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Diastereoselective Photochemical Synthesis of α-Amino-β-hydroxyketones by Photocycloaddition of Carbonyl Compounds to 2,5-Dimethyl-4-isobutyloxazole

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Summary. The photocycloaddition of aldehydes and α-ketoesters to 2,5-dimethyl-4-isobutyloxazole leads to bicyclic oxetanes with high to moderate (*exo*) diastereoselectivity that can be easily ring-opened to give α-amino-β-hydroxyketones.

Keywords. Photocycloaddition; 2,5-Dimethyl-4-isobutyloxazole; Carbonyl compounds; Oxetanes; α-Amino-β-hydroxyketones.

Introduction

Synthesis elegance and short reaction sequences are properties often observed for photochemical processes. Where sensitive reagents and low temperatures are needed for organometallic reactions, photochemical analogs need photons only and reactions can often be performed at room temperature. The photocycloaddition of electronically excited carbonyl compounds to alkenes (*Paterno-Büchi* reaction) is the important synthetic route to oxetanes, which can be subsequently transformed into polyfunctionalized products [1–10]. Concerning the regio- and especially diastereoselectivity of the *Paterno-Büchi* reaction, recent experimental and theoretical work brought a remarkable increase in our understanding of triplet 1,4-biradical behavior [11, 12], which also improved the synthesis significance of this reaction [13]. *Griesbeck* and *Fiege* published the photocycloaddition of the commercially available 2,4,5-trimethyloxazole to carbonyl compounds as a convenient protocol for the stereoselective synthesis of α-amino-β-hydroxyketones [14]. In previous work we developed a new synthetic method for the stereoselective synthesis of *erythro*-

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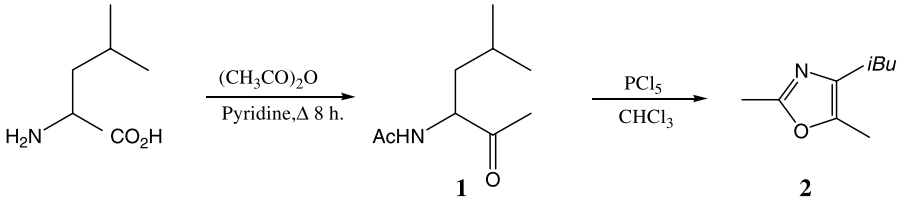
α-amino-β-hydroxycarboxylic acid derivatives [15, 16] and *erythro*-β-hydroxy dimethyl aspartates [17]. The key reaction is the cycloaddition of electronically excited carbonyl compounds (aldehydes and α-ketoesters) to 5-methoxyoxazoles.

In continuation of our interest in the synthesis of novel stereoselective α-amino-β-hydroxyketones, we report herein a facile synthesis of the title compounds *via* the photocycloaddition of 2,5-dimethyl-4-isobutyloxazole with carbonyl compounds.

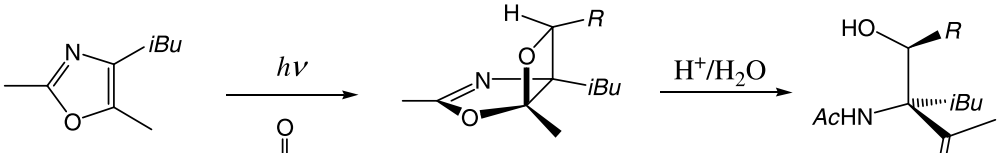
Results and Discussion

2,5-Dimethyl-4-isobutyloxazole (**2**) [18] was prepared using a modified literature procedure from leucin *via* double acylation by refluxing with a mixture of acetic anhydride and pyridine (1:1) to furnish 3-acetamido-5-methyl-2-hexanone (**1**), which underwent dehydrocyclization upon warming with PCl_5 in chloroform to afford **2** *via Robinson-Gabriel* synthesis as depicted in Scheme 1.

In order to probe the versatility of the oxazole–carbonyl photocycloaddition as a synthesis approach to α-amino-β-hydroxyketones, the *Paterno-Büchi* reaction of 2,5-dimethyl-4-isobutyloxazole with aliphatic and aromatic aldehydes was investigated. First of all, the photoreactions ($\lambda_{ex} = 300$ nm) of aldehydes with 2,5-dimethyl-4-isobutyloxazole were carried out in *n*-hexane at 10°C. In all cases, only the regioisomers **3a**–**3e** were formed with excellent (*exo*) diastereoselectivity (>98:2) in good yields (see Scheme 2). The formation of the acid-labile bicyclic oxetanes **3a**–**3e** was proven by the characteristic ^{13}C NMR signals of the acetal carbon ($\delta_c \sim 115$ ppm). The stereochemical assignment of the bicyclic oxetanes **3a**–**3e** was confirmed on the basis of ^1H NMR analysis (especially the strong ring current induced upfield-shift for the phenylated product **3a**).



Scheme 1



		d.r.	yield/%
3a	*R* = *Ph*	> 98:2	74
3b	*R* = *Et*	> 98:2	66
3c	*R* = *Pr*	> 98:2	73
3d	*R* = *iPr*	> 98:2	60
3e	*R* = *iBu*	> 98:2	72

Scheme 2

The chemical structures of the photoadducts **3a**–**3e** were established on the basis of the spectroscopic data. The IR spectra showed strong absorption bands around 1625 cm^{-1} attributed to the C=N group. The ^{1}H NMR spectrum of **3a** showed two doublets at 0.62 and 0.70 ppm due to the isopropyl group and confirmed the *exo-Ph* configuration of the photoadduct. In addition, there are three singlets at 1.43, 2.11, and 5.51 ppm corresponding to the CH_3 group at C-5, CH_3 group at C-3, and H-7 of the oxetane ring. In the ^{13}C NMR spectrum, the characteristic signals for the oxetane ring resonate at 79.9, 93.4, and 116.4 ppm for C-1, C-7, and C-5.

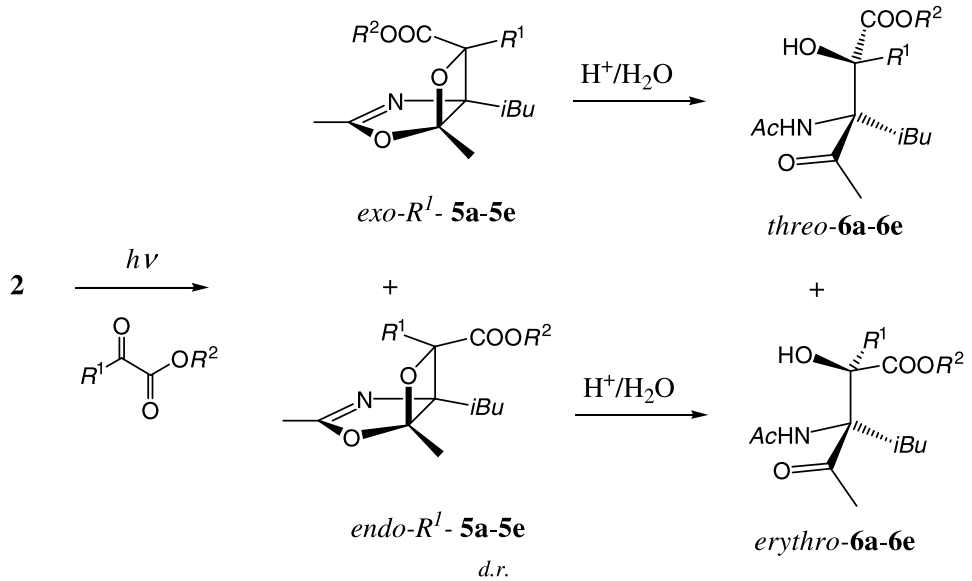
The primary photoproducts **3a**–**3e** were hydrolytically unstable and underwent twofold ring opening to give *erythro*-α-amino-β-hydroxyketones **4a**–**4e**. The ring opening of the bicyclic oxetanes proceeded with retention of configuration. In most cases, the diastereomeric ratio (*d.r.*) of the ring-opened products matched the *d.r.* of the oxetane precursors. The relative configuration of compounds **4a**–**4e** were confirmed by NMR spectroscopy and spectral comparison with literature known products [14].

In order to evaluate the influence of steric as well as electronic factors on the stereoselectivity of the *Paterno-Büchi* reaction of oxazole with aliphatic as well as aromatic α-ketoesters, the photocycloaddition of **2** with methyl pyruvate, methyl trimethylpyruvate, and different types of alkyl phenylglyoxylates were investigated. Photolysis of equimolar amounts of methyl pyruvate with **2** in *n*-hexane using a Rayonet photoreactor at 350 nm afforded the bicyclic oxetane **5a** with very high regio- and (*exo*-CO_2CH_3) stereoselectivity in good yield.

In contrast to methyl pyruvate, photolysis of methyl trimethylpyruvate in the presence of **2** afforded the bicyclic oxetane **5b** with the *exo-tert*-butyl substituent at position C-7. Again, the relative configurations of **5a** and **5b** were confirmed by NMR spectroscopy and spectral comparison with similar known products [17].

Phenylglyoxylates have been reported to add photochemically to electron-rich cycloalkenes with high diastereocontrol [19–20]. Thus, we also investigated the photocycloaddition of **2** with alkyl phenylglyoxylate. In contrast to the results with aliphatic α-ketoesters, the bicyclic oxetanes **5c**–**5e** were formed only with moderate *simple* diastereoselectivities favoring the *exo-Ph* products. Interestingly, the *exo*/*endo* diastereomeric ratios of the photoadducts were affected by the size of the alkyl substituent of phenylglyoxylates (see Scheme 3). In all cases, the diastereomeric *exo* and *endo* oxetane products were stable under the reaction conditions and could even be separated by preparative chromatography on silica when pretreated with 1% of triethylamine in methylene chloride.

The relative configurations of the *exo*- and *endo-Ph* diastereoisomers of compound **5c** were unambiguously determined by N*O*E measurement. For the *endo-Ph* isomer, cross peaks between the phenyl protons at 7.48 ppm and methyl protons at 1.78 ppm indicate a strong N*O*E effect and hence spatial proximity (*cis* relationship between *Ph* and methyl group). Other N*O*E effects between the phenyl protons and methylene protons at 2.11/1.53 ppm were observed. For the *exo-Ph* isomer, no interaction between the phenyl protons and methyl protons at C-3 is observable while a strong one is present for phenyl protons at 7.72 ppm and the methyl protons on C-5 at 1.64 ppm. Furthermore, a cross peak between the methylene protons at 1.72/0.97 ppm and phenyl protons at 7.72 ppm was observed again indicating their proximity.



			d.r. *exo* : *endo*	yield/%
5a	$R^1 = Me$	$R^2 = Me$	98:2	85
5b	$R^1 = tBu$	$R^2 = Me$	98:2	79
5c	$R^1 = Ph$	$R^2 = Me$	71:29	86
5d	$R^1 = Ph$	$R^2 = Et$	67:33	78
5e	$R^1 = Ph$	$R^2 = tBu$	55:45	80

Scheme 3

Treatment of the major diastereoisomers *exo*-**5a**–**5e** with catalytic amounts of HCl in chloroform or direct chromatography on silica delivered the (*2R**,*3S**)-bis-quaternary α-amino-β-hydroxyketones **6a**–**6e** in high yields (Scheme 3). The diastereomeric oxetanes *endo*-**5a**–**5e** were likewise transformed into the (*2R**,*3R**)-bis-quaternary α-amino-β-hydroxyketones **6a**–**6e**.

The relative configurations of **6a**–**6e** were determined on the basis of the characteristic signals in NMR spectra of the diastereoisomeric aldol products. For example, in the ^{1}H NMR spectra of the *erythro*-isomer, the acetyl group appears at 2.1 ± 0.05 ppm, whereas in the *threo*-isomer this absorption is shifted upfield to 1.8 ± 0.05 ppm due to ring current effect of the benzene ring. Also the chemical shifts of the diastereotopic protons of the methylene group at C-3 appear at higher field in the *erythro*-isomer than in the *threo*-isomer.

The regioselectivity of the *Paterno-Büchi* reaction of carbonyls with 2,5-dimethyl-4-isobutyloxazole is high and corresponds to the classical biradical stabilization concept. The stereochemistry of the triplet 1,4-biradical is attributed to a conformational memory effect during the intersystem crossing (ISC) process of the triplet 1,4-biradical. According to *Salem-Rowland* rules [21], strong spin-orbit coupling (SOC) occurs when the p-orbitals at the spin-bearing atoms are orthogonal to each other. The possible conformers (**A**–**C**) of the triplet 1,4-biradical are represented by the *Newman* projections (Fig. 1). Among these three conformers, **A** and **B** are expected to be similar populated whereas **C** is higher in energy. ISC from **A** leads to immediate C–C bond formation, whereby the *R*=*Ph* group is

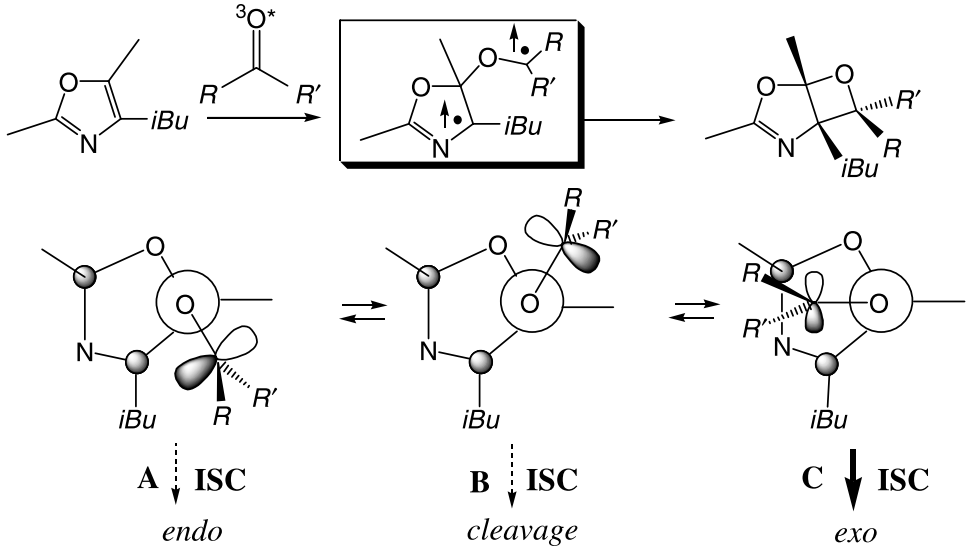


Fig. 1. Mechanistic scenario for oxazole–carbonyl photocycloaddition

rotated over the former oxazole ring plane resulting in the *endo-Ph* product. ISC from **B** leads to cleavage of the initially formed C–O bond restoring the starting materials. Similarly, ISC from **C** gives the *exo-Ph* product. The experimental results show that the *exo-Ph* product is dominant, thus an interaction between the allylic and exocyclic radical in triplet 1,4-biradical, secondary orbital interaction (SOI) as depicted in conformer **C** must be crucial for the dominance of this 1,4-biradical geometry for rapid ISC [11, 12]. The relative stabilities of **A** and **C** depend on the size of both the substituent *iBu* in the oxazole moiety and the size of the R and R' groups of the carbonyl compounds.

Aldehydes (R'=H) show strong preference for bond formation *via* conformer **C** and thus give *exo* oxetanes with high stereoselectivities. For α-ketoesters (R = alkyl, aryl; R'=CO_2R'') structure **A** is preferred and they give preferentially the *endo* diastereoisomers. If, however, the ring terminus of the triplet biradical is isobutyl substituted, additional steric interactions disfavor structure **A**.

In conclusion, we have shown that the oxazole–carbonyl photocycloaddition serves as an excellent route to the regio- and diastereoselective preparation of *erythro-* and *threo-*β-aminoalcohols from aldehydes and α-ketoesters.

Experimental

All reactions were carried out in oven-dried glassware (100°C). All solvents were dried before use. Ether was distilled from Na/benzophenone, $CHCl_3$ and CH_2Cl_2 from CaH_2. Aldehydes and α-ketoesters were purchased from Aldrich and were distilled before use. Methyl trimethylpyruvate [22] and *tert*-butyl phenylglyoxylate [23] were prepared according to reported methods. Mixtures of ethyl acetate and *n*-hexane were used as eluents. TLC: Commercially precoated polygram© SIL-G/UV 254 plates (Macherey-Nagel). Spots were detected with UV light or in an I_2 chamber. IR spectra were recorded on a Mattson 5000 FTIR spectrophotometer. ^{1}H NMR: Bruker AC 300 (300 MHz). ^{13}C NMR: Bruker AC 300 (75.5 MHz), carbon multiplicities were determined by DEPT. Mass spectra were measured on a GCMS-QP1000 EX spectrometer at 70 eV. Preparative thin layer chromatography:

Silica gel (2–25 μm) on TLC plates (Fluka), layer thickness 0.25 mm, medium pore diameter 60 Å, 20×20 cm on glass plates. Elemental analyses were performed with a Perkin-Elmer elemental analyzer 240-c; the results were in satisfactory agreement with the calculated values. Rayonet® chamber photoreactors RPR-208 (8×3000 Å lamps, *ca.* 800 W, $\lambda = 300 \pm 10$ nm) and phosphor-coated mercury low-pressure lamps ($\lambda = 350 \pm 10$ nm) were used for irradiation.

3-Acetamido-5-methyl-2-hexanone (**1**)
A mixture of 15 g leucin (0.115 mol), 50 cm^3 pyridine, and 50 cm^3 acetic anhydride was heated on a steam-bath for 8 h. At the end of heating, the reaction solution was steam distilled to decompose the acetic anhydride and to remove acetic acid and pyridine. After 1 h the condensate was neutral to litmus. The residue in the distilling flask was reduced to a volume of 20 cm^3 by external heating during the steam distillation. This residue was treated with 5% $NaHCO_3$, then extracted with ether, washed with brine and H_2O, then dried ($MgSO_4$), the ether was evaporated under *vacuo*, and the residue was fractionated to give 15 g (76%) **1**, bp 122–134°C at 2–3 mm [18]. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 6.5$ Hz, CH_3), 0.84 (d, $J = 6.5$ Hz, CH_3), 1.35 (m, CH), 1.52 (m, CH_2), 1.89 (s, CH_3CO), 2.08 (s, CH_3CO), 4.52 (ddd, $J = 7.4$, 4.1, 4.0 Hz, CHN), 6.55 (d, $J = 7.4$ Hz, NH) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 21.5$ (q, CH_3), 22.7 (q, CH_3), 23.0 (q, CH_3), 24.7 (q, CH_3), 26.9 (d, CH), 39.8 (t, CH_2), 57.0 (d, CHN), 170.1 (s, CON), 207.6 (s, CO) ppm.

2,5-Dimethyl-4-isobutyloxazole (**2**)
To a stirred solution of 17.1 g **1** (0.1 mol) in 25 cm^3 $CHCl_3$ were added 20.8 g PCl_5 (0.1 mol) in 250 cm^3 round bottemed flask fitted with $CaCl_2$ tube. The solution was warmed 2 h on a water bath. Then, the flask was cooled in an ice-bath, and 50 cm^3 of ether were added. To the cold mixture, 10% aqueous NaOH was added dropwise with vigorous stirring until neutralization. The mixture was kept at room temperature for 15 min. The organic layer was subsequently separated and the aqueous layer was extrated with 2×50 cm^3 ether. The combined ether extracts were washed with H_2O, brine, and dried (Na_2SO_4), then evaporated under reduced pressure to give a residue. The residual oil was fractionated to give 13.0 g (85%) **2** as a colorless liquid, bp 175–177°C [18]. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 6.6$ Hz, $2CH_3$), 1.87 (m, CH), 2.11 (s, CH_3), 2.15 (d, $J = 7.1$ Hz, CH_2), 2.31 (s, CH_3) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 9.8$ (q, CH_3), 13.7 (q, CH_3), 22.2 (q, $2CH_3$), 28.2 (d, CH), 34.6 (t, CH_2), 133.3 (s, C-4), 143.2 (s, C-5), 158.7 (s, C-2) ppm.

Photolyses of 2,5-Dimethyl-4-isobutyloxazole with Aldehydes
A mixture of **2** (5 mmol) and aldehydes (5 mmol) was dissolved in 50 cm^3 *n*-hexane, the solution transferred to a vacuum jacket SiO_2 tube and degassed with a steady stream of N_2. The reaction mixture was irradiated at 10°C in a Rayonet photoreactor (RPR-208) for 24 h. The solvent was evaporated under vacuum, and the residue was purified by preparative thick layer chromatography (*EA* = ethyl acetate, *H* = *n*-hexane).

(exo)-1-Isobutyl-3,5-dimethyl-7-phenyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene
(**3a**, C_{16} $H_{21}NO_2$)
A solution of 0.53 g benzaldehyde (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.8 g (62%) **3a** as a colorless oil. $R_f = 0.43$ (*H*:*EA* = 4:1); IR (film): $\bar{\nu} = 2993$ (C–H), 1625 (C=N), 1600 (*Ph*), 1100 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.62$ (d, $J = 6.6$ Hz, CH_3), 0.70 (d, $J = 6.6$ Hz, CH_3), 0.98 (m, CH), 1.29 (m, CH), 1.43 (s, CH_3), 1.93 (m, CH), 2.11 (s, CH_3), 5.51 (s, CH), 7.42 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 9.6$ (q, CH_3), 13.3 (q, CH_3), 14.4 (q, CH_3), 19.6 (q, CH_3), 21.9 (q, CH_3), 23.6 (q, CH_3), 23.9 (q, CH_3), 28.0 (d, CH), 36.8 (t, CH_2), 79.9 (s, C-1), 93.4 (s, C-7), 116.4 (s, C-5), 125.9 (d, CH_{Ar}), 127.4 (d, $2CH_{Ar}$), 130.5 (d, $2CH_{Ar}$), 134.1 (s, Cq_{Ar}), 165.9 (s, C-3) ppm; MS: m/z (%) = 259 (M^+, 15).

(exo)-7-Ethyl-1-isobutyl-3,5-dimethyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene
(**3b**, $C_{12}H_{21}NO_2$)
A solution of 0.29 g propionaldehyde (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.74 g (70%) **3b** as a colorless oil. $R_f = 0.56$ (*H*:*EA* = 4:1); IR (film): $\bar{\nu} = 2989$ (C–H), 1628 (C=N), 1105 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.88$ (d, $J = 6.6$ Hz, CH_3), 0.92 (d, $J = 6.6$ Hz, CH_3), 0.97 (t, $J = 7.5$ Hz, $\underline{CH_3}CH_2$), 0.99 (d, $J = 6.2$ Hz, $\underline{CH_2}CH$), 1.59 (s, CH_3), 1.83 (m, CH), 1.96 (s, CH_3), 2.21 (m, $\underline{CH_2}CH_3$), 4.22 (dd, $J = 9.4$, 4.7 Hz, H_7) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 8.7$ (q, CH_3), 14.1 (q, CH_3), 21.9 (q, CH_3), 23.4 (q, CH_3), 23.7 (q, CH_3), 25.1 (d, CH), 27.1 (t, CH_2), 35.2 (t, CH_2), 74.5 (s, C-1), 93.5 (d, C-7), 115.7 (s, C-5), 178.1 (s, C-3) ppm; MS: m/z (%) = 211 (M^+, 25).

(exo)-1-Isobutyl-3,5-dimethyl-7-propyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene
(**3c**, $C_{13}H_{23}NO_2$)
A solution of 0.36 g butyraldehyde (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.96 g (68%) **3c** as a colorless oil. $R_f = 0.46$ (*H*:*EA* = 4:1); IR (film): $\bar{\nu} = 2993$ (C–H), 1630 (C = N), 1102 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.84$ (d, $J = 6.6$ Hz, $2CH_3$), 0.95 (t, $J = 7.5$ Hz, CH_3), 1.13 (m, CH), 1.21 (sextet, $J = 7.5$ Hz, CH_2), 1.31 (m, CH_2), 1.35 (m, CH), 1.52 (s, CH_3), 1.87 (m, CH), 2.08 (s, CH_3), 2.16 (d, $J = 7.2$ Hz, CH_2), 4.04 (dd, $J = 10.1$, 4.2 Hz, H_7) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 9.6$ (q, CH_3), 13.4 (q, CH_3), 22.1 (q, $2CH_3$), 23.8 (d, CH), 24.1 (d, CH), 27.1 (q, CH_3), 28.1 (q, CH_3), 34.3 (t, CH_2), 93.1 (s, C-1), 97.1 (d, C-7), 117.1 (s, C-5), 179.5 (s, C-3) ppm.

(exo)-1-Isobutyl-7-isopropyl-3,5-dimethyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene
(**3d**, $C_{13}H_{23}NO_2$)
A solution of 0.36 g isobutyraldehyde (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.75 g (67%) **3d** as a colorless oil. $R_f = 0.40$ (*H*:*EA* = 4:1); IR (film): $\bar{\nu} = 2986$ (C–H), 1624 (C=N), 1100 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 6.6$ Hz, $2CH_3$), 1.10 (d, $J = 6.9$ Hz, CH_3), 1.17 (d, $J = 6.9$ Hz, CH_3), 1.32 (m, CH), 1.55 (s, CH_3), 1.87 (m, CH), 2.11 (s, CH_3), 2.16 (d, $J = 7.2$ Hz, CH_2), 3.94 (d, $J = 10.1$ Hz, H_7) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.4$ (q, CH_3), 16.4 (t, CH_2), 22.1 (q, $2CH_3$), 23.8 (d, CH), 24.1 (d, CH), 27.1 (q, CH_3), 28.1 (q, CH_3), 33.6 (t, CH_2), 34.3 (t, CH_2), 90.1 (s, C-1), 95.1 (d, C-7), 115.1 (s, C-5), 170.5 (s, C-3) ppm; MS: m/z (%) = 225 (M^+, 18).

(exo)-1,7-Diisobutyl-3,5-dimethyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (**3e**, $C_{14}H_{25}NO_2$)
A solution of 0.43 g 3-methyl butyraldehyde (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.81 g (68%) **3e** as a colorless oil. $R_f = 0.45$ (*H*:*EA* = 4:1); IR (film): $\bar{\nu} = 2982$ (C–H), 1628 (C=N), 1105 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.78$ (d, $J = 6.6$ Hz, $2CH_3$), 0.85 (d, $J = 6.8$ Hz, $2CH_3$), 0.87 (m, CH), 0.90 (m, CH), 1.43 (m, CH_2), 1.56 (s, CH_3), 1.95 (m, CH_2), 2.29 (s, CH_3), 4.49 (dd, $J = 10.7$, 2.7 Hz, H_7) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): 9.6 (q, CH_3), 13.4 (q, CH_3), 22.0 (q, CH_3), 23.9 (q, CH_3), 24.1 (q, CH_3), 24.2 (q, CH_3), 28.1 (d, CH), 30.2 (d, CH), 35.6 (t, CH_2), 43.3 (t, CH_2), 74.9 (s, C-1), 90.6 (d, C-7), 115.8 (s, C-5), 171.3 (s, C-3) ppm.

Synthesis of erythro α-Amino-β-Hydroxyketones (**4a**–**4e**)
To a solution of the bicyclic oxetane **3a**–**3e** (0.002 mol) in 20 cm^3 CH_2Cl_2, 0.5 cm^3 of conc. HCl were added. The mixture was stirred in an open flask at room temperature for 4 h and the reaction mixture was quenched with H_2O and extracted with CH_2Cl_2 (3×20 cm^3). The organic layer was washed with

5% $NaHCO_3$, brine, and dried ($MgSO_4$). The solvent was removed in *vacuo* and the residual oil was purified by preparative chromatography.

(erythro)-3-N-Acetamido-3-(hydroxyphenylmethyl)-5-methyl-2-hexanone (**4a**, $C_{16}H_{23}NO_3$)
According to the above general procedure, 0.52 g **3a** (2 mmol) were cleaved hydrolytically in 4 h. Preparative chromatography yielded 0.39 g (70%) **4a** as a colorless oil. $R_f = 0.34$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3500$ (OH), 3347 (NH), 2983, 2894 (C–H), 1715 (C=O), 1660 (CON), 1605 (Ph), 1118 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (d, $J = 6.5$ Hz, CH_3), 0.90 (d, $J = 6.5$ Hz, CH_3), 0.97 (d, $J = 6.6$ Hz, CH_2), 1.36 (m, CH), 1.94 (s, CH_3CO), 2.47 (s, CH_3CO), 5.12 (s, CH), 7.00 (bs, NH), 7.19–7.47 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 22.9$ (q, CH_3), 23.5 (q, CH_3), 24.4 (d, CH), 25.0 (q, CH_3), 25.6 (q, CH_3), 40.5 (t, CH_2), 75.5 (s, C-2), 78.0 (d, CHOH), 125.5 (d, $2CH_{Ar}$), 128.9 (d, $2CH_{Ar}$), 133.4 (d, CH_{Ar}), 140.1 (s, Cq_{Ar}) 172.4 (s, CON), 205.3 (s, CO) ppm; MS: m/z (%) = 277 (M^+, 40).

(erythro)-3-N-Acetamido-3-(1-hydroxypropyl)-5-methyl-2-hexanone (**4b**, $C_{12}H_{23}NO_3$)
According to the above general procedure, 0.42 g **3b** (2 mmol) were cleaved hydrolytically in 4 h. Preparative chromatography yielded 0.34 g (75%) **4b** as a colorless oil. $R_f = 0.41$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3450$ (OH), 3345 (NH), 2988, 2894 (C–H), 1725 (C=O), 1668 (CON), 1113 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.83$ (d, $J = 6.6$ Hz, $2CH_3$), 0.99 (t, $J = 7.5$ Hz, CH_3), 1.22 (m, CH), 1.40 (m, CH_2), 1.82 (dd, $J = 15.4$, 4.7 Hz, CH), 2.06 (s, CH_3CO), 2.22 (s, CH_3CO), 2.64 (dd, $J = 15.4$, 8.1 Hz, CH), 3.75 (dd, $J = 10.9$, 2.4 Hz, CHOH), 5.70 (d, $J = 10.9$ Hz, OH), 7.17 (bs, NH) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 10.9$ (q, CH_3), 23.3 (q, CH_3), 23.8 (q, CH_3), 24.3 (q, CH_3), 24.7 (q, CH_3), 24.9 (d, CH), 26.6 (t, CH_2), 39.5 (t, CH_2), 75.0 (s, C-2), 76.9 (d, CHOH), 171.4 (s, CON), 206.7 (s, CO) ppm; MS: m/z (%) = 229 (M^+, 32).

(erythro)-3-N-Acetamido-3-isobutyl-4-hydroxy-2-heptanone (**4c**, $C_{13}H_{25}NO_3$)
According to the above general procedure, 0.57 g **3c** (2 mmol) were cleaved hydrolytically in 4 h. Preparative chromatography yielded 0.35 g (72%) **4c** as a colorless oil. $R_f = 0.41$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3490$ (OH), 3335 (NH), 2983, 2894 (C–H), 1718 (C=O), 1662 (CON), 1115 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.81$ (d, $J = 6.6$ Hz, CH_3), 0.87 (d, $J = 6.8$ Hz, CH_3), 0.94 (t, $J = 7.5$ Hz, CH_3), 0.97 (m, CH_2), 1.32 (m, CH_2), 1.73 (dd, $J = 14.9$, 7.7 Hz, CH), 2.08 (s, CH_3CO), 2.18 (s, CH_3CO), 2.36 (dd, $J = 14.9$, 4.7 Hz, CH), 4.01 (dd, $J = 16.3$, 7.7 Hz, CHOH), 5.80 (d, $J = 4.7$ Hz, CHOH), 6.68 (bs, NH) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.6$ (q, CH_3), 13.8 (q, CH_3), 18.6 (t, CH_2), 23.4 (q, CH_3), 23.8 (q, CH_3), 24.1 (q, CH_3), 26.6 (d, CH), 31.6 (t, CH_2), 39.1 (t, CH_2), 70.9 (s, C-2), 75.2 (d, CHOH), 172.2 (s, CON), 206.3 (s, CO) ppm.

(erythro)-3-N-Acetamido-3-isobutyl-4-hydroxy-5-methyl-2-hexanone (**4d**, $C_{13}H_{25}NO_3$)
According to the above general procedure, 0.45 g **3d** (2 mmol) were cleaved hydrolytically in 4 h. Preparative chromatography yielded 0.33 g (68%) **4d** as a colorless oil. $R_f = 0.38$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3548$ (OH), 3363 (NH), 2989, 2897 (C–H), 1719 (C=O), 1663 (CON), 1104 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.98$ (d, $J = 6.6$ Hz, $2CH_3$), 1.04 (d, $J = 6.8$ Hz, $2CH_3$), 1.67 (d, $J = 6.9$ Hz, CH_2), 1.87 (m, CH), 1.92 (m, CH), 2.19 (s, CH_3CO), 2.21 (s, CH_3CO), 4.08 (dd, $J = 6.6$, 2.6 Hz, CHOH), 5.72 (d, $J = 10.8$ Hz, CHOH), 7.26 (bs, NH) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 16.2$ (q, $2CH_3$), 17.6 (q, CH_3), 18.2 (q, CH_3), 21.0 (d, CH), 22.4 (q, $2CH_3$), 26.0 (d, CH), 36.6 (t, CH_2), 70.1 (s, C-2), 86.9 (d, CHOH), 169.2 (s, CON), 210.0 (CO) ppm.

(erythro)-3-N-Acetamido-3-isobutyl-4-hydroxy-6-methyl-2-heptanone (**4e**, $C_{14}H_{27}NO_3$)
According to the above general procedure, 0.48 g **3e** (2 mmol) were cleaved hydrolytically in 4 h. Preparative chromatography yielded 0.38 g (74%) **4e** as a colorless oil. $R_f = 0.34$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3495$ (OH), 3342 (NH), 2983, 2890 (C–H), 1722 (C=O), 1665 (CON), 1124 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.83$ (d, $J = 6.6$ Hz, $2CH_3$), 0.86 (d, $J = 6.8$ Hz, $2CH_3$), 1.31 (m, CH),

1.43 (m, CH_2), 1.82 (dd, $J = 15.4$, 6.4 Hz, CH), 2.19 (s, CH_3CO), 2.21 (s, CH_3CO), 2.64 (dd, $J = 15.4$, 8.1 Hz, CH), 3.94 (dd, $J = 5.4$, 2.6 Hz, CHOH), 5.74 (d, $J = 10.7$ Hz, CHOH), 7.17 (bs, NH) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.7$ (q, CH_3), 20.4 (q, CH_3), 21.6 (q, CH_3), 22.9 (q, CH_3), 23.5 (q, CH_3), 23.6 (q, CH_3), 23.8 (d, CH), 24.2 (d, CH), 35.9 (t, CH_2), 41.5 (t, CH_2), 78.1 (s, C-2), 90.9 (d, CHOH), 165.2 (s, CON), 200.0 (CO) ppm.

Photolyses of α-Ketoesters with 2,5-Dimethyl-4-isobutyloxazole

Under a nitrogen atmosphere, a solution of α-ketoester substrates (5 mmol) and **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated in a Rayonet photoreactor (350 nm) at 10°C for 24 h. The solvent was evaporated in *vacuo*, and the residue was analyzed by ^{1}H NMR spectroscopy to determine the diastereoselectivity. Purification was carried out by preparative chromatography using silica gel which was firstly neutralized by elution with 1% *TEA*/CH_2Cl_2. The thermally and hydrolytically unstable primary products could in most cases not be characterized by combustion analysis and were hydrolyzed subsequently to the more stable bis-quaternery α-amino-β-hydroxyketones.

7-Methoxycarbonyl-1-isobutyl-3,5,7-trimethyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (**5a**, $C_{13}H_{21}NO_4$)

A solution of 0.51 g methyl pyruvate (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.99 g (78%) **5a** as a colorless oil. $R_f = 0.52$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 2998$ (C–H), 1725 (C=O), 1627 (C=N), 1100 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.65$ (d, $J = 6.6$ Hz, CH_3), 0.71 (d, $J = 6.6$ Hz, CH_3), 1.28 (dd, $J = 14.0$, 5.8 Hz, CH), 1.32 (s, CH_3), 1.54 (s, CH_3), 1.56 (dd, $J = 14.0$, 6.0 Hz, CH), 1.84 (m, CH), 1.97 (s, CH_3), 3.62 (s, OCH_3) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.9$ (q, CH_3), 18.2 (q, CH_3), 18.8 (q, CH_3), 21.8 (q, CH_3), 23.2 (d, CH), 23.5 (q, CH_3), 37.2 (t, CH_2), 51.8 (q, OCH_3), 80.4 (s, C-1), 91.7 (s, C-7), 114.9 (s, C-5), 166.4 (s, C-3), 172.1 (s, COO) ppm; MS: m/z (%) = 255 (M^+, 8).

7-Methoxycarbonyl-7-tert-butyl-1-isobutyl-3,5-dimethyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (**5b**, $C_{16}H_{27}NO_4$)

A solution of 0.72 g methyl trimethylpyruvate (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 1.11 g (75%) **5b** as a colorless oil. $R_f = 0.48$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 2995$ (C–H), 1735 (C=O), 1632 (C=N), 1113 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.85$ (d, $J = 6.8$ Hz, CH_3), 0.92 (d, $J = 6.9$ Hz, CH_3), 1.08 (s, $3CH_3$), 1.43 (s, CH_3), 1.52 (m, CH), 1.78 (m, CH_2), 2.07 (s, CH_3), 3.64 (s, OCH_3) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.4$ (q, CH_3), 16.7 (q, CH_3), 18.9 (q, CH_3), 19.4 (q, CH_3), 25.8 (q, 3 CH_3), 27.3 (d, CH), 39.7 (s, Cq), 40.2 (t, CH_2), 51.3 (q, OCH_3), 92.5 (s, C-1), 96.2 (s, C-7), 117.3 (s, C-5), 169.2 (s, C-3), 173.4 (s, COO) ppm; MS: m/z (%) = 297 (M^+, 24).

7-Methoxycarbonyl-1-isobutyl-3,5-dimethyl-7-phenyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (***exo*-5c**, $C_{18}H_{23}NO_4$)

A solution of 0.82 g methyl phenylglyoxlate (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.8 g (62%) **5c** as a colorless oil. $R_f = 0.43$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 2986$ (C–H), 1718 (C=O), 1635 (C=N), 1600 (*Ph*), 1108 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.68$ (d, $J = 6.8$ Hz, CH_3), 0.84 (d, $J = 6.5$ Hz, CH_3), 0.92 (dd, $J = 14.4$, 6.8 Hz, CH), 1.20 (m, CH), 1.64 (s, CH_3), 1.73 (dd, $J = 14.4$, 5.6 Hz, CH), 2.11 (s, CH_3), 3.74 (s, OCH_3), 7.35–7.74 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.4$ (q, CH_3), 19.7 (q, CH_3), 23.7 (q, CH_3), 23.8 (q, CH_3), 24.1 (d, CH), 38.1 (t, CH_2), 52.5 (q, OCH_3), 83.5 (s, C-1), 93.7 (s, C-7), 114.1 (s, C-5), 126.4 (d, CH_{Ar}), 127.0 (d, $2CH_{Ar}$), 128.2 (d, CH_{Ar}), 135.3 (s, Cq_{Ar}), 166.6 (s, C-3), 169.9 (s, COO) ppm; MS: m/z (%) = 317 (M^+, 100).

7-Methoxycarbonyl-1-isobutyl-3,5-dimethyl-7-phenyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (***endo*-5c**)

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.83$ (d, $J = 6.8$ Hz, CH_3), 0.95 (d, $J = 6.6$ Hz, CH_3), 1.20 (dd, $J = 14.0$, 5.6 Hz, CH), 1.54 (dd, $J = 14.0$, 6.4 Hz, CH), 1.77 (s, CH_3), 2.07 (m, CH), 3.96 (s, OCH_3), 7.46–8.00 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.9$ (q, CH_3), 19.2 (q, CH_3), 23.7 (q, CH_3), 24.2 (q, CH_3), 24.3 (d, CH), 38.6 (t, CH_2), 52.5 (q, OCH_3), 83.5 (s, C-1), 94.1 (s, C-7), 114.9 (s, C-5), 126.3 (d, CH_{Ar}), 127.7 (d, $2CH_{Ar}$), 130.1 (d, $2CH_{Ar}$), 134.9 (s, Cq_{Ar}), 163.6 (s, C-3), 166.9 (s, COO) ppm.

7-Ethoxycarbonyl-1-isobutyl-3,5-dimethyl-7-phenyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (***exo*-5d**, $C_{19}H_{25}NO_4$)

A solution of 0.89 g ethyl phenylglyoxalate (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.8 g (62%) **5d** as a colorless oil. $R_f = 0.43$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 2997$ (C–H), 1726 (C=O),1630 (C=N), 1605 (*Ph*), 1118 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.62$ (d, $J = 6.6$ Hz, CH_3), 0.73 (d, $J = 6.6$ Hz, CH_3), 1.27 (t, $J = 7.5$ Hz, CH_3), 1.39 (m, CH), 1.42 (s, CH_3), 1.56 (m, CH_2), 1.58 (m, CH), 2.05 (s, CH_3), 4.22 (q, $J = 7.5$ Hz, Hz, OCH_2), 7.26–7.52 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.8$ (q, CH_3), 14.0 (q, CH_3), 18.3 (q, CH_3), 22.6 (q, CH_3), 23.5 (q, CH_3), 25.7 (d, CH), 36.5 (t, CH_2), 62.1 (t, OCH_2), 81.7 (s, C-1), 91.5 (s, C-7), 115.3 (s, C-5), 126.3 (d, CH_{Ar}), 127.3 (d, $2CH_{Ar}$), 128.5 (d, $2CH_{Ar}$), 134.2 (s, Cq_{Ar}), 165.5 (s, C-3), 169.9 (s, COO) ppm.

7-Ethoxycarbonyl-1-isobutyl-3,5-dimethyl-7-phenyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (***endo*-5d**)

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 6.6$ Hz, CH_3), 0.93 (d, $J = 6.6$ Hz, CH_3), 1.29 (t, $J = 7.2$ Hz, CH_3), 1.35 (m, CH), 1.56 (dd, $J = 14.4$, 7.2 Hz, CH), 1.76 (s, CH_3), 1.77 (s, CH_3), 2.11 (dd, $J = 14.4$, 5.3 Hz, CH), 4.27 (q, $J = 7.2$ Hz, OCH_2), 7.23–7.31 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.9$ (q, CH_3), 14.2 (q, CH_3), 19.2 (q, CH_3), 23.7 (d, CH), 24.1 (q, CH_3), 38.7 (t, CH_2), 61.9 (t, OCH_2), 83.5 (s, C-1), 93.9 (s, C-7), 114.9 (s, C-5), 126.3 (d, CH_{Ar}), 127.6 (d, $2CH_{Ar}$), 128.2 (d, $2CH_{Ar}$), 136.3 (s, Cq_{Ar}), 165.2 (s, C-3), 170.3 (s, COO) ppm.

1-Isobutyl-3,5-dimethyl-7-phenyl-7-tert-butoxycarbonyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (***exo*-5e**, $C_{21}H_{29}NO_4$)

A solution of 1.03 g *tert*-butyl phenylglyoxlate (5 mmol) and 0.77 g **2** (5 mmol) in 50 cm^3 *n*-hexane was irradiated for 24 h according to the above general procedure. The crude product was purified by preparative chromatography to give 0.8 g (62%) **5e** as a colorless oil. $R_f = 0.43$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 2988$ (C–H), 1736 (C=O), 1630 (C=N), 1600 (*Ph*), 1108 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.67$ (d, $J = 6.6$ Hz, CH_3), 0.80 (d, $J = 6.6$ Hz, CH_3), 0.92 (dd, $J = 14.0$, 6.5 Hz, CH), 1.45 (s, $3CH_3$), 1.61 (s, CH_3), 1.65 (m, CH), 2.09 (s, CH_3), 7.28–7.70 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.5$ (q, CH_3), 19.8 (q, CH_3), 23.6 (d, CH), 23.7 (q, CH_3), 24.1 (q, CH_3), 27.9 (q, $3CH_3$), 38.2 (t, CH_2), 82.4 (s, Cq), 83.5 (s, C-1), 93.3 (s, C-7), 113.7 (s, C-5), 126.4 (d, CH_{Ar}), 127.9 (d, $2CH_{Ar}$), 128.1 (d, $2CH_{Ar}$), 135.9 (s, Cq_{Ar}), 165.6 (s, C-3), 168.3 (s, COO) ppm; MS: m/z (%) = 359 (M^+, 20).

1-Isobutyl-3,5-dimethyl-7-phenyl-7-tert-butoxycarbonyl-4,6-dioxa-2-azabicyclo[3.2.0]hept-2-ene (***endo*-5e**)

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (d, $J = 6.5$ Hz, CH_3), 0.97 (d, $J = 6.5$ Hz, CH_3), 1.49 (s, $3CH_3$), 1.64 (m, CH), 1.65 (dd, $J = 14.0$, 8.0 Hz, CH), 1.79 (s, CH_3), 1.81 (s, CH_3), 2.18 (dd, $J = 14.0$, 5.0 Hz, CH), 7.25–7.50 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.9$ (q, CH_3), 19.3 (q, CH_3), 23.7 (d, CH), 24.1 (q, CH_3), 24.2 (q, CH_3), 27.9 (q, $3CH_3$), 38.9 (t, CH_2), 82.9 (s, Cq), 83.3 (s, C-1), 93.9 (s, C-7), 114.8 (s, C-5), 126.4 (d, 2CH), 127.4 (d, 2CH), 136.7 (s, Cq), 164.9 (s, C-3), 169.3 (s, COO) ppm.

Synthesis of erythro- and threo-bis-Quaternery α-Amino-β-hydroxyketones (**6a**–**6e**)
To a stirred solution of the bicyclic oxetane **5a**–**5e** (2 mmol) in 10 cm^3 $CHCl_3$ was added 0.5 cm^3 1 N HCl. After 4 h at rt, the course of reaction was monitored by *TLC*. Upon complete conversion, the reaction mixture was diluted with $CHCl_3$, washed with $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$), and concentrated in *vacuo*. The crude product was purified by preparative thick-layer chromatography over silica gel using a mixture of ethylacetate/*n*-hexane as an eluent.

(erythro)-Methyl 3-acetamido-3-acetyl-2-hydroxy-2,5-dimethylhexanoate (**6a**, $C_{13}H_{23}NO_5$)
Following the general procedure, 0.51 g **5a** (2 mmol) were hydrolyzed in 5 h. Preparative chromatography yielded 0.46 g (85%) **6a** as a colorless oil. $R_f = 0.42$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3448$ (OH), 3330 (NH), 2993, 2898 (C–H), 1735, 1718 (2C=O), 1667 (CON), 1124 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (d, $J = 6.6$ Hz, CH_3), 0.95 (d, $J = 6.6$ Hz, CH_3), 1.41 (m, CH), 1.56 (s, CH_3), 1.89 (m, CH_2), 2.04 (s, CH_3CO), 2.14 (s, CH_3CO), 3.66 (s, OCH_3), 6.53 (bs, NH) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.3$ (q, CH_3), 17.9 (q, CH_3), 18.5 (q, CH_3), 23.4 (q, CH_3), 24.5 (q, CH_3), 43.3 (t, CH_2), 52.4 (q, OCH_3), 82.4 (s, C-3), 89.7 (s, C-2), 164.7 (s, CON), 171.3 (s, COO), 195.2 (s, CO) ppm; MS: m/z (%) = 273 (M^+, 37).

(threo)-Methyl 2-tert-butyl-3-acetamido-3-acetyl-2-hydroxy-5-methylhexanoate
(**6b**, $C_{16}H_{29}NO_5$)
Following the general procedure, 0.59 g **5b** (2 mmol) were hydrolyzed in 4 h. Preparative chromatography yielded 0.50 g (80%) **6b** as a colorless oil. $R_f = 0.51$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3440$ (OH), 3345 (NH), 2989, 2890 (C–H), 1730, 1715 (2C=O), 1660 (CON), 1120 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.93$ (d, $J = 6.8$ Hz, $2CH_3$), 1.05 (s, $3CH_3$), 1.23 (m, CH), 1.53 (m, CH_2), 2.12 (s, CH_3CO), 2.23 (s, CH_3CO), 3.65 (s, OCH_3) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.8$ (q, CH_3), 18.9 (q, CH_3), 19.3 (q, CH_3), 19.5 (q, CH_3), 26.4 (q, $3CH_3$), 27.5 (d, CH), 39.5 (t, CH_2), 40.2 (s, Cq), 52.2 (q, OCH_3), 82.5 (s, C-3), 84.0 (s, C-2), 165.6 (s, CON), 171.8 (s, COO), 194.6 (s, CO) ppm; MS: m/z (%) = 315 (M^+, 46).

(threo)-Methyl 3-acetamido-3-acetyl-2-hydroxy-5-methyl-2-phenylhexanoate
(***threo*-6c**, $C_{18}H_{25}NO_5$)
Following the general procedure, 0.63 g ***exo*-5c** (2 mmol) were hydrolyzed in 4 h. Preparative chromatography yielded 0.52 g (78%) ***threo*-6c** as a colorless oil. $R_f = 0.55$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3470$ (OH), 3359 (NH), 2993, 2893 (C–H), 1735, 1726 (2C=O), 1665 (CON), 1118 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.88$ (d, $J = 6.6$ Hz, CH_3), 0.95 (d, $J = 6.6$ Hz, CH_3), 1.35 (dd, $J = 13.3$, 5.7 Hz, CH), 1.80 (m, CH), 1.87 (s, CH_3CO), 2.27 (s, CH_3CO), 2.37 (dd, $J = 13.3$, 6.1 Hz, CH), 3.38 (s, 3H, OCH_3), 7.25–7.55 (m, 5H, Ar′H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.2$ (q, CH_3), 15.5 (q, CH_3), 23.3 (q, CH_3), 24.5 (q, CH_3), 25.8 (d, CH), 43.9 (t, CH_2), 52.8 (q, OCH_3), 86.5 (s, C-3), 93.0 (s, C-2), 125.6 (d, CH_{Ar}), 126.4 (d, $2CH_{Ar}$), 127.5 (d, $2CH_{Ar}$), 134.8 (s, Cq_{Ar}), 164.6 (s, CON), 168.6 (s, COO), 194.5 (s, CO) ppm.

(erythro)-Methyl 3-acetamido-3-acetyl-2-hydroxy-5-methyl-2-phenylhexanoate (***erythro*-6c**)
Following the general procedure, 0.63 g ***endo*-5c** (2 mmol) were hydrolyzed in 4 h. Preparative chromatography yielded 0.54 g (80%) ***erythro*-6c** as a colorless oil. $R_f = 0.36$ (*H:EA* = 4:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.81$ (d, $J = 6.6$ Hz, CH_3), 0.92 (d, $J = 6.6$ Hz, CH_3), 1.61 (dd, $J = 13.4$, 5.8 Hz, CH), 1.72 (s, CH_3CO), 1.83 (m, CH), 2.02 (dd, $J = 13.4$, 6.1 Hz, CH), 2.35 (s, CH_3CO), 3.76 (s, OCH_3), 7.26–7.37 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.4$ (q, CH_3), 15.9 (q, CH_3), 23.1 (q, CH_3), 24.1 (q, CH_3), 25.6 (d, CH), 37.1 (t, CH_2), 52.3 (q, OCH_3), 83.1 (s, C-3), 93.1 (s, C-2), 126.7 (d, CH_{Ar}), 127.3 (d, $2CH_{Ar}$), 129.2 (d, $2CH_{Ar}$), 135.7 (s, Cq_{Ar}), 165.1 (s, CON), 168.6 (s, COO), 194.0 (s, CO) ppm.

(threo)-Ethyl 3-acetamido-3-acetyl-2-hydroxy-5-methyl-2-phenylhexanoate
(***threo*-6d**, $C_{19}H_{27}NO_5$)
Following the general procedure, 0.66 g ***exo*-5d** (2 mmol) were hydrolyzed in 4 h. Preparative chromatography yielded 0.57 g (82%) ***threo*-6d** as a colorless oil. $R_f = 0.53$ (*H:EA* = 4:1); IR (film):

$\bar{\nu} = 3456$ (OH), 3327 (NH), 2996, 2898 (C–H), 1735, 1716 (2C=O), 1665 (CON), 1116 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (d, $J = 6.8$ Hz, CH_3), 0.97 (d, $J = 6.6$ Hz, CH_3), 1.28 (t, $J = 7.2$ Hz, CH_3), 1.39 (dd, $J = 13.4$, 5.9 Hz, CH), 1.80 (m, CH), 1.94 (s, CH_3CO), 2.26 (s, CH_3CO), 2.38 (dd, $J = 13.4$, 6.0 Hz, CH), 4.25 (q, $J = 7.2$ Hz, OCH_2), 7.25–7.56 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.9$ (q, CH_3), 14.2 (q, CH_3), 15.5 (q, CH_3), 23.3 (q, CH_3), 24.5 (q, CH_3), 25.8 (d, CH), 43.9 (t, CH_2), 62.2 (t, OCH_2), 86.4 (s, C-3), 92.9 (s, C-2), 125.6 (d, CH_{Ar}), 126.4 (d, $2CH_{Ar}$), 127.5 (d, $2CH_{Ar}$), 134.8 (s, Cq_{Ar}), 164.7 (s, CON), 168.1 (s, COO), 193.7 (s, CO) ppm.

(erythro)-Ethyl 3-acetamido-3-acetyl-2-hydroxy-5-methyl-2-phenylhexanoate (***erythro*-6d**)
Following the general procedure, 0.66 g ***endo*-5d** (2 mmol) were hydrolyzed in 4 h. Preparative chromatography yielded 0.56 g (80%) ***erythro*-6d** as a colorless oil. $R_f = 0.41$ (*H:EA* = 4:1); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.75$ (d, $J = 6.6$ Hz, CH_3), 0.90 (d, $J = 6.8$ Hz, CH_3), 1.27 (t, $J = 7.5$ Hz, CH_3), 1.41 (m, CH), 1.60 (m, CH_2), 1.89 (s, CH_3CO), 2.10 (s, CH_3CO), 4.25 (q, $J = 7.5$ Hz, OCH_2), 7.26–7.35 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 13.9$ (q, CH_3), 14.2 (q, CH_3), 15.5 (q, CH_3), 22.6 (q, CH_3), 23.7 (q, CH_3), 25.7 (d, CH), 37.1 (t, CH_2), 61.7 (t, OCH_2), 83.5 (s, C-3), 91.6 (s, C-2), 126.7 (d, CH), 126.7 (d, CH), 127.3 (d, CH), 129.2 (d, CH), 135.7 (s, Cq), 165.7 (s, CON), 169.2 (s, COO), 193.8 (s, CO) ppm.

(threo)-tert-Butyl 3-acetamido-3-acetyl-2-hydroxy-5-methyl-2-phenylhexanoate
(***threo*-6e**, $C_{21}H_{31}NO_5$)
Following the general procedure, 0.72 g ***exo*-5e** (2 mmol) were hydrolyzed in 4 h. Preparative chromatography yielded 0.59 g (79%) ***threo*-6e** as a colorless oil. $R_f = 0.58$ (*H:EA* = 4:1); IR (film): $\bar{\nu} = 3465$ (OH), 3324 (NH), 2993, 2890 (C–H), 1730, 1720 (2C=O), 1669 (CON), 1120 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.88$ (d, $J = 6.6$ Hz, CH_3), 0.95 (d, $J = 6.6$ Hz, CH_3), 1.35 (dd, $J = 13.3$, 5.7 Hz, CH), 1.49 (s, $3CH_3$), 1.81 (m, CH), 1.98 (s, CH_3CO), 2.13 (s, CH_3CO), 2.37 (dd, $J = 13.3$, 6.1 Hz, CH), 7.25–7.55 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.2$ (q, CH_3), 15.3 (q, CH_3), 23.3 (q, CH_3), 24.5 (q, CH_3), 25.8 (d, CH), 27.9 (q, $3CH_3$), 43.9 (t, CH_2), 83.7 (s, Cq), 86.1 (s, C-3), 93.2 (s, C-2), 125.6 (d, CH_{Ar}), 126.4 (d, $2CH_{Ar}$), 127.5 (d, $2CH_{Ar}$), 134.8 (s, Cq_{Ar}), 163.7 (s, CON), 164.9 (s, COO), 193.7 (s, CO) ppm; MS: m/z (%) = 377 (M^+, 38).

(erythro)-tert-Butyl 3-acetamido-3-acetyl-2-hydroxy-5-methyl-2-phenyl hexanoate (***erythro*-6e**)
Following the general procedure, 0.72 g ***endo*-5e** (2 mmol) were hydrolyzed in 4 h. Preparative chromatography yielded 0.62 g (83%) ***erythro*-6e** as a colorless oil. $R_f = 0.46$ (*H:EA* = 4:1); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.81$ (d, $J = 6.6$ Hz, CH_3), 0.92 (d, $J = 6.6$ Hz, CH_3), 1.47 (s, $3CH_3$), 1.61 (dd, $J = 13.4$, 5.8 Hz, CH), 1.72 (s, CH_3CO), 1.83 (m, CH), 2.02 (dd, $J = 13.4$, 6.1 Hz, CH), 2.14 (s, CH_3CO), 7.26–7.37 (m, Ar′H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.4$ (q, CH_3), 15.5 (q, CH_3), 23.1 (q, CH_3), 24.1 (q, CH_3), 25.6 (d, CH), 28.3 (q, $3CH_3$), 37.1 (t, CH_2), 82.9 (s, Cq), 83.1 (s, C-3), 93.1 (s, C-2), 126.7 (d, CH_{Ar}), 127.3 (d, $2CH_{Ar}$), 129.2 (d, $2CH_{Ar}$), 135.7 (s, Cq_{Ar}), 165.1 (s, CON), 168.6 (s, COO), 192.8 (s, CO) ppm.

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