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Asymmetric Synthesis of α-Methyl-α-Amino Acids via Diastereoselective Alkylation of (1*S*)-(+)-3-Carene Derived Tricyclic Iminolactone

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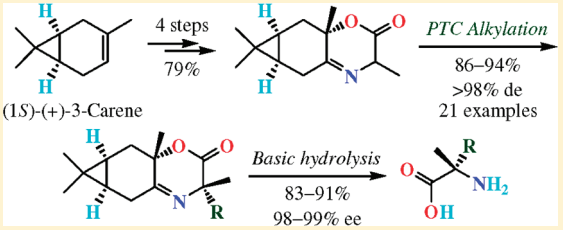
Supporting Information

ABSTRACT: A novel carene-based alanine-equivalent tricyclic iminolactone **16** has been synthesized via stereoselective dihydroxylation of the double bond, IBX oxidation of the secondary alcohol, esterification of the tertiary alcohol, deprotection of the resulting ester, and subsequent cyclization from commercially available (1*S*)-(+)-3-carene in 79% overall yield. The iminolactone **16** demonstrated high reactivity toward alkylation with a wide range of electrophiles at room temperature under phase-transfer catalysis conditions. The alkylated products were produced with excellent diastereoselectivities (>98% de) in good isolated yields (86−94%). High yields (83−91%) of optically pure (*S*)-α-methyl-α-substituted-α-amino acids were obtained by basic hydrolysis of the dialkylated iminolactones with the recovery of the chiral auxiliary **15** (78−87%).



The synthesis of optically active, unnatural nonproteinogenic α,α-dialkyl-α-amino acids has attracted much attention[1] not only because of their capability to restrict the conformational freedom of peptides but also owing to their potential biological activities.[2] In the class of α-quaternary α-amino acids, α-methyl-α-amino acids are known to play an important role in bioorganic chemistry.[3] For instance, (*S*)-α-methylDOPA (Aldomet),[4] a competitive inhibitor of the enzyme DOPA decarboxylase, is a psychoactive drug used as an antihypertensive, (*R*)-α-methylcysteine is a potential enzyme inhibitor,[5] α-methyltrypophan is a substrate for tryptophan hydrolase,[6] and α-methylaspartic acid exhibits the competitive inhibition of aspartate amino transferase.[7] Moreover, enantiomerically pure α-methyl-α-amino acids serve as valuable building blocks in the conformational design of peptides.[8] For example, isovaline, the simplest chiral α,α-dialkyl-α-amino acid, has been found to be able to construct α- or 3_{10}-helical peptides,[9] α-methylleucine[10] and α-methylphenylalanine[11] are efficient *β*-turn and helix formers, and the latter is much stronger than its demethylated analogue phenylalanine. Owing to the versatilities and bioactivities of α-methyl-α-amino acids, the development of efficient methods for their asymmetric synthesis is a growing demand. Among these approaches, chiral cyclic alanine-equivalent templates are of great interest due to their ability in allowing for a more rigid transition state than the corresponding acyclic ones to exploit the steric effect of the auxiliary in controlling the stereochemistry of the reaction. In addition, a cyclic template will generate only the *Z*-enolate after deprotonation, which in turn will give a single alkylated product if the electrophile approaches specifically from one of the diastereomeric faces. Some representative examples are (1) the bis-lactim ethers **1** of Schöllkopf,[12] (2) the imidazolidinone **2** and oxazolidinones **3** of Seebach,[13] (3) the diphenyloxazinones **4** of Williams,[14] (4) the oxazinones **5** and pyrazinones **6** of Nájera,[15] (5) the oxazinone **7** of Wanner,[16] (6) the morpholindiones **8** of Sandri,[17] (7) the diketopiperazine (DKP) **9** and monolactim ether **10** of Davies,[18] and (8) the camphor-derived tricyclic iminolactones **11** and **12** of Lu (Figure 1).[19] However, there are several existing problems among some of these synthetic routes such as using strong bases and dry solvents, being carried out at low reaction temperatures, and poor recovery of the chiral auxiliary.

Phase-transfer catalysis is an exceedingly practical method that has the advantages of mild reaction conditions, simple experimental operations, environment-friendly and low-cost reagents and solvents, and scalability. Hence, it has been applied to synthesize various α-amino acids using either chiral or achiral phase-transfer catalysts.[20]

In 2008, we reported an efficient method for the synthesis of α-methyl-α-amino acids employing the diastereoselective alkylation of the monocyclic iminolactones **13** that was prepared from α-methyl-*trans*-cinnamaldehyde (Figure 2).[21] Herein, we report the development of a new carene-based tricyclic iminolactone as an alanine-equivalent and its application to the asymmetric synthesis of α-methyl-α-amino acids employing phase-transfer catalytic alkylation.

RESULTS AND DISCUSSION

In the course of our study on the asymmetric synthesis of α-amino acids, we were required to prepare an α-hydroxy ketone

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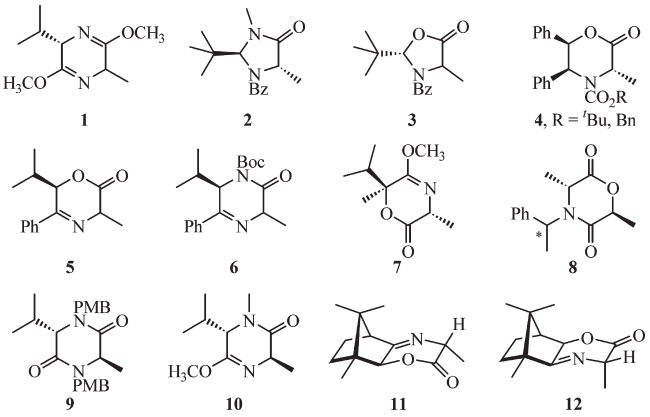


Figure 1. Some representative chiral cyclic alanine-equivalent templates.

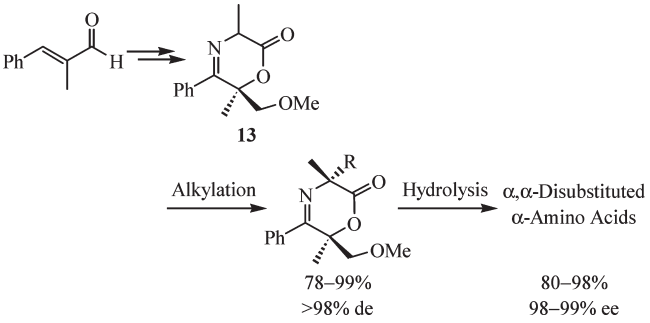
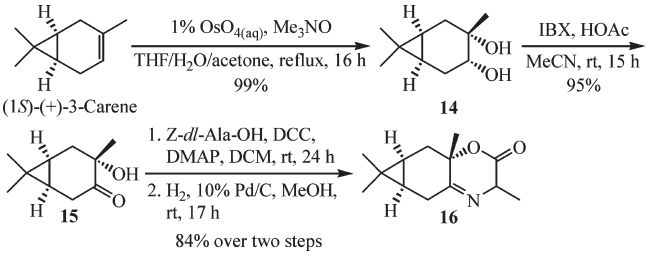


Figure 2. Asymmetric synthesis of α-methyl-α-amino acids via monocyclic iminolactones.

Scheme 1. Synthesis of Iminolactone 16



as a chiral auxiliary that could be synthesized from the corresponding 1,2-diol. To meet our goal, commercially available (1*S*)-(+)-3-carene was chosen as the starting material. The preparation of the required iminolactone is illustrated in Scheme 1. First, dihydroxylation of (1*S*)-(+)-3-carene by osmium tetroxide was carried out under reflux to give diol **14** as a single stereoisomer in 99% yield.[22] The resulting diol **14** was oxidized by treatment with IBX (*o*-iodoxybenzoic acid) in acetonitrile in the presence of a stoichiometric amount of acetic acid to obtain the chiral auxiliary, α-hydroxy ketone **15**, in 95% yield.[23] It is worthy to note that other oxidation conditions such as Jones oxidation,[24] PCC (pyridinium chlorochromate),[25] PDT (P_2O_5/DMSO/Et_3N, phosphorus pentoxide/dimethyl sulfoxide/triethylamine),[26] or Swern oxidation[27] were not able to afford the desired product in good yields. DCC/DMAP-mediated esterification[28] of the tertiary hydroxyl group of compound **15** with *N*-carbobenzyloxyalanine (*Z*-*dl*-Ala-OH) and subsequent removal of the protecting group with the spontaneous cyclization under catalytic hydrogenation conditions led to the chiral template, iminolactone **16**, as a 17:1 mixture of inseparable diastereomers ($C_{3\alpha}$-methyl/$C_{3\beta}$-methyl), in 84% yield over two steps.

Iminolactone **16** was then subjected to alkylation under phase-transfer catalysis conditions, and the results are summarized in Table 1.

The results of the alkylation of the iminolactone **16** are found to be strongly dependent on the reaction conditions. Initially, the alkylation of the potassium enolate of iminolactone **16** was performed with 3 equiv of benzyl bromide in the presence of catalytic amount (0.1 equiv) of tetrabutylammonium bromide (TBAB) in toluene/water at room temperature. The starting material was consumed within 30 min; however, only 83% of α-hydroxy ketone **15**, the hydrolyzed product, was obtained (Table 1, entry 1) because alkylation and hydrolysis of iminolactone **16** are competing reactions in aqueous solution. As a result, the yields of compound **17a** were significantly improved by increasing the amount of TBAB from 0.1 to 1 equiv with a concomitant reduction of the amount of the undesired product **15** (Table 1, entries 2−5). Moreover, when 1.5 equiv of benzyl bromide was used, the yield of compound **17a** was further improved to 90% (Table 1, entry 6). The stereoselectivity of the benzylation of iminolactone **16** exceeded 98% de as determined by NMR. Furthermore, other phase-transfer catalysts, e.g., tetrabutylammonium iodide (TBAI), tetrabutylammonium chloride (TBAC), TEAPTS, Aliquat 336, and Triton B, have been also employed in the alkylation reaction. Unfortunately, compared to TBAB, unsatisfactory results were observed (Table 1, entries 7−11). In entry 11, when using Triton B as the phase-transfer catalyst, α-hydroxy ketone **15** was obtained exclusively in 88% yield.

The alkylation was subsequently performed with a number of activated and nonactivated electrophiles under the optimum reaction conditions developed in Table 1. The alkylation reaction delivered the α-methyl-α-alkylated products in high yields with excellent control of the stereochemistry of the newly formed stereocenter for a wide range of electrophiles. As summarized in Tables 2 and 3, the results of alkylation of iminolactone **16** clearly demonstrate the generality and effectiveness of our method.

Comparison of the results of different benzyl chlorides (Table 2, entries 1−6) demonstrates that those with an electron-withdrawing group on the benzene ring showed lower reactivity toward iminolactone **16**, which required 3 equiv of the chloride to avoid the formation of α-hydroxy ketone **15** (Table 2, entries 3 and 4). When the alkylation of compound **16** was carried out with benzyl, allyl, and activated alphatic bromides, 1.5 equiv of the electrophiles was enough to give the desired products within 20 min in good yields (86−94%, Table 2, entries 7−19). In addition, 4-nitro and 4-bromo benzyl iodides are as efficient as their corresponding bromides (Table 2, entries 20 and 21).

In the alkylation of compound **16** employing nonactivated ethyl and *n*-propyl bromides, 3 and 9 equiv of the electrophiles were required, respectively, to afford high yields of the corresponding products (Table 3, entries 1 and 2) and to prevent the formation of significant amounts of α-hydroxy ketone **15**. In addition, the Michael addition of iminolactone **16** generated the product **17p** smoothly with good facial selectivity (Table 3, entry 3). Other nonactivated aliphatic bromides and iodides were also examined in the alkylation (Table 3, entries 4−11). Large excess of *n*-butyl and isobutyl bromides and iodides were needed to

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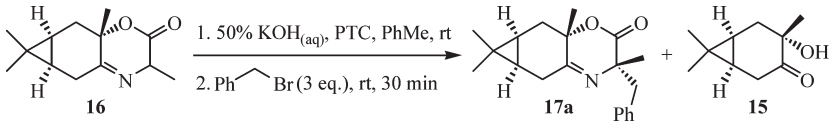
Table 1. Optimization of Conditions for Phase-Transfer Alkylation of Iminolactone 16



entry	PTC	equiv of PTC	yield (%) of **17a**[a]	yield (%) of **15**[a]	de[b] (%)
1	TBAB	0.1		83	
2	TBAB	0.2	15	62	>98
3	TBAB	0.4	46	35	>98
4	TBAB	0.6	88		>98
5	TBAB	1	86		>98
6[c]	TBAB	0.6	90		>98
7	TBAI	0.6	72	13	>98
8	TBAC	0.6	65	21	>98
9	TEAPTS[d]	0.6	57	24	>98
10	Aliquat 336[e]	0.6	60		>98
11	Triton B[f]	0.6		88	

[a] The yields are isolated yields after column chromatography. [b] Diastereomeric excess was estimated by ^{1}H NMR analysis of the crude reaction mixtures on a 400 MHz spectrometer. [c] 1.5 equiv of benzyl bromide was used. [d] Tetraethylammonium *p*-toluenesulfonate. [e] Trioctylmethylammonium chloride. [f] Benzyltrimethylammonium hydroxide solution (40 wt % in H_2O).

afford the desired products in 50−55% yields along with the formation of compound **15** (25−33%) (Table 3, entries 4, 6, 8, and 10). Although isopropyl and 2-phenylethyl bromides and iodides were used in large excess (6−12 equiv), only 70−75% of α-hydroxy ketone **15** were obtained (Table 3, entries 5, 7, 9, and 11). It is noteworthy that when the alkylation was performed with 2-phenylethyl bromide or iodide, the elimination product, styrene, was detected in the crude ^{1}H NMR spectra. Presumably, under the reaction conditions, deprotonation of these alkyl halides containing *β*-protons occurred faster than that of the alkylation and hence significantly decreased the available amount of the electrophile. As a result, the hydrolysis of compound **16** competes favorably with the alkylation.

Compared to direct alkylation of iminolactone **16** with *n*-butyl and isobutyl halides (Table 3, entries 4, 6, 8, and 10), compounds **17q** and **17r** can be obtained in much better yields via a two-step process, i.e., alkylation with allylic halides and followed by hydrogenation (90% and 91%, respectively, Scheme 2). Compounds **17h** and **17k** were also hydrogenated under standard conditions to give the saturated products **17s** and **17t** in high yields.

The stereochemistry of the newly created stereocenter of the dialkylated products is deduced from the following evidence. The ^{1}H NMR spectra of compounds **17a**−**h** with a $C_{3\alpha}$-substituent containing a benzene ring show a remarkable stereochemistry-dependent shielding effect on the chemical shifts of the protons on C_{5a}, C_{6a}, and C_7. The chemical shifts of characteristic protons of compounds **17a**−**h** are listed in Table 4.

For example, the chemical shifts of the C_{5a}-H, C_{6a}-H, and C_7-H^α of the iminolactone **16** appear at *δ* 0.81, 0.70, and 2.32, respectively (Table 4, entry 1). After benzylation, those three protons of the benzylated product **17a** move to much higher fields of *δ* 0.47, −0.02, and 2.04, respectively (Table 4, entry 2). The shielding effect of the C_3−benzyl group is apparently responsible for this upfield shift, indicating that the C_3−benzyl group and the C_{5a}-H, C_{6a}-H, and C_7-H^α are on the same side of the tricyclic iminolactone ring. Similar chemical shift changes are also observed for compounds **17b**−**d** and **17f** (Table 4, entries 3−5 and 7). The C_{5a}-H, C_{6a}-H, and C_7-H^α are shielded more efficiently ($\Delta\delta_{C_{5a}\text{-}H} = 1.93$, $\Delta\delta_{C_{6a}\text{-}H} = 1.24$, and $\Delta\delta_{C_7-H^\alpha} = 0.44$, compared to compound **16**) by the C_3−1-naphthylmethyl group of compound **17e** suggesting that the shielding zone gets closer to those protons (Table 4, entry 6). A similar trend was also found for compound **17g** (Table 4, entry 8). The chemical shifts of the C_{5a}-H, C_{6a}-H, and C_7-H^α of compound **17h** show much smaller difference than those of other compounds with a $C_{3\alpha}$-substituent containing a benzene ring indicating that the shielding zone is further apart from those protons (Table 4, entry 9).

Furthermore, X-ray diffraction analyses of the single crystals of compounds **17a**, **17e**, **17g**, **17l**, **17m**, and **17o**,[29] recrystallized from ether/hexanes, confirm the absolute configuration of the dialkylated products. It is evident that the iminolactone ring, fused with the boat carene skeleton, adopts a boat conformation with the $C_{3\alpha}$-methyl and C_{7a}-methyl groups being at the flagpole positions (Figures 3−5). The X-ray structure of compound **17a** clearly shows that the C_{5a}-H, C_{6a}-H, and C_7-H^α fall in the shielding zone of the $C_{3\alpha}$-substituent's benzene ring. Consequently, X-ray structure clearly supports the stereochemical assignment of the alkylated products by ^{1}H NMR. Besides, the stereochemistry of the alkylated products demonstrates that electrophiles reacted with the enolate of iminolactone **16** from the opposite side of the C_{7a}-methyl group in the alkylation step.

A plausible mechanism for the highly stereoselective alkylation reaction is proposed in Scheme 3. The crystal structures of compounds **17a**, **17e**, **17g**, **17l**, **17m**, and **17o** indicate that the C_{7a}-methyl group sits on the top face of the iminolactone ring. Deprotonation of the tricyclic iminolactone **16** would generate intermediate **I** in which the top face is effectively blocked by this C_{7a}-methyl group. Since the bottom face is much more accessible for the alkylation, a high degree of diasteroselectivity resulted.

At first, hydrolysis of the dialkylated iminolactone was carried out with 8 N HCl aqueous solution in a sealed tube at 90 °C for 2 h (Scheme 4)[30] to give high yield and excellent enantiomeric excess of the corresponding amino acid hydrogen chloride salt. Unfortunately, the chiral auxiliary **15** was not recovered probably because of the decomposition of the sensitive cyclopropane ring

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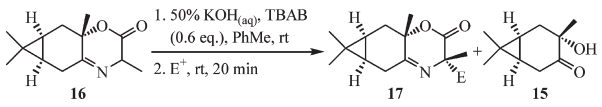
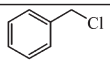
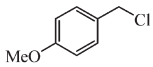
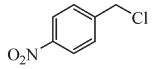
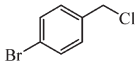
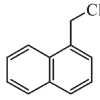
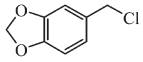
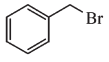
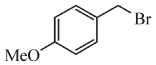
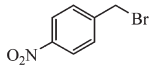
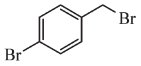
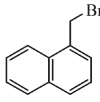
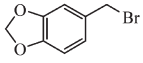
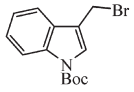
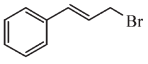
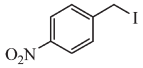
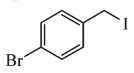
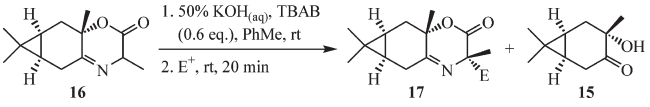
Table 2. Alkylations of Iminolactone 16 with Activated Electrophiles

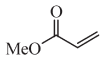
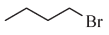


Entry	Electrophile	Equiv of E^+	Yield (%) of **17**[a]	Yield (%) of **15**[a]	de[b] (%)
1		1.5	88 (**17a**)	–	>98
2		1.5	89 (**17b**)	–	>98
3		3	89 (**17c**)	–	>98
4		3	90 (**17d**)	–	>98
5		1.5	88 (**17e**)	–	>98
6		1.5	91 (**17f**)	–	>98
7		1.5	90 (**17a**)	–	>98
8		1.5	88 (**17b**)	–	>98
9		1.5	92 (**17c**)	–	>98
10		1.5	91 (**17d**)	–	>98
11		1.5	87 (**17e**)	–	>98
12		1.5	90 (**17f**)	–	>98
13		1.5	86 (**17g**)	–	>98
14		1.5	90 (**17h**)	–	>98
15		1.5	92 (**17i**)	–	>98
16		1.5	93 (**17j**)	–	>98
17		1.5	93 (**17k**)	–	>98
18		1.5	94 (**17l**)	–	>98
19		1.5	90 (**17m**)	–	>98
20		1.5	88 (**17e**)	–	>98
21		1.5	90 (**17d**)	–	>98

[a] The yields are isolated yields after column chromatography. [b] Diastereomeric excess was estimated by ^{1}H NMR analysis of the crude reaction mixtures on a 400 MHz spectrometer.

Table 3. Alkylations of Iminolactone 16 with Nonactivated Electrophiles



Entry	Electrophile	Equiv of E^+	Yield (%) of **17**[a]	Yield (%) of **15**[a]	de[b] (%)
1		3	93 (**17n**)	–	>98
2		9	94 (**17o**)	–	>98
3		10	92 (**17p**)	–	>98
4		9–12	55 (**17q**)	27	>98
5		9–12	–	72	–
6		9–12	50 (**17r**)	31	>98
7		9–12	–	74	–
8		6–9	54 (**17q**)	25	>98
9		6–9	–	70	–
10		6–9	52 (**17r**)	33	>98
11		6–9	–	75	–

[a] The yields are isolated yields after column chromatography. [b] Diastereomeric excess was estimated by ^{1}H NMR analysis of the crude reaction mixtures on a 400 MHz spectrometer.

of compound **15** under strongly acidic conditions. A further evidence of the acid-sensitivity of the system was observed in one of our attempts to prepare iminolactone **16**. The chiral auxiliary **15** was coupled with *N-tert*-butoxycarbonylalanine (Boc-*dl*-Ala-OH) to give the corresponding ester. However, attempted deprotection of the Boc group by bubbling gasous hydrogen chloride to the ester only gave an unidentified mixture of complicated products. It suggests that the acid-sensitive cyclopropane ring is unstable under the deprotection conditions.

Finally, after studying a wide varieties of conditions, hydrolysis of representative dialkylated iminolactones was achieved along with the recovery of the chiral auxiliary **15** (78−87%) under basic conditions. The results are compiled in Table 5. Several bioactive α-methyl-α-amino acids such as α-methylphenylalanine (**19a**), α-methylDOPA (**19c**), α-methyltryptophan (**19d**), α-methylaspartic acid (**19f**), isovaline (**19g**), and α-methylleucine (**19i**) are produced by this liberation method in good yields (83−91%) and optical purities (98−99% ee) (Table 5, entries 1, 2, 4, 5, 8, 9, and 12). A dialkylated iminolactone bearing a benzene ring shows a dramatic solvent effect on the reaction time. When compound **19a** was exposed to 50% aqueous cesium hydroxide in a sealed tube at 70 °C for 14 h giving α-methylphenylalanine in 84% yield (Table 5, entry 1). When ethanol is used as a cosolvent, the reaction time can be significantly reduced to 2 h (Table 5, entry 2). On the contrary, a dialkylated iminolactone without a benzene ring can be hydrolyzed in either the presence or absence of ethanol in short reaction time (2−3 h) (Table 5, entries 6−12). The *S*-configuration of the resulting amino acids, determined by comparing the optical rotation of the products with

Scheme 2. Hydrogenation of Compounds 17h and 17j−l

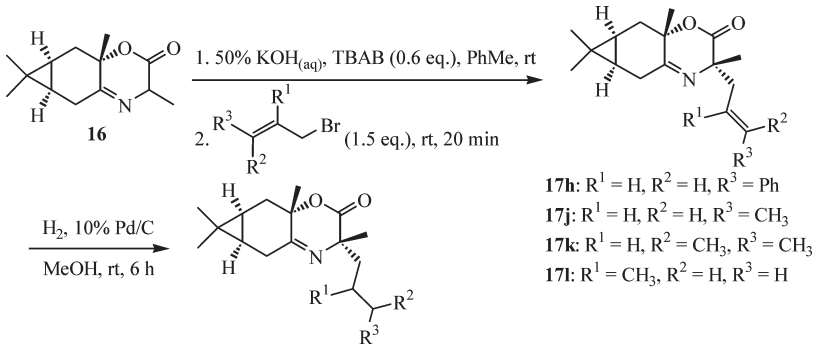
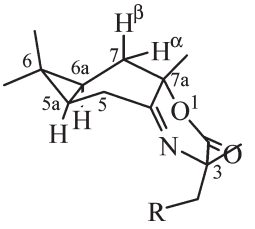
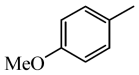
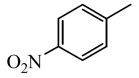
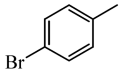
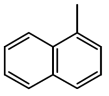
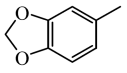
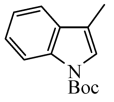
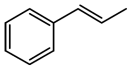


Table 4. Chemical Shifts (ppm) of Characteristic Protons of Compounds 16 and 17a−h



Entry	Compound	RCH_2	$\delta_{C_{5a}-H}$	$\Delta\delta_{C_{5a}-H}$[a]	$\delta_{C_{6a}-H}$	$\Delta\delta_{C_{6a}-H}$[a]	δ_{C_7-H}[a]	$\Delta\delta_{C_7-H}$[a a]
1	**16**	–	0.81	–	0.70	–	2.32	–
2	**17a**		0.47	0.34	–0.02	0.72	2.04	0.28
3	**17b**		0.53	0.28	0.04	0.66	2.06	0.26
4	**17c**		0.41	0.40	–0.03	0.73	2.06	0.26
5	**17d**		0.44	0.37	0.05	0.65	2.08	0.24
6	**17e**		–1.12	1.93	–0.54	1.24	1.88	0.44
7	**17f**		0.68	0.13	0.16	0.54	2.11	0.21
8	**17g**		–0.04	0.85	–0.19	0.89	2.07	0.25
9	**17h**		0.72	0.09	0.43	0.27	2.26	0.06

[a] The difference in chemical shift compared to the same proton of compound **16**.

literature values,[31] is in consistent with the assigned stereochemistry of the dialkylated iminolactones. The recovered compound **15** was recycled to generate the template **16** without loss of optical integrity.

dx.doi.org/10.1021/jo1022537 |J. Org. Chem. 2011, 76, 1621–1633

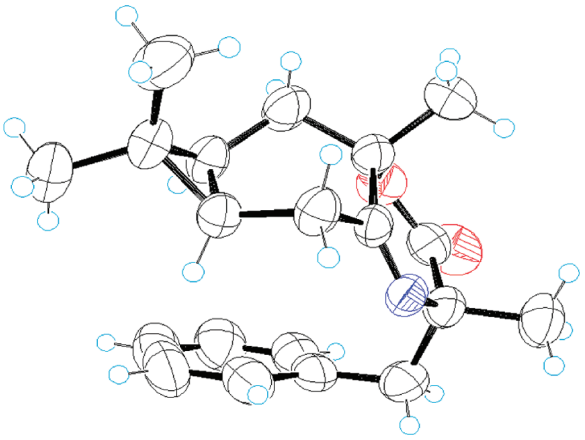


Figure 3. X-ray-derived ORTEP of compound **17a**.

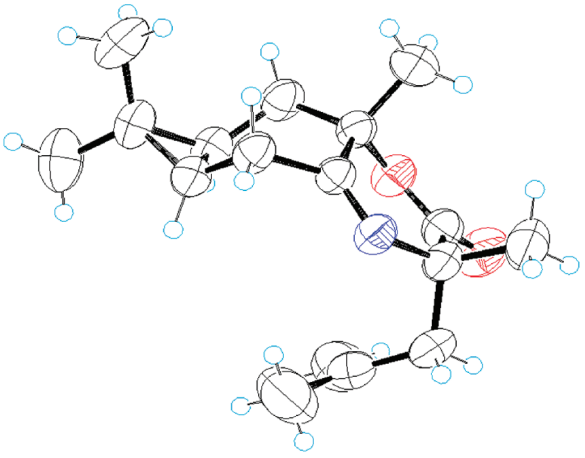


Figure 4. X-ray-derived ORTEP of compound **17l**.

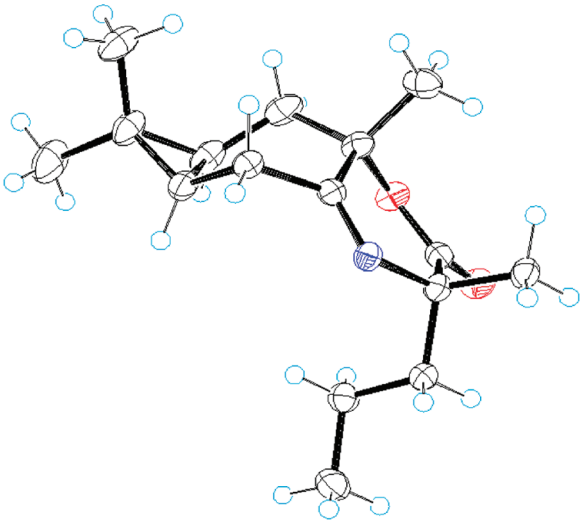


Figure 5. X-ray-derived ORTEP of compound **17o**.

CONCLUSION

In conclusion, an efficient and practical method for the synthesis of various α-methyl-α-substituted-α-amino acids via diastereoselective alkylation of an alanine-equivalent tricyclic iminolactone **16**, obtained in 79% yield over four steps from (1*S*)-(+)-3-carene, under phase-transfer catalysis conditions has been achieved. The iminolactone **16** reacted smoothly with a variety of electrophiles such as benzyl, allyl, and aliphatic halides and Michael acceptor in a well-controlled stereochemical manner to afford the alkylated products in good yields and excellent stereoselectivities. Hydrolysis of the alkylated products provided good yields and enantiomeric excesses of α-methyl-α-amino acids along with recovered chiral auxiliary **15** under basic conditions. Thus, an effective, economical, environmentally benign, and highly facial selective methodology for the preparation of α-methyl-α-amino acids has been established. Other useful chiral auxiliaries are currently being studied in our laboratories.

EXPERIMENTAL SECTION

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a 400 or 600 MHz spectrometer. Chloroform (δ = 7.26) or deuterium oxide (δ = 4.60) was used as internal standard in ^{1}H NMR spectra. The center peak of deuterochloroform (δ = 77.0) was used as internal standard in ^{13}C NMR spectra. High-resolution mass spectrometry (HRMS) analyses were determined on a mass spectrometer. Elemental analyses were measured on an elemental analyzer. X-ray data were collected on a diffractometer equipped with graphite-monochromator Mo Kα radiation (λ = 0.71073 Å). Optical rotations were measured in $CHCl_3$, H_2O, MeOH, or 1 N $HCl_{(aq)}$ solution with a cuvette of 1 dm length on a polarimeter. IR spectra were recorded with a FT-IR spectrometer and only structurally important peaks are listed. Melting points were measured on a melting point apparatus with a capillary melting point tube. Thin-layer chromatography (TLC) plates visualized by exposure to ultraviolet light at 254 nm and/or immersion in a staining solution (phosphomolybdic acid) followed by heating on a hot plate. Flash chromatography was carried out utilizing silica gel 60, 70−230 mesh ASTM. For facial alkylations, diastereomeric ratios were determined by the integration of the ^{1}H NMR spectra of the crude mixtures. The ee values of the α-amino acids obtained from hydrolysis of the alkylated iminolactones were determined by HPLC analysis performed on a Crownpak CR(+) column (4 mm ×150 mm).

Materials. Reagents and solvents are commercially available. All alkyl halides were pretreated with copper powder. Methanol, toluene, dichloromethane, and acetonitrile were distilled from calcium hydride immediately prior to use. *o*-iodoxybenzoic acid,[32] *N*-carbobenzyloxy-alanine,[33] and *N*-*tert*-butoxycarbonyl-3-bromomethylindole[34] were prepared according to the literature procedures.

*(1S,3S,4R,6R)-3,7,7-Trimethylbicyclo[4.1.0]heptane-3,4-diol (**14**)*[22]. To a solution of trimethylamine *N*-oxide dehydrate (10.21 g, 90 mmol) in tetrahydrofuran/deionized water/acetone (112/13/38 mL) was added (1*S*)-(+)-carene (11 mL, 60 mmol) and 1% aqueous solution of osmium tetroxide (15 mL, 0.6 mmol) at room temperature. The mixture was then heated to reflux overnight (16 h). The solvents were removed under reduced pressure. The residue was dissolved in deionized water (30 mL), and the aqueous layer was extracted with ethyl acetate (50 mL × 3). The combined organic layers were dried over anhydrous magnesium sulfate and concentrated to afford the crude mixture. Flash column chromatography [silica gel (63−200 μm), hexanes/EtOAc 1:2] afforded diol **14** as a white solid (10.11 g, 99%). Mp = 65−67 °C; $[\alpha]_D^{23}$ = +18.6° (*c* 1.14, $CHCl_3$); IR (KBr, $CHCl_3$) 3413 (br), 2929 (ms) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.10 (dd, *J* = 16.8, 7.8 Hz, 1 H, C_4−H), 2.57 (d, *J* = 7.8 Hz, 1 H, C_4−OH), 2.35 (s, 1 H, C_3−OH), 2.02 (dd, *J* = 15.6, 9.6 Hz, 1 H, C_2−H_2), 1.94 (dd, *J* = 14.4, 7.2 Hz, 1 H, C_5−H_2), 1.64 (ddd, *J* = 14.4, 9.6, 8.4 Hz, 1 H, C_5−H_2), 1.14 (dd, *J* = 15.6, 4.8 Hz, 1 H, C_2−H_2), 1.12 (s, 3 H, C_3−CH_3), 0.92 (s, 3 H, C_7−CH_3), 0.82 (s, 3 H, C_7−CH_3), 0.77 (t, *J* = 8.4 Hz, 1 H, C_6−H), 0.55

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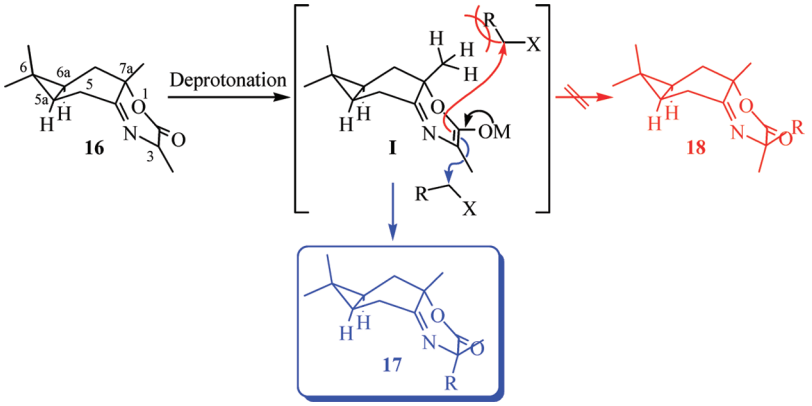
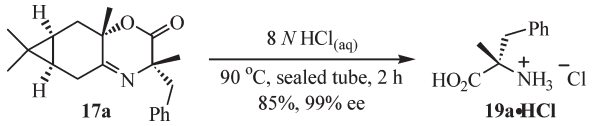
Scheme 3. Plausible Transition State for the Alkylation of Iminolactome 16



Scheme 4. Hydrolysis of Dialkylated Iminolactone 17a under Acidic Conditions



(td, J = 9.0, 4.2 Hz, 1 H, C_1−H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 73.1 (C_4), 70.2 (C_3), 33.2 (C_2), 28.5 (C_7−CH_3), 26.7 (C_5), 25.5 (C_3−CH_3), 21.5 (C_6), 17.3 (C_1), 16.2 (C_7−CH_3), 15.3 (C_7); MS m/z 170 (M^+, 0.53), 152 (49.8), 137 (60.4), 119 (87.3), 109 (98.0), 95 (48.5), 91 (72.8), 82 (42.7), 81 (100.0), 67 (98.5), 55 (49.4); HRMS m/z calcd for $C_{10}H_{18}O_2$ M^+ 170.1307, found M^+ 170.1304. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.60; H, 10.93.

(1R,4S,6S)-4-Hydroxy-4,7,7-trimethylbicyclo[4.1.0]heptan-3-one (***15***)[35]. A suspension of diol **14** (1.703 g, 10 mmol), acetic acid (860 μL, 15 mmol), and *o*-iodoxybenzoic acid (4.200 g, 15 mmol) in acetonitrile (50 mL) was stirred vigorously at room temperature for 15 h. After completion of the reaction, the resulting mixture was filtered through a pad of Celite using ethyl acetate as the eluent. The solvents were removed under reduced pressure to obtain the crude product as a pale yellow oil. Flash column chromatography [silica gel (63−200 μm), hexanes/EtOAc 5:1] afforded α-hydroxy ketone **15** as a colorless liquid (1.598 g, 95%). $[\alpha]_D^{23} = -109.3°$ (*c* 0.75, $CHCl_3$); IR (KBr, $CHCl_3$) 3475 (br), 2933 (ms), 1713 (s) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.82 (dd, J = 16.8, 8.4 Hz, 1 H, C_2−H_2), 2.62 (s, 1 H, C_4−OH), 2.32 (dd, J = 15.6, 8.4 Hz, 1 H, C_5−H_2), 2.21 (dd, J = 16.8, 3.6 Hz, 1 H, C_2−H_2), 1.37 (dd, J = 15.6, 6.0 Hz, 1 H, C_5−H_2), 1.18 (s, 3 H, C_4−CH_3), 1.15 (td, J = 9.0, 3.6 Hz, 1 H, C_1−H), 1.06 (s, 3 H, C_7−CH_3), 0.90 (s, 3 H, C_7−CH_3), 0.88 (td, J = 9.0, 6.0 Hz, 1 H, C_6−H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 214.5 (C=O), 72.8 (C_4), 35.2 (C_5), 34.0 (C_2), 27.8 (C_7−CH_3), 23.2 (C_1), 23.0 (C_4−CH_3), 19.9 (C_7), 16.9 (C_6), 14.5 (C_7−CH_3); MS m/z 168 (M^+, 7.06), 125 (30.1), 107 (33.4), 97 (34.3), 82 (57.8), 67 (100.0), 55 (41.8); HRMS m/z calcd for $C_{10}H_{16}O_2$ M^+ 168.1150, found M^+ 168.1143. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 68.40; H, 10.90.

(5aR,6aS,7aS)-5,5a,6,6a,7,7a-Hexahydro-3,6,6,7a-tetramethylbicyclo-[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (***16***). To a solution of α-hydroxy ketone **15** (1.682 g, 10 mmol), *N*-carbobenzyloxyalanine (4.465 g, 20 mmol), and 4-(dimethylamino)pyridine (1.222 g, 10 mmol) in dry dichloromethane (37 mL) was added dropwise a solution of *N*,*N*′-dicyclohexylcarbodiimide (4.168 g, 20 mmol) in dry dichloromethane (13 mL) via a syringe over a period of 3 min at 0 °C. The mixture was allowed to warm to room temperature and kept stirring for 24 h. The mixture was diluted with hexanes. White precipitated 1,3-dicyclohexylurea (DCU) was filtered through a pad of Celite and washed with ethyl acetate. The solvents were removed under reduced pressure to obtain the crude product as a pale yellow oil. Flash column chromatography [silica gel (63−200 μm), hexanes/EtOAc 3:1] afforded the ester as a colorless viscous oil. A 100 mL round-bottom flask with a Claisen tube was charged with the above ester (10 mmol), 10% palladium on activated carbon (400 mg), and a magnetic stirbar. The flask was evacuated by an aspirator and filled with hydrogen through a balloon three times. Dry methanol (27 mL) was added to the mixture followed by evacuation and filling with hydrogen one more time. The mixture was stirred under hydrogen atmosphere at room temperature for 17 h. The catalyst was removed by filtration and the solvent was concentrated to give a yellow oil. The oil was dissolved in ethyl acetate and the white precipitate was filtered through a pad of Celite. The solvent was removed under reduced pressure to obtain the crude product as a pale yellow oil. Flash column chromatography [silica gel (63−200 μm), hexanes/EtOAc 1:1] afforded iminolactone **16** (1.859 g, 84%, $C_{3\alpha}$-methyl/$C_{3\beta}$-methyl, 17:1 inseparable mixture of diastereomers determined by ^{1}H NMR) as a white solid. IR (KBr, $CHCl_3$): 2932 (ms), 1736 (s), 1686 (m) cm^{-1}. Major diastereomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.02 (qd, J = 7.2, 3.6 Hz, 1 H, C_3−H), 2.51 (dd, J = 13.8, 7.8 Hz, 1 H, C_5−H_2), 2.32 (dd, J = 15.6, 7.8 Hz, 1 H, C_7−H_2), 1.70 (ddd, J = 13.8, 9.0, 3.6 Hz, 1 H, C_5−H_2), 1.56 (d, J = 7.2 Hz, 3 H, C_3−CH_3), 1.33 (dd, J = 15.6, 9.0 Hz, 1 H, C_7−H_2), 1.30 (s, 3 H, C_{7a}−CH_3), 1.02 (s, 3 H, C_6−CH_3), 0.97 (s, 3 H, C_6−CH_3), 0.81 (dd, J = 16.8, 9.0 Hz, 1 H, C_{5a}−H), 0.70 (dd, J = 16.8, 9.0 Hz, 1 H, C_{6a}−H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.4 (C=O), 172.4 (C=N), 81.3 (C_{7a}), 54.3 (C_3), 34.3 (C_5), 29.3 (C_7), 27.5 (C_6−CH_3), 24.0 (C_{5a}), 21.4 (C_{7a}−CH_3), 20.1 (C_6), 18.3 (C_3−CH_3), 17.1 (C_{6a}), 14.1 (C_6−CH_3); MS m/z 221 (M^+, 10.5), 177 (100.0), 162 (54.5), 134 (69.0), 119 (40.4), 115 (34.4), 93 (79.5), 31 (32.1), 67 (26.9); HRMS m/z calcd for $C_{13}H_{19}NO_2$ M^+ 221.1416, found M^+ 221.1418. Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 69.95; H, 9.00; N, 6.30.

Alkylation of Iminolactone 16. Synthesis of Compounds 17a−r. General Procedure. To a solution of iminolactone **16** (221 mg, 1 mmol) and tetrabutylammonium bromide (195 mg, 0.6 mmol) in toluene (3 mL) was added 50% aqueous solution of potassium hydroxide (2 mL, 18 mmol) and then an electrophile immediately via syringes at room temperature. The resulting mixture was stirred for 20 min (the reaction progress was monitored by TLC). After completion of the reaction, the aqueous layer was extracted with ethyl acetate (40 mL × 3). The combined organic layers were dried over anhydrous magnesium sulfate. The solvents were evaporated, and the residue was analyzed by

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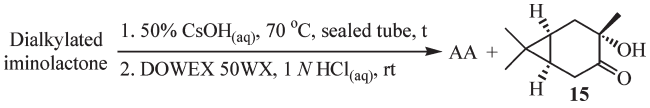
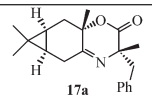
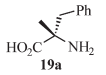
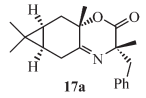
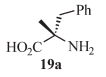
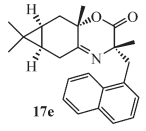
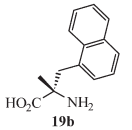
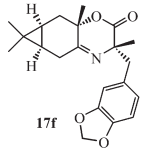
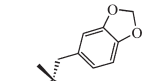
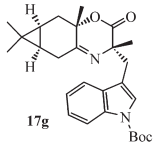
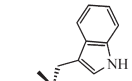
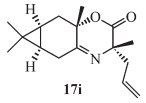
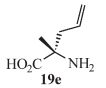
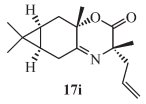
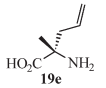
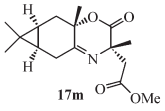
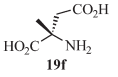
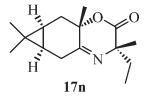
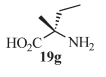
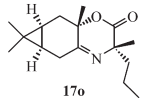
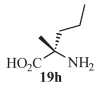
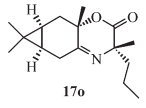
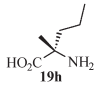
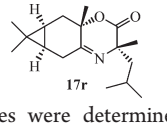
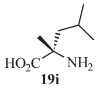
Table 5. Hydrolysis of Dialkylated Iminolactones under Basic Conditions



Entry	Dialkylated iminolactone	Cosolvent	t (h)	AA	Yield of AA (%)	% ee of AA[a]	Yield of **15** (%)
1	 **17a**	–	14	 **19a**	84	99	78
2	 **17a**	EtOH	2	 **19a**	86	99	85
3	 **17e**	EtOH	3	 **19b**	85	97	82
4	 **17f**	EtOH	4	 **19c**	88	98	85
5	 **17g**	EtOH	4	 **19d**	86	99	82
6	 **17i**	–	2	 **19e**	90	99	83
7	 **17i**	EtOH	2	 **19e**	88	99	84
8	 **17m**	–	3	 **19f**	91	98	85
9	 **17n**	–	3	 **19g**	87	98	87
10	 **17o**	–	2.5	 **19h**	89	98	82
11	 **17o**	EtOH	2	 **19h**	87	98	80
12	 **17r**	–	3	 **19i**	83	99	84

[a] Values were determined by HPLC analysis utilizing a Crownpak CR(+) column.

^{1}H NMR (400 MHz) to determine the diastereomeric excess. Flash column chromatography [silica gel (63−200 μm), hexanes/EtOAc 3:1] afforded the alkylated product.

*(3S,5aR,6aS,7aS)-3-Benzyl-5,5a,6,6a,7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17a**).* Yield: 280 mg (90%). White solid. Mp = 88−91 °C; $[\alpha]_D^{23}$ = −199.3° (*c* 0.54, $CHCl_3$); IR (KBr, $CHCl_3$) 3008 (m), 2934 (ms), 1735 (s), 1687 (m) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18−7.10 (m, 5 H, ArH), 3.42 (d, *J* = 12.6 Hz, 1 H, C_3−CH_2), 3.04 (d, *J* = 12.6 Hz, 1 H, C_3−CH_2), 2.43 (dd, *J* = 13.2, 4.8 Hz, 1 H, C_5−H_2), 2.04 (dd, *J* = 16.8, 8.4 Hz, 1 H, C_7−H_2), 1.61 (s, 3 H, C_{7a}−CH_3), 1.59 (dd, *J* = 13.2, 9.0 Hz, 1 H, C_5−H_2), 1.29 (s, 3 H, C_3−CH_3), 1.25 (dd, *J* = 16.8, 9.0 Hz, 1 H, C_7−H_2), 0.94 (s, 3 H, C_6−CH_3), 0.87 (s, 3 H, C_6−CH_3), 0.47 (dd, *J* = 16.8, 9.0 Hz, 1 H, C_{5a}−H), −0.02 (dd, *J* = 17.4, 8.4 Hz, 1 H, C_{6a}−H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8 (C═O), 170.3 (C═N), 136.6 (ArC), 130.5 (ArC), 127.7 (ArC), 126.5 (ArC), 81.8 (C_{7a}), 62.9 (C_3), 49.0 (C_3−CH_2), 35.0 (C_7), 30.1 (C_5), 27.9 (C_6−CH_3), 27.5 (C_3−CH_3), 26.8 (C_{7a}−CH_3), 25.7 (C_{5a}), 20.6 (C_6), 17.4 (C_{6a}), 14.3 (C_6−CH_3); MS *m*/*z* 311 (M^+, 6.39), 267 (100.0), 224 (19.6), 176 (65.2), 107 (17.2), 91 (44.9); HRMS *m*/*z* calcd for $C_{20}H_{25}NO_2$ M^+ 311.1885, found M^+ 311.1880. Anal. Calcd for $C_{20}H_{25}NO_2$: C, 77.14; H, 8.09; N, 4.50. Found: C, 77.14; H, 8.25; N, 4.77.

*(3S,5aR,6aS,7aS)-3-(4-Methoxybenzyl)-5,5a,6,6a,7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17b**).* Yield: 300 mg (88%). White solid. Mp = 80−83 °C; $[\alpha]_D^{23}$ = −180.6° (*c* 0.64, $CHCl_3$); IR (KBr, $CHCl_3$) 3009 (m), 2934 (ms), 1735 (s), 1686 (m) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.4 Hz, 2 H, ArH), 6.69 (d, *J* = 8.4 Hz, 2 H, ArH), 3.69 (s, 3 H, OCH_3), 3.36 (d, *J* = 12.6 Hz, 1 H, C_3−CH_2), 2.99 (d, *J* = 12.6 Hz, 1 H, C_3−CH_2), 2.44 (dd, *J* = 13.2, 7.2 Hz, 1 H, C_5−H_2), 2.06 (dd, *J* = 16.2, 8.4 Hz, 1 H, C_7−H_2), 1.60 (dd, *J* = 13.2, 9.0 Hz, 1 H, C_5−H_2), 1.59 (s, 3 H, C_{7a}−CH_3), 1.29 (s, 3 H, C_3−CH_3), 1.27 (dd, *J* = 16.2, 8.4 Hz, 1 H, C_7−H_2), 0.96 (s, 3 H, C_6−CH_3), 0.89 (s, 3 H, C_6−CH_3), 0.53 (dd, *J* = 16.8, 9.0 Hz, 1 H, C_{5a}−H), 0.04 (dd, *J* = 16.8, 8.4 Hz, 1 H, C_{6a}−H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8 (C═O), 170.3 (C═N), 158.4 (ArC), 131.5 (ArC), 128.7 (ArC), 113.0 (ArC), 81.7 (C_{7a}), 63.0 (C_3), 55.1 (OCH_3), 48.3 (C_3−CH_2), 35.0 (C_7), 30.1 (C_5), 27.9 (C_6−CH_3), 27.6 (C_3−CH_3), 26.6 (C_{7a}−CH_3), 25.8 (C_{5a}), 20.6 (C_6), 17.6 (C_{6a}), 14.3 (C_{6a}−CH_3); MS *m*/*z* 341 (M^+, 4.05), 176 (7.29), 121 (100.0); HRMS *m*/*z* calcd for $C_{21}H_{27}NO_3$ M^+ 341.1991, found M^+ 341.1986. Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10. Found: C, 73.69; H, 7.79; N, 3.94.

*(3S,5aR,6aS,7aS)-3-(4-Nitrobenzyl)-5,5a,6,6a,7,7a-hexahydro-3,6,-6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17c**).* Yield: 328 mg (92%). White solid. Mp = 119−121 °C; $[\alpha]_D^{23}$ = −258.4° (*c* 1.04, $CHCl_3$); IR (KBr, $CHCl_3$) 3078 (m), 2938 (ms), 1735 (s), 1683 (m), 1520 (s), 1346 (s) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 2 H, ArH), 7.35 (d, *J* = 8.4 Hz, 2 H, ArH), 3.50 (d, *J* = 12.6 Hz, 1 H, C_3−CH_2), 3.14 (d, *J* = 12.6 Hz, 1 H, C_3−CH_2), 2.45 (dd, *J* = 13.2, 7.2 Hz, 1 H, C_5−H_2), 2.06 (dd, *J* = 16.2, 8.4 Hz, 1 H, C_7−H_2), 1.62 (s, 3 H, C_{7a}−CH_3), 1.61 (dd, *J* = 13.2, 9.0 Hz, 1 H, C_5−H_2), 1.31 (s, 3 H, C_3−CH_3), 1.28 (dd, *J* = 16.2, 9.0 Hz, 1 H, C_7−H_2), 0.95 (s, 3 H, C_6−CH_3), 0.84 (s, 3 H, C_6−CH_3), 0.41 (dd, *J* = 16.8, 9.0 Hz, 1 H, C_{5a}−H), −0.03 (dd, *J* = 16.8, 9.0 Hz, 1 H, C_{6a}−H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.2 (C═O), 171.3 (C═N), 146.8 (ArC), 144.5 (ArC), 131.5 (ArC), 122.6 (ArC), 82.0 (C_{7a}), 62.7 (C_3), 48.4 (C_3−CH_2), 35.0 (C_7), 30.1 (C_5), 27.6 (C_3−CH_3), 27.6 (C_6−CH_3), 26.9 (C_{7a}−CH_3), 25.9 (C_{5a}), 20.6 (C6), 17.4 (C_{6a}), 14.1 (C_6−CH_3); MS *m*/*z* 356 (M^+, 1.44), 312 (76.4), 269 (14.7), 220 (9.93), 176 (100.0), 135 (19.2), 107 (18.4), 93 (22.4); HRMS *m*/*z* calcd for $C_{20}H_{24}N_2O_4$ M^+ 356.1736, found M^+ 356.1735. Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.35; H, 6.63; N, 7.66.

*(3S,5aR,6aS,7aS)-3-(4-Bromobenzyl)-5,5a,6,6a,7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17d**).* Yield: 355 mg (91%). White solid. Mp = 114−115 °C; $[\alpha]_D^{23}$ = −195.6° (*c* 0.46, $CHCl_3$); IR (KBr, $CHCl_3$) 3010 (m),

2934 (ms), 1735 (s), 1685 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, J = 8.4 Hz, 2 H, ArH), 7.05 (d, J = 8.4 Hz, 2 H, ArH), 3.40 (d, J = 13.2 Hz, 1 H, C_3-CH_2), 2.98 (d, J = 13.2 Hz, 1 H, C_3-CH_2), 2.42 (dd, J = 13.2, 7.8 Hz, 1 H, C_5-H_2), 2.08 (dd, J = 16.2, 8.4 Hz, 1 H, C_7-H_2), 1.61 (s, 3 H, $C_{7a}-CH_3$), 1.60 (dd, J = 13.2, 9.0 Hz, 1 H, C_5-H_2), 1.31 (s, 3 H, C_3-CH_3), 1.28 (dd, J = 16.2, 8.4 Hz, 1 H, C_7-H_2), 0.97 (s, 3 H, C_6-CH_3), 0.95 (s, 3 H, C_6-CH_3), 0.44 (dd, J = 16.8, 9.0 Hz, 1 H, $C_{5a}-H$), 0.05 (dd, J = 16.8, 8.4 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5 (C=O), 170.5 (C=N), 135.6 (ArC), 132.2 (ArC), 130.6 (ArC), 120.4 (ArC), 81.8 (C_{7a}), 62.6 (C_3), 48.3 (C_3-CH_2), 34.9 (C_7), 30.0 (C_5), 27.7 (C_3-CH_3), 27.5 (C_6-CH_3), 26.6 ($C_{7a}-CH_3$), 25.7 (C_{5a}), 20.5 (C_6), 17.4 (C_{6a}), 14.2 (C_6-CH_3); MS m/z 389 (M^+, 5.52), 347 (33.8), 345 (33.6), 20 (29.5), 176 (100.0), 169 (26.7), 135 (32.1), 123 (36.6), 115 (26.4), 107 (51.3), 91 (40.4), 77 (21.8); HRMS m/z calcd for $C_{20}H_{24}BrNO_2$ M^+ 389.0990, found M^+ 389.0981. Anal. Calcd for $C_{20}H_{24}BrNO_2$: C, 61.54; H, 6.20; N, 3.59. Found: C, 61.50; H, 6.12; N, 3.17.

*(3S,5aR,6aS,7aS)-5,5a,6,6a,7,7a-Hexahydro-3,6,6,7a-tetramethyl-3-[(naphthalen-1-yl)methyl]bicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]-oxazin-2(3H)-one (**17e**).* Yield: 314 mg (87%). White solid. Mp = 126−129 °C; $[\alpha]_D^{23}$ = −197.4° (c 0.70, $CHCl_3$); IR (KBr, $CHCl_3$) 3061 (m), 2935 (ms), 1735 (s), 1687 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.36 (d, J = 8.4 Hz, 1 H, ArH), 7.71 (d, J = 7.8 Hz, 1 H, ArH), 7.64 (d, J = 7.8 Hz, 1 H, ArH), 7.50−7.32 (m, 4 H, ArH), 3.85 (d, J = 13.2 Hz, 1 H, C_3-CH_2), 3.64 (d, J = 13.2 Hz, 1 H, C_3-CH_2), 2.03 (dd, J = 13.2, 7.8 Hz, 1 H, C_5-H_2), 1.88 (dd, J = 16.2, 8.4 Hz, 1 H, C_7-H_2), 1.76 (s, 3 H, $C_{7a}-CH_3$), 1.33 (dd, J = 13.2, 9.0 Hz, 1 H, C_5-H_2), 1.23 (s, 3 H, C_3-CH_3), 1.10 (dd, J = 16.2, 8.4 Hz, 1 H, C_7-H_2), 0.79 (s, 3 H, C_6-CH_3), 0.63 (s, 3 H, C_6-CH_3), −0.54 (dd, J = 17.4, 9.0 Hz, 1 H, $C_{6a}-H$), −1.12 (dd, J = 16.8, 9.0 Hz, 1 H, $C_{5a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8 (C=O), 169.4 (C=N), 133.7 (ArC), 133.3 (ArC), 133.2 (ArC), 128.2 (ArC), 127.9 (ArC), 127.2 (ArC), 126.5 (ArC), 125.3 (ArC), 125.3 (ArC), 124.8 (ArC), 81.9 (C_{7a}), 64.2 (C_3), 44.7 (C_3-CH_2), 34.8 (C_7), 29.7 (C_5), 28.1 (C_3-CH_3), 27.2 (C_6-CH_3), 26.7 ($C_{7a}-CH_3$), 24.5 (C_{6a}), 20.0 (C_6), 16.9 (C_{5a}), 14.1 (C_6-CH_3); MS m/z 361 (M^+, 22.8), 176 (24.3), 141 (100.0), 107 (10.2); HRMS m/z calcd for $C_{24}H_{27}NO_2$ M^+ 361.2042, found M^+ 361.2035. Anal. Calcd for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.87. Found: C, 79.40; H, 7.40; N, 3.16.

*(3S,5aR,6aS,7aS)-3-[(Benzo[d][1,3]dioxol-6-yl)methyl]-5,5a,6,6a,-7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno-[3,4-b][1,4]oxazin-2(3H)-one (**17f**).* Yield: 320 mg (90%). Colorless oil. $[\alpha]_D^{23}$ = −217.5° (c 0.77, $CHCl_3$); IR (KBr, $CHCl_3$) 3007 (m), 2934 (ms), 1734 (s), 1686 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.72 (s, 1 H, ArH), 6.64 (s, 1 H, ArH), 6.64 (s, 1 H, ArH), 5.84 (d, J = 1.2 Hz, 1 H, OCH_2O), 5.80 (d, J = 1.2 Hz, 1 H, OCH_2O), 3.32 (d, J = 12.6 Hz, 1 H, C_3-CH_2), 2.99 (d, J = 12.6 Hz, 1 H, C_3-CH_2), 2.50 (dd, J = 13.2, 7.8 Hz, 1 H, C_5-H_2), 2.11 (dd, J = 16.8, 8.4 Hz, 1 H, C_7-H_2), 1.65 (dd, J = 13.2, 9.0 Hz, 1 H, C_5-H_2), 1.59 (s, 3 H, $C_{7a}-CH_3$), 1.32 (dd, J = 16.8, 8.4 Hz, 1 H, C_7-H_2), 1.32 (s, 3 H, C_3-CH_3), 1.00 (s, 3 H, C_6-CH_3), 0.95 (s, 3 H, C_6-CH_3), 0.68 (dd, J = 16.8, 9.0 Hz, 1 H, $C_{5a}-H$), 0.16 (dd, J = 17.4, 8.4 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.6 (C=O), 170.4 (C=N), 146.5 (ArC), 146.1 (ArC), 130.3 (ArC), 123.7 (ArC), 111.1 (ArC), 107.7 (ArC), 100.6 (OCH_2O), 81.8 (C_{7a}), 63.1 (C_3), 48.7 (C_3-CH_2), 35.0 (C_7), 30.2 (C_5), 27.9 (C_6-CH_3), 27.7 (C_3-CH_3), 26.6 (C_7-CH_3), 25.9 (C_{5a}), 20.7 (C_6), 17.6 (C_{6a}), 14.3 (C_6-CH_3); MS m/z 355 (M^+, 7.91), 176 (10.5), 135 (100.0); HRMS m/z calcd for $C_{21}H_{25}NO_4$ M^+ 355.1784, found M^+ 355.1788. Anal. Calcd for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94. Found: C, 70.50; H, 7.55; N, 3.40.

*tert-Butyl 3-{[3S,5aR,6aS,7aS)-2,3,5,5a,6,6a,7,7a-octahydro-3,6,6,-7a-tetramethyl-2-oxobicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-3-yl]methyl}-1H-indole-1-carboxylate (**17g**).* Yield: 387 mg (86%). White solid. Mp = 126−129 °C; $[\alpha]_D^{23}$ = −172.6° (c 0.53, $CHCl_3$); IR (KBr, $CHCl_3$) 3054 (m), 2934 (ms), 1732 (s), 1685 (m), 1367 (s), 1158 (s) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, J = 6.0 Hz, 1 H, ArH), 7.69 (d, J = 7.8 Hz, 1 H ArH), 7.38 (s, 1 H, C=CHN), 7.23−7.18 (m, 2 H, ArH), 3.48 (d, J = 13.8 Hz, 1 H, C_3-CH_2), 3.20 (d, J = 13.8 Hz, 1 H, C_3-CH_2), 2.31 (dd, J = 13.2 Hz, 7.8 Hz, 1 H, C_5-H_2), 2.07 (dd, J = 16.8, 8.4 Hz, 1 H, C_7-H_2), 1.67 (s, 3 H, $C_{7a}-CH_3$), 1.61 [s, 9 H, $OC(CH_3)_3$], 1.52 (dd, J = 13.2, 9.0 Hz, 1 H, C_5-H_2), 1.30 (s, 3 H, C_3-CH_3), 1.24 (dd, J = 16.8, 8.4 Hz, 1 H, C_7-H_2), 0.90 (s, 3 H, C_6-CH_3), 0.78 (s, 3 H, C_6-CH_3), −0.04 (s, 1 H, $C_{5a}-H$), −0.19 (s, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9 (C=O), 170.5 (C=N), 149.6 (C=O), 134.9 (ArC), 131.3 (ArC), 124.6 (C=CHN), 123.9 (ArC), 122.1 (ArC), 120.5 (ArC), 116.0 (C=CHN), 114.6 (ArC), 83.3 [$OC(CH_3)_3$], 81.9 (C_{7a}), 63.2 (C_3), 38.6 (C_3-CH_2), 35.0 (C_5), 30.0 (C_7), 28.1 [$OC(CH_3)_3$], 27.8 (C_3-CH_3), 27.3 (C_6-CH_3), 26.5 ($C_{7a}-CH_3$), 24.7 (C_{5a}), 20.3 (C_6), 17.2 (C_{6a}), 14.2 (C_6-CH_3); MS m/z 450 (M^+, 4.47), 221 (16.5), 174 (28.5), 130 (100.0), 57 (28.7); HRMS m/z calcd for $C_{27}H_{34}N_2O_4$ M^+ 450.2519, found M^+ 450.2526. Anal. Calcd for $C_{27}H_{34}N_2O_4$: C, 71.97; H, 7.61; N, 6.22. Found: C, 72.19; H, 7.60; N, 5.99.

*(3S,5aR,6aS,7aS)-3-Cinnamyl-5,5a,6,6a,7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17h**).* Yield: 304 mg (90%). Colorless oil. $[\alpha]_D^{23}$ = −187.1° (c 0.76, $CHCl_3$); IR (KBr, $CHCl_3$) 3027 (m), 2935 (ms), 1737 (s), 1685 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.23−7.10 (m, 5 H, ArH), 6.42 (d, J = 15.6 Hz, 1 H, CH_2CH=C*H*Ph), 6.01−5.95 (m, 1 H, CH_2CH=CHPh), 2.95 (dd, J = 13.2, 6.6 Hz, 1 H, C_3-CH_2), 2.64 (dd, J = 12.6, 8.4 Hz, 1 H, C_3-CH_2), 2.51 (dd, J = 13.2, 7.2 Hz, 1 H, C_5-H_2), 2.26 (dd, J = 16.8, 8.4 Hz, 1 H, C_7-H_2), 1.69 (dd, J = 13.2, 9.0 Hz, 1 H, C_5-H_2), 1.55 (s, 3 H, C_3-CH_3), 1.38 (dd, J = 16.8, 8.4 Hz, 1 H, C_7-H_2), 1.35 (s, 3 H, $C_{7a}-CH_3$), 0.99 (s, 3 H, C_6-CH_3), 0.74 (s, 3 H, C_6-CH_3), 0.72 (dd, J = 16.8, 9.0 Hz, 1 H, $C_{5a}-H$), 0.43 (dd, J = 16.8, 8.4 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9 (C=O), 170.9 (C=N), 137.2 (ArC), 134.0 (CH_2CH=CHPh), 128.3 (ArC), 127.1 (ArC), 125.9 (ArC), 124.4 (CH_2CH=CHPh), 82.0 (C_{7a}), 62.3 (C_3), 46.5 (C_3-CH_2), 35.1 (C_7), 30.3 (C_5), 27.8 ($C_{7a}-CH_3$), 27.3 (C_6-CH_3), 26.6 (C_{5a}), 26.1 (C_3-CH_3), 20.8 (C_6), 17.6 (C_{6a}), 14.4 (C_6-CH_3); MS m/z 337 (M^+, 23.2), 176 (35.4), 117 (100.0), 91 (17.4); HRMS m/z calcd for $C_{22}H_{27}NO_2$ M^+ 337.2042, found M^+ 337.2047. Anal. Calcd for $C_{22}H_{27}NO_2$: C, 78.30; H, 8.06; N, 4.15. Found: C, 76.49; H, 8.75; N, 3.89.

*(3S,5aR,6aS,7aS)-3-Allyl-5,5a,6,6a,7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17i**).* Yield: 240 mg (92%). White solid. Mp = 57−60 °C; $[\alpha]_D^{23}$ = −175.0° (c 0.60, $CHCl_3$); IR (KBr, $CHCl_3$) 3011 (m), 2937 (ms), 1738 (s), 1684 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.63−5.56 (m, 1 H, CH_2CH=CH_2), 5.12−5.02 (m, 2 H, CH_2CH=CH_2), 2.78 (dd, J = 13.2, 7.2 Hz, 1 H, C_3-CH_2), 2.55 (dd, J = 13.2, 7.2 Hz, 1 H, C_5-H_2), 2.54 (dd, J = 13.2, 7.8 Hz, 1 H, C_3-CH_2), 2.37 (dd, J = 16.8, 7.8 Hz, 1 H, C_7-H_2), 1.73 (dd, J = 13.2, 9.0 Hz, 1 H, C_5-H_2), 1.49 (s, 3 H, $C_{7a}-CH_3$), 1.47 (dd, J = 16.8, 9.0 Hz, 1 H, C_7-H_2), 1.38 (s, 3 H, C_3-CH_3), 1.07 (s, 3 H, C_6-CH_3), 1.05 (s, 3 H, C_6-CH_3), 0.94 (dd, J = 16.8, 9.0 Hz, 1 H, $C_{5a}-H$), 0.74 (dd, J = 17.4, 8.4 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8 (C=O), 171.0 (C=N), 132.7 (CH_2CH=CH_2), 119.0 (CH_2CH=CH_2), 81.6 (C_{7a}), 62.0 (C_3), 47.3 (C_3-CH_2), 35.4 (C_7), 30.2 (C_5), 27.7 (C_6-CH_3), 27.7 (C_3-CH_3), 26.4 ($C_{7a}-CH_3$), 26.2 (C_{5a}), 20.8 (C_6), 17.7 (C_{6a}), 14.5 (C_6-CH_3); MS m/z 261 (M^+, 43.6), 217 (38.4), 202 (32.8), 176 (100.0), 174 (30.4), 135 (33.8), 123 (26.0), 110 (37.9), 107 (56.2), 93 (42.1), 91 (32.7), 79 (25.7), 67 (40.8); HRMS m/z calcd for $C_{16}H_{23}NO_2$ M^+

261.1729, found M^+ 261.1736. Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 71.88; H, 8.25; N, 4.99.

*(3S,5aR,6aS,7aS)-3-[(E)-But-2-enyl]-5,5a,6,6a,7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17j**).* Yield: 256 mg (93%). White solid. Mp = 68−70 °C; $[\alpha]_D^{23}$ = −138.4° (*c* 0.32, $CHCl_3$); IR (KBr, $CHCl_3$) 2936 (ms), 1738 (s), 1686 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.55−5.49 (m, 1 H, $CH_2CH{=}CHCH_3$), 5.26−5.21 (m, 1 H, $CH_2CH{=}CHCH_3$), 2.71 (dd, *J* = 13.2, 7.2 Hz, 1 H, $C_3{-}CH_2$), 2.55 (dd, *J* = 13.2, 7.2 Hz, 1 H, $C_5{-}H_2$), 2.46 (dd, *J* = 13.2, 7.8 Hz, 1 H, $C_3{-}CH_2$), 2.36 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_7{-}H_2$), 1.74 (dd, *J* = 13.2, 9.6 Hz, 1 H, $C_5{-}H_2$), 1.57 (d, *J* = 6.0 Hz, 3 H, $CH_2CH{=}CHCH_3$), 1.49 (s, 3 H, $C_{7a}{-}CH_3$), 1.47 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_7{-}H_2$), 1.38 (s, 3 H, $C_3{-}CH_3$), 1.08 (s, 3 H, $C_6{-}CH_3$), 1.05 (s, 3 H, $C_6{-}CH_3$), 0.93 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{5a}{-}H$), 0.72 (dd, *J* = 17.4, 8.4 Hz, 1 H, $C_{6a}{-}H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.1 (C=O), 170.5 (C=N), 129.5 ($CH_2CH{=}CHCH_3$), 125.4 ($CH_2CH{=}CHCH_3$), 81.7 (C_{7a}), 62.3 (C_3), 46.2 ($C_3{-}CH_2$), 35.3 (C_7), 30.3 (C_5), 27.8 ($C_6{-}CH_3$), 27.8 ($C_3{-}CH_3$), 26.5 (C_{5a}), 26.1 ($C_{7a}{-}CH_3$), 20.8 (C_6), 18.0 ($CH_2CH{=}CHCH_3$), 17.8 (C_{6a}), 14.4 ($C_6{-}CH_3$); MS *m*/*z* 275 (M^+, 60.7), 216 (40.1), 176 (100.0), 123 (51.2), 110 (43.9), 91 (45.9), 67 (43.1); HRMS *m*/*z* calcd for $C_{17}H_{25}NO_2$ M^+ 275.1885, found M^+ 275.1883. Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.03; H, 9.45; N,. 4.68.

*(3S,5aR,6aS,7aS)-5,5a,6,6a,7,7a-Hexahydro-3,6,6,7a-tetramethyl-3-(3-methylbut-2-enyl)bicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17k**).* Yield: 269 mg (93%). White solid. Mp = 85−88 °C; $[\alpha]_D^{23}$ = −148.3° (*c* 0.58, $CHCl_3$); IR (KBr, $CHCl_3$) 2932 (ms), 1738 (s), 1686 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.93 [td, *J* = 7.2, 1.2 Hz, 1 H, $CH_2CH{=}C(CH_3)_2$], 2.74 (dd, *J* = 13.2, 7.8 Hz, 1 H, $C_3{-}CH_2$), 2.51 (dd, *J* = 13.8, 7.8 Hz, 1 H, $C_5{-}H_2$), 2.45 (dd, *J* = 13.8, 7.2 Hz, 1 H, $C_3{-}CH_2$), 2.34 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_7{-}H_2$), 1.72 (dd, *J* = 13.8, 9.6 Hz, 1 H, $C_5{-}H_2$), 1.60 [s, 3 H, $CH_2CH{=}C(CH_3)_2$], 1.59 [s, 3 H, $CH_2CH{=}C(CH_3)_2$], 1.48 (s, 3 H, $C_{7a}{-}CH_3$), 1.44 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_7{-}H_2$), 1.35 (s, 3 H, $C_3{-}CH_3$), 1.06 (s, 3 H, $C_6{-}CH_3$), 1.03 (s, 3 H, $C_6{-}CH_3$), 0.90 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{5a}{-}H$), 0.71 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{6a}{-}H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.2 (C=O), 170.3 (C=N), 135.3 [$CH_2CH{=}C(CH_3)_2$], 118.6 [$CH_2CH{=}C(CH_3)_2$], 81.6 (C_{7a}), 62.2 (C_3), 42.0 ($C_3{-}CH_2$), 35.2 (C_7), 30.2 (C_5), 27.8 ($C_3{-}CH_3$), 27.8 ($C_6{-}CH_3$), 26.2 (C_{5a}), 26.0 ($C_{7a}{-}CH_3$), 25.9 [$CH_2CH{=}C(CH_3)_2$], 20.7 (C_6), 18.2 [$CH_2CH{=}C(CH_3)_2$], 17.8 (C_{6a}), 14.4 ($C_6{-}CH_3$); MS *m*/*z* 289 (M^+, 4.53), 221 (100.0), 206 (16.6), 176 (73.7), 107 (22.7), 93 (18.9), 69 (30.4); HRMS *m*/*z* calcd for $C_{18}H_{27}NO_2$ M^+ 289.2042, found M^+ 289.2048. Anal. Calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.22; H, 9.55; N, 4.30.

*(3S,5aR,6aS,7aS)-5,5a,6,6a,7,7a-Hexahydro-3,6,6,7a-tetramethyl-3-(2-methylallyl)bicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17l**).* Yield: 259 mg (94%). White solid. Mp = 72−76 °C; $[\alpha]_D^{23}$ = −171.4° (*c* 1.06, $CHCl_3$); IR (KBr, $CHCl_3$) 3013 (m), 2937 (ms), 1734 (s), 1681 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.73 (s, 1 H, $H_3CC{=}CH_2$), 4.66 (s, 1 H, $H_3CC{=}CH_2$), 2.83 (d, *J* = 13.8 Hz, 1 H, $C_3{-}CH_2$), 2.52 (dd, *J* = 13.2, 7.8 Hz, 1 H, $C_5{-}H_2$), 2.48 (d, *J* = 13.8 Hz, 1 H, $C_3{-}CH_2$), 2.35 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_7{-}H_2$), 1.71 (dd, *J* = 13.2, 8.4 Hz, 1 H, $C_5{-}H_2$), 1.64 (s, 3 H, $H_3CC{=}CH_2$), 1.46 (s, 3 H, $C_{7a}{-}CH_3$), 1.45 (dd, *J* = 15.6, 9.0 Hz, 1 H, $C_7{-}H_2$), 1.36 (s, 3 H, $C_3{-}CH_3$), 1.03 (s, 3 H, $C_6{-}CH_3$), 1.01 (s, 3 H, $C_6{-}CH_3$), 0.91 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{5a}{-}H$), 0.68 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_{6a}{-}H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8 (C=O), 170.0 (C=N), 141.2 ($H_3CC{=}CH_2$), 114.1 ($H_3CC{=}CH_2$), 81.6 (C_{7a}), 61.7 (C_3), 50.1 ($C_3{-}CH_2$), 35.4 (C_7), 30.1 (C_5), 27.7 ($C_{7a}{-}CH_3$), 27.7 ($C_3{-}CH_3$), 27.6 ($C_6{-}CH_3$), 25.7 (C_{5a}), 24.1 ($H_3CC{=}CH_2$), 20.7 (C_6), 17.8 (C_{6a}), 14.4 ($C_6{-}CH_3$); MS *m*/*z* 275 (M^+, 64.6), 231 (29.1), 188 (24.5), 176 (100.0), 150 (21.8), 135 (51.8), 107 (70.7), 96 (51.6), 93 (53.5), 55 (66.7); HRMS *m*/*z* calcd for $C_{17}H_{25}NO_2$ M^+ 275.1885, found M^+ 275.1887. Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.01; H, 9.59; N, 4.70.

*Methyl 2-[(3S,5aR,6aS,7aS)-2,3,5,5a,6,6a,7,7a-Octahydro-3,6,6,7a-tetramethyl-2-oxobicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-3-yl]-acetate (**17m**).* Yield: 264 mg (90%). White solid. Mp = 112−115 °C; $[\alpha]_D^{23}$ = −173.3° (*c* 0.75, $CHCl_3$); IR (KBr, $CHCl_3$) 2943 (ms), 1739 (s), 1685 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.57 (s, 3 H, OCH_3), 3.28 (d, *J* = 16.2 Hz, 1 H, $C_3{-}CH_2$), 2.82 (d, *J* = 16.2 Hz, 1 H, $C_3{-}CH_2$), 2.48 (dd, *J* = 14.4, 6.6 Hz, 1 H, $C_5{-}H_2$), 2.47 (dd, *J* = 16.2, 9.0 Hz, 1 H, $C_7{-}H_2$), 1.73 (dd, *J* = 14.4, 8.4 Hz, 1 H, $C_5{-}H_2$), 1.52 (dd, *J* = 16.2, 7.8 Hz, 1 H, $C_7{-}H_2$), 1.47 (s, 3 H, $C_{7a}{-}CH_3$), 1.43 (s, 3 H, $C_3{-}CH_3$), 1.07 (s, 3 H, $C_6{-}CH_3$), 1.04 (s, 3 H, $C_6{-}CH_3$), 0.90 (dd, *J* = 12.6, 9.0 Hz, 1 H, $C_{5a}{-}H$), 0.88 (dd, *J* = 16.2, 8.4 Hz, 1 H, $C_{6a}{-}H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.3 (C=O), 171.3 (C=O), 170.3 (C=N), 82.3 (C_{7a}), 59.0 (C_3), 51.4 (OCH_3), 47.2 ($C_3{-}CH_2$), 36.0 (C_7), 30.2 (C_5), 27.7 ($C_3{-}CH_3$), 27.6 ($C_6{-}CH_3$), 26.4 ($C_{7a}{-}CH_3$), 25.8 (C_{5a}), 20.7 (C_6), 17.9 (C_{6a}), 14.5 ($C_6{-}CH_3$); MS *m*/*z* 293 (M^+, 9.85), 249 (100.0), 234 (41.0), 190 (28.2), 132 (29.7), 119 (26.1), 93 (21.9); HRMS *m*/*z* calcd for $C_{16}H_{23}NO_4$ M^+ 293.1627, found M^+ 293.1624. Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.51; H, 7.90; N, 4.77. Found: C, 65.49; H, 7.79; N, 4.45.

*(3S,5aR,6aS,7aS)-3-Ethyl-5,5a,6,6a,7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17n**).* Yield: 232 mg (93%). White solid. Mp = 97−99 °C; $[\alpha]_D^{23}$ = −202.9° (*c* 1.06, $CHCl_3$); IR (KBr, $CHCl_3$) 2937 (ms), 1733 (s), 1685 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.53 (dd, *J* = 13.2, 7.8 Hz, 1 H, $C_5{-}H_2$), 2.35 (dd, *J* = 16.2, 7.8 Hz, 1 H, $C_7{-}H_2$), 2.10 (td, *J* = 13.2, 7.8 Hz, 1 H, $C_3{-}CH_2$), 1.75 (dd, *J* = 13.2, 6.0 Hz, 1 H, $C_3{-}CH_2$), 1.72 (dd, *J* = 13.2, 9.6 Hz, 1 H, $C_5{-}H_2$), 1.45 (dd, *J* = 16.2, 8.4 Hz, 1 H, $C_7{-}H_2$), 1.44 (s, 3 H, $C_{7a}{-}CH_3$), 1.36 (s, 3 H, $C_3{-}CH_3$), 1.05 (s, 3 H, $C_6{-}CH_3$), 1.01 (s, 3 H, $C_6{-}CH_3$), 0.94 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{5a}{-}H$), 0.72 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_{6a}{-}H$), 0.72 (t, *J* = 7.8 Hz, CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.4 (C=O), 171.2 (C=N), 81.6 (C_{7a}), 62.2 (C_3), 36.5 ($C_3{-}CH_2$), 35.3 (C_7), 30.3 (C_5), 27.6 ($C_3{-}CH_3$), 27.6 ($C_6{-}CH_3$), 26.8 ($C_{7a}{-}CH_3$), 26.1 (C_{5a}), 20.7 (C_6), 17.6 (C_{6a}), 14.4 ($C_6{-}CH_3$), 8.8 (CH_2CH_3); MS *m*/*z* 249 (M^+, 0.49), 205 (100.0), 190 (60.2), 162 (59.5), 96 (21.0), 55 (20.4); HRMS *m*/*z* calcd for $C_{15}H_{23}NO_2$ M^+ 249.1729, found M^+ 249.1720. Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 71.99; H, 9.13; N, 5.34.

*(3S,5aR,6aS,7aS)-5,5a,6,6a,7,7a-Hexahydro-3,6,6,7a-tetramethyl-3-propylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17o**).* Yield: 248 mg (94%). White solid. Mp = 92−94 °C; $[\alpha]_D^{23}$ = −196.7° (*c* 0.84, $CHCl_3$); IR (KBr, $CHCl_3$) 2952 (ms), 1734 (s), 1686 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.55 (dd, *J* = 13.8, 7.8 Hz, 1 H, $C_5{-}H_2$), 2.39 (dd, *J* = 16.2, 8.4 Hz, 1 H, $C_7{-}H_2$), 2.07 (td, *J* = 12.6, 4.2 Hz, 1 H, $C_3{-}CH_2$), 1.75 (dd, *J* = 13.8, 7.2 Hz, 1 H, $C_5{-}H_2$), 1.71 (td, *J* = 10.2, 4.2 Hz, 1 H, $C_3{-}CH_2$), 1.48 (dd, *J* = 16.2, 9.0 Hz, 1 H, $C_7{-}H_2$), 1.47 (s, 3 H, $C_{7a}{-}CH_3$), 1.39 (s, 3 H, $C_3{-}CH_3$), 1.25−1.19 (m, 1 H, $CH_2CH_2CH_3$), 1.09−1.04 (m, 1 H, $CH_2CH_2CH_3$), 1.08 (s, 3 H, $C_6{-}CH_3$), 1.06 (s, 3 H, $C_6{-}CH_3$), 0.98 (dd, *J* = 16.8, 9.0 Hz, 1H, $C_{5a}{-}H$), 0.88 (t, *J* = 7.2 Hz, 3 H, $CH_2CH_2CH_3$), 0.76 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_{6a}{-}H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.6 (C=O), 170.8 (C=N), 81.6 (C_{7a}), 61.8 (C_3), 45.7 ($C_3{-}CH_2$), 35.4 (C_7), 30.3 (C_5), 27.7 ($C_3{-}CH_3$), 27.6 ($C_6{-}CH_3$), 27.1 ($C_{7a}{-}CH_3$), 26.0 (C_{5a}), 20.7 (C_6), 17.8 ($CH_2CH_2CH_3$), 17.6 (C_{6a}), 14.5 ($C_6{-}CH_3$), 13.9 ($CH_2CH_2CH_3$); MS *m*/*z* 263 (M^+, 0.86), 219 (83.1), 204 (50.4), 190 (35.2), 176 (100.0), 119 (28.8), 69 (25.0); HRMS *m*/*z* calcd for $C_{16}H_{25}NO_2$ M^+ 263.1885, found M^+ 263.1879. Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.69; H, 9.25; N, 4.89.

*Methyl 3-[(3S,5aR,6aS,7aS)-2,3,5,5a,6,6a,7,7a-Octahydro-3,6,6,7a-tetramethyl-2-oxobicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-3-yl]-propanoate (**17p**).* Yield: 283 mg (92%). White solid. Mp = 40−43 °C; $[\alpha]_D^{23}$ = −173.1° (*c* 0.67, $CHCl_3$); IR (KBr, $CHCl_3$) 2944 (ms), 1739 (s), 1684 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.63 (s, 3 H, OCH_3), 2.53 (dd, *J* = 13.8, 7.8 Hz, 1 H, C_3-H_2), 2.44−2.41 (m, 1 H, C_3-CH_2), 2.39 (dd, *J* = 16.8, 8.4 Hz, 1 H, C_7-H_2), 2.24−2.17 (m, 2 H, $CH_2CH_2CO_2CH_3$), 2.16−2.12 (m, 1 H, C_3-CH_2), 1.74 (dd, *J* = 13.8, 9.0 Hz, 1 H, C_5-H_2), 1.50 (s, 3 H, $C_{7a}-CH_3$), 1.49 (dd, *J* = 16.8, 8.4 Hz, 1 H, C_7-H_2), 1.40 (s, 3 H, C_3-CH_3), 1.07 (s, 3 H, C_6-CH_3), 1.05 (s, 3 H, C_6-CH_3), 0.97 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{5a}-H$), 0.77 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8 (C═O), 173.2 (C═O), 172.0 (C═N), 81.9 (C_{7a}), 60.8 (C_3), 51.6 (OCH_3), 38.0 ($CH_2CH_2CO_2CH_3$), 35.5 (C_7), 30.3 (C_5), 29.5 (C_3-CH_2), 27.6 (C_6-CH_3), 27.4 (C_3-CH_3), 26.8 ($C_{7a}-CH_3$), 26.0 (C_{5a}), 20.8 (C_6), 17.5 (C_{6a}), 14.4 (C_6-CH_3); MS *m*/*z* 307 (M^+, 6.12), 263 (100.0), 248 (55.5), 220 (59.4), 190 (49.5), 176 (27.6), 119 (29.4), 108 (26.8), 91 (22.2), 55 (21.9); HRMS *m*/*z* calcd for $C_{17}H_{25}NO_4$ M^+ 307.1784, found M^+ 307.1790. Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.28; H, 8.39; N, 4.29.

*(3S,5aR,6aS,7aS)-3-Butyl-5,5a,6,6a,7,7a-hexahydro-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17q**).* Yield: 153 mg (55%). White solid. Mp = 50−51 °C; $[\alpha]_D^{23}$ = −217.0° (*c* 0.40, $CHCl_3$); IR (KBr, $CHCl_3$) 2956 (ms), 1739 (s), 1685 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.53 (dd, *J* = 13.8, 7.8 Hz, 1 H, C_5-H_2), 2.36 (dd, *J* = 16.2, 8.4 Hz, 1 H, C_7-H_2), 2.07 (td, *J* = 12.6, 4.8 Hz, 1 H, C_3-CH_2), 1.72 (dd, *J* = 13.8, 8.4 Hz, 1 H, C_5-H_2), 1.71 (td, *J* = 8.4, 4.2 Hz, 1 H, C_3-CH_2), 1.46 (dd, *J* = 16.2, 8.4 Hz, 1 H, C_7-H_2), 1.45 (s, 3 H, $C_{7a}-CH_3$), 1.37 (s, 3 H, C_3-CH_3), 1.26 (td, *J* = 14.4, 7.2 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 1.16−1.13 (m, 1 H, $CH_2CH_2CH_2CH_3$), 1.06 (s, 3 H, C_6-CH_3), 1.03 (s, 3 H, C_6-CH_3), 1.01−0.98 (m, 1 H, $CH_2CH_2CH_2CH_3$), 0.95 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{5a}-H$), 0.82 (t, *J* = 7.2 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 0.74 (dd, *J* = 16.2, 8.4 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.5 (C═O), 170.7 (C═N), 81.6 (C_{7a}), 61.7 (C_3), 43.2 (C_3-CH_2), 35.4 (C_7), 30.2 (C_5), 27.6 (C_3-CH_3), 27.6 (C_6-CH_3), 27.0 ($C_{7a}-CH_3$), 26.6 ($CH_2CH_2CH_2CH_3$), 26.0 (C_{5a}), 22.5 ($CH_2CH_2CH_2CH_3$), 20.6 (C_6), 17.6 (C_{6a}), 14.4 (C_6-CH_3), 13.8 ($CH_2CH_2CH_2CH_3$); MS *m*/*z* 277 (M^+, 2.51), 233 (60.7), 218 (44.4), 191 (100.0), 176 (98.1), 119 (39.9), 81 (30.5), 67 (29.6); HRMS *m*/*z* calcd for $C_{17}H_{27}NO_2$ M^+ 277.2042, found M^+ 277.2048. Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.83; H, 9.48; N, 4.64.

*(3S,5aR,6aS,7aS)-5,5a,6,6a,7,7a-Hexahydro-3-isobutyl-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17r**).* Yield: 144 mg (52%). White solid. Mp = 67−70 °C; $[\alpha]_D^{23}$ = −131.2° (*c* 0.68, $CHCl_3$); IR (KBr, $CHCl_3$) 2952 (ms), 1738 (s), 1682 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.53 (dd, *J* = 13.8, 7.8 Hz, 1 H C_5-H_2), 2.39 (dd, *J* = 16.8, 8.4 Hz, 1 H, C_7-H_2), 2.05 (dd, *J* = 13.2, 7.8 Hz, 1 H, C_3-CH_2), 1.75 (dd, *J* = 13.8, 5.4 Hz, 1 H, C_5-H_2), 1.73 (dd, *J* = 13.2, 9.0 Hz, 1 H, C_3-CH_2), 1.64−1.60 [m, 1 H, $CH_2CH(CH_3)_2$], 1.48 (dd, *J* = 16.8, 8.4 Hz, 1 H, C_7-H_2), 1.41 (s, 3 H, $C_{7a}-CH_3$), 1.38 (s, 3 H, C_3-CH_3), 1.05 (s, 3 H, C_6-CH_3), 1.02 (s, 3 H, C_6-CH_3), 0.95 (dd, *J* = 16.2, 9.0 Hz, 1 H, $C_{5a}-H$), 0.86 [d, *J* = 7.2 Hz, 3 H, $CH_2CH(CH_3)_2$], 0.75 [d, *J* = 7.2 Hz, 3 H, $CH_2CH(CH_3)_2$], 0.73 (dd, *J* = 16.2, 8.4 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.9 (C═O), 170.1 (C═N), 81.5 (C_{7a}), 60.7 (C_3), 51.4 (C_3-CH_2), 35.5 (C_7), 30.2 (C_5), 28.3 ($C_{7a}-CH_3$), 27.7 (C_3-CH_3), 27.6 (C_6-CH_3), 25.8 (C_{5a}), 25.1 [$CH_2CH(CH_3)_2$], 23.8 [$CH_2CH(CH_3)_2$], 22.0 [$CH_2CH(CH_3)_2$], 20.7 (C_6), 17.8 (C_{6a}), 14.4 (C_6-CH_3); MS *m*/*z* 277 (M^+, 3.77), 204 (21.3), 176 (100.0), 148 (40.0), 134 (28.8), 91 (36.8), 55 (48.7); HRMS *m*/*z* calcd for $C_{17}H_{27}NO_2$ M^+ 277.2042, found M^+ 277.2049. Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.70; H, 9.54; N, 4.74.

Hydrogenation of Compounds 17h and 17j−l. Synthesis of Compounds 17q−t. Representative Procedure. A 50 mL round-bottom flask with a Claisen tube was charged with compound **17h** (337 mg, 1 mmol), 10% palladium on activated carbon (40 mg) and a magnetic stirbar. The flask was evacuated by an aspirator and filled with hydrogen through a balloon three times. Dry methanol (2.7 mL) was added to the mixture followed by evacuation and filling with hydrogen one more time. The mixture was stirred under hydrogen atmosphere at room temperature for 6 h. The catalyst was removed by filtration and the solvent was evaporated to give pale yellow oil. Flash column chromatography [silica gel (63−200 μm), hexanes/EtOAc 4:1] afforded iminolactone **17s**.

*Compound **17q**.* Yield: 269 mg (97%). White solid.

*Compound **17r**.* Yield: 269 mg (97%). White solid.

*(3S,5aR,6aS,7aS)-5,5a,6,6a,7,7a-Hexahydro-3,6,6,7a-tetramethyl-3-(3-phenylpropyl)bicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17s**).* Yield: 336 mg (99%). White solid. Mp = 130−132 °C; $[\alpha]_D^{23}$ = −110.1° (*c* 0.92, $CHCl_3$); IR (KBr, $CHCl_3$) 2943 (ms), 1735 (s), 1688 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26−7.12 (m, 5 H, ArH), 2.60 (t, *J* = 7.8 Hz, 2 H, $CH_2CH_2CH_2Ph$), 2.56 (dd, *J* = 13.2, 7.8 Hz, 1 H, C_5-H_2), 2.20 (dd, *J* = 16.2, 8.4 Hz, 1 H, C_7-H_2), 2.17 (td, *J* = 12.6, 5.4 Hz, 1 H, C_3-CH_2), 1.82 (td, *J* = 12.6, 4.2 Hz, 1 H, C_3-CH_2), 1.75 (dd, *J* = 13.8, 9.0 Hz, 1 H, C_5-H_2), 1.56−1.50 (m, 1 H, $CH_2CH_2CH_2Ph$), 1.49 (dd, *J* = 16.2, 8.4 Hz, 1 H, C_7-H_2), 1.48 (s, 3 H, $C_{7a}-CH_3$), 1.45−1.39 (m, 1 H, $CH_2CH_2CH_2Ph$), 1.40 (s, 3 H, C_3-CH_3), 1.08 (s, 3 H, C6−CH_3), 1.03 (s, 3 H, C_6-CH_3), 0.95 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{5a}-H$), 0.73 (dd, *J* = 16.8, 8.4 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.4 (C═O), 171.0 (C═N), 142.0 (ArC), 128.2 (ArC), 128.2 (ArC), 125.6 (ArC), 81.7 (C_{7a}), 61.6 (C_3), 43.2 (C_3-CH_2), 35.6 ($CH_2CH_2CH_2Ph$), 35.4 (C_7), 30.2 (C_5), 27.6 (C_3-CH_3), 27.6 (C_6-CH_3), 27.1 ($C_{7a}-CH_3$), 26.1 ($CH_2CH_2CH_2Ph$), 26.1 (C_{5a}), 20.7 (C_6), 17.6 (C_{6a}), 14.4 (C_6-CH_3); MS *m*/*z* 339 (M^+, 29.8), 222 (100.0), 191 (92.7), 176 (99.3), 148 (30.5), 91 (55.7); HRMS *m*/*z* calcd for $C_{22}H_{29}NO_2$ M^+ 339.2198, found M^+ 339.2209. Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.66; H, 8.71; N, 3.79.

*(3S,5aR,6aS,7aS)-5,5a,6,6a,7,7a-Hexahydro-3-isopentyl-3,6,6,7a-tetramethylbicyclo[4.1.0]hept-1(6)-eno[3,4-b][1,4]oxazin-2(3H)-one (**17t**).* Yield: 286 mg (98%). Colorless oil. $[\alpha]_D^{23}$ = −176.9° (*c* 1.08, $CHCl_3$); IR (KBr, $CHCl_3$) 2955 (ms), 1739 (s), 1685 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.53 (dd, *J* = 13.2, 7.8 Hz, 1 H, C_5-H_2), 2.36 (dd, *J* = 16.2, 8.4 Hz, 1 H, C_7-H_2), 2.06 (td, *J* = 12.6, 4.2 Hz, 1 H, C_3-CH_2), 1.72 (dd, *J* = 13.2, 9.0 Hz, 1 H, C_5-H_2), 1.71 (td, *J* = 8.4, 4.2 Hz, 1 H, C_3-CH_2), 1.48−1.44 [m, 1 H, $CH_2CH_2CH(CH_3)_2$], 1.47 (dd, *J* = 16.2, 9.0 Hz, 1 H, C_7-H_2), 1.45 (s, 3 H, $C_{7a}-CH_3$), 1.37 (s, 3 H, C_3-CH_3), 1.08−1.03 [m, 1 H, $CH_2CH_2CH(CH_3)_2$], 1.06 (s, 3 H, C_6-CH_3), 1.03 (s, 3 H, C_6-CH_3), 0.94 (dd, *J* = 16.2, 8.4 Hz, 1 H, $C_{5a}-H$), 0.89−0.84 [m, 1 H, $CH_2CH_2CH(CH_3)_2$], 0.81 [d, *J* = 6.0 Hz, 6 H, $CH_2CH_2CH(CH_3)_2$], 0.73 (dd, *J* = 16.8, 9.0 Hz, 1 H, $C_{6a}-H$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.5 (C═O), 170.7 (C═N), 81.6 (C_{7a}), 61.7 (C_3), 41.4 (C_3-CH_2), 35.4 (C_7), 33.4 [$CH_2CH_2CH(CH_3)_2$], 30.2 (C_5), 27.9 [$CH_2CH_2CH(CH_3)_2$], 27.7 (C_3-CH_3), 27.7 (C_6-CH_3), 27.0 ($C_{7a}-CH_3$), 26.1 (C_{5a}), 22.5 [$CH_2CH_2CH(CH_3)_2$], 22.4 [$CH_2CH_2CH(CH_3)_2$], 20.7 (C_6), 17.7 (C_{6a}), 14.4 (C_6-CH_3); MS *m*/*z* 291 (M^+, 6.41), 222 (49.1), 191 (100.0), 176 (64.6), 55 (19.3); HRMS *m*/*z* calcd for $C_{18}H_{29}NO_2$ M^+ 291.2198, found M^+ 291.2193. Anal. Calcd for $C_{18}H_{29}NO_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 73.05; H, 10.26; N, 4.15.

Hydrolysis of Dialkylated Iminolactones 17a, 17e−g, 17i, 17m−o, and 17r. Synthesis of Compounds 19a−i. Representative Procedure. To a solution of compound **17a** (78 mg, 0.25 mmol) in deionized water (1.2 mL) and ethanol (600 μL) in a sealed tube with a Teflon screw cap was added a 50% aqueous solution of cesium hydroxide (380 μL, 1.25 mmol), and the mixture was stirred at 70 °C for 2 h. After the mixture was cooled to room temperature, the

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mixture was extracted with dichloromethane (5 mL). The chiral auxiliary **15** was recovered from the dichloromethane layer after the removal of the solvent. And the aqueous layer was passed through a short path of the ion-exchange resin (DOWEX 50WX8-100) eluting with 1 N aqueous hydrochloric acid (2 mL), after evaporating the solvents, to afford α-methyl-α-amino acid **19a**.

*(S)-α-Methylphenylalanine (**19a**).* Yield: 39 mg (86%). White solid. $[\alpha]_D^{23} = -22.1°$ (*c* 1.03, H_2O) [lit.[36] $[\alpha]_D^{25} = -19.7°$ (*c* 1.16, H_2O)]; ^1H NMR (400 MHz, D_2O) δ 7.27 (s, 3 H, ArH), 1.15 (s, 2 H, ArH), 3.25 (d, *J* = 14.0 Hz, 1 H, CH_2), 2.99 (d, *J* = 14.0 Hz, 1 H, CH_2), 1.52 (s, 3 H, CH_3); ^{13}C NMR (D_2O) δ 173.8, 133.5, 130.6, 129.6, 128.7, 61.2, 42.7, 22.1; recovered **15** (36 mg, 85%).

*(S)-α-(2-Naphthylmethyl)alanine (**19b**).* Yield: 49 mg (85%). White solid. $[\alpha]_D^{23} = -17.8°$ (*c* 0.87, MeOH) [lit.[37] (*R*)-isomer $[\alpha]_D^{22} = +18.1°$ (*c* 0.16, MeOH)]; ^1H NMR (400 MHz, D_2O) δ 7.56−7.06 (m, 7 H, ArH), 3.42 (d, *J* = 14.4 Hz, 1 H, CH_2), 3.20 (d, *J* = 14.4 Hz, 1 H, CH_2), 1.56 (s, 3 H, CH_3); ^{13}C NMR (D_2O) δ 174.0, 134.0, 132.5, 129.8, 129.7, 129.4, 129.2, 127.2, 126.7, 126.1, 123.9, 61.3, 38.6, 22.0; recovered **15** (34 mg, 82%).

*(S)-2-Amino-3-benzo[1,3]dioxol-5-yl-2-methylpropanoic acid (**19c**).* Yield: 49 mg (88%). Pale yellow solid. $[\alpha]_D^{23} = -6.8°$ (*c* 0.75, 1 N HCl); ^1H NMR (400 MHz, D_2O) δ 6.76−6.61 (m, 3 H, ArH), 5.84 (s, 2 H, OCH_2O), 3.15 (d, *J* = 14.4 Hz, 1 H, CH_2), 2.86 (d, *J* = 14.4 Hz, 1 H, CH_2), 1.46 (s, 3 H, CH_3); ^{13}C NMR (D_2O) δ 173.8, 147.9, 147.4, 127.1, 124.3, 110.8, 109.4, 101.8, 61.2, 42.3, 22.1; recovered **15** (36 mg, 85%).

*(S)-α-Methyltryptophan (**19d**).* Yield: 47 mg (86%). Pale yellow solid. $[\alpha]_D^{23} = -11.1°$ (*c* 0.97, H_2O) [lit.[15d] $[\alpha]_D^{25} = -11.3°$ (*c* 1.10, H_2O)]; ^1H NMR (400 MHz, D_2O) δ 7.65 (d, *J* = 8.0 Hz, 1 H, ArH), 7.58 (d, *J* = 8.0 Hz, 1 H, ArH), 7.20 (s, 1 H, (s, 1 H, C=CHN), 7.14 (t, *J* = 8.0 Hz, 1 H, ArH), 7.06 (t, *J* = 8.0 Hz, 1 H, ArH), 3.43 (d, *J* = 15.2 Hz, 1 H, CH_2), 3.20 (d, *J* = 15.2 Hz, 1 H, CH_2), 1.56 (s, 3 H, CH_3); ^{13}C NMR (D_2O) δ 174.5, 136.5, 127.6, 126.7, 122.9, 120.4, 119.3, 112.8, 106.5, 61.1, 33.2, 22.1; recovered **15** (34 mg, 82%).

*(S)-α-Allylalanine (**19e**).* Yield: 29 mg (90%). White solid. $[\alpha]_D^{23} = -28.3°$ (*c* 1.23, H_2O) [lit.[19] $[\alpha]_D^{22} = -28.0°$ (*c* 0.88, H_2O)]; ^1H NMR (400 MHz, D_2O) δ 5.67 (td, *J* = 16.8, 8.4 Hz, 1 H, C*H*=CH_2CH_2), 5.23−5.19 (m, 2 H, CH=C$H_2$$CH_2$), 2.64 (dd, *J* = 14.4, 6.8 Hz, 1 H, CH=CH_2CH_2), 2.48 (dd, *J* = 14.4, 8.0 Hz, 1 H, CH=CH_2CH_2), 1.48 (s, 3 H, CH_3); ^{13}C NMR (D_2O) δ 173.9, 130.1, 123.5, 60.2, 41.3, 22.0; ^{13}C NMR (D_2O) δ 173.8, 173.5, 57.8, 40.6, 22.9; recovered **15** (35 mg, 83%).

*(S)-α-Methylaspartic Acid (**19f**).* Yield: 33 mg (91%). White solid. $[\alpha]_D^{23} = +54.9°$ (*c* 1.14, H_2O) [lit.[15d] $[\alpha]_D^{25} = -52.5°$ (*c* 1.00, H_2O)]; ^1H NMR (400 MHz, D_2O) δ 3.10 (d, *J* = 18.0 Hz, 1 H, CH_2), 2.83 (d, *J* = 18.0 Hz, 1 H, CH_2), 1.47 (s, 3 H, CH_3); recovered **15** (36 mg, 85%).

*(S)-Isovaline (**19g**).* Yield: 25 mg (87%). White solid. $[\alpha]_D^{23} = +12.1°$ (*c* 1.03, H_2O) [lit.[38] $[\alpha]_D^{25} = +11.1°$ (*c* 5.00, H_2O)]; ^1H NMR (400 MHz, D_2O) δ 1.90 (td, *J* = 14.4, 7.2 Hz, 1 H, C$H_2$$CH_3$), 1.78 (td, *J* = 14.4, 6.8 Hz, 1 H, C$H_2$$CH_3$), 1.46 (s, 3 H, CH_3), 0.86 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3); ^{13}C NMR (D_2O) δ 176.1, 62.0, 30.8, 22.5, 8.3; recovered **15** (37 mg, 87%).

*(S)-α-Propylalanine (**19h**).* Yield: 29 mg (89%). White solid. $[\alpha]_D^{23} = +2.3°$ (*c* 1.01, 1 N HCl) [lit.[16] (*R*)-isomer $[\alpha]_D = -1.4°$ (*c* 0.86, 1 N HCl)]; ^1H NMR (400 MHz, D_2O) δ 1.84−1.66 (m, 2 H, C$H_2$$CH_2CH_3$), 1.44 (s, 3 H, CH_3), 1.33−1.27 (m, 1 H, CH_2C$H_2$$CH_3$), 1.19−1.13 (m, 1 H, CH_2C$H_2$$CH_3$), 0.82 (t, *J* = 7.6 Hz, 3 H, CH_2CH_2CH_3); ^{13}C NMR (D_2O) δ 174.7, 60.8, 39.3, 22.4, 17.2, 14.1; recovered **15** (34 mg, 82%).

*(S)-α-Methylleucine (**19i**).* Yield: 30 mg (83%). White solid. $[\alpha]_D^{23} = +37.8°$ (*c* 1.12, H_2O) [lit.[15a] $[\alpha]_D^{25} = +38.2°$ (*c* 2.00, H_2O)]; ^1H NMR (400 MHz, D_2O) δ 1.80 [dd, *J* = 15.2, 8.4 Hz, 1 H, C$H_2$$CH(CH_3)_2$], 1.69 [dd, *J* = 15.2, 4.4 Hz, 1 H, C$H_2$$CH(CH_3)_2$], 1.63−1.57 [m, 1 H, CH_2C$H$$(CH_3)_2$], 1.44 (s, 3 H, CH_3), 0.81 [d, *J* = 6.4 Hz, 3 H, $CH_2CH(CH_3)_2$], 0.76 [d, *J* = 6.4 Hz, 3 H, $CH_2CH(CH_3)_2$]; ^{13}C NMR (D_2O) δ 175.4, 60.3, 45.9, 24.3, 24.0, 23.9, 22.4; recovered **15** (35 mg, 84%).

■ ASSOCIATED CONTENT

Supporting Information. Copies of spectral data for all new compounds and X-ray data of compounds **17a**, **17e**, **17g**, **17l**, **17m**, and **17o**. This material is available free of charge via the Internet at http://pubs.acs.org.

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