} = +31.8$ (*c* = 0.97, EtOH). IR (neat): 3075, 1710, 1640. ^{1}H-NMR: 5.82–5.69 (*m*, 1 H); 5.13–5.05 (*m*, 2 H); 4.13, 3.75 (*AB* of *ABX*, $J_{AB} = 8.6$, $J_{AX} = 7.9$, $J_{BX} = 6.7$, 2 H); 3.60–3.52 (*m*, 1 H); 2.55–2.48 (*m*, 1 H); 2.33–2.21 (*m*, 2 H); 2.11–2.02 (*m*, 2 H); 1.65–1.23 (*m*, 5 H); 1.41 (*s*, 3 H); 1.00 (*d*, *J* = 6.6, 3 H); 0.84 (*d*, *J* = 6.6, 3 H). ^{13}C-NMR: 183.6 (*s*); 134.5 (*d*); 118.1 (*t*); 98.0 (*s*); 70.4 (*t*); 61.6, 61.1 (2*d*); 51.4 (*s*); 41.8, 37.1 (2*t*); 34.1 (*d*); 28.4, 26.5 (2*t*); 26.4, 20.7, 18.9 (3*q*). Anal. calc. for $C_{16}H_{25}NO_2$ (263.383): C 72.97, H 9.57; found: C 72.82, H 9.75.

4.6. *(3*S*,5a*R*,8a*S*,8b*R)-5a-(4-Bromobenzyl)-2,3,5a,6,7,8,8a,8b-octahydro-3-isopropyl-8b-methyl-5*H*-cyclopenta[3,4]pyrrolo[2,1-*b*]oxazol-5-one* (**65**). Analogously to *1.1* with **61** (176 mg, 0.79 mmol), LDA (1.2 mmol), DMPU (2 ml), and 4-bromobenzyl bromide (650 mg, 2.6 mmol). Chromatography (AcOEt/hexane 1:9) gave 306 mg (99%) of **65**. $[\alpha]_D^{23} = +50.8$ (*c* = 0.75, EtOH). IR (neat): 1710. ^{1}H-NMR: 7.26–7.23 (*m*, 2 H); 6.94–6.92 (*m*, 2 H); 3.45–3.28 (*m*, 3 H); 3.02 (*d*, *J* = 13.3, 1 H); 2.50–2.43 (*m*, 1 H); 2.46 (*d*, *J* = 13.3, 1 H); 2.04–1.99 (*m*, 1 H); 1.81–1.76 (*m*, 1 H); 1.52–1.15 (*m*, 5 H); 1.14 (*s*, 3 H); 0.92 (*d*, *J* = 6.6, 3 H); 0.71 (*d*, *J* = 6.6, 3 H). ^{13}C-NMR: 185.4, 137.2 (2*s*); 131.7, 130.6 (2*d*, 2 C each); 120.3, 99.2 (2*s*); 68.8 (*t*); 63.9, 60.1 (2*d*); 49.0 (*s*); 42.2, 38.0 (2*t*); 33.9 (*d*); 29.1, 25.5 (2*t*); 20.8, 19.8, 18.9 (3*q*).

4.7. *(3*S*,5a*R*,8a*S*,8b*R)-2,3,5a,6,7,8,8a,8b-Octahydro-3-isopropyl-5a,8b-dimethyl-5*H*-cyclopenta[3,4]oxazol-5-one* (**66**). Analogously to *1.1* with **61** (176 mg, 0.79 mmol), LDA (1.2 mmol), DMPU (2 ml), and MeI (439 mg, 2.6 mmol). Chromatography (AcOEt/hexane 3:7) gave 183 mg (98%) of **66**.

A mixture of **51** (30 mg, 0.13 mmol) and 10% Pd/C (10 mg) in AcOEt (3 ml) of was stirred under H_2 (1 atm) for 18 h and then filtered through a pad of *Celite*. Evaporation yielded 25.7 mg (85%) of **66**. $[\alpha]_D^{23} = +13.5$ ($c = 1.55$, EtOH). IR (neat): 1715. ^{1}H-NMR: 4.11 (*t*, $J = 8.1$, 1 H); 3.71–3.55 (*m*, 2 H); 2.39–2.35 (*m*, 1 H); 2.07–1.35 (*m*, 7 H); 1.33 (*s*, 3 H); 1.24 (*s*, 3 H); 1.03 (*d*, $J = 6.6$, 3 H); 0.86 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 187.2, 99.6 (2*s*); 69.1 (*t*); 64.1, 54.2 (2*d*); 54.1 (*s*); 39.3 (*t*); 34.1 (*d*); 29.1, 26.2 (2*t*); 25.3, 20.9, 29.8, 19.0 (4*q*). Anal. calc. for $C_{14}H_{23}NO_2$ (237.345): C 70.85, H 9.77; found: C 71.11, H 9.80.

4.8. *(3S,5aR,8aS,8bR)-5a-(But-3-enyl)-2,3,5a,6,7,8,8a,8b-octahydro-3-isopropyl-8b-methyl-5*H*-cyclopenta-[3,4]pyrrolo[2,1-b]oxazol-5-one* (**67**). Analogously to *1.1* with **61** (176 mg, 0.79 mmol), LDA (1.2 mmol), DMPU (2 ml), and 4-bromobut-1-ene (351 mg, 2.6 mmol). Chromatography (AcOEt/hexane 3:7) gave 206 mg (99%) of **64**. $[\alpha]_D^{23} = +26.8$ ($c = 0.44$, EtOH). IR (neat): 3080, 1710, 1660. ^{1}H-NMR: 5.81–5.68 (*m*, 1 H); 5.00–4.86 (*m*, 2 H); 4.08, 3.69 (*AB* of *ABX*, $J_{AB} = 8.5$, $J_{AX} = 8.5$, $J_{BX} = 6.9$, 2 H); 3.61–3.53 (*m*, 1 H); 2.52–2.49 (*m*, 1 H); 2.12–1.32 (*m*, 11 H); 1.32 (*s*, 3 H); 1.02 (*d*, $J = 6.6$, 3 H); 0.85 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR: 186.0 (*s*); 138.4 (*d*); 114.2 (*t*); 99.3 (*s*); 68.9 (*t*); 63.9, 58.3 (2*d*); 50.3 (*s*); 38.2, 37.1 (2*t*); 34.0 (*d*); 29.7, 29.2, 25.5 (3*t*); 20.8, 19.6, 18.9 (3*q*). Anal. calc. for $C_{17}H_{27}NO_2$ (277.410): C 73.61, H 9.81; found: C 73.50, H 9.99.

5. *Conversion to the Fused Cyclopentenones.* 5.1. *(1R,5S)-4,5-Dimethylbicyclo[3.3.0]oct-3-en-2-one* (**68**) *and (1S,5R)-1,4-Dimethylbicyclo[3.3.0]oct-3-en-2-one* (**69**). A soln. of **63** (1.20 g, 5.06 mmol) in THF (100 ml) was cooled to −78° and 1.3M MeLi in Et_2O (8.2 ml, 10.6 mmol) was added. The mixture was warmed up to −25°, stirred for 2 d, quenched with sat. NH_4Cl soln. (5 ml), and warmed to 23°. After removal of the volatiles *in vacuo*, the mixture was extracted with Et_2O. The org. extracts were washed with brine, dried (K_2CO_3), and evaporated. The crude mixture of enamine and amino alcohol was dissolved in abs. EtOH (30 ml) and treated with 1M aq. $(Bu_4N)H_2PO_4$ soln. (70 ml) at 23° for 1 h and at reflux for 16 h. The bulk of the solvent was removed by distillation through a short-path distillation head at ambient pressure and the residue extracted with Et_2O/pentane 1:1. The combined org. extracts were washed with H_2O and brine, dried, and concentrated in the rotary evaporator at ambient pressure: crude dicarbonyl compound. This crude intermediate was dissolved in abs. EtOH (75 ml) and treated with a freshly prepared soln. of EtONa in EtOH (140 mg (6.08 mmol) of Na dissolved in 5 ml of EtOH) for 25 h at 23°. The mixture was neutralized with 10% aq. HCl soln., the bulk of the solvents was evaporated through a short-path distillation head at ambient pressure, and the residue extracted with Et_2O/pentane 1:1. The org. extracts were washed with H_2O and brine, dried, and concentrated in the rotary evaporator at ambient pressure. Chromatography (Et_2O/pentane gradient) gave 183 mg (24%; slightly contaminated) of **68** and 205 mg (27%) of **69**. Anal. samples were obtained by microdistillation.

Data of **68**: $[\alpha]_D^{23} = -12.5$ ($c = 1.22$, EtOH). IR (neat): 1705, 1620. ^{1}H-NMR: 5.81 (*q*, $J = 1.2$, 1 H); 2.29–2.26 (*m*, 1 H); 2.00 (*d*, $J = 1.2$, 3 H); 1.84–1.12 (*m*, 6 H); 1.25 (*s*, 3 H). ^{13}C-NMR: 211.5, 183.3 (2*s*); 130.6 (*d*); 58.6 (*s*); 54.7 (*d*); 36.1, 29.5, 25.0 (3*t*); 24.2, 14.7 (2*q*). Spectra in agreement with literature reports [19].

Data of **69**: $[\alpha]_D^{23} = +81.1$ ($c = 1.24$, EtOH). IR (neat): 1705, 1620. ^{1}H-NMR: 5.84 (*q*, $J = 1.1$, 1 H); 2.66 (*q*, $J = 9.2$, 1 H); 2.05 (*t*, $J = 1.1$, 3 H); 1.91–1.64 (*m*, 6 H); 1.16 (*s*, 3 H). ^{13}C-NMR: 214.5, 178.7 (2*s*); 129.9 (*d*); 57.7 (*s*); 55.9 (*d*); 37.2, 28.4, 24.7 (3*t*); 22.3, 17.7 (2*q*). Spectra in agreement with literature reports [21].

5.2. *(1R,5R)-5-Allyl-4-methylbicyclo[3.3.0]oct-3-en-2-one* (**70**) *and (1R,5R)-1-Allyl-4-methylbicyclo[3.3.0]-oct-3-en-2-one* (**71**). Analogously to *5.1* with **64** (1.33 g, 5.06 mmol) and MeLi (10.6 mmol). Chromatography gave 164 mg (18%) of **70** and 173 mg (19%) of **71**.

Data of **70**: $[\alpha]_D^{23} = +40.9$ ($c = 1.03$, EtOH). IR (neat): 3080, 1705, 1640, 1620. ^{1}H-NMR: 5.88 (*q*, $J = 1.2$, 1 H); 5.64–5.50 (*m*, 1 H); 5.09–5.00 (*m*, 2 H); 2.46–2.39 (*m*, 2 H); 2.31–2.24 (*m*, 1 H); 2.01 (*t*, $J = 1.2$, 3 H); 1.89–1.19 (*m*, 6 H). ^{13}C-NMR: 211.2, 181.5 (2*s*); 134.0, 132.1 (2*d*); 118.2 (*t*); 58.5 (*s*); 55.0 (*d*); 34.8, 34.4, 29.6, 24.5 (4*t*); 15.0 (*q*). FAB-HR-MS: 177.1285 ($C_{12}H_{16}O^+$; calc. 177.1279).

Data of **71**: $[\alpha]_D^{23} = +55.4$ ($c = 1.49$, EtOH). IR (neat): 3080, 1705, 1640, 1620. ^{1}H-NMR: 5.86 (*q*, $J = 1.0$, 1 H); 5.69–5.56 (*m*, 1 H); 5.06–4.95 (*m*, 2 H); 2.82–2.78 (*m*, 1 H); 2.45–2.37 (*m*, 1 H); 2.21–2.13 (*m*, 1 H); 2.05 (*t*, $J = 1.0$, 3 H); 1.86–1.80 (*m*, 1 H); 1.71–1.54 (*m*, 3 H); 1.44–1.34 (*m*, 1 H); 1.27–1.17 (*m*, 1 H). ^{13}C-NMR: 213.7, 179.3 (2*s*); 134.3, 130.8 (2*d*); 117.7 (*t*); 59.7 (*s*); 54.2 (*d*); 40.2, 35.3, 28.3, 24.1 (4*t*); 17.7 (*q*). FAB-HR-MS: 177.1283 ($C_{12}H_{16}O^+$; calc. 177.1279).

5.3. *(1S,5S)-5-(But-3-enyl)-4-methylbicyclo[3.3.0]oct-3-en-2-one* (**72**) *and (1S,5S)-1-(But-3-enyl)-4-methyl-bicyclo[3.3.0]oct-3-en-2-one* (**73**). Analogously to *5.1* with **67** (1.40 g, 5.06 mmol) and MeLi (10.6 mmol). Chromatography gave 280 mg (29%) of **72** and 135 mg (14%; slightly contaminated) of **73**.

Data of **72**: $[\alpha]_D^{23} = -56.6$ ($c = 1.78$, EtOH). IR (neat): 3080, 1700, 1640, 1620. ^{1}H-NMR: 5.89 (*s*, 1 H); 5.82–5.68 (*m*, 1 H); 4.99–4.89 (*m*, 2 H); 2.41 (*d*, $J = 9.7$, 1 H); 1.89 (*d*, $J = 1.1$, 3 H); 1.91–1.53 (*m*, 8 H); 1.43–1.17 (*m*, 2 H). ^{13}C-NMR: 211.4, 181.8 (2*s*); 138.0, 132.3 (2*d*); 114.8 (*t*); 58.8 (*s*); 54.9 (*d*); 35.5, 35.1 (2*t*); 29.8 (*t*, 2 C); 24.2 (*t*); 14.9 (*q*). FAB-HR-MS: 191.1435 ($C_{13}H_{18}O^+$; calc. 191.1436).

Data of **71**: $[\alpha]_D^{23} = -57.4$ ($c = 2.09$, EtOH). IR (neat): 3080, 1705, 1640, 1620. ^{1}H-NMR: 5.88 (*q*, $J = 0.9$, 1 H); 5.81–5.67 (*m*, 1 H); 4.99–4.86 (*m*, 2 H); 2.83–2.79 (*m*, 1 H); 2.07 (*t*, $J = 0.9$, 3 H); 1.99–1.12 (*m*, 10 H). ^{13}C-NMR: 214.0, 179.3 (2*s*); 138.4, 131.1 (2*d*); 114.4 (*t*); 59.9 (*s*); 54.7 (*d*); 36.0, 35.3, 29.6, 28.3, 23.8 (5*t*); 17.7 (*q*). FAB-HR-MS: 191.1432 ($C_{13}H_{18}O^+$; calc. 191.1436).

5.4. *(1S,5R)-4,5,8-Trimethylbicyclo[3.3.0]octa-3,7-dien-2-one* (**74**) *and (1R,5R)-1,4,6-Trimethylbicyclo-[3.3.0]octa-3,6-dien-2-one* (**75**). Analogously to *5.1* with **50** (44.0 mg, 0.18 mmol) and MeLi (0.88 mmol; without treatment with EtONa). Chromatography (Et_2O/hexane 1:8) gave 13.8 mg (48%) of **74** and 2.7 mg (9%) of **75**.

Data of **74**: $[\alpha]_D^{23} = +62.2$ ($c = 0.60$, $CHCl_3$). IR (neat): 3045, 1700, 1660, 1620. ^{1}H-NMR: 5.71 (*m* ('*d*'), $J = 1.4$, 1 H); 5.15 (*m* ('br. *s*'), 1 H); 2.87 (br. *s*, 1 H); 2.51–2.18 (*m*, 2 H); 2.06 (*d*, $J = 1.2$, 3 H); 1.82–1.80 (*m* 3 H); 1.33 (*s*, 3 H). ^{1}H-NOE: irrad. at 2.06 → NOE at 5.71 (0.8%) and 2.51–2.18 (1.1%); irrad. at 1.33 → NOE at 2.87 (2.4%) and 2.51–2.18 (1.6%); irrad. at 1.82–1.80 → NOE at 5.15 (1.3%) and 2.87 (1.1%). ^{13}C-NMR: 207.9, 182.6, 137.6 (3*s*); 126.6, 123.6, 69.1 (3*d*); 53.9 (*s*); 42.1 (*t*); 24.6, 14.93, 14.87 (3*q*).

Data of **75**: IR (neat): 3010, 1700, 1615. ^{1}H-NMR: 5.77 (*t*, $J = 1.2$, 1 H); 5.23 (*m* ('br. *s*'), 1 H); 3.15 (br. *s*, 1 H); 2.60–2.45 (*m*, 1 H); 2.22–2.05 (*m*, 4 H); 1.87–1.85 (*m*, 3 H); 1.25 (*s*, 3 H). ^{1}H-NOE: irrad. at 1.25 → NOE at 3.15 (1.6%) and 2.60–2.45 (0.6%); irrad. at 2.22 → NOE at 5.77 and 3.15; irrad. at 1.87–1.85 → NOE at 5.23 (0.4%) and 3.15 (0.4%). ^{13}C-NMR: 214.0, 178.9, 138.3 (3*s*); 128.2, 126.0, 68.6 (3*d*); 55.7 (*s*); 41.2 (*t*); 24.0, 19.3, 16.7 (*q*).

5.5. *(1S,5S)-5,8-Dimethylbicyclo[3.3.0]octa-3,7-dien-2-one* (**76**) *and (R)-2-Acetyl-1,3-dimethylcyclopent-2-ene-1-carbaldehyde* (**77**). Analogously to *5.1* with **50** (30.0 mg, 0.12 mmol) and sodium dihydridobis(methoxyethoxy)aluminate (*Red-Al®*; 0.12 mmol; without treatment with EtONa). Chromatography (Et_2O/hexane 1:4) gave 4.5 mg (26%; contaminated) of **76** and 10.3 mg (52%) of **77**.

Data of **76**: ^{1}H-NMR (relevant signals from unpure compound): 7.43 (*d*, $J = 5.6$, 1 H); 5.95 (*d*, $J = 5.6$, 1 H); 5.21–5.19 (*m*, 1 H); 2.80–2.78 (*m*, 1 H); 2.40–2.34 (*m*, 2 H); 1.81–1.76 (*m*, 3 H); 1.35 (*s*, 3 H).

Data of **77**: IR (neat): 3020, 2860, 2715, 1720, 1650. ^{1}H-NMR: 9.58 (*s*, 1 H); 2.78–2.50 (*m*, 2 H); 2.34 (*s*, 3 H); 2.15 (*t*, $J = 1.1$, 3 H); 2.13–2.02 (*m*, 1 H); 1.59–1.47 (*m*, 1 H); 1.30 (*s*, 3 H). ^{13}C-NMR: 202.9 (*d*); 196.5, 156.0, 142.0, 61.4 (4*s*); 39.8, 31.6 (2*t*); 30.7, 18.9, 17.5 (3*q*).

5.6. *(R)-6-Acetyl-6-methylcyclohex-1-ene-1-carbaldehyde* (**78**). Analogously to *5.1* with **55** (185 mg, 0.74 mmol) and MeLi (3.0 mmol; without treatment with EtONa). Chromatography (AcOEt/hexane 1:8) gave 64 mg (53%) of **78**. $[\alpha]_D^{20} = +12.6$ ($c = 2.10$, $CHCl_3$). IR (neat): 1710, 1680, 1635. ^{1}H-NMR: 9.30 (*s*, 1 H); 6.59 (*t*, $J = 4.0$, 1 H); 2.45–2.35 (*m*, 2 H); 2.06 (*s*, 3 H); 1.80–1.66 (*m*, 3 H); 1.60–1.50 (*m*, 1 H); 1.33 (*s*, 3 H). ^{13}C-NMR: 210.4 (*s*); 193.3 (*d*); 153.1 (*s*); 145.2 (*d*); 48.5 (*s*); 33.4 (*t*); 26.4, 25.2 (2*q*); 21.6, 17.9 (2*t*).

5.7. *(R)-6-Methylbicyclo[4.3.0]nona-1,8-dien-7-one* (**79**). A soln. of **78** (52 mg, 0.31 mmol) in Et_2O (25 ml) was treated with 0.5M NaOH in EtOH (6 ml) for 14 h at 23°. H_2O was added and the mixture extracted with CH_2Cl_2. The org. extracts were washed with H_2O and brine, dried (K_2CO_3), and evaporated. Chromatography (AcOEt/hexane 1:8) gave 27 mg (61%) of **79**. $[\alpha]_D^{23} = +105.6$ ($c = 0.5$, $CHCl_3$). IR (neat): 1705. ^{1}H-NMR: 7.63 (*d*, $J = 5.6$, 1 H); 6.01 (*d*, $J = 5.6$, 1 H); 5.84 (*dd*, $J = 4.1$, 3.9, 1 H); 2.46–2.34 (*m*, 1 H); 2.22–2.07 (*m*, 1 H); 1.91–1.80 (*m*, 1 H); 1.19 (*s*, 1 H); 1.35–1.09 (*m*, 2 H). ^{13}C-NMR: 211.7, 155.3 (2*s*); 146.0, 129.0, 124.2 (3*d*); 45.3 (*s*); 27.3, 24.7, 22.6 (3*t*); 17.6 (*q*). Spectra in agreement with the literature reports [22].

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