Pergamon

Bioorganic & Medicinal Chemistry 10 (2002) 3829–3848

BIOORGANIC & MEDICINAL CHEMISTRY

Synthesis of Derivatives of (1*S*,2*R*)-1-Phenyl-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (PPDC) Modified at the 1-Aromatic Moiety as Novel NMDA Receptor Antagonists: The Aromatic Group is Essential for the Activity

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Received 24 May 2002; accepted 1 August 2002

Abstract—(1*S*,2*R*)-1-Phenyl-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (PPDC, **4a**), which is a conformationally restricted analogue of antidepressant milnacipran [(±)-**1**], is a new class of potent noncompetitive NMDA receptor antagonists. A series of PPDC analogues modified at the 1-phenyl moiety, that is, the analogue **6** lacking 1-phenyl group, the 1-(fluorophenyl) analogues **4b**,**c**,**d**, the 1-(methylphenyl) analogues **4e**–**g** and the 1-(naphthyl) analogues **4h**,**i** were synthesized. Analogue **6**, lacking the 1-phenyl group, was completely inactive showing that the aromatic moiety is essential for the NMDA receptor binding. Among the analogues synthesized, the 1-*o*-fluorophenyl and 1-*m*-fluorophenyl analogues **4b** and **4c** showed potent affinities for the NMDA receptor [$IC_{50} = 0.16 \pm 0.001$ μM (**4b**), 0.15 ± 0.02 μM (**4c**)], which were improved to some extent compared to those of the parent compound PPDC ($IC_{50} = 0.20 \pm 0.02$ μM). On the other hand, compounds **4b** and **4c** showed none of the 5-HT-uptake inhibitory effect, while PPDC turned out to be a weak 5-HT-uptake inhibitor.

Introduction

There have been attempts to develop novel agents that block the activation of NMDA (*N*-methyl-D-aspartic acid) receptors by glutamate or related excitatory neurotransmitters, and a large number of competitive and non-competitive NMDA receptor antagonists have been developed.[1–3] Although a number of studies clearly indicate that these competitive and noncompetitive antagonists are effective in experimental models of epilepsy and stroke, clinical studies of these NMDA receptor antagonists have proven unsuccessful.[1–3] Non-competitive inhibitors have produced serious behavioral effects[4] and have caused neuronal vacuolization in some cases,[5] while competitive inhibitors are often inactive in vivo because of poor transport to the brain.[6] Considering these results, the development of another type of efficient NMDA receptor antagonists is eagerly desired.

(±)-(*Z*)-2-Aminomethyl-1-phenyl-*N*,*N*-diethylcyclopropanecarboxamide [milnacipran, (±)-**1**],[7] a clinically efficient antidepressant due to competitive inhibition of the re-uptake of serotonin (5-HT) in the CNS,[8] is also recognized as a non-competitive NMDA receptor antagonist.[9] Although the binding affinity of (±)-**1** for the NMDA receptor is not very high, the compound has the advantage of sufficiently penetrating the brain without serious side effects,[8d,e] making it a clinically useful antidepressant and therefore a good lead for an efficient NMDA receptor antagonist. This may be because the structure of milnacipran is clearly different from that of previous NMDA receptor antagonists.

We designed and synthesized four types of conformationally restricted analogues of (±)-**1**, each having a different stereochemistry; that is, Type-1 (**2** and **4a**), Type-2 (**3** and **5**), and their enantiomers Type-3 (***ent*-2** and ***ent*-4a**) and Type-4 (***ent*-3** and ***ent*-5**), as shown in Figure 1.[10] In these analogues, an alkyl group introduced at the α-position of the amino function of (±)-**1** restricts the

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PII: S0968-0896(02)00346-2

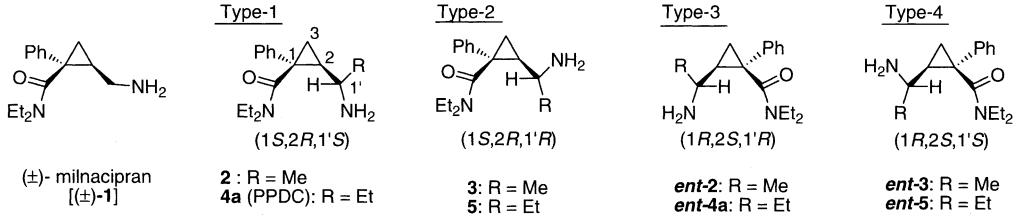


Figure 1. Milnacipran and its conformationally restricted analogues.

location of the amino group in space, which is essential for binding to the NMDA receptor,[9] due to steric repulsion of the diethylcarbamoyl group.[11a] Therefore, we expected the conformation of these compounds to be determined by the configuration of the alkyl group introduced; conformer B would be predominant in the conformationally restricted analogues with the Type-1 configuration and its enantiomer (Type-3), while conformer A would be predominant in Type-2 analogues and its enantiomer (Type-4), as shown in Figure 2. In fact, the structural analysis by X-ray crystallographic, NMR, and computational calculation studies showed that these compounds are conformationally restricted, as we had hypothesized (Fig. 3).[10a,k,m]

The biological evaluations of these conformationally restricted analogues demonstrated that: (1) the conformational restriction can improve activity;[10d] (2) analogues with a (1*S*,2*R*)-configuration (Type-1 and Type-2) are more potent than the corresponding enantiomers (Type-3 and Type-4), and Type-1 analogues are more potent than the corresponding Type-2 analogues,[10d–f] and (3) introduction of a substituent bulkier than an ethyl group, such as a propyl or isobutyl group, at the 1′-position significantly reduces the activity.[10d] Thus, we found that analogues with a Type-1 configuration, i.e., the 1′-methyl analogue **2** and the 1′-ethyl analogue **4a** (PPDC) were potent NMDA receptor antagonists which significantly inhibited the binding of [^{3}H] MK-801 with IC_{50} values approximately 30-fold stronger than (±)-**1**.[10e,f] Among these compounds, PPDC (**4a**) is likely to be the most desirable, since the compound is a potent NMDA receptor antagonist almost devoid of inhibitory effect on 5-HT-uptake, while the 1′-methyl analogue **2** is a strong 5-HT-uptake inhibitor, like the parent compound milnacipran.[10h]

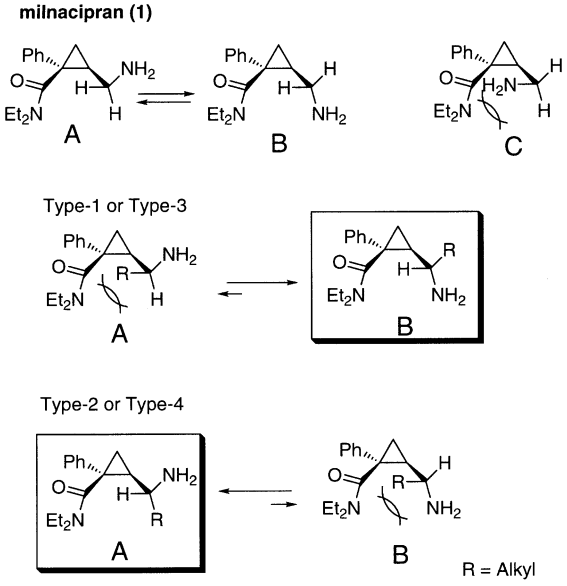


Figure 2. Conformational restriction of milnacipran by introducing an alkyl substituent at the 1′-position.

Pharmacological studies on PPDC have shown that: (1) it binds to the receptor in an agonist-independent manner, whereas the binding affinities of known non-competitive NMDA receptor antagonists are affected by agonist concentration;[10h] (2) the release of PPDC and the previous non-competitive antagonists, such as MK-801, from their binding sites was quite different with respect to their dependence on the direction of ionic currents flowing through the channel pores of NMDA receptors, that is, outward currents had no effect on the channel block of PPDC, while the release of MK-801 was significantly accelerated under outward current conditions in the voltage-clamp experiments,[10f] and (3) PPDC was selective to GluRε2/ζ1, GluRε3/ζ1 and GluRε4/ζ1 subtypes, while previous antagonists were nonselective or selective to the GluRε1/ζl, GluRε2/ζl and/or GluRε3/ζl subtypes.[10j] These results, together with the structural features of PPDC, which are clearly different from those of the previous antagonists, suggest that it is a new class of NMDA receptor antagonists.

These encouraging results prompted us to synthesize PPDC analogues in the hope of finding further useful compounds and of clarifying their structure–activity relationship. Therefore, we designed the PPDC derivative **6** without a 1-phenyl group. Biological evaluation of **6** showed that the aromatic ring was essential for the NMDA receptor binding affinity. Consequently, we designed and synthesized the novel 1′-aromatic group-modified PPDC analogues **4b–i** (Fig. 3) with the same stereochemistry as for PPDC. In this paper we describe the results of these studies.

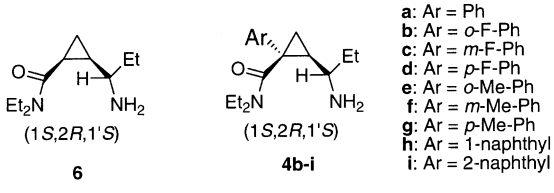
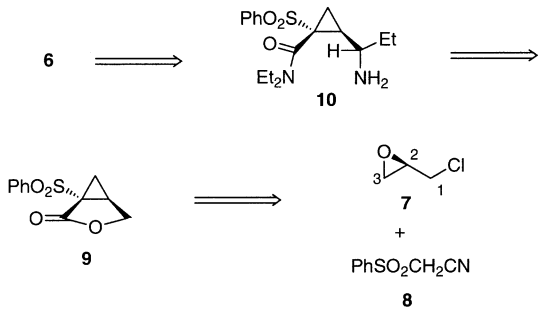


Figure 3. Derivatives of the PPDC modified at the 1-aromatic moiety.

Results and Discussion

Synthesis of the PPDC analogue lacking the phenyl group

We first tried to synthesize the PPDC derivative **6**, which lacks the 1-phenyl group. Biological evaluation of **6** would clarify the role of the phenyl group for the binding to the receptor in PPDC and its congeners. For the synthesis of **6**, an efficient construction of a chiral 1,2-*cis*-carbonsubstituted cyclopropane structure was needed. In recent years, stereoselective preparation of biologically important cyclopropane derivatives has been extensively studied.[11–14] We have developed a synthetic procedure for chiral cyclopropanes with (*R*)- or (*S*)-epichlorohydrin as a synthon.[10a–c,15] The procedure is particularly useful, since the both chiral epichlorohydrins are commercially available in high optical purity and also cyclopropane products of high optical purity can be obtained on a rather large scale. Thus, we planned to synthesize the target **6** using (*R*)-epichlorohydrin (**7**) as a synthon. The retrosynthetic analysis is shown in Scheme 1. The final product **6** is obtained by reductive removal of the phenylsolfonyl group of **10**, can be obtained from the (1*R*,2*S*)-1-(phenylsulfonyl)cyclopropane derivative **9**. The cyclopropane structure having a phenylsulfonyl group is constructed from (*R*)-epichlorohydrin (**7**) and phenylsulfonylacetonitrile (**8**) by the procedure recently developed by us.[15]

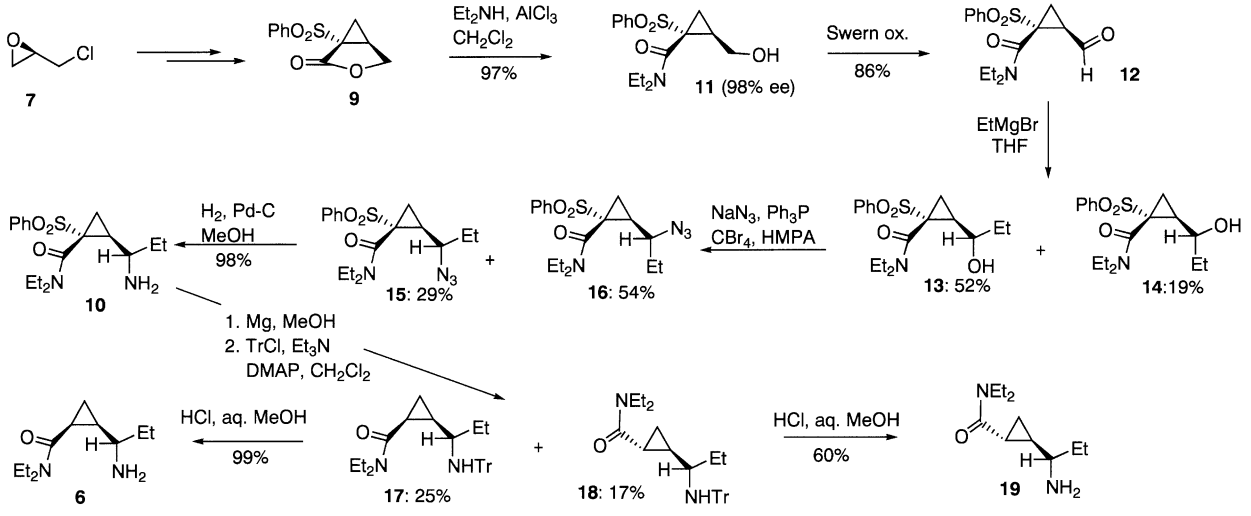


Scheme 1.

Compound **6** was successfully synthesized as summarized in Scheme 2. Aminolysis of the (1*R*,2*S*)-1-(phenylsulfonyl)-cyclopropane derivative **9**, prepared via the condensation between **7** and **8** under basic conditions, with $Et_2NH/AlCl_3$ gave the cyclopropylmethyl alcohol **11**, the optical purity of which was determined as 98% ee by chiral HPLC analysis. Grignard reaction of the aldehyde **12**, which was prepared by Swern oxidation of **11**, with EtMgBr in THF gave a major addition product **13** in 52% yield and its 1′-diastereomer **14** in 19% yield.

The relative stereochemistries were confirmed by ^1H NMR analysis. We previously demonstrated that the 1′-configurations of the conformationally rigid 1′*S*-methyl lactone **20** and its 1′*R*-diastereomer **21** can be determined based on their ^1H NMR coupling constant between the H-2 and the H-1′, as shown in Figure 4. Thus, in this study, the major and minor products **13** and **14** of the Grignard reaction were heated with HCl in MeOH to convert them into the corresponding lactones **22** and **23**, and their 1′-configuration were confirmed as *S* ($J_{2,1'}=0$ Hz) and *R* ($J_{2,1'}=4.6$ Hz), respectively.

Mitsunobu-type azidation of **13** with a $NaN_3/Ph_3P/CBr_4$ system[16] in HMPA gave the 1′-azido derivative **16** in 54% yield and its diastereomer **15** in 29% yield. As described below, similar reactions with the corresponding 1-phenyl substrates **29a–i** proceeded stereoselectively via the neighboring amido-oxygen-participation pathway. In the reaction of **13**, such a neighboring participation would not work effectively due to the electron-withdrawing sulfony group at the 1-position. Although the 1′-*S*-azide **16** is required for synthesizing the target compound **6**, the 1′-configuration of the major product **16** was determined as *R* by its X-ray crystallographic analysis. Catalytic hydrogenation of **15** with Pd-C in MeOH gave the corresponding amine **10**. The reductive removal of the phenylsulfonyl group of **10** with Mg/MeOH[15,17] was performed, and the products were isolated after protection of the amino function by a trityl group. Treatment of **10** with Mg/MeOH at 50 °C gave only the *trans* product **18**. However, the desired *cis*-product **17** was



Scheme 2.

obtained as the major product, when the reductive treatment of **10** was carried out at 0 °C. Although we also examined desulfonylation by SmI2, it was unsuccessful and **10** was recovered. Finally, acidic detritylation of **17** with HCl/MeOH gave the target compound **6** as a hydrochloride. The corresponding *trans*-isomer **19** was obtained by a similar deprotection of **18**. The *cis*/*trans*-geometry of **6** and **19** were confirmed by the NOE experiments as shown in Figure 5.

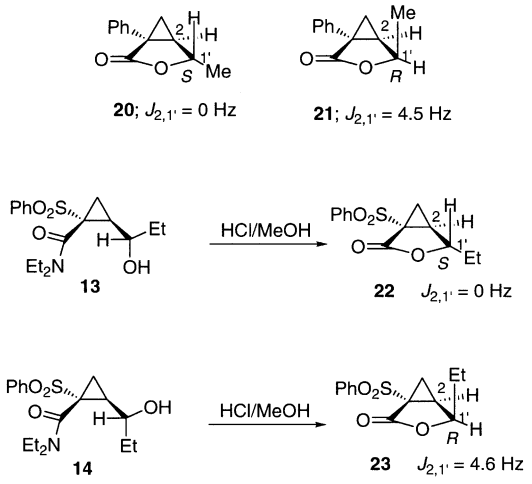


Figure 4. Determinations of the 1′-configurations of **13** and **14**.

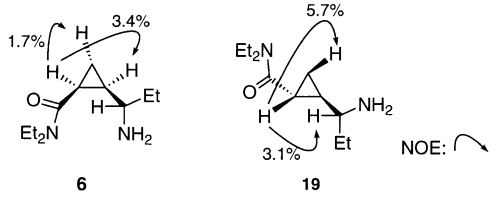
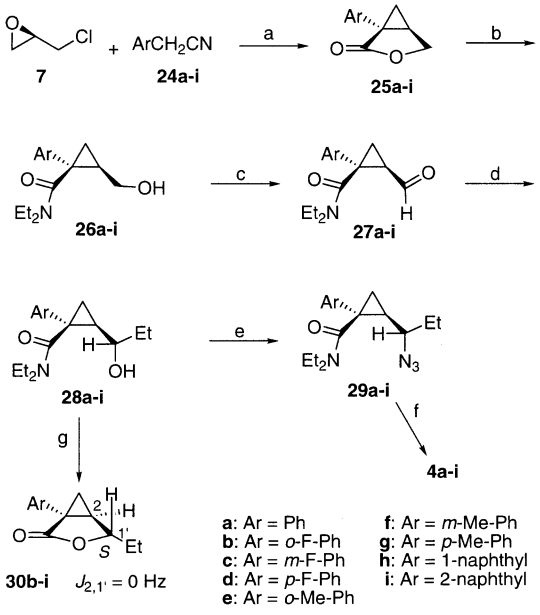


Figure 5. Determinations of stereochemistry of **6** and **19**.



Scheme 3.

Synthesis of PPDC analogues having a Substituted-phenyl group at the 1-position

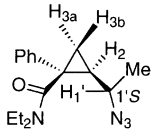
The target compounds **4b–i** were synthesized, as shown in Scheme 3, according to the procedure developed previously for the synthesis of a series of conformationally restricted analogues of milnacipran, such as PPDC, having a phenyl group at the 1-position on the cyclopropane ring.[10] In the previous synthesis, all of the target compounds with Type-1 stereochemistry [(1*S*,2*R*,1′*S*)-configuration] were prepared via the key-intermediate (1*S*,2*R*)-lactone **25a**, which was readily prepared from (*R*)-epichlorohydrin (**7**) and phenylacetonitrile (**24a**).[10a] Therefore, similar reactions with the substituted phenylacetonitriles **24b–i** and **7** were thought to provide the corresponding (1*S*,2*R*)-lactones **25b–i**, from which the target compounds **4b–i** would be synthesized.

Reactions of **7** and the carbanions, prepared by treating the substituted phenylacetonitriles **24b–i** with $NaNH_2$, in benzene at room temperature, followed by alkaline hydrolysis of the nitrile group and subsequent acidic treatment gave the desired (1*S*,2*R*)-lactone **25a–i** in 28–63% yields with a high optical purity (94–96% ee).[18] Diethyl-aminolyses of the lactones **25b–i** and subsequent Swern oxidation readily gave the cyclopropylcarbaldehydes **27b–i**.

Grignard reactions of **27b–i** with EtMgBr in THF were performed to give the corresponding 1′*S*-products **28b–i** highly diastereoselectively in 77–94% yields. The 1′-configurations of **28b–i** were determined by the $J_{2,1'}$ values, after converting **28b–i** into the lactones **30b–i**. As we previously reported,[10a,b] addition of the Grignard reagent to the cyclopropylcarbaldehydes **27b–i** would proceed from the least-hindered *si*-face in the bisected *s-trans* conformation, which would be preferred due to the peculiar stereo-electronic effect of the cyclopropane ring, to produce 1′*S*-addition products **28b–i** highly stereoselectively.[10a,b] Treatment of **28b–i** with a NaN_3/PPh_3/CBr_4 system[16] gave the 1′*S*-azide **29b–i** with retention of configuration in 69–99% yield. We have demonstrated that the reaction occurs via the neighboring amido-oxygen-participation to give the corresponding azido derivatives with retention of configuration.[10a,d,e] The 1′-configurations of **29a–i** were supported by the chemical shifts in ^1H NMR spectra as summarized in Table 1. The 1′-cyclopropylazide derivatives show a typical chemical shift pattern depending on the 1′-configuration. Table 1 shows the ^1H NMR spectral data of the known stereochemistry of the 1′*R*-azides **32**[10a] and **33**,[10a] and the 1′*S*-azides **31**[10a] and **29a**.[10a] In the 1′*S*-azide series, the H-2, H-3a, and H-3b signals are separately observed around δ 2.0, 0.9, and 1.6 ppm, respectively, while signals of the three protons overlap in the spectra of the 1′*R* azides. Thus the 1′-configurations of **29b–i** were confirmed as *S* based on the separately observed signals of the three protons, as shown in Table 1.

Catalytic hydrogenations of **29b–i** finally gave the target compounds **4b–i** in high yields.

Table 1. ^{1}H NMR chemical shifts of the 1′-azido derivatives in $CDCl_3$



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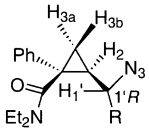
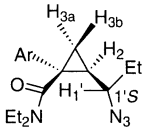


32: R = Me
33: R = Et



29a-i

a: Ar = Ph
b: Ar = *o*-F-Ph
c: Ar = *m*-F-Ph
d: Ar = *p*-F-Ph
e: Ar = *o*-Me-Ph
f: Ar = *m*-Me-Ph
g: Ar = *p*-Me-Ph
h: Ar = 1-naphthyl
i: Ar = 2-naphthyl

Compd	R	1′-Config.	Chemical shift, δ (multiplicity)			
			H-1′	H-2	H-3a	H-3b
31	Me	*S*	2.98–3.08 (m)	1.95 (ddd)	0.91 (dd)	1.61 (dd)
29a	Et	*S*	2.86 (ddd)	1.96 (ddd)	0.95 (dd)	1.65 (dd)
32	Me	*R*	3.33–3.38 (m)	1.48–1.52 (m)	1.48–1.52 (m)	1.48–1.52 (m)
33	Et	*R*	3.12–3.26 (m)	1.47–1.60 (m)	1.47–1.60 (m)	1.47–1.60 (m)
29b	Et	*S*	2.87 (m)	2.05 (ddd)	0.89 (dd)	1.93 (dd)
29c	Et	*S*	2.86 (m)	1.91 (ddd)	0.97 (m)	1.67 (dd)
29d	Et	*S*	2.87 (m)	1.89 (ddd)	0.92 (dd)	1.64 (dd)
29e	Et	*S*	2.85–2.94 (m)	2.05 (ddd)	0.73 (dd)	1.99 (dd)
29f	Et	*S*	2.85 (m)	1.95 (ddd)	0.93 (dd)	1.64 (dd)
29g	Et	*S*	2.85 (m)	1.95 (ddd)	0.92 (dd)	1.62 (dd)
29h	Et	*S*	3.00–3.07 (m)	2.15–2.20 (m)	0.88 (dd)	2.15–2.20 (m)
29i	Et	*S*	2.97 (m)	2.10 (ddd)	1.01 (dd)	1.73 (dd)

Affinity for the NMDA receptor of rat cerebral cortex

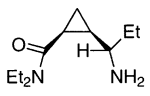
The synthesized compounds were evaluated for their binding affinity for the NMDA receptor of cerebral cortical synaptic membranes from rats with [^{3}H] MK-801 as a radioligand.[19] The results, together with those of several previously reported compounds,[10d,e] are shown in Table 2.

Compound **6**, a PPDC analogue lacking the phenyl group, completely lost the affinity for the receptor. Thus, it is clear that the aromatic moiety is essential for the activity.

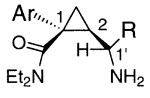
In the fluorophenyl series, **4b**, **4c**, and **4d**, the *para*-substituted **4d** showed the binding affinity with IC_{50} value of $2.8 \pm 0.04\,\mu M$, which was lower than that of PPDC ($IC_{50} = 0.20 \pm 0.02\,\mu M$). However, when a fluoro substituent was introduced at the *ortho*- or the *meta*-position, i.e., **4b** and **4c**, respectively, the affinity was somewhat improved [$IC_{50} = 0.16 \pm 0.001\,\mu M$ (**4b**), $0.15 \pm 0.02\,\mu M$ (**4c**)], compared with the parent compound PPDC.

On the other hand, the binding affinity of the methylphenyl and naphthyl derivatives was relatively weak compared with that of the fluoro compounds above. The *o*-methylphenyl (**4e**), *m*-methylphenyl (**4f**) and 2-naphthyl (**4h**) derivatives showed rather potent binding affinity for the receptor ($IC_{50} = 0.24 \pm 0.03\,\mu M$, $0.29 \pm 0.4\,\mu M$, and $0.38 \pm 0.05\,\mu M$, respectively), whereas the values were weaker than those of PPDC. The binding affinity for the *p*-methylphenyl (**4g**) and 3-naphthyl (**4i**) derivatives was insignificant.

Table 2. Effects of the compounds on NMDA receptor binding and 5-HT uptake



6



2, **4a-i**

Compd	Ar	R	NMDA receptor binding[a] (IC_{50}, μM)	5-HT uptake[b] (K_i, μM)	Selectivity index[c] (5-HT/NMDA)
(±)-**1**	Ph	H	6.3 ± 0.3	0.0085 ± 0.0006	0.0013
2	Ph	Me	0.35 ± 0.08	0.014 ± 0.002	0.040
4a	Ph	Et	0.20 ± 0.02	24 ± 0.9	120
6	H	Et	> 100	> 100	—
4b	*o*-F–Ph	Et	0.16 ± 0.001	> 100	> 630
4c	*m*-F–Ph	Et	0.15 ± 0.02	> 100	> 670
4d	*p*-F–Ph	Et	2.8 ± 0.04	> 100	36
4e	*o*-Me–Ph	Et	0.24 ± 0.03	> 100	420
4f	*m*-Me–Ph	Et	0.29 ± 0.4	> 100	340
4g	*p*-Me–Ph	Et	33 ± 2.1	> 100	3.0
4h	2-Naphthyl	Et	0.48 ± 0.05	> 100	210
4i	3-Naphthyl	Et	4.2 ± 0.2	> 100	> 24

[a]Assay was done with cerebral cortical synaptic membrane of rats using [^{3}H]MK-801.
[b]Assay was done with cerebral cortical synaptic membrane of rats using [^{3}H]paroxetine.
[c]The ratio: 5-HT uptake inhibition (K_i)/NMDA receptor binding (IC_{50}).

These results suggested that although the presence of a substituent at the *ortho*- or the *meta*-position of the 1-phenyl moiety of PPDC is tolerated in binding to the receptor, a *para*-substituent is likely to disturb this binding, probably due to a steric effect.

Inhibition on the 5-HT-Uptake

The inhibitory effects of the compounds on the uptake of 5-HT by nerve terminals of cerebral cortical synaptic membrane from rats were next evaluated with [^{3}H] paroxetine as a radioligand,[10d] since the lead compound milnacipran [(±)-**1**] is a potent inhibitor of 5-HT uptake. The results are also summarized in Table 1. Compound **2**, the 1′-methyl congener of PPDC, significantly inhibits the 5-HT uptake, whereas PPDC has a very weak inhibitory effect.

As a result, all of the newly synthesized compounds were completely inactive in this system, which explains the absence of affinity for the nerve terminal 5-HT-transporter when a substitution is introduced at the 1-phenyl moiety. The selectivity index [5-HT uptake inhibition (Ki)/NMDA receptor binding (IC_{50})] of the fluoro derivatives **4b** and **4c** surpassed that of PPDC.

Conclusion

We have synthesized a series of PPDC analogues modified at the 1-phenyl moiety as novel NMDA receptor antagonists. Analogue **6**, which lacked the 1-phenyl group, was completely inactive, while all of the other synthesized analogues with an aromatic ring at the 1-position had affinity for the receptor, indicating that the aromatic moiety is essential for activity. The *ortho*- and *meta*-fluorophenyl derivatives **4b** and **4c** were identified as the most selective NMDA receptor antagonists in this series of compounds. Further pharmacological evaluations of **4b** and **4c** are now in progress.[20]

Experimental

Melting points were determined on a Yanagimoto MP-3 micro-melting point apparatus and are uncorrected. The NMR spectra were recorded with a Jeol EX-270,-400, or Bruker AMX 500 spectrometer with tetramethylsilane as an internal standard. Chemical shifts were reported in parts per million (δ), and signals are expressed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad). Mass spectra were measured on a Jeol JMS-D300 spectrometer. Thin-layer chromatography was done on Merck coated plate $60F_{254}$. Silica gel chromatography was done with Merck silica gel 5715. Reactions were performed under argon.

(1*R*,2*S*)-1-Phenylsulfonyl-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (11). To a mixture of **9** (35.7 g, 150 mmol) and $AlCl_3$ (40.0 g, 300 mmol) in CH_2Cl_2 (400 mL) was added Et_2NH (62.7 mL, 600 mmol) slowly at 0 °C, and the mixture was stirred at room temperature for 5 h. After addition of 1 N HCl, the resulting mixture was partitioned. The organic layer was washed with 1 N HCl and brine, dried (Na_2SO_4), evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:3) to give **11** as yellow crystals (45.2 g, 96.8%), of which optical purity was determined as 98% ee by a chiral HPLC (CHIRALCEL OJ, 0.46×25 cm, Daicel Chemical Industries Co., Ltd.; hexane/EtOH, 1:1; 0.5 mL/min; 265 nm): mp (hexane, AcOEt, Et_2O) 61 °C; $[\alpha]_D^{28}$ −45.34 (*c* 1.010, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.24 (1H, dd, H-3a, $J_{3a,3b}$ = 5.5, $J_{3a,2}$ = 5.5 Hz), 1.26 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 2.16 (1H, m, H-3b), 2.23 (1H, dd, H-3b, $J_{3b,3a}$ = 5.5, $J_{3b,2}$ = 9.5 Hz), 2.84 (1H, ddd, H-1′a, $J_{1'a,OH}$ = 1.5, $J_{1'a,2}$ = 12.0, $J_{1'a,\ 1'b}$ = 12.0 Hz), 3.23 (1H, m, –$N\underline{CH_2}CH_3$), 3.47–3.58 (2H, m, –$N\underline{CH_2}CH_3$), 3.85 (1H, dd, –OH, $J_{OH,1'a}$ = 1.5, $J_{OH,1'b}$ = 12.0 Hz), 3.91–4.00 (2H, m, –$N\underline{CH_2}CH_3$ and H-1′), 7.56 (2H, dd, H-3″ and H-5″, J = 7.5, J = 7.5 Hz), 7.67 (1H, dd, H-4″, J = 7.5, J = 7.5 Hz), 7.86 (2H, d, H-2″ and H-6″, J = 7.5 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 12.02 (–$NCH_2\underline{CH_3}$), 13.48 (–$NCH_2\underline{CH_3}$), 15.89 (C-3), 28.09 (C-2), 40.06 (–$N\underline{CH_2}CH_3$), 43.13 (–$N\underline{CH_2}CH_3$), 49.35 (C-1), 62.63 (C-1′), 128.75 (C-2″ and C-6″), 128.79 (C-3″ and C-5″), 133.96 (C-4″), 137.86 (C-1″), 163.56 (C=O); HR-MS (EI) calcd $C_{15}H_{21}NO_4S$ 311.1191; obs 311.1203 (M^+). Anal. calcd for $C_{15}H_{21}NO_4S$: C, 57.86; H, 6.80; N, 4.50; S, 10.30. Found: C, 57.67; H, 6.78; N, 4.42; S, 10.24.

(1*R*,2*S*)-1-Phenylsulfonyl-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (12). To a solution of oxalyl chloride (6.11 mL, 70.0 mmol) in CH_2Cl_2 (20 mL) was slowly added a mixture of DMSO (9.93 mL, 140 mmol) and CH_2Cl_2 (10 mL) at −78 °C, and then **11** (10.9 g, 35.0 mmol) in CH_2Cl_2 (30 mL) was added dropwise. The resulting mixture was stirred at the same temperature for 2 h, and then Et_3N (39.4 mL, 280 mmol) was added. After being stirring at −78 °C for further 30 min, the reaction was quenched with saturated NH_4Cl, and then CH_2Cl_2 was added and partitioned. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:4) to give **12** as white an oil (9.27 g, 85.6%): $[\alpha]_D^{26}$ −49.39 (*c* 1.166, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.09 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.27 (4H, m, –$NCH_2\underline{CH_3}$ and H-3a), 2.11 (1H, m, H-3b), 3.27–3.49 (3H, m, –$N\underline{CH_2}CH_3$), 3.86 (1H, m, –$N\underline{CH_2}CH_3$), 7.57 (2H, m, aromatic), 7.65 (1H, m, aromatic), 7.83 (2H, m, aromatic), 9.13 (1H, d, H-1′, $J_{1',2}$ = 4.0 Hz); ^{13}C NMR (67.8 MHz, CDCl3) δ 12.56 (–$NCH_2\underline{CH_3}$), 14.00 (–$NCH_2\underline{CH_3}$), 18.04 (C-3), 33.28 (C-2), 40.42 (–$N\underline{CH_2}CH_3$), 43.38 (–$N\underline{CH_2}CH_3$), 54.22 (C-1), 128.79 (C-2″ and C-6″), 129.47 (C-3″ and C-5″), 134.83 (C-4″), 137.75 (C-1″), 160.41 (C=O), 195.04 (C-1′); HR-MS (EI) calcd $C_{15}H_{19}NO_4S$ 309.1035; obs 309.1044 (M^+). Anal. calcd for $C_{15}H_{19}NO_4S$: C, 58.23; H, 6.19; N, 4.53; S, 10.36. Found: C, 58.06; H, 6.19; N, 4.46; S, 10.32.

(1*R*,2*S*)-1-Phenylsulfonyl-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (13) and (1*R*,2*S*)-1-Phenylsulfonyl-2-[(*R*)-1-hydroxypropyl]-*N*,*N*-diethylcyclo-

propanecarboxamide (14). A mixture of **12** (7.43 g, 24.0 mmol) and EtMgBr (0.95 M in THF, 100 mL, 95.0 mmol) in THF (10 mL) was stirred at −20 °C for 5 h. The reaction was quenched with saturated NH_4Cl, and the resulting mixture was concentrated in vacuo (for removing THF and Et_2O), to which AcOEt and H_2O was added and partitioned. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated The reside was purified by column chromatography (silica gel; AcOEt/hexane 1:4) to give **13** as an oil (4.26 g, 52.3%) and **14** as an oil (1.57 g, 19.3%). **13:** mp (hexane, AcOEt, $CHCl_3$) 95 °C; $[\alpha]_D^{20}$ −45.57 (*c* 1.055, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.94 (3H, t, H-3′, $J_{3',2'}$ = 7.5 Hz), 1.13 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.22 (1H, dd, H-3a, $J_{3a,3b}$ = 5.8, $J_{3a,2}$ = 5.8 Hz), 1.26 (3H, m, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.54–1.68 (2H, m, H-2′), 1.90 (1H, ddd, H-2, $J_{2,3a}$ = 5.8, $J_{2,3b}$ = 9.6, $J_{2,1'}$ = 9.6 Hz), 2.23 (1H, dd, H-3b, $J_{3b,3a}$ = 5.8, $J_{3b,2}$ = 9.6 Hz), 2.74 (1H, m, H-1′), 3.20 (1H, m, –$N\underline{CH_2}CH_3$), 3.49–3.58 (2H, m, –$N\underline{CH_2}CH_3$), 3.97 (1H, m, –$N\underline{CH_2}CH_3$), 4.42 (1H, d, –OH, $J_{OH,1'}$ = 0.6 Hz), 7.55 (2H, dd, H-3″ and H-5″, J = 7.5, J = 7.8 Hz), 7.65 (1H, dd, H-4″, J = 7.5, J = 7.5 Hz), 7.85 (2H, d, H-2″ and H-6″, J = 7.8 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 9.98 (C-3′), 12.02 (–$NCH_2\underline{CH_3}$), 13.52 (–$NCH_2\underline{CH_3}$), 16.12 (C-3), 28.65 (C-2′), 32.29 (C-2), 40.02 (–$N\underline{CH_2}CH_3$), 43.07 (–$N\underline{CH_2}CH_3$), 48.34 (C-1), 73.71 (C-1′), 128.79 (C-2″ and C-6″), 129.22 (C-3″ and C'-5), 133.98 (C-4″), 137.83 (C-1″), 163.70 (C=O); HR-MS (EI) calcd $C_{17}H_{25}NO_4S$ 339.1504; obs 339.1516 (M^+). Anal. calcd for $C_{17}H_{25}NO_4S$: C, 60.15; H,7.42; N, 4.13; S, 9.45. Found: C, 60.19; H,7.36; N, 3.97; S, 9.37. **14:** $[\alpha]_D^{25}$ −83.54 (*c* 0.505, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.90 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.12 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.0 Hz), 1.24 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.37 (1H, m, H-2′a), 1.46 (1H, m, H-2′b) 1.62 (1H, dd, H-3a, $J_{3a,3b}$ = 5.3, $J_{3a,2}$ = 7.6 Hz), 1.84 (1H, m, H-3b), 2.05–2.12 (2H, m, –OH and H-2), 3.24 (1H, m,-$NCH_2\underline{CH_3}$), 3.41–3.52 (2H, m, –$NCH_2\underline{CH_3}$), 3.78 (1H, m, H-1′), 3.94 (1H, m, –$NCH_2\underline{CH_3}$), 7.54 (2H, m, aromatic), 7.65 (1H, m, aromatic), 7.82 (2H, m, aromatic); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 9.81 (C-3′), 11.97 (–$NCH_2\underline{CH_3}$), 13.37 (–$NCH_2\underline{CH_3}$), 14.02 (C-3), 29.11 (C-2′), 30.42 (C-2), 39.93 (–$N\underline{CH_2}CH_3$), 43.16 (–$N\underline{CH_2}CH_3$), 46.87 (C-1), 67.66 (C-1′), 128.63 (C-2″ and C-6″), 129.20 (C-3″ and C-5″), 133.64 (C-4″), 138.53 (C-1″), 163.70 (C=O); HR-MS (EI) calcd $C_{17}H_{25}NO_4S$ 339.1504; obs 339.1505 (M^+). Anal. calcd for $C_{17}H_{25}NO_4S$: C, 60.15; H,7.42; N, 4.13; S, 9.45. Found: C, 59.95; H,7.35; N, 4.02; S, 9.30.

(1*R*,2*S*)-1-Phenylsulfonyl-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (15) and (1*R*,2*S*)-1-Phenylsulfonyl-2-[(*R*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (16). A mixture of **15** (289 mg, 1.00 mmol), PPh_3 (787 mg, 3.00 mmol), and CBr_4 (995 mg, 3.00 mmol) in HMPA (10 mL) was stirred at 0 °C for 30 min. After addition of NaN_3 (650 mg, 10.0 mmol), the resulting mixture was stirred at room temperature for 8 h, and then AcOEt and H_2O were added and partitioned. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The reside was purified by flash column chromatography (silica gel; AcOEt/hexane 1:9) to give **16** as white crystals (3.95 g, 54%) and **15** as white crystals (2.14 g, 29%). **15:** mp (hexane, AcOEt, $CHCl_3$, Et_2O, H_2O) 73–74 °C; $[\alpha]_D^{26}$ −71.07 (*c* 1.135, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.14 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.24 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.0 Hz), 1.44 (1H, m, H-2′a), 1.52–1.67 (2H, m, H-3a and H-2′b), 1.79 (1H, m, H-2), 2.21 (1H, dd, H-3b, $J_{3b,3a}$ = 5.8, $J_{3b,2}$ = 9.7 Hz), 3.17–3.27 (2H, m, –$N\underline{CH_2}CH_3$ and H-1′), 3.34–3.58 (2H, m, –$N\underline{CH_2}CH_3$), 3.89 (1H, m, –$N\underline{CH_2}CH_3$), 7.54 (2H, m, aromatic), 7.65 (1H, m, aromatic), 7.80 (2H, m, aromatic); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 10.17 (C-3′), 12.19 (–$NCH_2\underline{CH_3}$), 13.55 (–$NCH_2\underline{CH_3}$), 15.69 (C-3), 28.14 (C-2′), 28.38 (C-2), 39.93 (–$N\underline{CH_2}CH_3$), 42.81 (–$N\underline{CH_2}CH_3$), 47.42 (C-1), 62.23 (C-1′), 128.73 (C-2″ and C-6″), 128.88 (C-3″ and C-5″), 133.93 (C-4″), 138.17 (C-1″), 161.76 (C=O); HR-MS (EI) calcd $C_{17}H_{25}N_4O_3S$ 365.1647; obs 365.1654 $(M+1)^+$. Anal. calcd for $C_{17}H_{24}N_4O_3S$: C, 56.02; H, 6.64; N, 15.37; S, 8.80. Found: C, 55.98; H, 6.60; N, 15.10; S, 8.80. **16:** mp (hexane, AcOEt, $CHCl_3$, Et_2O, H_2O) 88–89 °C; $[\alpha]_D^{26}$ −67.98 (*c* 1.110, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.94 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.13 (3H, t, –$NCH_2\underline{CH_3}$ J = 7.1 Hz), 1.23–1.36 (4H, m, –$NCH_2\underline{CH_3}$ and H-3a), 1.53–1.62 (2H, m, H-2′), 1.91 (1H, br, H-2), 2.17 (1H, br, H-3b), 2.93 (1H, br, H-1′), 3.27 (1H, m, –$N\underline{CH_2}CH_3$), 3.42–3.54 (2H, m, –$N\underline{CH_2}CH_3$), 3.96 (1H, m, –$N\underline{CH_2}CH_3$), 7.54 (2H, m, aromatic), 7.65 (1H, m, aromatic), 7.86 (2H, m, aromatic); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 10.19 (C-3′), 12.15 (–$NCH_2\underline{CH_3}$), 13.61 (–$NCH_2\underline{CH_3}$), 15.85 (C-3), 27.46 (C-2′), 29.98 (C-2), 40.22 (–$N\underline{CH_2}CH_3$), 43.27 (–$N\underline{CH_2}CH_3$), 49.45 (C-1), 62.39 (C-1′), 128.77 (C-2″ and C-6″), 129.22 (C-3″ and C-5″), 134.34 (C-4″), 138.58 (C-1″), 162.08 (C=O); HR-MS (EI) calcd $C_{17}H_{24}N_4O_3S$ 364.1569; obs 364.1595. Anal. calcd for $C_{17}H_{24}N_4O_3S$: C, 56.02; H,6.64; N, 15.37; S, 8.80. Found: C, 55.95; H, 6.64; N, 15.24; S, 8.84.

(1*R*,2*S*)-1-Phenylsulfonyl-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide Hydrochloride (10). A mixture of **15** (500 mg, 1.37 mmol) and 10% Pd-charcoal (100 mg) in MeOH (10 mL) was stirred under atmospheric pressure of hydrogen at room temperature for 15 h, and then the catlayst was filtered off. The filtrate was evaporated, and the residue was purified by column chromatography (silica gel; $CHCl_3$/MeOH 10:1) to give the free amine of **10** as an oil (456 mg, 99%): ^1H NMR (270 MHz, $CDCl_3$) δ 0.91 (3H, t, H-3′, $J_{3',2'}$ = 7.6 Hz), 1.14 (3H, t, –$NCH_2\underline{CH_3}$ J = 7.0 Hz), 1.19–1.26 (4H, m, –$NCH_2\underline{CH_3}$ and H-3a), 1.36–1.74 (5H, m, H-2 and H-2′ and –NH_2), 2.00 (1H, m, H-1′), 2.21 (1H, dd, H-3b, $J_{3b,3a}$ = 5.6, $J_{3b,2}$ = 9.9 Hz), 3.21 (1H, m, –$N\underline{CH_2}CH_3$), 3.41–3.54 (2H, m, –$N\underline{CH_2}CH_3$), 3.95 (1H, m, –$N\underline{CH_2}CH_3$), 7.55 (2H, m, aromatic), 7.64 (1H, m, aromatic), 7.86 (2H, m, aromatic); HR-MS (EI) calcd $C_{17}H_{27}N_2O_3S$ 339.1742; obs 339.1728 $(M+1)^+$. Anal. calcd for $C_{17}H_{26}N_2O_3S$: C, 60.33; H, 7.74; N, 8.28; S, 9.47. Found: C, 60.01; H, 7.61; N, 8.09; S, 9.58. A solution of the free amine of **10** (338 mg, 1.00 mmol) in MeOH was put on a column of Diaion WA-30 resin (Cl^- form), and the column was developed with MeOH. The solvent was evaporated, and the residue was treated with *i*-Pr_2O to give hydrochloride of **10** as white crystals (372 mg, quant): mp (hexane, AcOEt, $CHCl_3$, Et_2O) 224–225.5 °C; $[\alpha]_D^{28}$ −37.84

(*c* 1.065, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 0.96 (3H, t, H-3′, $J_{3',\ 2'}=7.5$ Hz), 1.01 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.11 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.60 (1H, dd, H-3a, $J_{3a,3b}=6.5$, $J_{3a,2}=6.5$ Hz), 1.76 (1H, m, H-2′), 1.95 (1H, ddd, H-2, $J_{2,3a}=6.5$, $J_{2,3b}=9.8$, $J_{2,1'}=9.8$ Hz), 2.22 (1H, dd, H-3b, $J_{3b,3a}=6.5$, $J_{3b,2}=9.8$ Hz), 2.45 (1H, m, H-1′), 3.09 (1H, m, –$N\underline{CH_2}CH_3$), 3.23 (1H, m, –$N\underline{CH_2}CH_3$), 3.45 (1H, m, –$N\underline{CH_2}CH_3$), 3.57 (1H, m, –$N\underline{CH_2}CH_3$), 7.59 (2H, dd, H-3″ and H-5″, $J=7.5$, $J=7.5$ Hz), 7.71 (1H, dd, H-4″, $J=7.5$, $J=7.5$ Hz), 7.79 (2H, d, H-2″ and H-6″, $J=7.5$ Hz); ^{13}C NMR (67.8 MHz, CD_3OD) δ 10.29 (C-3′), 12.49 (–$NCH_2\underline{CH_3}$), 13.48 (–$NCH_2\underline{CH_3}$), 18.42 (C-3), 27.15 (C-2′), 27.58 (C-2), 41.51 (–$N\underline{CH_2}CH_3$), 44.67 (–$N\underline{CH_2}CH_3$), 50.33 (C-1), 55.92 (C-1′), 130.31 (C-2″ and C-6″), 130.74 (C-3″ and C-5″), 135.88 (C-4″), 138.70 (C-1″), 164.70 (C=O); HR-MS (FAB) calcd $C_{17}H_{27}N_2O_3S$ 339.1742; obs 339.1760 $(M\text{-}Cl)^+$. Anal. calcd for $C_{17}H_{27}ClN_2O_3S$: C, 54.46; H, 7.26; Cl, 9.46; N, 7.47; S, 8.55. Found: C, 54.35; H, 7.12; Cl, 9.52; N, 7.52; S, 8.63.

(1*S*,2*R*)-2-[(*S*)-1-Triphenylmethylaminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (17) and (1*R*,2*R*)-2-[(*S*)-1-Triphenylmethylaminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (18). A mixture of Mg turnings (100 mg) in dry MeOH (10 mL) was heated to 55 °C with stirring until gas evolution started (15 min). To the mixture a solution of **10** (135 mg, 0.40 mmol) in dry MeOH (10 mL) was added in one portion and the resulting mixture was stirred at 0 °C for 36 h. The resulting mixture was filtered through Celite, the filtrate was evaporated. A mixture of the residue, TrCl (167 mg, 0.60 mmol), Et_3N (83.6 mL, 0.60 mmol) and DMAP (9.80 mg, 8.00 μmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 24 h, and the reaction was quenched with MeOH. The resulting mixture was concentrated in vacuo (for removing methanol), and the residue was partitioned between H_2O and AcOEt. The organic layer was washed with brine, dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:4) to give **17** (44 mg, 25%) and **18** (29 mg, 17%) as yellow solids. **17**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.46 (3H, t, H-3′, $J_{3',\ 2'}=7.4$ Hz), 0.77 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 0.94 (1H, m, H-3a), 1.05 (1H, m, H-2), 1.17–1.23 (5H, t, –$NCH_2\underline{CH_3}$ and H-3b and H-2′a), 1.43 (1H, m, H-2′b), 1.62 (1H, m, H-1), 1.87 (1H, brs, –NH–), 2.06 (1H, dt, H-1′, $J_{1',\ 2'}=2.2$, $J_{1',\ 2}=9.0$ Hz), 3.07 (1H, m, –$N\underline{CH_2}CH_3$), 3.15 (2H, m, –$N\underline{CH_2}CH_3$), 3.71 (1H, m, –$N\underline{CH_2}CH_3$), 7.13 (3H, dd, aromatic, $J=7.0$, $J=7.0$ Hz), 7.23 (6H, dd, aromatic, $J=7.0$, $J=8.0$ Hz), 7.46 (6H, d, aromatic, $J=8.0$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.56 (C-3′), 11.57 (C-3), 12.92 (–$NCH_2\underline{CH_3}$), 14.72 (–$NCH_2\underline{CH_3}$), 15.57 (C-2), 28.33 (C-2′), 28.38 (C-1), 40.39 (–$N\underline{CH_2}CH_3$), 42.08 (–$N\underline{CH_2}CH_3$), 54.94 (C-1′), 70.44 (–$\underline{C}Ph_3$), 125.95, 127.33, 129.40, 146.90 (the above mentioned, aromatic), 169.60 (C=O); HR-MS (EI) calcd $C_{30}H_{36}N_2O$ 440.2828; obs 440.2830 (M^+). **18:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.59 (1H, m, H-3a), 0.66–0.71 (4H, m, H-3′ and H-2), 1.02–1.15 (8H, m, –$NCH_2\underline{CH_3}\times6$ and H-3b and H-1), 1.70 (2H, m, H-2′), 1.81 (1H, m, H-1′), 1.84 (1H, m, –NH–), 3.23 (2H, m, –$N\underline{CH_2}CH_3$), 3.35 (2H, m, –$N\underline{CH_2}CH_3$), 7.15 (3H, dd, aromatic, $J=7.0$, $J=7.0$ Hz), 7.23 (6H, dd, aromatic, $J=7.0$, $J=8.0$ Hz), 7.54 (6H, d, aromatic, $J=8.0$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.69 (C-3′), 13.24 (–$NCH_2\underline{CH_3}$), 14.68 (C-3), 14.79 (–$NCH_2\underline{CH_3}$), 17.50 (C-2), 27.27 (C-1), 28.38 (C-2′), 40.68 (–$N\underline{CH_2}CH_3$), 41.79 (–$N\underline{CH_2}CH_3$), 57.15 (C-1′), 71.24 (–$\underline{C}Ph_3$), 126.16, 127.59, 128.84, 147.00 (the above mentioned, aromatic), 172.02 (C=O); HR-MS (EI) calcd $C_{30}H_{36}N_2O$ 440.2828; obs 440.2839 (M^+).

(1*S*,2*R*)-2-[(*S*)-1-Aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide Hydrochloride (6). A solution of **17** (100 mg, 227 mol) in MeOH (3.0 mL) and 1 N HCl (2.0 mL) was stirred at room temperature for 1 h. The solvent was evaporated, and the residue was partitioned between H_2O and AcOEt. The aqueous layer was washed with Et_2O and evaporated, and the residue was purified by column chromatography (silica gel; AcOEt/hexane 1:1 then MeOH/$CHCl_3$ 1:9) to give the hydrochloride of **6** as a solid (53 mg, 99%): $[\alpha]_D^{23}$ +65.82 (*c* 0.165, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 0.80 (3H, br, H-3a), 1.00 (3H, t, H-3′, $J_{3',\ 2'}=7.4$ Hz) 1.04 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.0$ Hz), 1.16 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.0$ Hz), 1.21–1.29 (2H, m, H-2 and H-3b), 1.68–1.78 (2H, m, H-2′), 1.92 (1H, m, H-1′), 3.07 (1H, m, H-1′), 3.26 (1H, m, –$N\underline{CH_2}CH_3$), 3.36 (1H, m, –$N\underline{CH_2}CH_3$), 3.50 (2H, m, –$N\underline{CH_2}CH_3$); NOE (400 MHz, CD_3OD) 35.2% (H-1→–$N\underline{CH_2}CH_3$), 20.0% (H-1→–$NCH_2\underline{CH_3}$), 3.4% (H-1→H-2), 1.7% (H-1→H-3a); ^{13}C NMR (125 MHz, CD_3OD) δ 10.48 (C-3′), 13.17 (–$NCH_2\underline{CH_3}$), 13.66 (C-3), 14.50 (–$NCH_2\underline{CH_3}$), 17.96 (C-2), 22.46 (C-1), 28.14 (C-2′), 41.81 (–$N\underline{CH_2}CH_3$), 43.91 (–$N\underline{CH_2}CH_3$), 55.32 (C-1′), 172.89 (C=O); HR-MS (EI) calcd $C_{11}H_{22}N_2O$ 198.1732; obs 198.1739 $(M\text{–}HCl)^+$. Anal. calcd for $C_{11}H_{23}ClN_2O\cdot3H_2O$: C, 45.75; H, 10.12; N, 9.70. Found: C, 45.36; H, 10.01; N, 9.44.

(1*R*,2*R*)-2-[(*S*)-1-Aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide Hydrochloride (19). Compound **19** was prepared from **18** in 60% yield as described above for **6**: $[\alpha]_D^{22}$ −69.10 (*c* 0.210, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 0.92 (1H, m, H-3a), 0.95–1.02 (7H, m, –$NCH_2\underline{CH_3}$ and H-3′ and H-3b), 1.19 (1H, m, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.53 (1H, m, H-2), 1.70 (2H, m, H-2′), 2.01 (1H, m, H-1), 2.56 (1H, m, H-1′), 3.23 (1H, m, –$N\underline{CH_2}CH_3$), 3.30–3.42 (2H, m, –$N\underline{CH_2}CH_3$), 3.69 (1H, m, –$N\underline{CH_2}CH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 10.48 (C-3′), 13.32 (–$NCH_2\underline{CH_3}$), 14.67 (C-3), 14.91 (–$NCH_2\underline{CH_3}$), 18.09 (C-2), 23.44 (C-1), 27.70 (C-2′), 42.33 (–$N\underline{CH_2}CH_3$), 43.59 (–$N\underline{CH_2}CH_3$), 57.44 (C-1′), 172.86 (C=O); NOE (400 MHz, CD_3OD) 5.7% (H-1→H-3a), 3.1% (H-1→H-1′), 2.9% (H-1→–$N\underline{CH_2}CH_3$); HR-MS (EI) calcd $C_{11}H_{22}N_2O$ 199.1810; obs 199.1826 $(M-HCl)^+$. Anal. calcd for $C_{11}H_{23}ClN_2O\cdot H_2O$: C, 52.27; H, 9.97; N, 11.08. Found: C, 52.64; H, 9.42; N, 10.84.

(1*R*,4*S*,5*S*)-2-Oxo-4-ethyl-1-phenylsulfonyl-3-oxabicyclo[3.1.0]hexane (22). A solution of **13** (169 mg, 0.50 mmol) in MeOH (5 mL) and 6 N HCl (5 mL) was heated under reflux for 2 h. The solvent was evaporated, and then the residue was partitioned between saturated aqueous $NaHCO_3$ and AcOEt. The organic layer was washed

with brine, dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:4) to give **22** as white crystals (106 mg, 80%): mp (hexane, AcOEt, H_2O) 84.5–85 °C; $[\alpha]_D^{24}$ −92.30 (*c* 1.160, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.92 (3H, t, H-2′, $J_{2',1'}$ = 7.3 Hz), 1.44 (1H, dd, H-6a, $J_{6a,6b}$ = 5.3, $J_{6a,5}$ = 5.3 Hz), 1.66 (2H, m, H-1′), 2.15 (1H, dd, H-6b, $J_{6b,6a}$ = 5.3, $J_{6b,5}$ = 8.6 Hz), 2.89 (1H, dd, H-5, $J_{5,6a}$ = 5.3, $J_{5,6b}$ = 8.6 Hz), 4.24 (1H, t, H-4, $J_{4,1'}$ = 6.3 Hz), 7.59 (2H, m, H-3″ and H-5″), 7.67 (1H, m, H-4″), 8.03 (2H, m, H-2″ and H-6″); HR-MS (EI) calcd $C_{13}H_{14}O_4S$ 266.0613; obs 266.0594 (M^+). Anal. calcd for $C_{13}H_{14}O_4S$: C, 58.62; H, 5.30; S, 12.04. Found: C, 58.57; H, 5.39; S, 12.04.

(1*R*,4*R*,5*S*)-2-Oxo-4-ethyl-1-phenylsulfonyl-3-oxabicyclo [3.1.0]hexane (23). Compound **23** was prepared from **14** in 59% yield as described above for **22:** mp (hexane, AcOEt, H_2O) 113 °C; $[\alpha]_D^{25}$ −111.60 (*c* 1.160, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 1.00 (3H, t, H-2′, $J_{2',1'}$ = 7.3 Hz), 1.49 (1H, dd, H-6a, $J_{6a,6b}$ = 5.3, $J_{6a,5}$ = 5.3 Hz), 1.53 (1H, m, H-1′a), 1.67 (1H, m, H-1′b), 2.02 (1H, dd, H-6b, $J_{6b,6a}$ = 5.3, $J_{6b,5}$ = 8.6 Hz), 3.12 (1H, ddd, H-5, $J_{5,4}$ = 4.6, $J_{5,6a}$ = 5.3, $J_{5,6b}$ = 8.6 Hz), 4.52 (1H, dt, H-4, $J_{4,5}$ = 4.6, $J_{4,1'}$ = 6.6 Hz), 7.61 (2H, m, aromatic), 7.69 (1H, m, aromatic), 8.07 (2H, m, aromatic); HR-MS (EI) calcd $C_{13}H_{14}O_4S$ 266.0613; obs 266.0621 (M^+). Anal. calcd for $C_{13}H_{14}O_4S$: C, 58.62; H, 5.30; S, 12.04. Found: C, 58.55; H, 5.38; S, 11.86.

General procedure for preparing lactones 25b–i. To a suspension of $NaNH_2$ (858 mg, 22.0 mmol) in benzene (20 mL) was added slowly a solution of phenylacetonitrile (**24b–i**, 10.0 mmol) in benzene (10 mL) at 0 °C, and the mixture was stirred at room temperature for 2 h. (*R*)-epichlorohydrin was added to the resulting mixture at 0 °C, and the whole was stirred at room temperature for 2 h. After the solvent was evaporated, AcOEt was added to residue. Insoluble salts were filtered off, and the filtrate was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane, 1:4) to give **25b–i** as an oil or crystals.

(1*S*,5*R*)-2-Oxo-1-(2-fluorophenyl)-3-oxabicyclo[3.1.0]-hexane (25b). Compound **25b** with 96% ee (CHIRALCEL OJ, 0.46×25 cm, Daicel; hexane/EtOH, 4:1; 0.5 mL/min; 265 nm) was obtained as crystals in 28% yield: mp (hexane, AcOEt) 82 °C; $[\alpha]_D^{23}$ −20.55 (*c* 1.080, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.32 (1H, dd, H-6a, $J_{6a,6b}$ = 5.0, $J_{6a,5}$ = 5.0 Hz), 1.70 (1H, dd, H-6b, $J_{6b,6a}$ = 5.0, $J_{6b,5}$ = 7.8 Hz), 2.43 (1H, ddd, H-5, $J_{5,4b}$ = 4.6, $J_{5,6a}$ = 5.0, $J_{5,6b}$ = 7.8 Hz), 4.29 (1H, d, H-4a, $J_{4a,4b}$ = 9.3 Hz), 4.52 (1H, dd, H-4b, $J_{4b,5}$ = 4.6, $J_{4b,4a}$ = 9.3 Hz), 7.06 (1H, m, aromatic), 7.13 (1H, m, aromatic), 7.27–7.36 (2H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.96 (C-6), 24.46 (C-5, $J_{C,F}$ = 5.5 Hz), 27.80 (C-1), 68.28 (C-4), 115.37 (C-3′, $J_{C,F}$ = 20 Hz), 115.21 (C-1′, $J_{C,F}$ = 14 Hz), 124.14 (C-6′, $J_{C,F}$ = 4 Hz), 130.02 (C-4′, $J_{C,F}$ = 9 Hz), 131.44 (C-5′, $J_{C,F}$ = 8 Hz), 162.03 (C-2′, $J_{C,F}$ = 246 Hz), 175.42 (C=O); HR-MS (EI) calcd $C_{11}H_9FO_2$ 192.0586; obs 192.0589 (M^+). Anal. calcd for $C_{11}H_9FO_2$: C, 68.74; H, 4.72. Found: C, 68.97; H, 4.92.

(1*S*,5*R*)-2-Oxo-1-(3-fluorophenyl)-3-oxabicyclo[3.1.0]-hexane (25c). Compound **25c** with 96% ee (CHIRALPAK AD-RH, 0.46×15 cm, Daicel; H_2O/CH_3CN, 4:1; 0.5 mL/min; 265 nm) was obtained as an oil in 63% yield: $[\alpha]_D^{23}$ −91.96 (*c* 1.390, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.38 (1H, dd, H-6a, $J_{6a,6b}$ = 5.0, $J_{6a,5}$ = 5.0 Hz), 1.62 (1H, dd, H-6b, $J_{6b,6a}$ = 5.0, $J_{6b,5}$ = 7.9 Hz), 2.59 (1H, ddd, H-5, $J_{5,4b}$ = 4.7, $J_{5,4a}$ = 5.0, $J_{5,6b}$ = 7.9 Hz), 4.27 (1H, d, H-4a, $J_{4a,4b}$ = 9.3 Hz), 4.44 (1H, dd, H-4b, $J_{4b,5}$ = 4.7, $J_{4b,4a}$ = 9.3 Hz), 6.97 (1H, m, aromatic), 7.18 (2H, m, aromatic), 7.30 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.59 (C-6), 25.31 (C-5), 31.09 (C-1), 67.88 (C-4, $J_{C,F}$ = 5 Hz), 114.44 (C-4′, $J_{C,F}$ = 21 Hz), 115.21 (C-2′, $J_{C,F}$ = 21 Hz), 123.50 (C-6′, $J_{C,F}$ = 3 Hz), 130.02 (C-5′, $J_{C,F}$ = 9 Hz), 136.59 (C-1′, $J_{C,F}$ = 8 Hz), 162.63 (C-3′, $J_{C,F}$ = 244 Hz), 175.30 (C=O); HR-MS (EI) calcd $C_{11}H_9FO_2$ 192.0586; obs 192.0588 (M^+). Anal. calcd for $C_{11}H_9FO_2$: C, 68.74; H, 4.72. Found: C, 68.75; H, 4.86.

(1*S*,5*R*)-2-Oxo-1-(4-fluorophenyl)-3-oxabicyclo[3.1.0]-hexane (25d). Compound **25d** with 94% ee (CHIRALPAK AD-RH, 0.46×15 cm, Daicel; H_2O/CH_3CN, 4:1; 0.5 mL/min; 265 nm) was obtained as an oil in 34% yield: $[\alpha]_D^{22}$ −60.44 (*c* 1.205, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (1H, dd, H-6a, $J_{6a,6b}$ = 4.9, $J_{6a,5}$ = 4.9 Hz), 1.59 (1H, dd, H-6b, $J_{6b,6a}$ = 4.9, $J_{6b,5}$ = 7.8 Hz), 2.54 (1H, ddd, H-5, $J_{5,4b}$ = 4.7, $J_{5,6a}$ = 4.9, $J_{5,6b}$ = 7.8 Hz), 4.27 (1H, d, H-4a, $J_{4a,4b}$ = 9.3 Hz), 4.45 (1H, dd, H-4b, $J_{4b,5}$ = 4.7, $J_{4b,4a}$ = 9.3 Hz), 7.01–7.06 (2H, m, aromatic), 7.37–7.40 (2H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.10 (C-6), 24.87 (C-5), 31.14 (C-1), 68.01 (C-4), 115.43 (C-3′ and C-5′, $J_{C,F}$ = 21 Hz), 129.87 (C-1′, $J_{C,F}$ = 3 Hz), 130.14 (C-2′ and C-6′, $J_{C,F}$ = 9 Hz), 162.16 (C-4′, $J_{C,F}$ = 245 Hz), 175.85 (C=O); HR-MS (EI) calcd $C_{11}H_9FO_2$ 192.0586; obs 192.0603 (M^+). Anal. calcd for $C_{11}H_9FO_2$: C, 68.74; H, 4.72. Found: C, 68.53; H, 4.82.

(1*S*,5*R*)-2-Oxo-1-(2-methylphenyl)-3-oxabicyclo[3.1.0]-hexane (25e). Compound **25e** with 94% ee (CHIRALPAK AD-RH, 0.46×15 cm, Daicel; H_2O/CH_3CN, 4:1; 0.5 mL/min; 265 nm) was obtained as crystals in 28% yield: mp (hexane/AcOEt) 105–106 °C; $[\alpha]_D^{22}$ +9.04 (*c* 1.105, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.34 (1H, dd, H-6a, $J_{6a,6b}$ = 4.7, $J_{6a,5}$ = 4.7 Hz), 1.64 (1H, dd, H-6b, $J_{6b,6a}$ = 4.7, $J_{6b,5}$ = 7.8 Hz), 2.37 (3H, s, Me-Ph-), 2.38 (1H, ddd, H-5, $J_{5,4b}$ = 4.5, $J_{5,6a}$ = 4.7, $J_{5,6b}$ = 7.8 Hz), 4.31 (1H, d, H-4a, $J_{4a,4b}$ = 9.3 Hz), 4.52 (1H, dd, H-4b, $J_{4b,5}$ = 4.5, $J_{4b,4a}$ = 9.3 Hz), 7.15–7.24 (4H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.26 (C-6), 19.44 (Me-Ph-), 24.59 (C-5), 31.82 (C-1), 68.22 (C-4), 125.96, 128.39, 130.29, 130.34, 132.44, 138.81 (the above mentioned, aromatic), 175.90 (C=O); HR-MS (EI) calcd $C_{12}H_{12}O_2$ 188.0837; obs 188.0823 (M^+). Anal. calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.73; H, 6.55.

(1*S*,5*R*)-2-Oxo-1-(3-methylphenyl)-3-oxabicyclo[3.1.0]-hexane (25f). Compound **25f** with 94% ee (CHIRALPAK AD-RH, 0.46×15 cm, Daicel; H_2O/CH_3CN, 4:1; 0.5 mL/min; 265 nm) was obtained as an oil in 46% yield: $[\alpha]_D^{23}$ −76.21 (*c* 2.025, $CHCl_3$); ^1H NMR

(500 MHz, $CDCl_3$) δ 1.29 (1H, dd, H-6a, $J_{6a,6b}=4.8$, $J_{6a,5}=4.8$ Hz), 1.60 (1H, dd, H-6b, $J_{6b,6a}=4.8$, $J_{6b,5}=7.8$ Hz), 2.33 (3H, s, Me-Ph-), 2.50 (1H, ddd, H-5, $J_{5,4b}=4.6$, $J_{5,6a}=4.8$, $J_{5,6b}=7.8$ Hz), 4.22 (1H, d, H-4a, $J_{4a,4b}=9.2$ Hz), 4.40 (1H, dd, H-4b, $J_{4b,2}=4.6$, $J_{4b,4a}=9.2$ Hz), 7.08 (1H, m, aromatic), 7.17–7.23 (3H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.76 (C-6), 21.15 (Me–Ph–), 24.88 (C-5), 31.49 (C-1), 67.92 (C-4), 125.17, 128.23, 128.26, 128.97, 133.88, 138.01 (the above mentioned, aromatic), 175.98 (C=O); HR-MS (EI) calcd $C_{12}H_{12}O_2$ 188.0837; obs 188.0851 (M^+). Anal. calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.64; H, 6.51.

(1*S*,5*R*)-2-Oxo-1-(4-methylphenyl)-3-oxabicyclo[3.1.0]-hexane (25g). Compound **25g** with 95% ee (CHIRALCEL OJ, 0.46×25 cm, Daicel; hexane/EtOH, 9:1; 0.5 mL/min; 265 nm) was obtained as an oil in 47% yield: $[\alpha]_D^{22}$ −74.89 (*c* 2.075, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.24 (1H, dd, H-6a, $J_{6a,6b}=4.8$, $J_{6a,5}=4.8$ Hz), 1.54 (1H, dd, H-6b, $J_{6b,6a}=4.8$, $J_{6b,5}=7.8$ Hz), 2.30 (3H, s, Me–Ph–), 2.45 (1H, ddd, H-5, $J_{5,4b}=4.7$, $J_{5,6a}=4.8$, $J_{5,6b}=7.8$ Hz), 4.18 (1H, d, H-4a, $J_{4a,4b}=9.3$ Hz), 4.36 (1H, dd, H-4b, $J_{4b,5}=4.7$, $J_{4b,4a}=9.3$ Hz), 7.12 (2H, d, aromatic, $J=8.0$ Hz), 7.27 (2H, m, aromatic, $J=8.0$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.64 (C-6), 20.73 (Me–Ph–), 24.70 (C-5), 31.14 (C-1), 67.82 (C-4), 127.99, 128.90, 130.91, 136.99 (the above mentioned, aromatic), 175.99 (C=O); HR-MS (EI) calcd $C_{12}H_{12}O_2$ 188.0837; obs 188.0842 (M^+). Anal. calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.46; H, 6.44.

(1*S*,5*R*)-2-Oxo-1-(1-naphthyl)-3-oxabicyclo[3.1.0]hexane (25h). Compound **25h** with 96% ee (CHIRALCEL OJ, 0.46×25 cm, Daicel; hexane/EtOH, 3:2; 0.5 mL/min; 265 nm) was obtained as crystals in 50% yield: mp (hexane, AcOEt, EtOH, $CHCl_3$) 172–173 °C; $[\alpha]_D^{24}$ +72.43 (*c* 1.555, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.53 (1H, dd, H-6a, $J_{6a,6b}=4.8$, $J_{6a,5}=4.8$ Hz), 1.76 (1H, dd, H-6b, $J_{6b,6a}=4.8$, $J_{6b,5}=7.7$ Hz), 2.54 (1H, ddd, H-5, $J_{5,6a}=4.8$, $J_{5,4b}=5.0$, $J_{5,6b}=7.7$ Hz), 4.45 (1H, d, H-4a, $J_{4a,4b}=9.5$ Hz), 4.74 (1H, dd, H-4b, $J_{4b,5}=5.0$, $J_{4b,4a}=9.5$ Hz), 7.42–7.58 (4H, m, aromatic), 7.82–7.89 (2H, m, aromatic), 7.97 (1H, d, aromatic, $J=8.4$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.71 (C-6), 24.75 (C-5), 31.29 (C-1), 68.36 (C-4), 124.05, 125.19, 126.05, 126.72, 128.48, 128.86, 129.26, 130.52, 132.67, 133.88 (the above mentioned, aromatic), 176.03 (C=O); HR-MS (EI) calcd $C_{15}H_{12}O_2$ 224.0837; obs 224.0837 (M^+). Anal. calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.28; H, 5.34.

(1*S*,5*R*)-2-Oxo-1-(2-naphthyl)-3-oxabicyclo[3.1.0]hexane (25i). Compound **25i** with 94% ee (CHIRALPAK AD-RH, 0.46×15 cm, Daicel; H_2O/CH_3CN, 3:2; 0.5 mL/min; 265 nm) was obtained as crystals in 45% yield: mp (hexane/AcOEt) 116 °C; $[\alpha]_D^{22}$ −64.51 (*c* 1.230, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.38 (1H, dd, H-6a, $J_{6a,6b}=4.8$, $J_{6a,5}=4.8$ Hz), 1.69 (1H, dd, H-6b, $J_{6b,6a}=4.8$, $J_{6b,5}=7.8$ Hz), 2.59 (1H, dd, H-5, $J_{5,4b}=4.6$, $J_{5,6a}=4.8$, $J_{5,6b}=7.8$ Hz), 4.27 (1H, d, H-4a, $J_{4a,4b}=9.3$ Hz), 4.74 (1H, dd, H-4b, $J_{4b,5}=4.6$, $J_{4b,4a}=9.3$ Hz), 7.43–7.48 (3H, m, aromatic), 7.78–7.81 (3H, m, aromatic), 7.88 (1H, d, aromatic, $J=0.7$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.16 (C-6), 25.15 (C-5), 31.80 (C-1), 68.04 (C-4), 125.92, 126.11, 126.28, 127.22, 127.53, 127.72, 128.29, 131.45, 132.59, 133.08 (the above mentioned, aromatic), 175.95 (C=O); HR-MS (EI) calcd $C_{15}H_{12}O_2$ 224.0837; obs 224.0817 (M^+). Anal. calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.38; H, 5.47.

General procedure for preparing compounds 26b–i. To a solution of **25b–i** (5.00 mmol) and $AlCl_3$ (1.33 g, 10.0 mmol) in CH_2Cl_2 (10 mL) was slowly added Et_2NH (2.08 mL, 20.0 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 8 h. The reaction was quenched with 1 N HCl, and then CH_2Cl_2 and H_2O was added and partitioned. The organic layer was washed with 1 N HCl and brine, dried (Na_2SO_4), evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:4, 3:7, 1:2, and 1:1) to give **26b–i**.

(1*S*,2*R*)-1-(2-Fluorophenyl)-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (26b). Compound **26b** was obtained as crystals quantitatively: mp (AcOEt, Hexane) 63–64 °C; $[\alpha]_D^{23}$ +42.79 (*c* 1.185, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.89 (3H, t, $-NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.09 (3H, t, $-NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.16 (1H, dd, H-3a, $J_{3a,3b}=5.0$, $J_{3a,2}=5.0$ Hz), 1.62–1.70 (2H, m, H-3b and H-2), 3.20 (1H, dd, H-1′a, $J_{1'a,\ 2}=10.0$, $J_{1'b,\ 1'a}=12.0$ Hz), 3.28 (1H, m, $-N\underline{CH_2}CH_3$), 3.38 (1H, m, $-N\underline{CH_2}CH_3$), 3.63 (2H, m, $-N\underline{CH_2}CH_3$), 4.04 (1H, dd, H-1′b, $J_{1'b,\ 2}=4.5$, $J_{1'b,\ 1'a}=12.0$ Hz), 7.00 (1H, m, aromatic), 7.11 (1H, m, aromatic), 7.22 (1H, m, aromatic), 7.50 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.34 ($-NCH_2\underline{CH_3}$), 13.23 ($-NCH_2\underline{CH_3}$), 16.66 (C-3, $J_{C,F}=15$ Hz), 29.57 (C-2), 30.63 (C-1), 39.89 ($-NCH_2CH_3$), 41.77 ($-N\underline{CH_2}CH_3$), 64.35 (C-1′), 116.06 (C-3″, $J_{C,F}=23$ Hz), 124.43 (C-6″, $J_{C,F}=4$ Hz), 127.22 (C-1″, $J_{C,F}=13$ Hz), 128.86 (C-4″, $J_{C,F}=9$ Hz), 131.26 (C-5″, $J_{C,F}=4$ Hz), 161.18 (C-2″, $J_{C,F}=248$ Hz), 170.38 (C=O); HR-MS (EI) calcd $C_{15}H_{20}FNO_2$ 265.1478; obs 265.1456 (M^+). Anal. calcd for $C_{15}H_{20}FNO_2$: C, 67.90; H, 7.60; N, 5.28. Found: C, 67.97; H, 7.64; N, 5.09.

(1*S*,2*R*)-1-(3-Fluorophenyl)-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (26c). Compound **26c** was obtained as crystals in 92% yield: mp (AcOEt, Hexane) 75–76 °C; $[\alpha]_D^{22}$ +63.11 (*c* 1.610, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (3H, t, $-NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.14 (1H, dd, H-3a, $J_{3a,3b}=5.5$, $J_{3a,2}=5.5$ Hz), 1.15 (3H, t, $-NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.57 (1H, dddd, H-2, $J_{2,1'b}=5.0$, $J_{2,3a}=5.5$, $J_{2,3b}=8.8$, $J_{2,1'a}=11.0$ Hz), 1.62 (1H, dd, H-3b, $J_{3b,3a}=5.5$, $J_{3a,2}=8.8$ Hz), 3.18 (1H, dd, H-1′a, $J_{1'a,\ 2}=11.0$, $J_{1'b,\ 1'a}=11.0$ Hz), 3.24–3.56 (4H, m, $-N\underline{CH_2}CH_3$), 4.02 (1H, ddd, H-1′b, $J_{1'b,\ 2}=5.0$, $J_{1'b,\ OH}=9.3$, $J_{1'b,\ 1'a}=11.0$ Hz), 4.69 (1H, d, –OH, $J_{OH,\ 1'b}=9.3$ Hz), 6.92 (2H, m, aromatic), 7.01 (1H, m, aromatic), 7.27 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.25 ($-NCH_2\underline{CH_3}$), 13.07 ($-NCH_2\underline{CH_3}$), 17.08 (C-3), 32.22 (C-2), 34.12 (C-1), 39.53 ($-N\underline{CH_2}CH_3$), 41.96 ($-N\underline{CH_2}CH_3$), 64.59 (C-1′), 112.67 (C-4″, $J_{C,F}=23$ Hz), 113.52 (C-2″, $J_{C,F}=21$ Hz),

121.25 (C-6″, $J_{C,F}=3$ Hz), 130.15 (C-5″, $J_{C,F}=9$ Hz), 143.05 (C-1″, $J_{C,F}=8$ Hz), 163.01 (C-3″, $J_{C,F}=245$ Hz), 170.57 (C=O); HR-MS (EI) calcd $C_{15}H_{20}FNO_2$ 265.1478; obs 265.1483 (M^+). Anal. calcd for $C_{15}H_{20}FNO_2$: C, 67.90; H, 7.60; N, 5.28. Found: C, 68.05; H, 7.67; N, 5.18.

(1*S*,2*R*)-1-(4-Fluorophenyl)-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (26d). Compound **26d** was obtained as an oil in 94% yield: $[\alpha]_D^{23}$ +63.64 (*c* 1.390, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.09 (1H, dd, H-3a, $J_{3a,3b}=5.5$, $J_{3a,2}=6.1$ Hz), 1.12 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.51 (1H, dddd, H-2, $J_{2,1'b}=4.8$, $J_{2,3a}=6.1$, $J_{2,3b}=8.8$, $J_{2,1'a}=11.7$ Hz), 1.60 (1H, dd, H-3b, $J_{3b,3a}=5.5$, $J_{3b,2}=8.8$ Hz), 3.16 (1H, dd, H-1′a, $J_{1'a,\ 2}=11.7$, $J_{1'b,\ 1'a}=11.7$ Hz), 3.32–3.43 (3H, m, –$N\underline{CH_2}CH_3$), 3.50 (3H, m, –$N\underline{CH_2}CH_3$), 4.02 (1H, ddd, H-1′b, $J_{1'b,\ 2}=4.8$, $J_{1'b,\ OH}=9.1$, $J_{1'b,\ 1'a}=11.7$ Hz), 4.73 (1H, d, –OH, $J_{OH,\ 1'b}=9.1$ Hz), 6.96–7.01 (2H, m, aromatic), 7.22–7.26 (2H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.28 (–$NCH_2\underline{CH_3}$), 13.13 (–$NCH_2\underline{CH_3}$), 16.55 (C-3), 31.55 (C-2), 33.87 (C-1), 39.53 (–$N\underline{CH_2}CH_3$), 41.89 (–$N\underline{CH_2}CH_3$), 64.69 (C-1′), 115.47 (C-3″ and C-5″, $J_{C,F}=23$ Hz), 127.64 (C-2″ and C-6″, $J_{C,F}=8$ Hz), 136.01 (C-1″, $J_{C,F}=4$ Hz), 161.54 (C-4″, $J_{C,F}=244$ Hz), 170.95 (C=O); HR-MS (EI) calcd $C_{15}H_{20}FNO_2$ 265.1478; obs 265.1464 (M^+). Anal. calcd for $C_{15}H_{20}FNO_2$: C, 67.90; H, 7.60; N, 5.28. Found: C, 67.71; H, 7.57; N, 5.12.

(1*S*,2*R*)-1-(2-Methylphenyl)-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (26e). Compound **26e** was obtained as an oil in 95% yield: $[\alpha]_D^{23}$ +31.91 (*c* 2.025, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.55 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.07 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.31 (1H, dd, H-3a, $J_{3a,3b}=4.8$, $J_{3a,2}=6.0$ Hz), 1.62 (1H, dd, H-3b, $J_{3b,3a}=4.8$, $J_{3b,2}=8.8$ Hz), 1.72 (1H, dddd, H-2, $J_{2,1'b}=5.3$, $J_{2,3a}=6.0$, $J_{2,3b}=8.8$, $J_{2,1'a}=9.7$ Hz), 2.49 (3H, s, Me—Ph–), 3.22–3.30 (2H, m, –$N\underline{CH_2}CH_3$), 3.41 (1H, dd, H-1′a, $J_{1'a,\ 2}=9.7$, $J_{1'b,\ 1'a}=12.0$ Hz), 3.47 (1H, m, –$N\underline{CH_2}CH_3$), 3.55 (1H, m, –$N\underline{CH_2}CH_3$), 4.02 (1H, dd, H-1′b, $J_{1'b,\ 2}=5.3$, $J_{1'b,\ 1'a}=12.0$ Hz), 7.13–7.15 (3H, m, aromatic), 7.27 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.44 (–$NCH_2\underline{CH_3}$), 12.79 (–$NCH_2\underline{CH_3}$), 16.90 (C-3), 20.24 (Me–Ph–), 28.35 (C-2), 34.47 (C-1), 40.55 (–$N\underline{CH_2}CH_3$), 42.11 (–$N\underline{CH_2}CH_3$), 63.95 (C-1′), 125.74, 127.07, 128.46, 130.99, 138.62, 140.28 (the above mentioned, aromatic), 170.18 (C=O); HR-MS (EI) calcd $C_{16}H_{23}NO_2$ 261.1729; obs 261.1728 (M^+). Anal. calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.25; H, 8.94; N, 5.33.

(1*S*,2*R*)-1-(3-Methylphenyl)-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (26f). Compound **26f** was obtained as an oil in 88% yield: $[\alpha]_D^{23}$ +54.12 (*c* 2.620, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.07 (1H, dd, H-3a, $J_{3a,3b}=5.3$, $J_{3a,2}=5.3$ Hz), 1.14 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.55 (1H, dddd, H-2, $J_{2,1'b}=4.8$, $J_{2,3a}=5.3$, $J_{2,3b}=8.8$, $J_{2,1'a}=10.4$ Hz), 1.62 (1H, dd, H-3b, $J_{3b,3a}=5.3$, $J_{3b,2}=8.8$ Hz), 2.31 (3H, s, Me–Ph–), 3.18 (1H, dd, H-1′a, $J_{1'a,\ 2}=10.4$, $J_{1'b,\ 1'a}=12.2$ Hz), 3.32–3.45 (3H, m, –$N\underline{CH_2}CH_3$), 3.52 (1H, m, –$N\underline{CH_2}CH_3$), 4.02 (1H, dd, H-1′b, $J_{1'b,\ 2}=4.8$, $J_{1'b,\ 1'a}=12.2$ Hz), 7.01–7.06 (3H, m, aromatic), 7.17 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.23 (–$NCH_2\underline{CH_3}$), 13.02 (–$NCH_2\underline{CH_3}$), 16.66 (C-3), 21.33 (Me–Ph–), 31.61 (C-2), 34.25 (C-1), 39.40 (–$N\underline{CH_2}CH_3$), 41.88 (–$N\underline{CH_2}CH_3$), 64.76 (C-1′), 122.58, 126.56, 127.28, 128.43, 138.19, 140.14 (the above mentioned, aromatic), 171.23 (C=O); HR-MS (EI) calcd $C_{16}H_{23}NO_2$ 261.1729; obs 261.1719 (M^+). Anal. calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.16; H, 8.91; N, 5.44.

(1*S*,2*R*)-1-(4-Methylphenyl)-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (26g). Compound **26g** was obtained as an oil in 89% yield: $[\alpha]_D^{22}$ +50.46 (*c* 3.620, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.92 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.05 (1H, dd, H-3a, $J_{3a,3b}=5.2$, $J_{3a,2}=5.2$ Hz), 1.13 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.51 (1H, dddd, H-2, $J_{2,1'b}=4.8$, $J_{2,3a}=5.2$, $J_{2,3b}=8.7$, $J_{2,1'a}=10.4$ Hz), 1.61 (1H, dd, H-3b, $J_{3b,3a}=5.2$, $J_{3b,2}=8.7$ Hz), 2.31 (3H, s, Me–Ph–), 3.15 (1H, dd, H-1′a, $J_{1'a,\ 2}=11.7$, $J_{1'b,\ 1'a}=11.7$ Hz), 3.32–3.44 (3H, m, –$N\underline{CH_2}CH_3$), 3.52 (1H, m, –$N\underline{CH_2}CH_3$), 4.03 (1H, dd, H-1′b, $J_{1'b,\ 2}=4.8$, $J_{1'b,\ 1'a}=11.7$ Hz), 7.09–7.13 (4H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.26 (–$NCH_2\underline{CH_3}$), 13.07 (–$NCH_2\underline{CH_3}$), 16.54 (C-3), 20.81 (Me–Ph–), 31.51 (C-2), 34.05 (C-1), 39.41 (–$N\underline{CH_2}CH_3$), 41.87 (–$N\underline{CH_2}CH_3$), 64.78 (C-1′), 125.65, 129.24, 136.13, 137.22 (the above mentioned, aromatic), 171.28 (C=O); HR-MS (EI) calcd $C_{16}H_{23}NO_2$ 261.1729; obs 261.1728 (M^+). Anal. calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.53; H, 8.87; N, 5.36.

(1*S*,2*R*)-1-(1-Naphthyl)-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (26h). Compound **26h** was obtained as crystals in 67% yield: mp (hexane/AcOEt) 136 °C; $[\alpha]_D^{22}$ −28.91 (*c* 1.580, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.46 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.0$ Hz), 0.99 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.0$ Hz), 1.46 (1H, dd, H-3a, $J_{3a,3b}=5.0$, $J_{3a,2}=8.5$ Hz), 1.52 (1H, dd, H-3b, $J_{3b,3a}=5.0$, $J_{3b,2}=5.0$ Hz), 1.92 (1H, m, H-2), 3.21 (2H, m, –$N\underline{CH_2}CH_3$), 3.49–3.58 (2H, m, H-1′a and –$N\underline{CH_2}CH_3$), 3.70 (1H, m, –$N\underline{CH_2}CH_3$), 4.11 (1H, m, H-1′b), 7.41 (1H, t, aromatic, $J=7.7$ Hz), 7.49 (1H, m, aromatic), 7.58 (1H, m, aromatic), 7.77 (1H, d, aromatic, $J=8.2$ Hz), 7.83 (1H, d, aromatic, $J=8.2$ Hz), 7.41 (1H, d, aromatic, $J=8.2$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.23 (–$NCH_2\underline{CH_3}$), 12.72 (–$NCH_2\underline{CH_3}$), 17.32 (C-3), 27.72 (C-2), 34.26 (C-1), 40.51 (–$N\underline{CH_2}CH_3$), 42.16 (–$N\underline{CH_2}CH_3$), 63.49 (C-1′), 124.89, 125.61, 125.86, 126.13, 126.33, 128.01, 128.16, 133.38, 133.82, 136.92 (the above mentioned, aromatic), 170.39 (C=O); HR-MS (EI) calcd C19H23NO2 297.1729; obs 297.1730 (M+). Anal. calcd for C19H23NO2: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.75; H, 7.72; N, 4.66.

(1*S*,2*R*)-1-(2-Naphthyl)-2-(hydroxymethyl)-*N*,*N*-diethylcyclopropanecarboxamide (26i). Compound **26i** was obtained as crystals in 91% yield: mp (hexane/AcOEt) 161–162 °C; $[\alpha]_D^{23}$ +61.76 (*c* 1.325, $CHCl_3$); ^{1}H NMR

(500 MHz, $CDCl_3$) δ 0.88 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.15 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.17 (1H, dd, H-3a, $J_{3a,3b}$ = 5.5, $J_{3a,2}$ = 5.5 Hz), 1.64 (1H, ddd, H-2, $J_{2,3a}$ = 5.5, $J_{2,1'b}$ = 8.5, $J_{2,3b}$ = 8.8, $J_{2,1'a}$ = 11.2 Hz), 1.79 (1H, dd, H-3b, $J_{3b,3a}$ = 5.5, $J_{3b,2}$ = 8.8 Hz), 3.23 (1H, dd, H-1′a, $J_{1'a,\ 2}$ = 8.8, $J_{1'a,\ 1'b}$ = 11.2 Hz), 3.33–3.48 (3H, m, –$N\underline{CH_2}CH_3$), 3.57 (1H, m, –$N\underline{CH_2}CH_3$), 4.07 (1H, m, H-1′b, $J_{1'b,\ 2}$ = 8.5, $J_{1'b,\ 1'a}$ = 11.2 Hz), 4.78 (1H, bs, –OH), 7.42–7.48 (3H, m, aromatic), 7.64 (1H, s, aromatic), 7.76–7.80 (3H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.35 (–$NCH_2\underline{CH_3}$), 13.19 (–$NCH_2\underline{CH_3}$), 16.64 (C-3), 31.87 (C-2), 34.67 (C-1), 39.55 (–$N\underline{CH_2}CH_3$), 41.96 (–$N\underline{CH_2}CH_3$), 64.85 (C-1′), 124.20, 124.41, 125.78, 126.26, 127.53, 127.61, 128.49, 132.21, 133.35, 137.77 (the above mentioned, aromatic), 171.14 (C=O); HR-MS (EI) calcd $C_{19}H_{23}NO_2$ 297.1729; obs 297.1733 (M^+). Anal. calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.48; H, 7.79; N, 4.70.

General procedure for preparing compounds 27b–i. To a solution of oxalyl chloride (3.49 mL, 40.0 mmol) in CH_2Cl_2 (30 mL) was slowly added a mixture of DMSO (6.19 mL, 80.0 mmol) in CH_2Cl_2 (20 mL) at −78 °C, and then **26b–i** (20.0 mmol) in CH_2Cl_2 (10 mL) was added dropwise. The resulting mixture was stirred at the same temperature for 2 h, and then Et_3N was added. After stirring at −78 °C for further 30 min, the reaction was quenched with saturated NH_4Cl, and then CH_2Cl_2 was added and partitioned. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:4) to give **29b–i** as an oil.

(1*S*,2*R*)-1-(2-Fluorophenyl)-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (27b). Compound **27b** was obtained as an oil in 87% yield: $[\alpha]_D^{22}$ −130.50 (*c* 2.375, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.66 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.07 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.75 (1H, dd, H-3a, $J_{3a,3b}$ = 5.4, $J_{3a,2}$ = 8.6 Hz), 2.39 (1H, dd, H-3b, $J_{3b,3a}$ = 5.4, $J_{3b,2}$ = 5.4 Hz), 2.57 (1H, ddd, H-2, $J_{2,3b}$ = 5.4, $J_{2,1'}$ = 6.1, $J_{2,3a}$ = 8.6 Hz), 3.21–3.31 (2H, m, –$N\underline{CH_2}CH_3$), 3.51 (1H, m, –$N\underline{CH_2}CH_3$), 3.51 (1H, m, –$N\underline{CH_2}CH_3$), 7.06 (1H, m, aromatic), 7.15 (1H, m, aromatic), 7.29 (1H, m, aromatic), 7.41 (1H, m, aromatic), 9.08 (1H, d, H-1′, $J_{1',\ 2}$ = 6.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.18 (–$NCH_2\underline{CH_3}$), 12.74 (–$NCH_2\underline{CH_3}$), 19.66 (C-3, $J_{C,F}$ = 9.5 Hz), 35.22 (C-2), 36.08 (C-1), 40.15 (–$N\underline{CH_2}CH_3$), 41.33 (–$N\underline{CH_2}CH_3$), 116.33 (C-3″, $J_{C,F}$ = 21 Hz), 124.67 (C-6″, $J_{C,F}$ = 4 Hz), 125.38 (C-1″, $J_{C,F}$ = 13 Hz), 129.56 (C-4″, $J_{C,F}$ = 9 Hz), 129.84 (C-5″, $J_{C,F}$ = 4 Hz), 161.00 (C-2″, $J_{C,F}$ = 249 Hz), 166.79 (C=O), 198.29 (C-1′); HR-MS (EI) calcd $C_{15}H_{18}FNO_2$ 263.1321; obs 263.1330 (M^+). Anal. calcd for $C_{15}H_{18}FNO_2$: C, 68.42; H, 6.89; N, 5.32. Found: C, 68.48; H, 6.90; N, 5.10.

(1*S*,2*R*)-1-(3-Fluorophenyl)-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (27c). Compound **27c** was obtained as crystals in 87% yield: mp (AcOEt, Hexane) 68–69 °C; $[\alpha]_D^{22}$ −136.91 (*c* 3.300, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.77 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.12 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.74 (1H, dd, H-3a, $J_{3a,3b}$ = 5.6, $J_{3a,2}$ = 8.4 Hz), 2.27 (1H, dd, H-3b, $J_{3b,3a}$ = 5.6, $J_{3b,2}$ = 5.6 Hz), 2.45 (1H, ddd, H-2, $J_{2,3b}$ = 5.6, $J_{2,1'}$ = 5.9, $J_{2,3a}$ = 8.4 Hz), 3.21 (1H, m, –$N\underline{CH_2}CH_3$), 3.28 (1H, m, –$N\underline{CH_2}CH_3$), 3.37–3.49 (2H, m, –$N\underline{CH_2}CH_3$), 6.98 (2H, m, aromatic), 7.06 (1H, m, aromatic), 7.32 (1H, m, aromatic), 9.07 (1H, d, H-1′, $J_{1',\ 2}$ = 5.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.20 (–$NCH_2\underline{CH_3}$), 12.82 (–$NCH_2\underline{CH_3}$), 20.06 (C-3), 36.48 (C-2), 39.66 (–$N\underline{CH_2}CH_3$), 39.70 (C-1, $J_{C,F}$ = 10 Hz), 41.54 (–$N\underline{CH_2}CH_3$), 113.02 (C-4″, $J_{C,F}$ = 23 Hz), 114.53 (C-2″, $J_{C,F}$ = 21 Hz), 121.51 (C-6″, $J_{C,F}$ = 3 Hz), 130.57 (C-5″, $J_{C,F}$ = 9 Hz), 140.59 (C-1″, $J_{C,F}$ = 8 Hz), 163.06 (C-3″, $J_{C,F}$ = 246 Hz), 166.83 (C=O), 197.55 (C-1′); HR-MS (EI) calcd $C_{15}H_{18}FNO_2$ 263.1321; obs 263.1315 (M^+). Anal. calcd for $C_{15}H_{18}FNO_2$: C, 68.42; H, 6.89; N, 5.32. Found: C, 68.32; H, 6.98; N, 5.33.

(1*S*,2*R*)-1-(4-Fluorophenyl)-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (27d). Compound **27d** was obtained as an oil in 82% yield: $[\alpha]_D^{22}$ −125.10 (*c* 3.365, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.75 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.10 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.73 (1H, dd, H-3a, $J_{3a,3b}$ = 5.5, $J_{3a,2}$ = 8.4 Hz), 2.25 (1H, dd, H-3b, $J_{3b,3a}$ = 5.5, $J_{3b,2}$ = 5.5 Hz), 2.42 (1H, ddd, H-2, $J_{2,3b}$ = 5.5, $J_{2,1'}$ = 6.1, $J_{2,3a}$ = 8.4 Hz), 3.19–3.30 (2H, m, –$N\underline{CH_2}CH_3$), 3.38–3.47 (2H, m, –$N\underline{CH_2}CH_3$), 7.00–7.08 (2H, m, aromatic), 7.26–7.31 (2H, m, aromatic), 9.06 (1H, d, H-1′, $J_{1',\ 2}$ = 6.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.18 (–$NCH_2\underline{CH_3}$), 12.81 (–$NCH_2\underline{CH_3}$), 19.80 (C-3), 36.32 (C-2), 39.55 (C-1), 39.63 (–$N\underline{CH_2}CH_3$), 41.45 (–$N\underline{CH_2}CH_3$), 115.86 (C-3″ and C-5″, $J_{C,F}$ = 23 Hz), 127.79 (C-2″ and C-6″, $J_{C,F}$ = 8 Hz), 133.77 (C-1″, $J_{C,F}$ = 3 Hz), 161.94 (C-4″, $J_{C,F}$ = 245 Hz), 167.16 (C=O), 197.77 (C-1′); HR-MS (EI) calcd $C_{15}H_{18}FNO_2$ 263.1321; obs 263.1310 (M^+). Anal. calcd for $C_{15}H_{18}FNO_2$: C, 68.42; H, 6.89; N, 5.32. Found: C, 68.48; H, 6.96; N, 5.20.

(1*S*,2*R*)-1-(2-Methylphenyl)-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (27e). Compound **27e** was obtained as an oil in 79% yield: $[\alpha]_D^{22}$ −114.64 (*c* 2.620, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.42 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.06 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.56 (1H, dd, H-3a, $J_{3a,3b}$ = 5.5, $J_{3a,2}$ = 8.7 Hz), 2.41 (3H, s, Me–Ph–), 2.46 (2H, m, H-3b and H-2), 3.13–3.21 (2H, m, –$N\underline{CH_2}CH_3$), 3.36 (1H, m, –$N\underline{CH_2}CH_3$), 3.49 (1H, m, –$N\underline{CH_2}CH_3$), 7.16–7.26 (4H, m, aromatic), 9.06 (1H, d, H-1′, $J_{1',\ 2}$ = 6.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.36 (–$NCH_2\underline{CH_3}$), 12.55 (–$NCH_2\underline{CH_3}$), 19.38 (C-3), 19.89 (Me–Ph–), 35.69 (C-2), 39.92 (C-1), 41.01 (–$N\underline{CH_2}CH_3$), 41.77 (–$N\underline{CH_2}CH_3$), 126.05, 127.67, 127.69, 131.10, 136.62, 138.98 (the above mentioned, aromatic), 167.25 (C=O), 199.08 (C-1′); HR-MS (EI) calcd $C_{16}H_{23}NO_2$ 259.1572; obs 259.1573 (M^+). Anal. calcd for $C_{16}H_{23}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.22; H, 8.06; N, 5.28.

(1*S*,2*R*)-1-(3-Methylphenyl)-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (27f). Compound **27f** was obtained as an oil in 94% yield: $[\alpha]_D^{23}$ −141.04 (*c* 2.795, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.71 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.10 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.70 (1H, dd, H-3a, $J_{3a,3b}$ = 5.5, $J_{3a,2}$ = 8.5 Hz), 2.26 (1H, dd,

H-3b, $J_{3b,3a}=5.5$, $J_{3b,2}=5.5$ Hz), 2.33 (3H, s, Me–Ph–), 2.48 (1H, ddd, H-2, $J_{2,3b}=5.5$, $J_{2,1'}=6.2$, $J_{2,3a}=8.5$ Hz), 3.18 (1H, m, –NCH$_2$CH$_3$), 3.26 (1H, m, –NCH$_2$CH$_3$), 3.38–3.44 (2H, m, –NCH$_2$CH$_3$), 7.03–7.09 (3H, s, aromatic), 7.22 (1H, s, aromatic), 9.04 (1H, d, H-1′, $J_{1',2}=6.2$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.13 (–NCH$_2$CH$_3$), 12.66 (–NCH$_2$CH$_3$), 19.92 (C-3), 21.24 (Me–Ph–), 36.22 (C-2), 39.51 (–NCH$_2$CH$_3$), 39.97 (C-1), 41.43 (–NCH$_2$CH$_3$), 122.68, 126.65, 128.14, 128.73, 137.75, 138.61 (the above mentioned, aromatic), 167.44 (C=O), 198.10 (C-1′); HR-MS (EI) calcd $C_{16}H_{23}NO_2$ 259.1572; obs 259.1595 (M^+). Anal. calcd for $C_{16}H_{23}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.43; H, 8.24; N, 5.35.

(1*S*,2*R*)-1-(4-Methylphenyl)-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (27g). Compound **27g** was obtained as an oil in 81% yield: $[\alpha]_D^{22}$ −138.88 (*c* 3.465, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.72 (3H, t, –NCH$_2$CH$_3$, $J=7.1$ Hz), 1.10 (3H, t, –NCH$_2$CH$_3$, $J=7.1$ Hz), 1.70 (1H, dd, H-3a, $J_{3a,3b}=5.5$, $J_{3a,2}=8.2$ Hz), 2.23 (1H, dd, H-3b, $J_{3b,3a}=5.5$, $J_{3b,2}=5.5$ Hz), 2.33 (3H, s, Me–Ph–), 2.44 (1H, ddd, H-2, $J_{2,3b}=5.5$, $J_{2,1'}=6.2$, $J_{2,3a}=8.2$ Hz), 3.19 (1H, m, –NCH$_2$CH$_3$), 3.26 (1H, m, –NCH$_2$CH$_3$), 3.38–3.48 (2H, m, –NCH$_2$CH$_3$), 7.14 (4H, s, aromatic), 9.04 (1H, d, H-1′, $J_{1',2}=6.2$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.20 (–NCH$_2$CH$_3$), 12.75 (–NCH$_2$CH$_3$), 19.94 (C-3), 20.87 (Me–Ph–), 36.29 (C-2), 39.55 (–NCH$_2$CH$_3$), 39.83 (C-1), 41.46 (–NCH$_2$CH$_3$), 125.75, 129.55, 134.88, 137.20 (the above mentioned, aromatic), 167.51 (C=O), 198.17 (C-1′); HR-MS (EI) calcd $C_{16}H_{23}NO_2$ 259.1572; obs 259.1575 (M^+). Anal. calcd for $C_{16}H_{23}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.16; H, 8.14; N, 5.35.

(1*S*,2*R*)-1-(1-Naphthyl)-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (27h). Compound **27h** was obtained as crystals in 73% yield: mp (hexane/AcOEt) 109 °C; $[\alpha]_D^{22}$ −79.36 (*c* 2.235, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.35 (3H, t, –NCH$_2$CH$_3$, $J=7.0$ Hz), 0.97 (3H, t, –NCH$_2$CH$_3$, $J=7.0$ Hz), 1.66 (1H, bs, H-3a), 2.46 (2H, bs, H-3b and H-2), 3.07 (1H, m, –NCH$_2$CH$_3$), 3.24 (1H, m, –NCH$_2$CH$_3$), 3.33 (1H, m, –NCH$_2$CH$_3$), 3.65 (1H, m, –NCH$_2$CH$_3$), 7.43 (1H, t, aromatic, $J=7.5$ Hz), 7.48 (1H, d, aromatic, $J=6.3$ Hz), 7.53 (1H, m, aromatic), 7.59 (1H, m, aromatic), 7.81 (1H, d, aromatic, $J=8.0$ Hz), 7.86 (1H, d, aromatic, $J=8.0$ Hz), 8.66 (1H, d, aromatic, $J=8.5$ Hz), 9.15 (1H, d, H-1′, $J_{1',2}=5.9$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.23 (–NCH$_2$CH$_3$), 12.75 (–NCH$_2$CH$_3$), 19.80 (C-3), 35.63 (C-2), 39.40 (C-1), 40.91 (–NCH$_2$CH$_3$), 41.71 (–NCH$_2$CH$_3$), 124.96, 125.26, 125.58, 126.30, 126.99, 128.39, 128.79, 133.07, 133.92, 134.67 (the above mentioned, aromatic), 167.48 (C=O), 198.85 (C-1′); HR-MS (EI) calcd $C_{19}H_{21}NO_2$ 295.1572; obs 295.1545 (M^+). Anal. calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.36; H, 6.99; N, 4.71.

(1*S*,2*R*)-1-(2-Naphthyl)-2-formyl-*N*,*N*-diethylcyclopropanecarboxamide (27i). Compound **27i** was obtained as crystals in 85% yield: mp (hexane/AcOEt) 90–91 °C; $[\alpha]_D^{22}$ −192.74 (*c* 1.505, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.67 (3H, t, –NCH$_2$CH$_3$, $J=7.1$ Hz), 1.12 (3H, t, –NCH$_2$CH$_3$, $J=7.1$ Hz), 1.83 (1H, dd, H-3a, $J_{3a,3b}=5.5$, $J_{3a,2}=8.3$ Hz), 2.34 (1H, dd, H-3b, $J_{3b,3a}=5.5$, $J_{3b,2}=5.5$ Hz), 2.59 (1H, ddd, H-2, $J_{2,3b}=5.5$, $J_{2,1'}=6.1$, $J_{2,3a}=8.3$ Hz), 3.19–3.32 (2H, m, –NCH$_2$CH$_3$), 3.43–3.51 (2H, m, –NCH$_2$CH$_3$), 7.41 (1H, dd, aromatic, $J=1.5$, $J=8.3$ Hz), 7.46–7.51 (2H, m, aromatic), 7.69 (1H, s, aromatic), 7.78–7.83 (3H, m, aromatic), 9.12 (1H, d, H-1′, $J_{1',2}=6.1$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.24 (–NCH$_2$CH$_3$), 12.83 (–NCH$_2$CH$_3$), 20.09 (C-3), 36.35 (C-2), 39.64 (–NCH$_2$CH$_3$), 40.31 (C-1), 41.52 (–NCH$_2$CH$_3$), 124.07, 124.47, 126.25, 126.56, 127.57, 127.67, 128.87, 132.47, 133.25, 135.37 (the above mentioned, aromatic), 167.33 (C=O), 198.03 (C-1′); HR-MS (EI) calcd $C_{19}H_{21}NO_2$ 295.1572; obs 295.1581 (M^+). Anal. calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.17; H, 7.27; N, 4.83.

General procedure for preparing compounds 28b–i. A mixture of **28b–i** (10.0 mmol) and EtMgBr (3.00 M in Et_2O, 13.3 mL, 40.0 mmol) in THF (20 mL) was stirred at −15 °C for 4 h. The reaction was quenched with saturated NH_4Cl, and the resulting mixture was concentrated in vacuo (for removing THF and Et_2O), to which AcOEt and H_2O was added and partitioned. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated The reside was purified by column chromatography (silica gel; AcOEt/hexane 1:4) to give **30b–i**.

(1*S*,2*R*)-1-(2-Fluorophenyl)-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (28b). Compound **28b** was obtained as crystals in 77% yield: mp (AcOEt, Hexane) 105–106 °C; $[\alpha]_D^{22}$ +61.13 (*c* 2.335, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (3H, t, –NCH$_2$CH$_3$, $J=7.1$ Hz), 1.00 (3H, t, H-3′, $J_{3',2'}=7.5$ Hz), 1.08 (3H, t, –NCH$_2$CH$_3$, $J=7.1$ Hz), 1.12 (1H, dd, H-3a, $J_{3a,3b}=5.5$, $J_{3a,2}=5.5$ Hz), 1.35 (1H, ddd, H-2, $J_{2,3a}=5.5$, $J_{2,3b}=8.8$, $J_{2,1}=8.8$ Hz), 1.60–1.72 (2H, m, H-2′), 1.76 (1H, dd, H-3b, $J_{3b,3a}=5.5$, $J_{3b,2}=8.8$ Hz), 3.08 (1H, m, H-1′), 3.28 (1H, m, –NCH$_2$CH$_3$), 3.40 (1H, m, –NCH$_2$CH$_3$), 3.63–3.68 (2H, m, –NCH$_2$CH$_3$), 5.26 (1H, bs, –OH), 6.99 (1H, m, aromatic), 7.09 (1H, m, aromatic), 7.21 (1H, m, aromatic), 7.51 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.23 (C-3′), 12.38 (–NCH$_2$CH$_3$), 13.35 (–NCH$_2$CH$_3$), 17.03 (C-3, $J_{C,F}=17$ Hz), 29.23 (C-2′), 29.66 (C-1), 34.31 (C-2), 39.82 (–NCH$_2$CH$_3$), 41.78 (–NCH$_2$CH$_3$), 75.27 (C-1′), 116.05 (C-3″, $J_{C,F}=23$ Hz), 124.44 (C-6″, $J_{C,F}=4$ Hz), 127.26 (C-1″, $J_{C,F}=11$ Hz), 128.84 (C-4″, $J_{C,F}=9$ Hz), 131.62 (C-5″, $J_{C,F}=4$ Hz), 161.12 (C-2″, $J_{C,F}=246$ Hz), 170.71 (C=O); HR-MS (EI) calcd $C_{17}H_{24}FNO_2$ 293.1791; obs 293.1795 (M^+). Anal. calcd for $C_{17}H_{24}FNO_2$: C, 69.60; H, 8.25; N, 4.77. Found: C, 69.68; H, 8.24; N, 4.82.

(1*S*,2*R*)-1-(3-Fluorophenyl)-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (28c). Compound **28c** was obtained as an oil in 83% yield: $[\alpha]_D^{22}$ +72.50 (*c* 3.000, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.96 (3H, t, –NCH$_2$CH$_3$, $J=7.1$ Hz), 1.00 (3H, t, H-3′, $J_{3',2'}=7.4$ Hz), 1.10 (1H, dd, H-3a, $J_{3a,3b}=6.1$, $J_{3a,2}=6.1$ Hz), 1.15 (3H, t, –NCH$_2$CH$_3$, $J=7.1$ Hz), 1.27 (1H, ddd, H-2, $J_{2,3a}=6.0$, $J_{2,3b}=9.4$, $J_{2,1'}=9.4$ Hz), 1.60–1.74 (3H,

m, H-3b and H-2′), 3.07 (1H, m, H-1′), 3.33–3.53 (4H, m, –NCH$_2$CH$_3$), 5.38 (1H, s,–OH), 6.91 (2H, m, aromatic), 7.01 (1H, m, aromatic), 7.26 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.22 (C-3′), 12.29 (–NCH$_2$CH$_3$), 13.15 (–NCH$_2$CH$_3$), 17.42 (C-3), 29.07 (C-2′), 33.12 (C-1, $J_{C,F}$ = 10 Hz), 37.07 (C-2), 39.50 (–NCH$_2$CH$_3$), 41.95 (–NCH$_2$CH$_3$), 75.57 (C-1′), 112.64 (C-4″, $J_{C,F}$ = 23 Hz), 113.50 (C-2″, $J_{C,F}$ = 21 Hz), 121.27 (C-6″, $J_{C,F}$ = 3 Hz), 130.15 (C-5″, $J_{C,F}$ = 9 Hz), 143.14 (C-1″, $J_{C,F}$ = 6 Hz), 163.05 (C-3″, $J_{C,F}$ = 244 Hz), 170.88 (C=O); HR-MS (EI) calcd $C_{17}H_{24}FNO_2$ 293.1791; obs 293.1820 (M^+). Anal. calcd for $C_{17}H_{24}FNO_2$: C, 69.60; H, 8.25; N, 4.77. Found: C, 69.73; H, 8.29; N, 4.81.

(1*S*,2*R*)-1-(4-Fluorophenyl)-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (28d). Compound **28d** was obtained as an oil in 94% yield: $[\alpha]_D^{22}$ +75.68 (*c* 2.530, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (3H, t, –NCH$_2$CH$_3$, *J* = 7.1 Hz), 1.00 (3H, t, H-3′, $J_{3',\ 2'}$ = 7.5 Hz), 1.06 (1H, dd, H-3a, $J_{3a,3b}$ = 6.0, $J_{3a,2}$ = 6.0 Hz), 1.13 (3H, t, –NCH$_2$CH$_3$, *J* = 7.1 Hz), 1.51 (1H, ddd, H-2, $J_{2,3a}$ = 6.0, $J_{2,3b}$ = 9.2, $J_{2,1'}$ = 9.2 Hz), 1.59–1.73 (3H, m, H-3b and H-2′), 3.05 (1H, m, H-1′), 3.32–3.44 (3H, m, –NCH$_2$CH$_3$), 3.52 (1H, m, –NCH$_2$CH$_3$), 5.43 (1H, s,–OH), 6.96–7.01 (2H, m, aromatic), 7.22–7.25 (2H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.22 (C-3′), 12.30 (–NCH$_2$CH$_3$), 13.18 (–NCH$_2$CH$_3$), 16.87 (C-3), 29.07 (C-2′), 32.82 (C-1), 36.33 (C-2), 39.47 (–NCH$_2$CH$_3$), 41.87 (–NCH$_2$CH$_3$), 75.60 (C-1′), 115.45 (C-3″ and C-5″, $J_{C,F}$ = 8 Hz), 127.64 (C-2″ and C-6″, $J_{C,F}$ = 8 Hz), 136.06 (C-1″, $J_{C,F}$ = 1 Hz), 161.53 (C-4″, $J_{C,F}$ = 245 Hz), 171.23 (C=O); HR-MS (EI) calcd $C_{17}H_{24}FNO_2$ 293.1791; obs 293.1766 (M^+). Anal. calcd for $C_{17}H_{24}FNO_2$: C, 69.60; H, 8.25; N, 4.77. Found: C, 69.56; H, 8.29; N, 4.76.

(1*S*,2*R*)-1-(2-Methylphenyl)-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (28e). Compound **28e** was obtained as an oil in 67% yield: $[\alpha]_D^{23}$ −316.62 (*c* 2.020, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.17 (3H, t, –NCH$_2$CH$_3$, *J* = 7.0 Hz), 0.73 (1H, dd, H-3a, $J_{3a,3b}$ = 4.2, $J_{3a,2}$ = 9.0 Hz), 1.08 (3H, t, H-3′, $J_{3',\ 2'}$ = 7.5 Hz), 1.11 (3H, t, –NCH$_2$CH$_3$, *J* = 7.0 Hz), 1.78–1.91 (2H, m, H-2′), 1.99 (1H, dd, H-3b, $J_{3b,3a}$ = 4.2, $J_{3b,2}$ = 6.2 Hz), 2.05 (1H, ddd, H-2, $J_{2,3b}$ = 6.2, $J_{2,3a}$ = 9.0, $J_{2,1'}$ = 9.0 Hz), 2.29 (3H, s, Me–Ph–), 2.85–2.94 (2H, m, H-1′ and –NCH$_2$CH$_3$), 3.13 (1H, m, –NCH$_2$CH$_3$), 3.42 (1H, m, –NCH$_2$CH$_3$), 3.89 (1H, m, –NCH$_2$CH$_3$), 7.11–7.18 (3H, m, aromatic), 7.29 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.28 (C-3′), 11.77 (–NCH$_2$CH$_3$), 12.43 (–NCH$_2$CH$_3$), 19.04 (C-3), 19.63 (Me–Ph–), 28.18 (C-2), 28.61 (C-2′), 35.28 (C-1), 41.22 (–NCH$_2$CH$_3$), 42.45 (–NCH$_2$CH$_3$), 63.95 (C-1′), 125.96, 126.82, 128.20, 130.43, 139.63, 139.75 (the above mentioned, aromatic), 169.35 (C=O); HR-MS (EI) calcd $C_{18}H_{26}N_4O$ 314.2106; obs 314.2119 (M^+). Anal. calcd for $C_{18}H_{26}N_4O$: C, 68.76; H, 8.33; N, 17.82. Found: C, 68.94; H, 8.24; N, 17.94.

(1*S*,2*R*)-1-(3-Methylphenyl)-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (28f). Compound **28f** was obtained as an oil in 91% yield: $[\alpha]_D^{23}$ +72.75(*c* 2.845, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (3H, t, –NCH$_2$CH$_3$, *J* = 7.1 Hz), 1.00 (3H, t, H-3′, $J_{3',\ 2'}$ = 7.5 Hz), 1.05 (1H, dd, H-3a, $J_{3a,3b}$ = 6.0, $J_{3a,2}$ = 6.0 Hz), 1.14 (3H, t, –NCH$_2$CH$_3$, *J* = 7.1 Hz), 1.25 (1H, ddd, H-2, $J_{2,3a}$ = 6.0, $J_{2,3b}$ = 8.8, $J_{2,1'}$ = 8.8 Hz), 1.60–1.73 (2H, m, H-2′), 1.69 (1H, dd, H-3b, $J_{3b,3a}$ = 6.0, $J_{3b,2}$ = 8.8 Hz), 2.31 (3H, s, Me–Ph–), 3.07 (1H, m, H-1′), 3.32–3.46 (3H, m, –NCH$_2$CH$_3$), 3.53 (1H, m, –NCH$_2$CH$_3$), 5.51 (1H, s,–OH), 7.00–7.06 (3H, m, aromatic), 7.17 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.22 (C-3′), 12.25 (–NCH$_2$CH$_3$), 13.08 (–NCH$_2$CH$_3$), 16.98 (C-3), 21.34 (Me–Ph–), 29.07 (C-2′), 33.16 (C-1), 36.42 (C-2), 39.33 (–NCH$_2$CH$_3$), 41.86 (–NCH$_2$CH$_3$), 75.66 (C-1′), 122.54, 126.52, 127.24, 128.40, 138.18, 140.17 (the above mentioned, aromatic), 171.51 (C=O); HR-MS (EI) calcd $C_{18}H_{27}NO_2$ 289.2042; obs 289.2026 (M^+). Anal. calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.49; H, 9.55; N, 4.81.

(1*S*,2*R*)-1-(4-Methylphenyl)-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (28g). Compound **28g** was obtained as crystals in 78% yield: mp (*i*-Pr$_2$O/AcOEt) 63–64 °C; $[\alpha]_D^{22}$ +77.48 (*c* 1.785, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (3H, t, –NCH$_2$CH$_3$, *J* = 7.1 Hz), 1.00 (3H, t, H-3′, $J_{3',\ 2'}$ = 7.5 Hz), 1.03 (1H, dd, H-3a, $J_{3a,3b}$ = 6.0, $J_{3a,2}$ = 6.0 Hz), 1.13 (3H, t, –NCH$_2$CH$_3$, *J* = 7.1 Hz), 1.22 (1H, ddd, H-2, $J_{2,3a}$ = 6.0, $J_{2,3b}$ = 8.4, $J_{2,1'}$ = 8.4 Hz), 1.59–1.73 (3H, m, H-3b and H-2′), 2.30 (3H, s, Me–Ph–), 3.06 (1H, m, H-1′), 3.31–3.45 (3H, m, –NCH$_2$CH$_3$), 3.53 (1H, m, –NCH$_2$CH$_3$), 5.43 (1H, s,–OH), 7.08–7.13 (4H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.29 (C-3′), 12.35 (–NCH$_2$CH$_3$), 13.20 (–NCH$_2$CH$_3$), 16.91 (C-3), 20.90 (Me–Ph–), 29.13 (C-2′), 33.02 (C-1), 36.40 (C-2), 39.41 (–NCH$_2$CH$_3$), 41.90 (–NCH$_2$CH$_3$), 75.73 (C-1′), 125.69, 129.30, 136.18, 137.34 (the above mentioned, aromatic), 171.63 (C=O); HR–MS (EI) calcd $C_{18}H_{27}NO_2$ 289.2042; obs 289.2055 (M^+). Anal. calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.70; H, 9.52; N, 4.90.

(1*S*,2*R*)-1-(1-Naphthyl)-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (28h). Compound **28h** was obtained as crystals in 91% yield: mp (hexane/AcOEt) 95–96 °C; $[\alpha]_D^{23}$ +26.58 (*c* 2.455, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.50 (3H, t, –NCH$_2$CH$_3$, *J* = 7.0 Hz), 0.99 (3H, t, –NCH$_2$CH$_3$, *J* = 7.0 Hz), 1.04 (3H, t, H-3′, $J_{3',\ 2'}$ = 7.4 Hz), 1.41 (1H, dd, H-3a, $J_{3a,3b}$ = 5.0, $J_{3a,2}$ = 5.0 Hz), 1.54 (1H, dd, H-3b, $J_{3b,3a}$ = 5.0, $J_{3b,2}$ = 8.7 Hz), 1.63 (1H, ddd, H-2, $J_{2,3a}$ = 5.0, $J_{2,3b}$ = 8.7, $J_{2,1'}$ = 8.7 Hz), 1.73 (2H, m, H-2′), 3.16 (1H, m, –NCH$_2$CH$_3$), 3.26 (1H, m, –NCH$_2$CH$_3$), 3.32 (1H, m, H-1′), 3.58 (1H, m, –NCH$_2$CH$_3$), 3.71 (1H, m, –NCH$_2$CH$_3$), 4.75 (1H, bs,–OH), 7.39 (1H, t, aromatic, *J* = 7.7 Hz), 7.47 (1H, t, aromatic, *J* = 7.7 Hz), 7.51 (1H, d, aromatic, *J* = 7.7 Hz), 7.58 (1H, t, aromatic, *J* = 7.7 Hz), 7.75 (1H, d, aromatic, *J* = 8.2 Hz), 7.81 (1H, d, aromatic, *J* = 8.2 Hz), 8.90 (1H, d, aromatic, *J* = 8.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.16 (C-3′), 12.26 (–NCH$_2$CH$_3$), 12.78 (–NCH$_2$CH$_3$), 17.80 (C-3), 29.77 (C-2′), 32.50 (C-2), 33.56 (C-1), 40.43 (–NCH$_2$CH$_3$), 42.29 (–NCH$_2$CH$_3$), 75.23 (C-1′), 124.80, 125.75, 125.82, 126.31, 126.42, 128.09, 128.10, 133.25, 133.83, 136.81 (the above mentioned, aromatic), 170.67 (C=O); HR-MS (EI) calcd $C_{21}H_{27}NO_2$ 325.2042; obs

325.2035 (M^+). Anal. calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.76; H, 8.58; N, 4.16.

(1*S*,2*R*)-1-(2-Naphthyl)-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (28i). Compound **28i** was obtained as crystals in 85% yield: mp (hexane/AcOEt) 99 °C; $[\alpha]_D^{25}$ +83.52 (*c* 1.660, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 1.02 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.13–1.16 (4H, t, –$NCH_2\underline{CH_3}$ and H-3a), 1.32 (1H, ddd, H-2, $J_{2,3a}$ = 5.6, $J_{2,3b}$ = 8.5, $J_{2,1'}$ = 8.5 Hz), 1.62–1.76 (2H, m, H-2′), 1.85 (1H, dd, H-3b, $J_{3b,3a}$ = 5.6, $J_{3b,2}$ = 8.5 Hz), 3.13 (1H, m, H-1′), 3.33–3.49 (3H, m, –$N\underline{CH_2}CH_3$), 3.58 (1H, m, –$N\underline{CH_2}CH_3$), 5.51 (1H, s,–OH), 7.42–7.47 (3H, m, aromatic), 7.64 (1H, s, aromatic), 7.75–7.79 (3H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.30 (C-3′), 12.35 (–$NCH_2\underline{CH_3}$), 13.22 (–$NCH_2\underline{CH_3}$), 17.01 (C-3), 29.17 (C-2′), 33.62 (C-1), 36.62 (C-2), 39.47 (–$N\underline{CH_2}CH_3$), 41.93 (–$N\underline{CH_2}CH_3$), 75.62 (C-1′), 124.17, 124.40, 125.73, 126.23, 127.52, 127.61, 128.45, 132.18, 133.35, 137.85 (the above mentioned, aromatic), 171.40 (C=O); HR-MS (EI) calcd $C_{21}H_{27}NO_2$ 325.2042; obs 325.2046 (M^+). Anal. calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.48; H, 8.25; N, 4.22.

General procedure for preparing compounds 29b–i. A mixture of **28b–i** (3.00 mmol), PPh_3 2.36 g, 9.00 mmol), and CBr_4 (2.978 g, 9.00 mmol) in HMPA (10 mL) was stirred at 0 °C for 30 min. After addition of NaN_3 (1.95 g, 30.0 mmol), the resulting mixture was stirred at room temperature for 8 h, and then AcOEt and H_2O were added and partitioned. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by flash column chromatography (silica gel; AcOEt/hexane 0:1, 1:9, and 1:4) to give **29b–i**.

(1*S*,2*R*)-1-(2-Fluorophenyl)-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (29b). Compound **29b** was obtained as an oil in 99% yield: $[\alpha]_D^{22}$ −249.30 (*c* 3.075, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.33 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 0.89 (1H, dd, H-3a, $J_{3a,3b}$ = 4.6, $J_{3a,2}$ = 9.3 Hz), 1.08 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.12 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 1.73–1.86 (2H, m, H-2′), 1.93 (1H, dd, H-3b, $J_{3b,3a}$ = 4.6, $J_{3b,2}$ = 6.5 Hz), 2.05 (1H, ddd, H-2, $J_{2,3b}$ = 6.5, $J_{2,3a}$ = 9.3, $J_{2,1'}$ = 9.3 Hz), 2.87 (1H, m, H-1′), 3.01 (1H, m, –$N\underline{CH_2}CH_3$), 3.18 (1H, m, –$N\underline{CH_2}CH_3$), 3.47 (1H, m, –$N\underline{CH_2}CH_3$), 3.78 (1H, m, –$N\underline{CH_2}CH_3$), 7.03 (1H, m, aromatic), 7.11 (1H, m, aromatic), 7.23 (1H, m, aromatic), 7.30 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.25 (C-3′), 11.88 (–$NCH_2\underline{CH_3}$), 12.29 (–$NCH_2\underline{CH_3}$), 19.36 (C-3), 27.41 (C-2), 28.12 (C-2′), 31.34 (C-1), 40.64 (–$N\underline{CH_2}CH_3$), 42.03 (–$N\underline{CH_2}CH_3$), 63.74 (C-1′), 115.92 (C-3″, $J_{C,F}$ = 23 Hz), 124.39 (C-6″, $J_{C,F}$ = 4 Hz), 128.55 (C-1″, $J_{C,F}$ = 11 Hz), 128.61 (C-4″, $J_{C,F}$ = 8 Hz), 129.27 (C-5″, $J_{C,F}$ = 4 Hz), 161.93 (C-2″, $J_{C,F}$ = 246 Hz), 168.75 (C=O); HR-MS (EI) calcd $C_{17}H_{23}FN_4O$ 318.1856; obs 318.1842 (M^+). Anal. calcd for $C_{17}H_{23}FN_4O$: C, 64.13; H, 7.28; N, 17.60. Found: C, 64.53; H, 7.40; N, 17.66.

(1*S*,2*R*)-1-(3-Fluorophenyl)-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (29c). Compound **29c** was obtained as an oil in 75% yield: $[\alpha]_D^{22}$ −169.35 (*c* 2.070, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.47 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 0.97 (1H, dd, H-3a, $J_{3a,3b}$ = 5.0, $J_{3a,2}$ = 9.3 Hz), 1.07 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.13 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 1.67 (1H, dd, H-3b, $J_{3b,3a}$ = 5.0, $J_{3b,2}$ = 6.4 Hz), 1.73–1.86 (2H, m, H-2′), 1.91 (1H, ddd, H-2, $J_{2,3b}$ = 6.4, $J_{2,3a}$ = 9.3, $J_{2,1'}$ = 9.3 Hz), 2.86 (1H, m, H-1′), 3.07 (1H, m, –$N\underline{CH_2}CH_3$), 3.19 (1H, m, –$N\underline{CH_2}CH_3$), 3.55 (1H, m, –$N\underline{CH_2}CH_3$), 3.67 (1H, m, –$N\underline{CH_2}CH_3$), 6.94 (2H, m, aromatic), 7.05 (1H, m, aromatic), 7.27 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.17 (C-3′), 11.94 (–$NCH_2\underline{CH_3}$), 12.24 (–$NCH_2\underline{CH_3}$), 19.84 (C-3), 27.86 (C-2), 28.18 (C-2′), 35.58 (C-1), 39.96 (–$N\underline{CH_2}CH_3$), 42.04 (–$N\underline{CH_2}CH_3$), 64.00 (C-1′), 113.62 (C-4″, $J_{C,F}$ = 23 Hz), 113.80 (C-2″, $J_{C,F}$ = 23 Hz), 122.63 (C-6″, $J_{C,F}$ = 4 Hz), 130.24 (C-5″, $J_{C,F}$ = 9 Hz), 143.51 (C-1″, $J_{C,F}$ = 8 Hz), 163.02 (C-3″, $J_{C,F}$ = 244 Hz), 168.86 (C=O); HR-MS (EI) calcd $C_{17}H_{23}FN_4O$ 318.1856; obs 318.1882 (M^+). Anal. calcd for $C_{17}H_{23}FN_4O$: C, 64.13; H, 7.28; N, 17.60. Found: C, 64.30; H, 7.44; N, 17.60.

(1*S*,2*R*)-1-(4-Fluorophenyl)-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (29d). Compound **29d** was obtained as an oil in 92% yield: $[\alpha]_D^{22}$ −154.68 (*c* 1.945, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.42 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 0.92 (1H, dd, H-3a, $J_{3a,3b}$ = 4.9, $J_{3a,2}$ = 9.3 Hz), 1.07 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.12 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 1.64 (1H, dd, H-3b, $J_{3b,3a}$ = 4.9, $J_{3b,2}$ = 6.1 Hz), 1.72–1.86 (2H, m, H-2′), 1.89 (1H, ddd, H-2, $J_{2,3b}$ = 6.1, $J_{2,3a}$ = 9.3, $J_{2,1'}$ = 9.6 Hz), 2.87 (1H, m, H-1′), 3.04 (1H, m, –$N\underline{CH_2}CH_3$), 3.18 (1H, m, –$N\underline{CH_2}CH_3$), 3.53 (1H, m, –$N\underline{CH_2}CH_3$), 3.70 (1H, m, –$N\underline{CH_2}CH_3$), 6.98–7.02 (2H, m, aromatic), 7.20–7.25 (2H, m, aromatic). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.21 (C-3′), 12.03 (–$NCH_2\underline{CH_3}$), 12.30 (–$NCH_2\underline{CH_3}$), 19.55 (C-3), 27.69 (C-2), 28.23 (C-2′), 35.30 (C-1), 40.02 (–$N\underline{CH_2}CH_3$), 42.00 (–$N\underline{CH_2}CH_3$), 64.16 (C-1′), 115.60 (C-3″ and C-5″, $J_{C,F}$ = 23 Hz), 128.70 (C-2″ and C-6″, $J_{C,F}$ = 8 Hz), 136.75 (C-1″, $J_{C,F}$ = 4 Hz), 161.52 (C-4″, $J_{C,F}$ = 245 Hz), 169.24 (C=O); HR-MS (EI) calcd $C_{17}H_{23}FN_4O$ 318.1856; obs 318.1835 (M^+). Anal. calcd for $C_{17}H_{23}FN_4O$: C, 64.13; H, 7.28; N, 17.60. Found: C, 64.43; H, 7.28; N, 17.36.

(1*S*,2*R*)-1-(2-Methylphenyl)-2-[(*S*)-1-hydroxypropyl]-*N*,*N*-diethylcyclopropanecarboxamide (29e). Compound **29e** was obtained as crystals in 87% yield: mp (hexane/AcOEt) 137–138 °C; $[\alpha]_D^{22}$ +94.76 (*c* 1.515, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.60 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.0 Hz), 1.01 (3H, t, H-3′, $J_{3',2'}$ = 7.5 Hz), 1.07 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.0 Hz), 1.20 (1H, dd, H-3a, $J_{3a,3b}$ = 5.5, $J_{3a,2}$ = 5.5 Hz), 1.36 (1H, ddd, H-2, $J_{2,3a}$ = 5.5, $J_{2,3b}$ = 8.8, $J_{2,1'}$ = 8.8 Hz), 1.51 (1H, dd, H-3b, $J_{3b,3a}$ = 5.5, $J_{3b,2}$ = 8.8 Hz), 1.65–1.74 (2H, m, H-2′), 2.53 (3H, s, Me–Ph–), 3.20–3.38 (3H, m, H-1′ and –$N\underline{CH_2}CH_3$), 3.53–3.57 (2H, m, –$N\underline{CH_2}CH_3$), 4.66 (1H, bs,–OH), 7.13–7.14 (3H, m, aromatic), 7.27 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.22 (C-3′), 12.45 (–$NCH_2\underline{CH_3}$), 12.84 (–$NCH_2\underline{CH_3}$), 17.37 (C-3), 20.36 (Me–Ph–), 29.66 (C-2′), 33.25 (C-2), 33.67 (C-1), 40.45 (–$N\underline{CH_2}CH_3$), 42.17 (–$N\underline{CH_2}CH_3$), 75.18 (C-1′),

125.67, 127.05, 128.55, 131.05, 138.60, 140.33 (the above mentioned, aromatic), 170.48 (C=O); HR–MS (EI) calcd $C_{18}H_{27}NO_2$ 289.2042; obs 289.2045 (M^+). Anal. calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.99; H, 9.22; N, 4.79.

(1*S*,2*R*)-1-(3-Methylphenyl)-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (29f). Compound **29f** was obtained as an oil in 69% yield: $[\alpha]_D^{23}$ −160.13 (*c* 2.730, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.39 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 0.93 (1H, dd, H-3a, $J_{3a,3b}$ = 4.8, $J_{3a,2}$ = 9.2 Hz), 1.07 (3H, t, H-3′, $J_{3',2'}$ = 7.5 Hz), 1.13 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.64 (1H, dd, H-3b, $J_{3b,3a}$ = 4.8, $J_{3b,2}$ = 5.5 Hz), 1.72–1.88 (2H, m, H-2′), 1.95 (1H, ddd, H-2, $J_{2,3b}$ = 5.5, $J_{2,3a}$ = 9.2, $J_{2,1'}$ = 9.2 Hz), 2.32 (3H, s, Me–Ph–), 2.85 (1H, m, H-1′), 3.03 (1H, m, –$N\underline{CH_2}CH_3$), 3.16 (1H, m, –$N\underline{CH_2}CH_3$), 3.54 (1H, m, –$N\underline{CH_2}CH_3$), 3.72 (1H, m, –$N\underline{CH_2}CH_3$), 7.02–7.07 (3H, m, aromatic), 7.19 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.25 (C-3′), 11.84 (–$NCH_2\underline{CH_3}$), 12.28 (–$NCH_2\underline{CH_3}$), 19.64 (C-3), 21.31 (Me–Ph–), 27.22 (C-2), 28.27 (C-2′), 35.83 (C-1), 39.92 (–$N\underline{CH_2}CH_3$), 42.05 (–$N\underline{CH_2}CH_3$), 64.25 (C-1′), 123.83, 127.35, 127.79, 128.59, 138.36, 140.72 (the above mentioned, aromatic), 169.60 (C=O); HR-MS (EI) calcd $C_{18}H_{26}N_4O$ 314.2106; obs 314.2100 (M^+). Anal. calcd for $C_{18}H_{26}N_4O$: C, 68.76; H, 8.33; N, 17.82. Found: C, 69.12; H, 8.56; N, 17.95.

(1*S*,2*R*)-1-(4-Methylphenyl)-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (29g). Compound **29g** was obtained as an oil in 90% yield: $[\alpha]_D^{23}$ −160.87 (*c* 2.545, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.40 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.0 Hz), 0.92 (1H, dd, H-3a, $J_{3a,3b}$ = 4.8, $J_{3a,2}$ = 9.2 Hz), 1.06 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.12 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.0 Hz), 1.62 (1H, dd, H-3b, $J_{3b,3a}$ = 4.8, $J_{3b,2}$ = 5.2 Hz), 1.74–1.87 (2H, m, H-2′), 1.92 (1H, ddd, H-2, $J_{2,3b}$ = 5.2, $J_{2,3a}$ = 9.2, $J_{2,1'}$ = 9.2 Hz), 2.31 (3H, s, Me–Ph–), 2.85 (1H, m, H-1′), 3.03 (1H, m, –$N\underline{CH_2}CH_3$), 3.18 (1H, m, –$N\underline{CH_2}CH_3$), 3.51 (1H, m, –$N\underline{CH_2}CH_3$), 3.71 (1H, m, –$N\underline{CH_2}CH_3$), 7.09–7.15 (4H, m, aromatic). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.21 (C-3′), 11.93 (–$NCH_2\underline{CH_3}$), 12.30 (–$NCH_2\underline{CH_3}$), 19.53 (C-3), 20.91 (Me–Ph–), 27.33 (C-2), 28.24 (C-2′), 35.55 (C-1), 39.92 (–$N\underline{CH_2}CH_3$), 42.05 (–$N\underline{CH_2}CH_3$), 64.23 (C-1′), 126.84, 129.33, 136.24, 137.84 (the above mentioned, aromatic), 169.63 (C=O); HR-MS (EI) calcd $C_{18}H_{26}N_4O$ 314.2106; obs 314.2107 (M^+). Anal. calcd for $C_{18}H_{26}N_4O$: C, 68.76; H, 8.33; N, 17.82. Found: C, 69.08; H, 8.58; N, 17.47.

(1*S*,2*R*)-1-(1-Naphthyl)-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (29h). Compound **29h** was obtained as crystals in 82% yield: mp (hexane/AcOEt) 94–95 °C; $[\alpha]_D^{22}$ −281.31 (*c* 1.115, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ −0.06 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.0 Hz), 0.88 (1H, dd, H-3a, $J_{3a,3b}$ = 3.6, $J_{3a,2}$ = 8.3 Hz), 1.02 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.0 Hz), 1.12 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.83–1.95 (2H, m, H-2′), 2.15–2.20 (2H, m, H-3b and H-2), 2.93 (1H, m, –$N\underline{CH_2}CH_3$), 3.00–3.07 (2H, m, H-1′ and –$N\underline{CH_2}CH_3$), 3.39 (1H, m, –$N\underline{CH_2}CH_3$), 4.04 (1H, m, –$N\underline{CH_2}CH_3$), 7.42 (1H, t, aromatic, J = 7.7 Hz), 7.46–7.54 (3H, m, aromatic), 7.76 (1H, t, aromatic, J = 8.2 Hz), 7.83 (1H, t, aromatic, J = 7.7 Hz), 8.40 (1H, t, aromatic, J = 8.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.33 (C-3′), 11.97 (–$NCH_2\underline{CH_3}$), 12.38 (–$NCH_2\underline{CH_3}$), 19.61 (C-3), 28.30 (C-2′), 28.59 (C-2), 35.12 (C-1), 41.26 (–$N\underline{CH_2}CH_3$), 42.44 (–$N\underline{CH_2}CH_3$), 64.01 (C-1′), 124.99, 125.23, 125.70, 125.99, 126.60, 127.81, 128.38, 133.53, 133.74, 137.82 (the above mentioned, aromatic), 169.73 (C=O); HR-MS (EI) calcd $C_{21}H_{26}N_4O$ 350.2106; obs 350.2111 (M^+). Anal. calcd for $C_{21}H_{26}N_4O$: C, 71.97; H, 7.48; N, 15.99. Found: C, 72.23; H, 7.67; N, 15.78.

(1*S*,2*R*)-1-(2-Naphthyl)-2-[(*S*)-1-azidopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (29i). Compound **29i** was obtained as an oil in 81% yield: $[\alpha]_D^{23}$ −252.85 (*c* 2.200, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.29 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.01 (1H, dd, H-3a, $J_{3a,3b}$ = 5.0, $J_{3a,2}$ = 9.3 Hz), 1.10 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.15 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.0 Hz), 1.73 (1H, dd, H-3b, $J_{3b,3a}$ = 5.0, $J_{3b,2}$ = 6.2 Hz), 1.77–1.92 (2H, m, H-2′), 2.10 (1H, ddd, H-2, $J_{2,3b}$ = 6.2, $J_{2,3a}$ = 9.3, $J_{2,1'}$ = 9.3 Hz), 2.92 (1H, m, H-1′), 3.07 (1H, m, –$N\underline{CH_2}CH_3$), 3.19 (1H, m, –$N\underline{CH_2}CH_3$), 3.56 (1H, m, –$N\underline{CH_2}CH_3$), 3.78 (1H, m, –$N\underline{CH_2}CH_3$), 7.39–7.48 (3H, m, aromatic), 7.66 (1H, d, aromatic, J = 0.7 Hz), 7.77–7.80 (3H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.24 (C-3′), 11.98 (–$NCH_2\underline{CH_3}$), 12.31 (–$NCH_2\underline{CH_3}$), 19.89 (C-3), 27.61 (C-2), 28.28 (C-2′), 36.09 (C-1), 39.94 (–$N\underline{CH_2}CH_3$), 42.03 (–$N\underline{CH_2}CH_3$), 64.23 (C-1′), 124.75, 125.73, 125.80, 126.29, 127.56, 128.42, 132.14, 133.44, 138.40 (the above mentioned, aromatic), 169.36 (C=O); HR-MS (EI) calcd $C_{21}H_{26}N_4O$ 350.2106; obs 350.2096 (M^+). Anal. calcd for $C_{21}H_{26}N_4O$: C, 71.97; H, 7.48; N, 15.99. Found: C, 72.36; H, 7.45; N, 15.79.

General procedure for preparing 4b–i. A mixture of **29b–i** (1.00 mmol) and 10% Pd-charcoal (50 mg) in MeOH (5 mL) was stirred under atmospheric pressure of hydrogen at room temperature for 3 h, and then the catalyst was filtered off. The filtrate was evaporated, and the residue was purified by column chromatography (silica gel; AcOEt/hexane 1:1 then $CHCl_3$/MeOH 4:1) to give free amine **4b–i** as an oil. A solution of the oil in MeOH (5 mL) was put on a column of Diaion WA-30 resin (Cl^- form), and the column was developed with MeOH. The solvent was evaporated, and the residue was treated with Et_2O to give white crystals of **4b–i** as hydrochloride.

(1*S*,2*R*)-1-(2-Fluorophenyl)-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide hydrochloride (4b). Yield 95%: $[\alpha]_D^{22}$ +153.87 (*c* 1.005, MeOH); mp (Et_2O) 231–232 °C; ^1H NMR (500 MHz, CD_3OD) δ 0.85 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.07 (3H, t, –$NCH_2\underline{CH_3}$, J = 7.1 Hz), 1.09 (3H, t, H-3′, $J_{3',2'}$ = 7.5 Hz), 1.20 (1H, ddd, H-2, $J_{2,3a}$ = 6.0, $J_{2,3b}$ = 9.0, $J_{2,1'}$ = 9.0 Hz), 1.40 (1H, dd, H-3a, $J_{3a,3b}$ = 6.0, $J_{3a,2}$ = 6.0 Hz), 1.77–1.96 (2H, m, H-2′), 2.17 (1H, dd, H-3b, $J_{3b,3a}$ = 6.0, $J_{3b,2}$ = 9.0 Hz), 2.87 (1H, m, H-1′), 3.28–3.39 (2H, m, –$N\underline{CH_2}CH_3$), 3.50 (1H, m, –$N\underline{CH_2}CH_3$), 3.76 (1H, m, –$N\underline{CH_2}CH_3$), 7.14 (1H, m, aromatic), 7.22 (1H, m, aromatic), 7.36 (1H, m, aromatic), 7.51 (1H, m, aromatic); ^{13}C NMR (125 MHz, CD_3OD) δ 10.45 (C-3′), 12.58 (–$NCH_2\underline{CH_3}$), 13.38

(–$NCH_2\underline{C}H_3$), 18.19 (C-3), 27.71 (C-2′), 30.25 (C-1), 30.82 (C-2), 41.34 (–$N\underline{C}H_2CH_3$), 43.44 (–$N\underline{C}H_2CH_3$), 57.62 (C-1′), 117.13 (C-3″, $J_{C,F}=23$ Hz), 126.05 (C-6″, $J_{C,F}=3$ Hz), 127.68 (C-1″, $J_{C,F}=13$ Hz), 131.06 (C-4″ and C-5″, $J_{C,F}=8$ Hz), 163.46 (C-2″, $J_{C,F}=246$ Hz), 171.55 (C=O); HR-MS (EI) calcd $C_{17}H_{25}FN_2O$ 292.1951; obs 292.1927 (M^+–HCl). Anal. calcd for $C_{17}H_{26}FClN_2O$: C, 62.09; H, 7.97; N, 8.52; Cl, 10.78. Found: C, 61.76; H, 7.91; N, 8.52; Cl, 10.91.

(1*S*,2*R*)-1-(3-Fluorophenyl)-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide hydrochloride (4c). Yield 86%: mp (Et_2O) 203–204 °C; $[\alpha]_D^{23}$ +87.22 (*c* 1.115, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 0.93 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.09 (3H, t, H-3′, $J_{3',\ 2'}=7.5$ Hz), 1.15 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.23 (1H, ddd, H-2, $J_{2,3a}=6.4$, $J_{2,3b}=9.1$, $J_{2,1'}=9.1$ Hz), 1.42 (1H, dd, H-3a, $J_{3a,3b}=6.4$, $J_{3a,2}=6.4$ Hz), 1.76–1.91 (2H, m, H-2′), 2.17 (1H, dd, H-3b, $J_{3b,3a}=6.4$, $J_{3b,2}=9.1$ Hz), 2.78 (1H, m, H-1′), 3.39 (1H, m, –$N\underline{C}H_2CH_3$), 3.43–3.50 (3H, m, –$N\underline{C}H_2CH_3$), 7.00–7.16 (3H, m, aromatic), 7.39 (1H, m, aromatic); ^{13}C NMR (125 MHz, CD_3OD) δ 10.33 (C-3′), 12.52 (–$NCH_2\underline{C}H_3$), 13.24 (–$NCH_2\underline{C}H_3$), 18.99 (C-3), 27.72 (C-2′), 33.19 (C-2), 34.31 (C-1), 41.00 (–$N\underline{C}H_2CH_3$), 43.60 (–$N\underline{C}H_2CH_3$), 57.64 (C-1′), 113.88 (C-4″, $J_{C,F}=23$ Hz), 115.15 (C-2″, $J_{C,F}=21$ Hz), 122.71 (C-6″, $J_{C,F}=3$ Hz), 131.95 (C-5″, $J_{C,F}=9$ Hz), 143.26 (C-1″, $J_{C,F}=8$ Hz), 164.60 (C-3″, $J_{C,F}=244$ Hz), 172.14 (C=O); HR-MS (EI) calcd $C_{17}H_{25}FN_2O$ 292.1951; obs 292.1944 (M^+–HCl). Anal. calcd for $C_{17}H_{26}FClN_2O$: C, 62.09; H, 7.97; N, 8.52; Cl, 10.78. Found: C, 62.25; H, 7.87; N, 8.41; Cl, 10.68.

(1*S*,2*R*)-1-(4-Fluorophenyl)-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide hydrochloride (4d). Yield 85%: mp (Et_2O) 215–217 °C; $[\alpha]_D^{22}$ +95.11 (*c* 1.115, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 0.90 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.08 (3H, t, H-3′, $J_{3',\ 2'}=7.5$ Hz), 1.12 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.16 (1H, ddd, H-2, $J_{2,3a}=6.2$, $J_{2,3b}=9.1$, $J_{2,1'}=10.1$ Hz), 1.37 (1H, dd, H-3a, $J_{3a,3b}=6.2$, $J_{3a,2}=6.2$ Hz), 1.75–1.90 (2H, m, H-2′), 2.13 (1H, dd, H-3b, $J_{3b,3a}=6.2$, $J_{3b,2}=9.1$ Hz), 2.75 (1H, m, H-1′), 3.36 (1H, m, –$N\underline{C}H_2CH_3$), 3.41 (1H, m, –$N\underline{C}H_2CH_3$), 3.44–3.52 (2H, m, –$N\underline{C}H_2CH_3$), 7.06–7.10 (2H, m, aromatic), 7.35–7.38 (2H, m, aromatic); ^{13}C NMR (125 MHz, CD_3OD) δ 10.35 (C-3′), 12.55 (–$NCH_2\underline{C}H_3$), 13.28 (–$NCH_2\underline{C}H_3$), 18.70 (C-3), 27.72 (C-2′), 32.60 (C-2), 34.04 (C-1), 40.96 (–$N\underline{C}H_2CH_3$), 43.53 (–$N\underline{C}H_2CH_3$), 57.71 (C-1′), 116.75 (C-3″ and C-5″, $J_{C,F}=21$ Hz), 129.14 (C-2″ and C-6″), 136.33 (C-1″), 163.34 (C-4″, $J_{C,F}=244$ Hz), 172.47 (C=O); HR-MS (EI) calcd $C_{17}H_{25}FN_2O$ 292.1951; obs 292.1956 (M^+–HCl). Anal. calcd for $C_{17}H_{25}FN_2O$: C, 62.09; H, 7.97; N, 8.52; Cl, 10.78. Found: C, 61.64; H, 7.87; N, 8.51; Cl, 11.10.

(1*S*,2*R*)-1-(2-Methylphenyl)-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide hydrochloride (4e). Yield 89%: mp (Et_2O) 192–193 °C ; $[\alpha]_D^{22}$ +230.34 (*c* 1.225, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 0.61 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.07 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.10 (3H, t, H-3′, $J_{3',\ 2'}=7.5$ Hz), 1.14 (1H, ddd, H-2, $J_{2,3a}=6.0$, $J_{2,3b}=9.0$, $J_{2,1'}=9.0$ Hz), 1.30 (1H, dd, H-3a, $J_{3a,3b}=6.0$, $J_{3a,2}=6.0$ Hz), 1.81–1.94 (2H, m, H-2′), 2.18 (1H, dd, H-3b, $J_{3b,3a}=6.0$, $J_{3b,2}=9.0$ Hz), 2.50 (3H, s, Me–Ph–), 2.91 (1H, m, H-1′), 3.23–3.39 (3H, m, –$N\underline{C}H_2\underline{C}H_3$), 3.78 (1H, m, –$N\underline{C}H_2CH_3$), 7.19–7.22 (3H, m, aromatic), 7.41 (1H, m, aromatic); ^{13}C NMR (125 MHz, CD_3OD) δ 10.56 (C-3′), 12.78 (–$NCH_2\underline{C}H_3$), 13.14 (–$NCH_2\underline{C}H_3$), 19.20 (C-3), 21.07 (Me–Ph–), 27.98 (C-2′), 30.18 (C-2), 35.08 (C-1), 41.81 (–$N\underline{C}H_2CH_3$), 43.65 (–$N\underline{C}H_2CH_3$), 58.19 (C-1′), 127.67, 129.04, 130.10, 132.45, 138.17, 140.34 (the above mentioned, aromatic), 172.22 (C=O); HR-MS (EI) calcd $C_{18}H_{28}N_2O$ 288.2201; obs 288.2225 (M^+–HCl). Anal. calcd for $C_{18}H_{29}ClN_2O$: C, 66.54; H, 9.00; N, 8.62; Cl, 10.91. Found: C, 66.49; H, 9.06; N, 8.52; Cl, 10.93.

(1*S*,2*R*)-1-(3-Methylphenyl)-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide hydrochloride (4f). Yield 93%: mp (Et_2O) 185–187 °C: $[\alpha]_D^{23}$ −160.13 (*c* 2.730, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.39 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 0.93 (1H, dd, H-3a, $J_{3a,3b}=4.8$, $J_{3a,2}=9.2$ Hz), 1.07 (3H, t, H-3′, $J_{3',\ 2'}=7.5$ Hz), 1.13 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.64 (1H, dd, H-3b, $J_{3b,3a}=4.8$, $J_{3b,2}=5.5$ Hz), 1.72–1.88 (2H, m, H-2′), 1.95 (1H, ddd, H-2, $J_{2,3b}=5.5$, $J_{2,3a}=9.2$, $J_{2,1'}=9.2$ Hz), 2.32 (3H, s, Me–Ph–), 2.85 (1H, m, H-1′), 3.03 (1H, m, –$N\underline{C}H_2CH_3$), 3.16 (1H, m, –$N\underline{C}H_2CH_3$), 3.54 (1H, m, –$N\underline{C}H_2CH_3$), 3.72 (1H, m, –$N\underline{C}H_2CH_3$), 7.02–7.07 (3H, m, aromatic), 7.19 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.25 (C-3′), 11.84 (–$NCH_2\underline{C}H_3$), 12.28 (–$NCH_2\underline{C}H_3$), 19.64 (C-3), 21.31 (Me–Ph–), 27.22 (C-2), 28.27 (C-2′), 35.83 (C-1), 39.92 (–$N\underline{C}H_2CH_3$), 42.05 (–$N\underline{C}H_2CH_3$), 64.25 (C-1′), 123.83, 127.35, 127.79, 128.59, 138.36, 140.72 (the above mentioned, aromatic), 169.60 (C=O); HR-MS (EI) calcd $C_{18}H_{26}N_4O$ 314.2106; obs 314.2100 (M^+). Anal. calcd for $C_{18}H_{26}N_4O$: C, 68.76; H, 8.33; N, 17.82. Found: C, 69.12; H, 8.56; N, 17.95.

(1*S*,2*R*)-1-(4-Methylphenyl)-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide hydrochloride (4g). Yield 87%; mp (Et_2O) 218–219 °C; $[\alpha]_D^{23}$ +88.74 (*c* 1.275, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 0.90 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.09 (3H, t, H-3′, $J_{3',\ 2'}=7.5$ Hz), 1.13 (3H, t, –$NCH_2\underline{CH_3}$, $J=7.1$ Hz), 1.15 (1H, ddd, H-2, $J_{2,3a}=6.0$, $J_{2,3b}=9.0$, $J_{2,1'}=9.0$ Hz), 1.35 (1H, dd, H-3a, $J_{3a,3b}=6.0$, $J_{3a,2}=6.0$ Hz), 1.78–1.91 (2H, m, H-2′), 2.12 (1H, dd, H-3b, $J_{3b,3a}=6.0$, $J_{3b,2}=9.0$ Hz), 2.30 (3H, s, Me–Ph–), 2.76 (1H, m, H-1′), 3.36 (1H, m, –$N\underline{C}H_2CH_3$), 3.41–3.48 (3H, m, –$N\underline{C}H_2CH_3$), 7.16–7.21 (4H, m, aromatic); ^{13}C NMR (125 MHz, CD_3OD) δ 10.35 (C-3′), 12.55 (–$NCH_2\underline{C}H_3$), 13.23 (–$NCH_2\underline{C}H_3$), 18.60 (C-3), 20.98 (Me–Ph–), 27.72 (C-2′), 32.66 (C-2), 34.19 (C-1), 40.90 (–$N\underline{C}H_2CH_3$), 43.53 (–$N\underline{C}H_2CH_3$), 57.81 (C-1′), 126.82, 130.67, 137.27, 138.29 (the above mentioned, aromatic), 172.85 (C=O); HR-MS (EI) calcd $C_{18}H_{28}N_2O$ 288.2201; obs 288.2192 (M^+–HCl). Anal. calcd for $C_{18}H_{29}ClN_2O$: C, 66.54; H, 9.00; N, 8.62; Cl, 10.91. Found: C, 66.69; H, 9.09; N, 8.62; Cl, 10.87.

(1*S*,2*R*)-1-(1-Naphthyl)-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide hydrochloride (4h). Yield

80%: mp (Et_2O) 132–134 °C; $[\alpha]_D^{22}$ +68.91 (*c* 1.075, MeOH); ^1H NMR (500 MHz, CD_3OD) δ 0.47 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.0 Hz), 0.99 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.0 Hz), 1.11 (3H, t, H-3′, $J_{3',2'}$ = 7.4 Hz), 1.22 (1H, ddd, H-2, $J_{2,3a}$ = 6.0, $J_{2,3b}$ = 8.4, $J_{2,1'}$ = 8.4 Hz), 1.44 (1H, dd, H-3a, $J_{3a,3b}$ = 6.0, $J_{3a,2}$ = 6.0 Hz), 1.79–1.92 (2H, m, H-2′), 2.33 (1H, dd, H-3b, $J_{3b,3a}$ = 6.0, $J_{3b,2}$ = 8.4 Hz), 3.05 (1H, m, –$N\underline{CH_2}CH_3$), 3.07 (1H, m, H-1′), 3.26 (1H, m, –$N\underline{CH_2}CH_3$), 3.42 (1H, m, –$N\underline{CH_2}CH_3$), 3.83 (1H, m, –$N\underline{CH_2}CH_3$), 7.48–7.55 (2H, m, aromatic), 7.61–7.67 (2H, m, aromatic), 7.86 (1H, d, aromatic, *J* = 8.0 Hz), 7.92 (1H, d, aromatic, *J* = 8.0 Hz), 8.61 (1H, d, aromatic, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ 10.45 (C-3′), 12.71 (–$NCH_2\underline{CH_3}$), 13.10 (–$NCH_2\underline{CH_3}$), 19.12 (C-3), 28.09 (C-2′), 30.78 (C-2), 35.09 (C-1), 41.89 (–$N\underline{CH_2}CH_3$), 43.73 (–$N\underline{CH_2}CH_3$), 57.99 (C-1′), 125.56, 126.59, 127.12, 127.82, 127.88, 130.03, 130.05, 134.33, 135.41, 136.34 (the above mentioned, aromatic), 172.72 (C=O); HR-MS (EI) calcd $C_{21}H_{28}N_2O$ 324.2202; obs 324.2181 (M^+–HCl). Anal. calcd for $C_{21}H_{29}ClN_2O\cdot H_2O$: C, 66.56; H, 8.25; N, 7.39; Cl, 9.36. Found: C, 66.72; H, 9.94; N, 7.06; Cl, 9.46.

(1*S*,2*R*)-1-(2-Naphthyl)-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide hydrochloride (4i). Yield 90%: mp (Et_2O) 216–217 °C; $[\alpha]_D^{22}$ +99.57 (*c* 1.285, MeOH); ^1H NMR (500 MHz, CD_3OD) δ 0.77 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 1.02 (3H, t, H-3′, $J_{3',2'}$ = 7.5 Hz), 1.07 (3H, t, –$NCH_2\underline{CH_3}$, *J* = 7.1 Hz), 1.17 (1H, ddd, H-2, $J_{2,3a}$ = 6.2, $J_{2,3b}$ = 9.0, $J_{2,1'}$ = 9.0 Hz), 1.37 (1H, dd, H-3a, $J_{3a,3b}$ = 6.2, $J_{3a,2}$ = 6.2 Hz), 1.70–1.81 (2H, m, H-2′), 2.24 (1H, dd, H-3b, $J_{3b,3a}$ = 6.2, $J_{3b,2}$ = 9.0 Hz), 2.74 (1H, m, H-1′), 3.30 (1H, m, –$N\underline{CH_2}CH_3$), 3.35–3.44 (3H, m, –$N\underline{CH_2}CH_3$), 7.36–7.41 (3H, m, aromatic), 7.69 (1H, s, aromatic), 7.73–7.78 (3H, m, aromatic); ^{13}C NMR (125 MHz, CD_3OD) δ 10.34 (C-3′), 12.57 (–$NCH_2\underline{CH_3}$), 13.21 (–$NCH_2\underline{CH_3}$), 18.69 (C-3), 27.76 (C-2′), 32.98 (C-2), 34.75 (C-1), 40.98 (–$N\underline{CH_2}CH_3$), 43.58 (–$N\underline{CH_2}CH_3$), 57.77 (C-1′), 124.97, 125.55, 127.32, 127.68, 128.70, 129.88, 133.93, 134.93, 137.68, (the above mentioned, aromatic), 172.66 (C=O); HR-MS (EI) calcd $C_{21}H_{28}N_2O$ 324.2202; obs 324.2181 (M^+–HCl). Anal. calcd for $C_{21}H_{29}ClN_2O$: C, 69.88; H, 8.10; N, 7.76; Cl, 9.82. Found: C, 69.81; H, 8.08; N, 7.74; Cl, 9.75.

General procedure for preparing 30b–i. A solution of **28a–i** (1.00 mmol) and 6 N HCl (1 mL) in MeOH (2 mL) was heated under reflux for 2 h. The solvent was evaporated, and then the residue was partitioned between saturated aqueous $NaHCO_3$ and AcOEt. The organic layer was washed with brine, dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:4) to give **32b–i**.

(1*S*,4*S*,5*R*)-2-Oxo-4-ethyl-1-(2-fluorophenyl)-3-oxabicyclo[3.1.0]hexane (30b). Compound **30b** was obtained quantitatively as crystals: mp (AcOEt, hexane) 85–86 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 1.09 (3H, t, H-2′, $J_{2',1'}$ = 7.5 Hz), 1.35 (1H, dd, H-6a, $J_{6a,5}$ = 4.6, $J_{6a,6b}$ = 5.0 Hz), 1.69 (1H, dd, H-6b, $J_{6b,6a}$ = 5.0, $J_{6b,5}$ = 7.8 Hz), 1.82 (1H, m, H-1′a), 1.95 (1H, m, H-1′b), 2.30 (1H, dd, H-5, $J_{5,6a}$ = 4.6, $J_{5,6b}$ = 7.8 Hz), 4.32 (1H, d, H-4, $J_{4,1'}$ = 6.7 Hz), 7.07 (1H, m, aromatic), 7.14 (1H, m, aromatic), 7.30–7.36 (2H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.23 (C-2′), 17.53 (C-6), 28.40 (C-1), 28.94 (C-5), 29.16 (C-1′), 81.83 (C-4), 115.62 (C-3″, $J_{C,F}$ = 21 Hz), 121.77 (C-1″, $J_{C,F}$ = 14 Hz), 124.25 (C-6″, $J_{C,F}$ = 4 Hz), 130.09 (C-4″, $J_{C,F}$ = 9 Hz), 131.63 (C-5″, $J_{C,F}$ = 3 Hz), 162.03 (C-2″, $J_{C,F}$ = 246 Hz), 175.01 (C=O); HR-MS (EI) calcd $C_{13}H_{13}FO_2$ 220.0899; obs 220.0881 (M^+).

(1*S*,4*S*,5*R*)-2-Oxo-4-ethyl-1-(3-fluorophenyl)-3-oxabicyclo[3.1.0]hexane (30c). Compound **30c** was obtained quantitatively as an oil: ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (3H, t, H-2′, $J_{2',1'}$ = 7.4 Hz), 1.38 (1H, dd, H-6a, $J_{6a,5}$ = 4.7, $J_{6a,6b}$ = 4.9 Hz), 1.62 (1H, dd, H-6b, $J_{6b,6a}$ = 4.9, $J_{6b,5}$ = 7.9 Hz), 1.81 (2H, m, H-1′), 2.36 (1H, dd, H-5, $J_{5,6a}$ = 4.7, $J_{5,6b}$ = 7.9 Hz), 4.36 (1H, t, H-4, $J_{4,1'}$ = 5.9 Hz), 6.98 (1H, m, aromatic), 7.16 (2H, m, aromatic), 7.31 (1H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.47 (C-2′), 20.47 (C-6), 29.20 (C-5), 29.86 (C-1′), 31.68 (C-1), 80.63 (C-4), 114.54 (C-4″, $J_{C,F}$ = 21 Hz), 115.26 (C-2″, $J_{C,F}$ = 23 Hz), 123.59 (C-6″, $J_{C,F}$ = 3 Hz), 130.10 (C-5″, $J_{C,F}$ = 9 Hz), 136.75 (C-1″, $J_{C,F}$ = 8 Hz), 162.74 (C-3″, $J_{C,F}$ = 244 Hz), 174.93 (C=O); HR-MS (EI) calcd $C_{13}H_{13}FO_2$ 220.0899; obs 220.0879 (M^+).

(1*S*,4*S*,5*R*)-2-Oxo-4-ethyl-1-(4-fluorophenyl)-3-oxabicyclo[3.1.0]hexane (30d). Compound **30d** was obtained as an oil in 94% yield: ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (3H, t, H-2′, $J_{2',1'}$ = 7.4 Hz), 1.35 (1H, dd, H-6a, $J_{6a,5}$ = 4.6, $J_{6a,6b}$ = 4.8 Hz), 1.58 (1H, dd, H-6b, $J_{6b,6a}$ = 4.8, $J_{6b,5}$ = 7.8 Hz), 1.81 (2H, m, H-1′), 2.32 (1H, dd, H-5, $J_{5,6a}$ = 4.6, $J_{5,6b}$ = 7.8 Hz), 4.35 (1H, t, H-4, $J_{4,1'}$ = 6.0 Hz), 7.03 (2H, t, aromatic, *J* = 8.5 Hz), 7.35–7.38 (2H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.61 (C-2′), 20.07 (C-6), 29.37 (C-1′), 29.52 (C-5), 31.75 (C-1), 80.79 (C-4), 115.56 (C-3″ and C-5″, $J_{C,F}$ = 23 Hz), 130.11 (C-1″, $J_{C,F}$ = 3 Hz), 130.21 (C-2″ and C-6″, $J_{C,F}$ = 9 Hz), 162.27 (C-4″, $J_{C,F}$ = 245 Hz), 175.55 (C=O); HR-MS (EI) calcd $C_{13}H_{13}FO_2$ 220.0899; obs 220.0889 (M^+).

(1*S*,4*S*,5*R*)-2-Oxo-4-ethyl-1-(2-methylphenyl)-3-oxabicyclo[3.1.0]hexane (30e). Compound **30e** was obtained as an oil in 62% yield: ^1H NMR (500 MHz, $CDCl_3$) δ 1.12 (3H, t, H-2′, $J_{2',1'}$ = 7.4 Hz), 1.39 (1H, dd, H-6a, $J_{6a,5}$ = 4.4, $J_{6a,6b}$ = 4.6 Hz), 1.52 (1H, dd, H-6b, $J_{6b,6a}$ = 4.6, $J_{6b,5}$ = 7.8 Hz), 1.84 (1H, m, H-1′a), 1.94 (1H, m, H-1′b), 2.35 (1H, dd, H-5, $J_{5,6a}$ = 4.5, $J_{5,6b}$ = 7.8 Hz), 2.47 (3H, s, Me–Ph–), 4.31 (1H, t, H-4, $J_{4,1'}$ = 6.6 Hz), 7.13–7.25 (4H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.24 (C-2′), 19.77 (Me–Ph–), 19.79 (C-6), 28.99 (C-5), 29.38 (C-1′), 32.33 (C-1), 81.51 (C-4), 125.78, 128.37, 130.07, 130.59, 132.32, 139.46 (the above mentioned, aromatic), 175.16 (C=O); HR-MS (EI) calcd $C_{14}H_{16}O_2$ 216.1150; obs 216.1139 (M^+).

(1*S*,4*S*,5*R*)-2-Oxo-4-ethyl-1-(3-methylphenyl)-3-oxabicyclo[3.1.0]hexane (30f). Compound **30f** was obtained as an oil in 49% yield: ^1H NMR (500 MHz, $CDCl_3$) δ 1.07 (3H, t, H-2′, $J_{2',1'}$ = 7.4 Hz), 1.33 (1H, dd, H-6a, $J_{6a,5}$ = 4.6, $J_{6a,6b}$ = 4.8 Hz), 1.62 (1H, dd, H-6b, $J_{6b,6a}$ = 4.8, $J_{6b,5}$ = 7.8 Hz), 1.82 (2H, m, H-1′), 2.31 (1H,

dd, H-5, $J_{5,6a}=4.6$, $J_{5,6b}=7.8$ Hz), 2.35 (3H, s, Me–Ph–), 4.34 (1H, d, H-4, $J_{4,1'}=6.0$ Hz), 7.10 (1H, d, aromatic, $J=7.5$ Hz), 7.18 (1H, m, aromatic), 7.22–7.26 (2H, m, aromatic); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.66 (C-2′), 19.82 (C-6), 21.38 (Me–Ph–), 29.38 (C-1′), 29.59 (C-5), 32.20 (C-1), 80.75 (C-4), 125.35, 128.46, 128.49, 129.16, 134.12, 138.29 (the above mentioned, aromatic), 175.72 (C=O); HR-MS (EI) calcd $C_{14}H_{16}O_2$ 216.1150; obs 216.1165 (M^+).

(1*S*,4*S*,5*R*)-2-Oxo-4-ethyl-1-(4-methylphenyl)-3-oxabicyclo [3.1.0]hexane (30g). Compound **30g** was obtained as an oil in 61% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (3H, t, H-2′, $J_{2',1'}=7.4$ Hz), 1.32 (1H, dd, H-6a, $J_{6a,6b}=4.6$, $J_{6a,5}=4.6$ Hz), 1.60 (1H, dd, H-6b, $J_{6b,6a}=4.6$, $J_{6b,5}=7.8$ Hz), 1.81 (2H, m, H-1′), 2.29 (1H, dd, H-5, $J_{5,6a}=4.6$, $J_{5,6b}=7.8$ Hz), 2.33 (3H, s, Me–Ph–), 4.34 (1H, t, H-4, $J_{4,1'}=6.0$ Hz), 7.16 (2H, d, aromatic, $J=8.0$ Hz), 7.28 (2H, m, aromatic, $J=8.0$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.58 (C-2′), 19.75 (C-6), 21.04 (Me–Ph–), 29.32 (C-5), 29.52 (C-1′), 31.98 (C-1), 80.70 (C-4), 128.26, 129.26, 131.19, 137.44 (the above mentioned, aromatic), 175.81 (C=O); HR-MS (EI) calcd $C_{14}H_{16}O_2$ 216.1150; obs 216.1165 (M^+).

(1*S*,4*S*,5*R*)-2-Oxo-4-ethyl-1-(1-naphthyl)-3-oxabicyclo [3.1.0]hexane (30h). Compound **30h** was obtained as an oil in 93% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (3H, t, H-2′, $J_{2',1'}=7.4$ Hz), 1.61 (1H, dd, H-6a, $J_{6a,5}=4.6$, $J_{6a,6b}=4.6$ Hz), 1.61 (1H, dd, H-6b, $J_{6b,6a}=4.6$, $J_{6b,5}=7.5$ Hz), 1.95 (1H, m, H-1′a), 2.05 (1H, m, H-1′b), 2.48 (1H, dd, H-5, $J_{5,6a}=4.6$, $J_{5,6b}=7.5$ Hz), 4.42 (1H, t, H-4, $J_{4,1'}=6.0$ Hz), 7.41 (2H, d, aromatic, $J=4.8$ Hz), 7.52 (1H, t, aromatic, $J=7.5$ Hz), 7.58 (1H, t, aromatic, $J=7.5$ Hz), 7.84 (1H, t, aromatic, $J=4.8$ Hz), 7.87 (1H, d, aromatic, $J=8.2$ Hz), 8.25 (1H, d, aromatic, $J=8.2$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.26 (C-2′), 20.25 (C-6), 29.00 (C-5), 29.65 (C-1′), 31.73 (C-1), 81.47 (C-4), 124.87, 124.95, 126.06, 126.46, 127.69, 128.62, 129.19, 130.52, 133.01, 133.98 (the above mentioned, aromatic), 175.22 (C=O); HR-MS (EI) calcd $C_{17}H_{16}O_2$ 252.1150; obs 252.1142 (M^+).

(1*S*,4*S*,5*R*)-2-Oxo-4-ethyl-1-(2-naphthyl)-3-oxabicyclo [3.1.0]hexane (30i). Compound **30i** was obtained as an oil in 89% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (3H, t, H-2′, $J_{2',1'}=7.4$ Hz), 1.40 (1H, dd, H-6a, $J_{6a,5}=4.6$, $J_{6a,6b}=4.8$ Hz), 1.71 (1H, dd, H-6b, $J_{6b,6a}=4.8$, $J_{6b,5}=7.8$ Hz), 1.84 (2H, m, H-1′), 2.39 (1H, dd, H-5, $J_{5,6a}=4.6$, $J_{5,6b}=7.8$ Hz), 4.37 (1H, t, H-4, $J_{4,1'}=6.0$ Hz), 7.45–7.49 (3H, m, aromatic), 7.79–7.82 (3H, m, aromatic), 7.86 (1H, d, aromatic, $J=0.7$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.59 (C-2′), 20.08 (C-6), 29.32 (C-1′), 29.76 (C-5), 32.32 (C-1), 80.74 (C-4), 125.94, 126.12, 126.30, 127.16, 127.56, 127.74, 128.33, 131.63, 132.63, 133.13 (the above mentioned, aromatic), 175.56 (C=O); HR-MS (EI) calcd $C_{17}H_{16}O_2$ 252.1150; obs 252.1139 (M^+).

X-ray crystallographic data of 16. $C_{17}H_{24}N_4O_3S$, $M=364.46$, Orthorhombic, $P2_12_12_1$, $a=13.436$ (3) Å, $b=16.504$ (3) Å, $c=9.033$ (1) Å, $V=2003.2$ (6) Å^3, $Z=4$, $D_x=1.209$ Mg cm^{-3}. Cell parameters were determined and refined from 21 reflections in the range $26.7°<\theta<29.9°$. A colorless crystal ($0.30\times0.20\times0.12$ mm) was mounted on a Mac Science MXC18 diffractometer with graphite-monochromated CuK_α radiation ($\lambda=1.54178$ Å). Data collection using the $\omega/2\theta$ scan technique gave 1791 reflections at room temperature, 1715 unique, of which 1365 with $I>2.00\,\sigma(I)$ reflections were used in calculations. The intensities were corrected for the Lorentz, polarization, and the extinction effect, but not for the absorption. The structure was solved by the direct method and refined by full-matrix least squares technique using maXus (ver. 2.0) as the computer program. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included by calculation, but these positions were not refined. The unweighted and weighted values were 0.057 and 0.081, respectively. No peak above 0.26 eÅ^{-3} in the last Fourier-difference map.

Binding assay. The binding affinity for the NMDA receptor was investigated according to previously reported methods.[19]

Inhibitory effects on the uptake of 5-HT. The assay was investigated according to the previously reported method.[10d]

Acknowledgements

This investigation was supported by a Grant-in-Aid for Creative Scientific Research (13NP0401) from the Japan Society for Promotion of Science. We are grateful to Daiso Co., Ltd. for the gift of chiral epichlorohydrins.

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