Accepted Manuscript

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PII: S0040-4020(18)30923-2

DOI: 10.1016/j.tet.2018.07.057

Reference: TET 29717

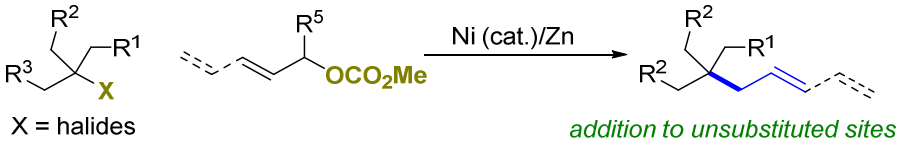
To appear in: *Tetrahedron*

Received Date: 11 May 2018

Revised Date: 20 July 2018

Accepted Date: 28 July 2018

Please cite this article as: Yu Y, Chen H, Qian Q, Yao K, Gong H, An extension of nickel-catalyzed reductive coupling between tertiary alkyl halides with allylic carbonates, *Tetrahedron* (2018), doi: 10.1016/j.tet.2018.07.057.



Tetrahedron
journal homepage: www.elsevier.com

An extension of nickel-catalyzed reductive coupling between tertiary alkyl halides with allylic carbonates

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Allylation
Chloro-cyclotryptamine
Nickel catalyzed
Extension
Dienyl carbonate

ABSTRACT

The nickel catalyzed reductive coupling of allylic carbonates with chloro-cyclotryptamine analogs to construct sterically congested all C(sp^3) quaternary centers has been achieved with emphasis on the substrate scope. And the using of dienyl methyleneyl carbonates coupling with a variety of tertiary alkyl halides furnished the dienylated products improved the reaction's applicability.

1. Introduction

The challenges in the construction of all C(sp^3) carbon quaternary stereogenic centers have evoked a number of synthetic strategies based on transition-metal-catalyzed conventional coupling of organometallic reagents with suitable electrophiles. [1-4] Among them, Cu-catalyzed Kumada assembly of tertiary alkyl-Grignard nucleophiles with alkyl electrophiles is of note. [1] The reactions display excellent compatibility with unactivated alkyl groups, although the functional group tolerance is constrained due to the use of alkyl-MgX reagents. The coupling of tertiary alkyl nucleophiles with allylic electrophiles has also been examined. [2] The allylation process often suffers from poor regioselective issues due to the competitive formation of α and γ products. Using allyl and benzyl zinc or magnesium as the nucleophiles, Oshima demonstrated the viability of formation of all carbon quaternary centers by their coupling with unactivated tertiary alkyl halides. [3] With Ag- or Co-catalysts, this coupling protocol also results in a mixture of α and γ isomers, when a 1- and/or 3-substituted allylic carbonate was subjected to the reaction conditions. [3c] When both allyl nucleophiles and allyl electrophiles are employed, excellent regioselectivities were observed in a Pd-catalyzed allyl-allyl coupling method, wherein the coupling of allyl-B(pin) with internal allyl electrophiles produces the quaternary centers when 3,3'-disubstituted allylic acetates were utilized (**Scheme 1**). [4]

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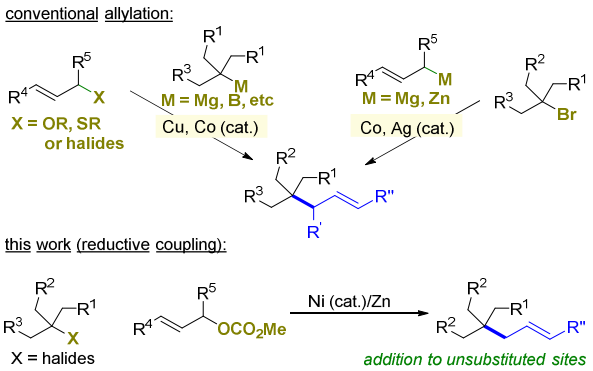


Scheme 1. Cross-coupling strategies for the construction of allyl containing all C (sp^3) quaternary carbon centers

Recently, we disclosed a Ni-catalyzed reductive coupling of tertiary alkyl halides with allylic carbonates, [5] which allows efficient preparation of all carbon quaternary congested centers constituting four C(sp^3)-C(sp^3) bonds. The mild reaction enables a wide set of unactivated tertiary alkyl halides and allylic carbonates with aryl- or alkyl-substitutes. Different substitution patterns were investigated. For 1- or 3-substituted alkyl or aryl allylic carbonates, the coupling results always favor the addition of tertiary alkyl group to the less hindered allylic carbon centers.

In this paper, we wish to provide more detailed studies on the reductive allylation method, with emphasis on the substrate scope. Firstly, we investigated the allylation of potential bio-activated cyclotryptamine structure. Then, we expanded the substrate scope to penta-dienyl carbonates.

2. Results and Discussion

(1) The coupling of chloro-cyclotryptamine derivatives

Cyclotryptamine derivatives are an important scaffold that can be found in a diverse set of natural products, alkaloids and pharmaceuticals. [6-8] The examples include bioactive compounds flustramine B which blocks voltage-activated potassium channels, [6] Fructigenine A which displays growth-inhibitory activity against Avena coleoptile and anti-inflammatory activity [7] and 5-N-acetylardeemin which is one of the most efficient inhibitors of multidrug resistance (MDR) toantitumor agents such as vinblastine, taxol, and doxorubicin (**Figure 1**). [7b, 8]

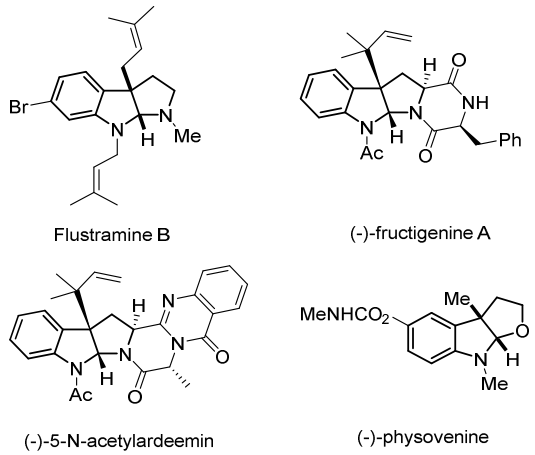


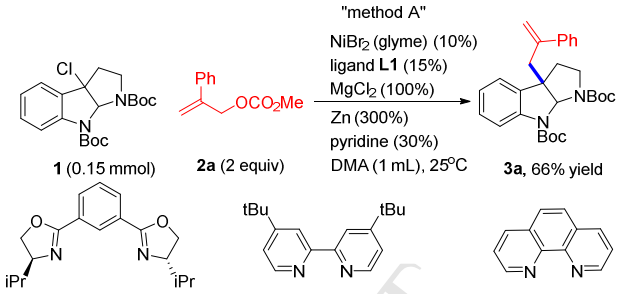
Figure 1. Examples of naturally-occurring products containing cyclotryptamine scaffold.

In our previous studies, we have showcased that use of Boc-protected chloro-cyclotryptamine precursor **1** effectively provided the allylated pyrroloindoline **3a** in 66% yield by coupling with 2-phenylallyl carbonate **2a**. Compound **3a** can be viewed as an analog of the natural products described in Figure 1. Such a result prompted us to quest the generality of the allylation reaction conditions, however, no improvement was attained (*method A*, **Table 1.**).

With the standard *method A* in hand, a number of 2-aryl allylic carbonates substituted with both electron-withdrawing and electron-donating groups on the aryl moieties were first explored. Good yields were obtained for **3b-f** regardless of the substitution patterns (**Figure 2**). By comparison, the unsubstituted allylic carbonate furnished **3g** in a moderate yield. Whereas 2-methyl-decorated allyl carbonate was much less effective, generating **3h** in 42% yield, the branched but-3-en-2-yl methyl carbonate delivered **3i** in 48% yield by addition of the tertiary alkyl group to the 1-position of the allyl substrate; product **3i** was also contaminated with a branched isomer with a 10:1 linear/branched ratio. Notably, for 1-methyl-substitted allylic carbonate, no appreciable coupling yield was observed.

Next, a variety of chloro-cyclotryptamine analogs of **1** were investigated for the methyl (2-aryl) allyl carbonates **2a**, which generated **4-13** in moderate to good yields. The chloro-substrates beating 5-methoxy and Cl gave **4-5** in preparatively useful yields. Different protecting groups on the nitrogen atoms of the chloro-substrates other than Boc- were effective. These include Cbz, Methoxycarbonyl and Tosyl as manifested in the example of **6-10**. More interestingly, a methyl substituent at C (2a)-position of the chloro-substrate delivered **11** in 45% yield which is composed of two consecutive quaternary carbon centers. To our delight, a chloro-substrate contacting a tetrahydrofuran ring was also competent, which offered **12** has 47% yield. This product can be viewed as a key scaffold for nature-occurring Physovenine (**Figure 1**). Finally, the more complex chloro-substrates derived from tryptophan were also examined, which gave **13** in 56% yield.

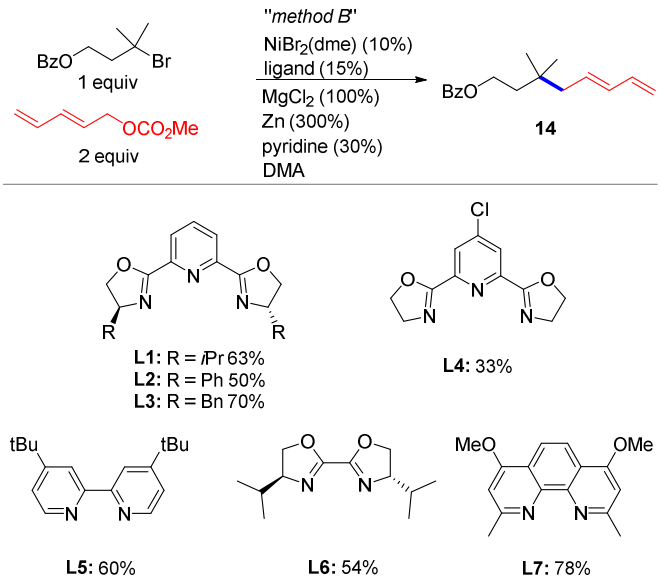
Table 1. Optimization for the coupling of 2-phenylallyl carbonate with chloro-cyclotryptamine 1**.**



Entry	Variation from the condition A	Yield[b]
1	none	66%[c]
2	no Ni	trace
3	no pyridine	57%
4	no ligand	8%
5	no $MgCl_2$	32%
6	no Zn	ND
7	$Ni(COD)_2$	60%
8	Ni(diglyme)	58%
9	NiI_2	63%
10	L5 instead of L1	trace
11	L8 instead of L1	12%

[a] **Standard conditions**: 1 (0.15mmol), allylic carbonate 2a (2 equiv), Ni (10%), ligand (15%), pyridine (30%), $MgCl_2$ (100%), Zn (300%), DMA (1 mL), 25°C. [b] NMR yield using 2,5-dimethylfuran as the internal reference. [c] Yield of isolate yield. COD=1,5-cycloocatadiene, DMA= N, N-dimethylacetamide.

(2) The coupling with penta-dienyl carbonates



Scheme 2. The optimal reaction conditions for **14**.

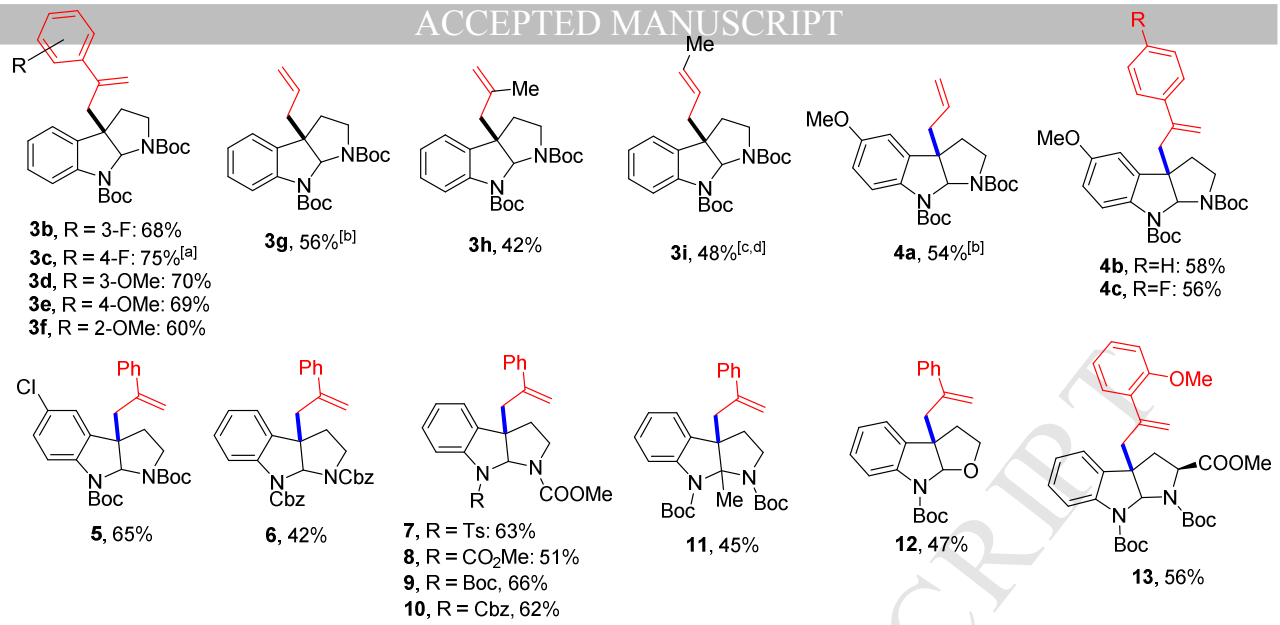


Figure 2. Substrate scope. [a] ph-pybox (L2, 15%) was used, no enantioselectivity was observed. [b] Standard conditions except that Ni $(COD)_2$ (10%), di-*t*bu-bipyridine (L5, 15%), 2,6-diamine-pyridine (30%) was used. [c] but-3-en-2-yl methyl carbonate was used, 10:1 ratio of linear/branched. [d] $NiBr_2$(diglyme) (10%), 4,7-dimethoxy-2,9-dimethyl-1,10-phenanthroline (L7, 15%), 2,6-diamine-pyridine (30%), $MgBr_2$ (100%), Mn (300%) was used.

To further expand the scope of the substrates, we explored the coupling of (*E*)-methyl penta-2,4-dien-1-yl carbonate with different tertiary alkyl halides. With ligand **L7**, a good yield was obtained for **14** (*method B*, **Scheme 2**). Extension the *method B* to other tertiary bromide generated **15-24** generally in moderate to good yields (**Figure 3**). The reaction conditions displayed excellent functional group tolerance even for a free phenolic group as evident in **17**. Similar to our previous findings, the primary bromide and tosylate were tolerated as in the products **19-20**, which provide a possibility of further transformations of these functional groups. In addition, the reaction also accommodates the chloro-cyclotryptamine derivatives which produced the dienyl products **21-24** in moderate yields.

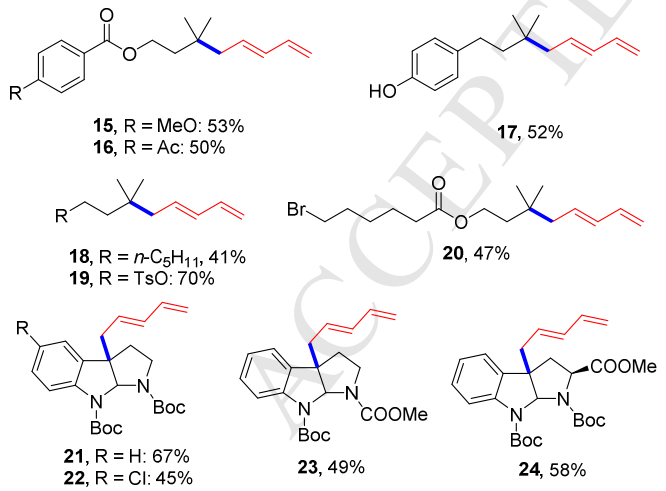
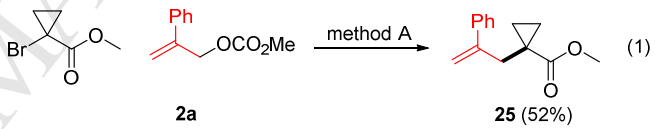


Figure 3. Substrate scope for the coupling of dienyl mehtylenyl carbonates

(3) The coupling of other substrates

With further investigation of the substrate scopes of the allylation event, we found that activated tertiary alkyl halides are also suitable for this protocol. For instance, the coupling of methyl 1-bromocyclopropane-1-carboxylate with **2a** furnished product **25** in 52% yield (**equation 1**). However, the reaction is not efficient for allyl substrates that bear two or more substituents may due to the steric hindrance.



Equation 1. Coupling of methyl 1-bromocyclopropane-1-carboxylate with 2a

3. Conclusions

In summary, an extension of nickel-catalyzed reductive coupling between tertiary alkyl halides with allylic carbonates to generate highly sterically congested all C(sp^3) quaternary centers is illustrated. We have developed the strategy of reductive allylation for chloro-cyclotryptamine derivatives, which is suitable for a variety of aryl and alkyl-substituted allylic carbonates and a number of chloro-cyclotryptamine analogs with different protecting groups. Installation of 1,3-dienyl methylenyl groups to the C3a-positions of the cyclotryptamine derivatives is also competent. In addition, penta-dienyl carbonate can efficiently coupling with tertiary alkyl halides. All these expansion, shows the potential value of this reaction.

4. Experimental section

4.1. General Information

Experiments were conducted under a nitrogen atmosphere in oven-dried or flame-dried glassware with magnetic stirring, unless otherwise specified. For product purification by flash column chromatography, silica gel (300−400 mesh) and petroleum ether (bp 60−90 °C) were used. NMR spectra were measured on a Bruker 600 MHz and a Bruker 500 MHz NMR instrument at room temperature. Reference peaks for chloroform in ^{1}H NMR and ^{13}C NMR spectra were set at 7.26 ppm and 77.0 ppm, respectively. High-resolution mass spectra (HRMS) were obtained using a IonSpec 4.7 TESLA FTMS. Melting point was

recorded on a micro melting point apparatus (X-4, YUHUA Co., Ltd, Gongyi, China). IR spectra was detected by AVATAR 370 FT-IR and recorded in wave number, cm^{-1}.

4.1.1 General Method A

To a flame-dried Schlenk tube equipped with a stir bar was loaded zinc power (58.8 mg, 0.9 mmol, 300 mol %), followed by addition of $MgCl_2$ (28.6 mg, 0.3 mmol, 100 mol %), iPr-box **L1** (13.6 mg, 0.045 mmol, 15 mol %), $NiBr_2$·glyme (9.2 mg, 0.03 mmol, 10 mol %). The tube was evacuated and refilled nitrogen (N_2) three time. DMA (1.0 mL) was added via syringe, followed by addition of chloro-cyclotryptamine/tertiary bromide (0.3 mmol, 100%), Allylic Carbonates (0.6 mmol, 200 mol %), Pyridine (0.09 mmol, 30 mol %). After the reaction mixture was allowed to stir for 12 hours under N_2 atmosphere at 25 °C. It was loaded onto a silica column. Flash column chromatography provided the product as oil or foam solid.

4.1.2 General Method B

To a flame-dried Schlenk tube equipped with a stir bar was loaded zinc power (58.8 mg, 0.9 mmol, 300 mol %), followed by addition of $MgCl_2$ (28.6 mg, 0.3 mmol, 100 mol %), **L7** (12.1 mg, 0.045 mmol, 15 mol %), $NiBr_2$·glyme (9.2 mg, 0.03 mmol, 10 mol %). The tube was evacuated and refilled nitrogen (N_2) three time. DMA (1.0 mL) was added via syringe, followed by addition of chloro-cyclotryptamine/tertiary bromide (0.3 mmol, 100%), Allylic Carbonates (0.6 mmol, 200 mol %), Pyridine (0.09 mmol, 30 mol %). After the reaction mixture was allowed to stir for 12 hours under N_2 atmosphere at 25 °C. It was loaded onto a silica column. Flash column chromatography provided the product as oil or solid.

4.2 Synthetic procedure and characterization data

4.2.1 Di-tert-butyl(3aS,8aR)-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydropyrrolo[2,3-b] indole-1,8-dicarboxylate (3a)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 66% yield (94.4 mg, 0.198 mmol) as foam solid. mp: 44-45 °C. The cis-structure was confirmed by NOESY spectrum wherein the allylic CH_2 protons correlate with the proton on the carbon adjacent to the two nitrogen atoms.

IR (KBr) ν **=** 2975, 2931, 1703, 1470, 1393, 1148, 864, 747. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.51 (s, 1H), 7.24-7.18 (m, 5H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.07 (s, 1H), 5.21 (s, 1H), 5.00 (s, 1H), 3.63-3.60 (m, 1H), 3.03 (d, *J* = 13.8 Hz, 1H), 2.86 (d, *J* = 13.8 Hz, 1H), 2.74-2.68 (m, 1H), 1.85-1.83 (m, 2H), 1.57 (s, 9H), 1.46 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 153.8, 152.3, 145.0, 142.7, 142.0, 134.2, 128.1, 128.0, 127.2, 126.3, 123.5, 122.6, 117.7, 116.4, 81.0, 79.9, 56.6, 45.9, 43.2, 28.4, 28.3. **HRMS** (APCI) exact mass calculated for [M+H$^+$] ($C_{29}H_{37}N_2O_4$): m/z 477.2748; found: 477.2910.

4.2.2 Di-*tert*-butyl(3aS)-3a-(2-(3-fluorophenyl) allyl)-2,3,3a,8a-tetrahy dropyrrolo [2,3-*b*] indole-1,8-dicarboxylate (3b)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 68% yield (100.9 mg, 0.204 mmol) as foam solid. mp: 100-101 °C.

IR (KBr) ν **=** 2972, 2929, 1704, 1476, 1390, 1158, 889, 750. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.47 (bs, 1H), 7.14 (q, *J* = 6.0 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 7.0 Hz, 2H), 6.86-6.79 (m, 3H), 6.06 (s, 1H), 5.21 (s, 1H), 5.06 (s, 1H), 3.64 (q, *J* = 11.2, 7.2 Hz, 1H), 3.01 (d, *J* = 13.7 Hz, 1H), 2.83 (d, *J* = 13.9 Hz, 1H), 2.76-2.71 (m, 1H), 1.93-1.85 (m, 2H), 1.58 (s, 9H), 1.46 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 163.3, 161.6, 153.8, 152.1, 144.3, 144.2, 144.0, 142.7, 129.5, 129.4, 128.1, 123.4, 122.6, 121.9, 118.5, 113.9, 113.8, 113.3, 113.1, 81.1, 79.6, 56.6, 53.3, 45.8, 43.3, 28.3, 28.2. **^{19}F NMR (564 MHz, Chloroform-*d*):** δ 113.6. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{29}H_{36}FN_2O_4$): m/z 495.2654; found: 495.2660.

4.2.3 Di-*tert*-butyl3a-(2-(4-fluorophenyl) allyl)-2,3,3a,8a-tetrahydro pyrrolo[2,3-*b*] indole-1,8-dicarboxylate (3c)

According to *method A*, except L2 was used, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 75% yield (111.2 mg, 0.225 mmol) as foam solid. mp: 102-104 °C. The cis-structure was confirmed by NOESY spectrum wherein the allylic CH_2 protons correlate with the proton on the carbon adjacent to the two nitrogen atoms.

IR (KBr) ν **=** 2973, 2928,1706, 1478, 1391, 1160, 894, 841, 751. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.50 (bs, 1H), 7.08 (t, *J* = 7.5 Hz, 3H), 6.91-6.82 (m, 4H), 6.04 (s, 1H), 5.13 (s, 1H), 5.01 (s, 1H), 3.64 (dd, *J* = 11.4, 7.8 Hz, 1H), 3.00 (d, *J* = 13.8 Hz, 1H), 2.84 (d, *J* = 13.2 Hz, 1H), 2.74-2.70 (m, 1H), 1.91-1.83 (m, 2H), 1.56 (s, 9H), 1.46 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 162.7, 161.1, 153.7, 152.1, 144.1, 142.7, 137.9, 133.8, 127.9, 127.8, 123.3, 122.5, 117.6, 116.1, 114.8, 114.7, 81.0, 79.6, 56.5, 53.3, 45.7, 43.6, 28.3, 28.2. **^{19}F NMR (564 MHz, Chloroform-*d*):** δ 115.3. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{29}H_{36}FN_2O_4$): m/z 495.2654; found: 495.2686.

4.2.4 Di-*tert*-butyl (3aS)-3a-(2-(3-methoxyphenyl) allyl)-2,3,3a,8a-tetrahydropyrrolo [2,3-*b*] indole-1,8-dicarboxylate (3d)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 70% yield (106.3 mg, 0.210 mmol) as foam solid. mp: 87-89 °C.

IR (KBr) ν **=** 2972, 2928, 1705, 1478, 1394, 1160, 891, 752. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.53 (bs, 1H), 7.15 (t, *J* = 12.0 Hz, 1H), 7.10 (t, *J* = 12.0 Hz, 1H), 6.94 (d, *J* = 6.0 Hz, 1H), 6.85 (t, *J* = 12.0 Hz, 1H), 6.81 (d, *J* = 6.0 Hz, 1H), 6.74 (dd, *J* = 12.0, 6.0 Hz, 1H), 6.67 (s, 1H), 6.06 (s, 1H), 5.22 (s, 1H), 4.99 (s, 1H), 3.76 (s, 3H), 3.63-3.60 (m, 1H), 3.00 (d, *J* = 12.0 Hz, 1H), 2.84 (d, *J* = 12.0 Hz, 1H), 2.71 (q, *J* = 12.0 Hz, 1H), 1.86 (t, *J* = 6.0 Hz, 2H), 1.57 (s,9H), 1.45 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 159.2, 152.2, 144.8, 143.5, 142.6, 129.0, 127.9, 123.5, 122.6, 118.8, 117.7, 112.7, 112.0, 81.0, 79.8, 56.6, 55.0, 53.4, 45.9, 43.2, 28.3, 28.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{30}H_{39}N_2O_5$): m/z 507.2853; found: 507.2831

4.2.5 Di-*tert*-butyl (3aS)-3a-(2-(4-methoxyphenyl) allyl)-2,3,3a,8a-tetrahydropyrrolo [2,3-*b*] indole-1,8-dicarboxylate (3e)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 69% yield (104.8 mg, 0.207 mmol) as foam solid. mp: 78-79 °C.

IR (KBr) ν **=** 2971, 2927, 1705, 1607, 1473, 1393, 1157, 1028, 892, 752. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.53 (bs, 1H), 7.14-7.10 (m, 3H), 6.95 (d, *J* = 6.0 Hz, 1H), 6.87 (t, *J* = 6.0 Hz, 1H), 6.76 (d, *J* = 6.0 Hz, 2H), 6.05 (s, 1H), 5.15 (s, 1H), 4.90 (s, 1H), 3.77 (s, 3H), 3.63-3.60 (m, 1H), 2.96 (d, *J* = 18.0 Hz, 1H), 2.82 (d, *J* = 18.0 Hz, 1H), 2.73-2.68 (m, 1H), 1.85-1.83 (m, 2H), 1.56 (s, 9H), 1.45 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 158.8, 153.8, 152.2, 144.2, 142.6, 134.3, 127.9, 127.4, 123.5,

122.5, 116.4, 113.5, 81.0, 79.8, 56.6, 55.1, 45.9, 43.1, 28.3, 28.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{30}H_{39}N_2O_5$): m/z 507.2853; found: 507.2839.

4.2.6 Di-*tert*-butyl(3aS)-3a-(2-(2-methoxyphenyl) allyl)-2,3,3a,8a-tetrahy dropyrrolo [2,3-*b*] indole-1,8-dicarboxylate (3f)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 60% yield (91.1 mg, 0.180 mmol) as foam solid. mp: 83-84 ^oC.

IR (KBr) *v* = 2972, 2927, 1706, 1480, 1391, 1160, 894, 750. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.48 (bs, 1H), 7.14(t, *J* = 7.8 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.83 (t, *J* = 7.8 Hz, 1H),6.79 (s, 1H), 6.74 (t, *J* = 7.2 Hz, 2H), 5.98 (s, 1H), 5.07 (s, 1H), 5.03 (s, 1H), 3.80 (s, 3H), 3.67-3.63 (m, 1H), 3.25 (d, *J* = 13.8 Hz, 1H), 2.85-2.80 (m, 1H), 2.69 (tt, *J* = 11.5, 6.0 Hz, 1H), 1.87-1.80 (m, 2H), 1.56 (s, 9H), 1.45 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 156.0, 153.8, 152.2, 145.1, 142.8, 131.2, 129.9, 128.5, 127.8, 123.3, 122.4, 120.5, 119.4, 110.2, 80.9, 79.7, 56.4, 55.1, 45.5, 43.9, 28.4, 28.3. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{30}H_{39}N_2O_5$): m/z 507.2853; found: 507.2849.

4.2.7 Di-*tert*-butyl (3aS)-3a-allyl-2,3,3a,8a-tetrahydropyrrolo[2,3-*b*] indole-1,8 -dicarboxylate (3g)

According to *method A*, except that Ni $(COD)_2$ 10%, L5 15%, 2,6-diamine-Pyridine 30% was used, flash column chromatography (SiO_2: 2% ethyl acetate in petroleum ether) provided this compound in 56% yield (67.3 mg, 0.168 mmol) as foam solid. mp: 89-91 ^oC.

IR (KBr) *v* = 2974, 2928, 1707, 1477, 1398, 1159, 1091, 887, 753. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.56 (bs, 1H), 7.20 (t, *J* = 12.0 Hz, 1H), 7.10 (d, *J* = 6.0 Hz, 1H), 7.02 (t, *J* = 12.0 Hz, 1H), 6.02 (s, 1H), 5.62-5.53 (m, 1H), 5.06-4.99 (m, 2H), 3.75-3.71 (m, 1H), 2.84 (td, *J* = 12.0, 6.0 Hz, 1H), 2.52-2.48 (m, 1H), 2.44-2.40 (m, 1H), 2.08-2.04 (m, 1H), 2.01-1.95 (m, 1H), 1.55 (s, 9H), 1.47 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 154.0, 152.4, 143.0, 133.1, 128.1, 123.1, 122.9, 118.7, 81.2, 79.9, 56.2, 45.8, 42.6, 28.4, 28.3. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{23}H_{33}N_2O_4$): m/z 401.2435; found: 401.2433.

4.2.8 Di-*tert*-butyl(3aS)-3a-(2-methylallyl)-2,3,3a,8a-tetrahydropyrrolo [2,3-*b*] indole -1,8-dicarboxylate (3h)

According to *method A*, flash column chromatography (SiO_2: 2% ethyl acetate in petroleum ether) provided this compound in 42% yield (52.2 mg, 0.126 mmol) as foamy semisolid.

IR (KBr) *v* = 2974, 2927, 1707, 1476, 1395, 1162, 892, 753. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.52 (bs, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 1H), 7.00 (t, *J* = 7.4 Hz,, 1H), 6.09 (s, 1H), 4.75 (s, 1H), 4.64 (s, 1H), 3.71 (dd, *J* = 10.8, 7.8 Hz, 1H), 2.82 (tt, *J* = 11.5, 5.2 Hz, 1H), 2.49 (d, *J* = 13.4 Hz, 1H), 2.41 (d, *J* = 13.4 Hz, 1H), 2.10-1.99 (m, 2H), 1.54 (s, 9H), 1.47 (s, 9H), 1.43 (s, 3H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 154.0, 152.3, 142.9, 141.4, 135.2, 128.1, 123.1, 115.2, 81.0, 79.7, 56.4, 53.4, 46.1, 45.6, 28.4, 28.3, 23.9. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{24}H_{35}N_2O_4$): m/z 415.2591; found: 415.2572.

4.2.9 Di-*tert*-butyl(E)-3a-(but-2-en-1-yl)-2,3,3a,8a-tetrahy dropyrrolo [2,3-*b*] indole-1,8- dicarboxylate (3i)

This compound can be prepared from the coupling of **but-3-en-2-yl methyl carbonate** with di-tert-butyl 3a-chloro-2,3,3a,8a-tetrahydropyrrolo[2,3-*b*] indole -1,8-dicarboxylate, using $NiBr_2$.diglyme (10 mol %) and $MgBr_2$ (100 mol %), Mn (300 mol %) and L7 (15 mol %). Flash column chromatography (SiO_2: 2% ethyl acetate in petroleum ether) provided a mixture of linear and branched isomer in overall 48% yield (59.7 mg, 0.144 mmol) as foamy semisolid. The ratio of the *linear* to *branched* was determined to be ~10:1 based on ^{1}H NMR analysis.

IR (KBr) *v* = 2974, 2928, 1707, 1476, 1395, 1160, 892, 753. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.57 (bs, 1H), 7.19 (t, *J* = Hz, 1H), 7.09 (d, *J* = 12.0 Hz, 1H), 7.01 (t, *J* = 6.0 Hz, 1H), 6.01 (s, 1H), 5.49-5.46 (m, 1H), 5.25-5.20 (m, 1H), 3.73 (t, *J* = 10.8, 7.8 Hz, 1H), 2.84 (td, *J* = 11.4, 5.4 Hz, 1H), 2.50-2.42(m, 1H), 2.36-2.33(m, 1H), 2.01-1.96 (m, 2H), 1.58 (d, *J* = 6.0 Hz, 3H), 1.57 (s, 9H), 1.48 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 153.8, 152.3, 142.8, 138.9, 135.2, 129.3, 128.7, 127.9, 127.3, 125.3, 122.9, 122.7, 116.5, 81.0, 79.7, 56.3, 45.7, 41.3, 36.0, 28.3, 28.2, 17.9. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{24}H_{35}N_2O_4$): m/z 415.2591; found: 415.2601.

4.2.10 Di-*tert*-butyl (3aS)-3a-allyl-5-methoxy-2,3,3a,8a-tetrahydro pyrrolo [2,3-*b*] indole-1,8- dicarboxylate (4a)

According to *method A*, except that Ni $(COD)_2$ 10%, L5 15%, 2,6-diamine-Pyridine 30% was used, flash column chromatography (SiO_2: 2% ethyl acetate in petroleum ether) provided this compound in 54% yield (69.7 mg, 0.162 mmol) as foam solid.

IR (KBr) *v* = 2971, 2927, 1704, 1485, 1394, 1256, 1158, 890, 761. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.43 (bs, 1H), 6.73 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.66 (d, *J* = 3.0 Hz, 1H), 5.98 (s, 1H), 5.56 (td, *J* = 16.8, 7.8 Hz, 1H), 5.05 (d, *J* = 16.8 Hz, 1H), 4.99 (d, *J* = 10.8 Hz, 1H), 3.78 (s, 3H), 3.71 (dd, *J* = 10.8, 7.8 Hz, 1H), 2.85 (td, *J* = 11.4, 5.4 Hz, 1H), 2.50-2.47 (m 1H), 2.40 (dd, *J* = 13.8, 7.8 Hz, 1H), 2.03-1.93 (m, 2H), 1.54 (s, 9H), 1.47 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 156.1, 153.9, 152.5, 136.6, 133.0, 118.7, 112.6, 109.1, 80.9, 80.1, 55.6, 45.6, 42.5, 28.4, 28.3. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{24}H_{35}N_2O_5$): m/z 431.2540; found: 431.2576.

4.2.11 Di-*tert*-butyl(3aS)-5-methoxy-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydropyrrolo[2,3-*b*] indole-1,8-dicarboxylate (4b)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 58% yield (88.2 mg, 0.174 mmol) as foam solid. mp: 117-119 ^oC.

IR (KBr) *v* = 2971, 2929, 1704, 1476, 1390, 1158, 889, 750. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.36 (bs, 1H), 7.22-7.15 (m, 5H), 6.62 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.43 (d, *J* = 1.2 Hz, 1H), 6.06 (s, 1H), 5.21 (s, 1H), 5.04 (s, 1H), 3.65 (s, 3H), 3.62-3.59 (m, 1H), 3.02 (d, *J* = 13.7 Hz, 1H), 2.84 (d, *J* = 13.7 Hz, 1H), 2.76-2.71 (m, 1H), 1.83-1.81 (m, 2H), 1.57 (s, 9H), 1.46 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 155.6, 153.7, 152.3, 144.9, 142.0, 136.3, 128.0, 127.1, 126.2, 117.6, 112.9, 109.5, 80.7, 80.2, 56.8, 55.4, 45.7, 43.1, 28.3, 28.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{30}H_{39}N_2O_5$): m/z 507.2583; found: 507.2845.

4.2.12 Di-*tert*-butyl3a-(2-(4-fluorophenyl) allyl)-5-methoxy-2,3,3a, 8a-tetrahydropyrrolo [2,3-*b*] indole-1,8-dicarboxylate (4c)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 56% yield (88.1 mg, 0.168 mmol) as foam solid.

IR (KBr) *v* = 2963, 2929, 1700, 1498, 1395, 1259, 828. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.40 (bs, 1H), 7.07 (s, 2H), 6.87 (t, *J* = 7.8 Hz, 2H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.41 (s, 1H), 6.03 (s,

1H), 5.14 (s, 1H), 5.05 (s, 1H), 3.67 (s, 3H), 3.64-3.62 (m, 1H), 3.00 (d, *J* = 13.2 Hz, 1H), 2.83 (d, *J* = 13.2 Hz, 1H), 2.77-2.73 (m, 1H), 1.88-1.87 (m, 2H), 1.56 (s, 9H), 1.46 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 162.7, 161.1, 155.7, 152.3, 144.1, 138.0, 127.9, 117.6, 114.8, 114.7, 112.7, 109.8, 80.8, 80.0, 56.9, 55.5, 45.7, 43.5, 28.4, 28.3. **^{19}F NMR (564 MHz, Chloroform-*d*):** δ 115.5. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{30}H_{38}FN_2O_5$): m/z 525.2759; found: 525.2770.

4.2.13 Di-*tert*-butyl (3aS)-5-chloro-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydro pyrrolo[2,3-*b*] indole-1,8-dicarboxylate (5)

According to *method A*, flash column chromatography (SiO_2: 2% ethyl acetate in petroleum ether) provided this compound in 65% yield (99.7 mg, 0.195 mmol) as foam solid. mp: 59-60 ^{o}C.

IR (KBr) *v* = 2973, 2927, 1707, 1475, 1385, 1159, 893, 773. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.40 (bs, 1H), 7.22-7.17 (m, 3H), 7.12 (d, *J* = 6.6 Hz, 2H), 7.00 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.83 (d, *J* = 1.8 Hz, 1H), 6.07 (s, 1H), 5.21 (s, 1H), 5.04 (s, 1H), 3.66-3.63 (m, 1H), 3.04 (d, *J* = 13.8 Hz, 1H), 2.84 (d, *J* = 13.8 Hz, 1H), 2.75-2.70 (m, 1H), 1.86-1.83 (m, 2H), 1.56 (s, 9H), 1.45 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ153.6, 152.0, 144.8, 141.5, 141.4, 135.9, 128.1, 127.9, 127.5, 127.3, 126.2, 123.8, 117.8, 81.4, 80.1, 56.7, 45.8, 43.3, 38.3, 28.3, 28.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{29}H_{36}ClN_2O_4$): m/z 511.2358; found: 511.2341.

4.2.14 Di-benzyl (3aS)-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydropyr rolo [2,3-*b*] indole -1,8- dicarboxylate (6)

According to *method A*, flash column chromatography (SiO_2: 3% ethyl acetate in petroleum ether) provided this compound in 42% yield (68.6 mg, 0.126 mmol) as foam solid.

IR (KBr) *v* = 1707, 1410, 1265, 1095, 904, 748, 698. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.63 (bs, 1H), 7.36-7.30 (m, 10H), 7.15 (d, *J* = 4.8 Hz, 4H), 7.11 (m, 2H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.93 (t, *J* = 7.2 Hz, 1H), 6.09 (s, 1H), 5.11 (s, 2H), 5.03 (d, *J* = 12.0 Hz, 2H), 4.91 (s, 2H), 3.75-3.72 (m, 1H), 3.01 (d, *J* = 8.4 Hz, 1H), 2.87-2.82 (m, 2H), 1.98-1.91 (m, 2H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 154.4, 153.1, 144.6, 142.0, 141.4, 137.8, 136.5, 136.2, 134.0, 128.3, 128.1, 128.0, 127.9, 127.3, 126.1, 123.3, 117.9, 116.5, 67.2, 66.9, 45.9, 43.0, 35.7. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{35}H_{33}N_2O_4$): m/z 545.2435; found: 545.2435.

4.2.15 Methyl (3aS)-3a-(2-phenylallyl)-8-tosyl-3,3a,8,8a-tetrahydro pyrrolo [2,3-*b*] indole-1(2H)-carboxylate (7)

According to *method A*, flash column chromatography (SiO_2: 10% ethyl acetate in petroleum ether) provided this compound in 63% yield (92.3 mg, 0.189 mmol) as foam solid. mp: 51-53 ^{o}C.

IR (KBr) *v* = 2925, 1708, 1598, 1449, 1374, 1168, 1000, 762, 662, 574. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.70 (bs, 2H), 7.49 (s, 1H), 7.23 (d, *J* = 6.0 Hz, 5H), 7.18 (t, *J* = 6.0 Hz, 1H), 7.14 (s, 2H), 6.91 (d, *J* = 24.0 Hz, 2H), 5.91 (s, 1H), 5.19 (t, *J* = 6.0 Hz, 1H), 4.67 (s, 1H), 3.66-3.61 (m, 4H), 2.72 (td, *J* = 12.0, 6.0 Hz, 1H), 2.67 (d, *J* = 12.0 Hz, 1H), 2.35 (s, 3H), 2.29 (d, *J* = 18.0 Hz, 1H), 1.85-1.79 (m, 1H), 1.68 (dd, *J* = 18.0, 6.0 Hz, 1H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 154.6, 143.9, 143.8, 141.5, 137.0, 135.1, 129.5, 128.5, 128.2, 127.4, 126.9, 126.2, 124.3, 118.1, 116.8, 83.2, 57.9, 52.4, 45.7, 42.2, 36.7, 35.3, 21.4. **HRMS** (ESI) exact mass calculated for [M+Na$^+$] ($C_{28}H_{28}N_2NaO_4S$): m/z 511.1662; found: 511.2437.

4.2.16 Di-methyl (3aS)-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydropyr rolo[2,3-*b*] indole-1,8- dicarboxylate (8)

According to *method A*, flash column chromatography (SiO_2: 3% ethyl acetate in petroleum ether) provided this compound in 51% yield (60.0 mg, 0.153 mmol) as colorless oil.

IR (KBr) *v* = 2922, 2853, 1716, 1449, 1380, 1257, 761. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.60 (bs, 1H), 7.24-7.21 (m, 3H), 7.19-7.14 (m, 3H), 7.01 (d, *J* = 6.0 Hz, 1H), 6.93 (t, *J* = 12.0 Hz, 1H), 5.92 (s, 1H), 5.20 (s, 1H), 4.92 (s, 1H), 3.76 (s, 3H), 3.67-3.66 (m, 1H), 3.65 (s, 3H), 2.99 (d, *J* = 12.0 Hz, 1H), 2.88 (d, *J* = 12.0 Hz, 1H), 2.82-2.77 (m, 1H), 1.96-1.95 (m, 2H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 153.8, 144.6, 144.5, 142.1, 141.5, 134.0, 128.4, 128.3, 127.5, 127.4, 126.3, 126.2, 123.3, 118.1, 116.3, 57.0, 52.6, 52.5, 45.8, 43.2, 43.1. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{23}H_{25}N_2O_4$): m/z 393.1809; found: 393.1823.

4.2.17 8-(Tert-butyl) 1-methyl (3aS)-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydropyrrolo [2,3-*b*] indole-1,8-dicarboxylate (9)

According to *method A*, flash column chromatography (SiO_2: 3% ethyl acetate in petroleum ether) provided this compound in 66% yield (86.0 mg, 0.198 mmol) as foam solid. mp: 81-82 ^{o}C.

IR (KBr) *v* = 2961, 2924, 1693, 1454, 1398, 1154, 906, 746. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.54 (bs, 1H), 7.24-7.19 (m, 5H), 7.12 (t, *J* = 12.0 Hz, 1H), 6.96 (d, *J* = 6.0Hz, 1H), 6.87 (t, *J* = 6.0 Hz, 1H), 5.99 (s, 1H), 5.24 (s, 1H), 5.00 (s, 1H), 3.68 (s, 3H), 3.66 (m, 1H), 3.00 (d, *J* = 13.8 Hz, 1H), 2.85 (d, *J* = 13.8 Hz, 1H), 2.80-2.75 (m, 1H), 1.91-1.88 (m, 2H), 1.56 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 155.1, 152.3, 144.8, 142.4, 141.8, 134.2, 128.2, 127.3, 126.2, 123.2, 122.9, 117.8, 116.5, 81.1, 57.0, 52.4, 45.9, 42.9, 28.3. **HRMS** (ESI) exact mass calculated for [M+Na$^+$] ($C_{26}H_{30}N_2NaO_4$): m/z 457.2098; found: 457.2075.

4.2.18 8-Benzyl-1-methyl (3aS)-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydro pyrrolo[2,3-*b*] indole-1,8-dicarboxylate (10)

According to *method A*, flash column chromatography (SiO_2: 3% ethyl acetate in petroleum ether) provided this compound in 62% yield (87.2 mg, 0.186 mmol) as colorless oil.

IR (KBr) *v* = 2948, 1706, 1398, 1265, 1030, 902, 751, 700. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.60 (bs, 1H), 7.43-7.41 (m, 2H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.17-7.11 (m, 6H), 7.00 (d, *J* = 7.2 Hz, 1H), 6.90 (t, *J* = 7.2 Hz, 1H), 6.01 (s, 1H), 5.22 (s, 2H), 5.13 (s, 1H), 4.91 (s, 1H), 3.68 (s, 1H), 3.45 (s, 3H), 3.01 (d, *J* = 13.8 Hz, 1H), 2.86 (d, *J* = 13.8 Hz, 1H), 2.82-2.76 (m, 1H), 1.96-1.92 (m, 2H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 155.0, 153.1, 152.9, 144.6, 142.0, 141.4, 136.2, 134.0, 128.4, 128.3, 128.2, 128.1, 128.0, 127.4, 127.3, 126.2, 126.1, 123.3, 117.9, 116.4, 67.4, 57.1, 52.2, 45.8, 43.2, 43.1. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{29}H_{29}N_2O_4$): m/z 469.2122; found: 469.2131.

4.2.19 Di-tert-butyl (3aS)-8a-methyl-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydropyrrolo [2,3-*b*] indole-1,8-dicarboxylate (11)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 45% yield (66.3 mg, 0.135 mmol) as foam solid. mp: 94-96 ^{o}C.

IR (KBr) *v* = 2979, 2929, 1705, 1475, 1375, 1150, 1056, 849, 748. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.65 (bs, 1H), 7.33-7.28 (m, 4H), 7.26-7.24 (m, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 6.6 Hz, 1H), 6.84 (t, *J* = 7.8 Hz, 1H), 5.24 (s, 1H), 4.68 (s, 1H), 3.25 (s, 1H), 2.93 (d, *J* = 12.0 Hz, 1H), 2.65 (d, *J* = 6.0 Hz, 1H), 2.45 (d, *J* = 12.0 Hz, 1H), 1.98 (s, 3H), 1.70-1.64 (m, 2H),

1.60 (s, 9H), 1.40 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 152.5, 144.1, 142.3, 133.3, 128.3, 127.7, 127.4, 126.4, 124.3, 122.0, 118.4, 89.5, 81.0, 58.7, 45.9, 39.3, 28.5, 20.6. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{30}H_{39}N_2O_4$): m/z 491.2904; found: 491.2916.

4.2.20 *Tert*-butyl (3aS)-3a-(2-phenylallyl)-2,3,3a,8a-tetrahydro-8H-furo [2,3-*b*] indole -8 -carboxylate (12)

According to *method A*, flash column chromatography (SiO_2: 3% ethyl acetate in petroleum ether) provided this compound in 47% yield (53.2 mg, 0.141 mmol) as foam solid.

IR (KBr) *ν* = 2975, 2930, 2870, 1706, 1480, 1388, 1161, 1029, 906, 755, 703. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.74 (bs, 1H), 7.25-7.17 (m, 6H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.92 (s, 1H), 5.52 (s, 1H), 5.11 (s, 1H), 4.88 (s, 1H), 3.87 (t, *J* = 7.8 Hz, 1H), 3.36-3.32 (m, 1H), 3.09 (d, *J* = 13.2 Hz, 1H), 2.97 (d, *J* = 13.8 Hz, 1H), 2.17-2.03 (m, 2H), 1.45 (s, 9H). **^{13}C NMR (100 MHz, Chloroform-*d*):** δ 151.9, 145.1, 142.9, 141.9, 133.3, 128.2, 127.4, 126.4, 123.5, 122.4, 117.7, 114.2, 96.0, 80.8, 67.1, 56.2, 43.4, 39.8, 28.3. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{24}H_{28}NO_3$): m/z 378.2064; found: 378.2074.

4.2.21 1, 8-Di-tert-butyl 2-methyl (3aS)-3a-(2-(2-methoxyphenyl) allyl)-2,3,3a,8a- tetrahydropyrrolo[2,3-*b*] indole-1,2,8-tricarboxylate (13)

According to *method A*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 56% yield (94.5 mg, 0.168 mmol) as foam solid. mp: 66-68 ^oC.

IR (KBr) *ν* = 2968, 2926, 2859, 1715, 1483, 1400, 1159, 1021, 903, 750. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.48 (bs, 1H), 7.16 (t, *J* = 12.0 Hz, 1H), 7.10 (t, *J* = 6.0 Hz, 1H), 6.90 (dd, *J* = 18.0, 6.0 Hz, 2H), 6.82 (t, *J* = 6.0 Hz, 1H), 6.78 (t, *J* = 6.0 Hz, 1H), 6.74 (d, *J* = 6.0 Hz, 1H), 6.02 (s, 1H), 5.09 (s, 1H), 5.07 (s, 1H), 3.79-3.75 (m, 1H), 3.76 (s, 3H), 3.67 (s, 3H), 3.14 (t, *J* = 6.0 Hz, 1H), 2.73 (d, *J* = 18.0Hz, 1H), 2.28 (q, *J* = 6.0 Hz, 1H), 2.01 (t, *J* = 12.0 Hz, 1H), 1.59 (s, 9H), 1.37 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 173.0, 156.0, 152.3, 144.1, 141.9, 134.8, 131.3, 129.9, 128.5, 128.2, 123.0, 120.6, 120.0, 110.4, 81.2, 80.5, 65.3, 59.4, 55.2, 51.9, 42.9, 41.9, 28.3, 28.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{32}H_{41}N_2O_7$): m/z 565.2908; found: 565.2929.

4.2.22 (E)-3,3-Dimethylocta-5,7-dien-1-yl benzoate (14)

According to *method B*, flash column chromatography (SiO_2: 1% ethyl acetate in petroleum ether) provided this compound in 78% yield (60.5 mg, 0.234 mmol) as colorless oil.

IR (KBr) *ν* = 2959, 2925, 2862, 1715, 1226, 1114, 947, 714. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 2H), 6.33 (dt, *J* = 17.4, 10.2 Hz, 1H), 6.07 (dd, *J* = 15.0, 10.2 Hz, 1H), 5.77-5.71 (m, 1H), 5.11 (d, *J* = 10.8 Hz, 1H), 4.98 (d, *J* = 10.2 Hz, 1H), 4.38 (t, *J* = 7.8 Hz, 2H), 2.07 (d, *J* = 7.8 Hz, 2H), 1.71 (t, *J* = 7.8 Hz, 2H), 0.98 (s, 6H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 166.6, 137.1, 133.7, 132.8, 131.2, 130.4, 129.5, 128.3, 115.2, 62.2, 45.6, 39.7, 33.1, 27.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{17}H_{23}O_2$): m/z 259.1693; found: 259.1693.

4.2.23 (E)-3,3-Dimethylocta-5,7-dien-1-yl 4-methoxybenzoate (15)

According to *method B*, flash column chromatography (SiO_2: 2% ethyl acetate in petroleum ether) provided this compound in 53% yield (45.9 mg, 0.159 mmol) as colorless oil.

IR (KBr) *ν* = 2960, 1708, 1607, 1264, 1171, 1111, 1027, 849, 771. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.98 (d, *J* = 9.0 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 6.33 (dt, *J* = 16.8, 10.2 Hz, 1H), 6.06 (dd, *J* = 15.0, 10.8 Hz, 1H), 5.76-5.71 (m, 1H), 5.10 (d, *J* = 16.8 Hz, 1H), 4.98 (d, *J* = 10.2 Hz, 1H), 4.35 (t, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 2.06 (d, *J* = 7.2 Hz, 2H), 1.69 (t, *J* = 7.2 Hz, 2H), 0.97 (s, 6H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 166.4, 163.2, 137.1, 133.6, 131.5, 131.3, 122.8, 115.2, 113.5, 61.9, 55.4, 45.6, 39.7, 33.1, 27.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{18}H_{25}O_3$): m/z 287.1798; found: 287.1807.

4.2.24 (E)-3,3-Dimethylocta-5,7-dien-1-yl 4-acetylbenzoate (16)

According to *method B*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 50% yield (45.1 mg, 0.150 mmol) as colorless oil

IR (KBr) *ν* = 2961, 2925, 1722, 1692, 1271, 1113, 1010, 958, 769, 697. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 8.10 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 6.33 (dt, *J* = 16.8, 10.2 Hz, 1H), 6.06 (dd, *J* = 15.0, 10.8 Hz, 1H), 5.75-5.70 (m, 1H), 5.10 (d, *J* = 16.8 Hz, 1H), 4.98 (d, *J* = 10.2 Hz, 1H), 4.40 (t, *J* = 7.8 Hz, 2H), 2.63 (s, 3H), 2.06 (d, *J* = 7.8 Hz, 2H), 1.72 (t, *J* = 7.8 Hz, 2H), 0.98 (s, 6H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 197.5, 165.8, 140.1, 137.0, 134.2, 133.7, 131.1, 129.7, 128.2, 115.3, 62.7, 45.6, 39.6, 33.1, 27.2, 26.8. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{19}H_{25}O_3$): m/z 301.1798; found: 301.1800.

4.2.25 (E)-4-(3,3-Dimethylocta-5,7-dien-1-yl) phenol (17)

According to *method B*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 52% yield (35.9 mg, 0.156 mmol) as colorless oil.

IR (KBr) *ν* = 3363, 2953, 2862, 1605, 1511, 1453, 1231, 1005, 835. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.05 (d, *J* = 7.8 Hz, 2H), 6.76 (d, *J* = 8.4 Hz, 2H), 6.35 (dt, *J* = 16.8, 10.2 Hz, 1H), 6.08 (dd, *J* = 15.0, 10.2 Hz, 1H), 5.78-5.73 (m, 1H), 5.12 (d, *J* = 16.8 Hz, 1H), 4.99 (d, *J* = 10.2 Hz, 1H), 2.52-2.49 (m, 2H), 2.06 (d, *J* = 7.8 Hz, 2H), 1.49-1.46 (m, 2H), 0.95 (s, 6H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 153.3, 137.2, 135.5, 133.2, 132.0, 129.3, 115.1, 114.9, 45.1, 44.4, 33.8, 29.7, 27.0. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{16}H_{23}O$): m/z 231.1743; found: 231.1746.

4.2.26 (E)-6,6-Dimethyltrideca-1,3-diene (18)

According to *method B*, flash column chromatography (SiO_2: 0.5% ethyl acetate in petroleum ether) provided this compound in 41% yield (25.6 mg, 0.123 mmol) as colorless oil.

IR (KBr) *ν* = 2926, 2859, 1703, 1462, 1374, 977, 724. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 6.33 (dt, *J* = 16.8, 10.2 Hz, 1H), 6.03 (dd, *J* = 15.6, 10.2 Hz, 1H), 5.74-5.69 (m, 1H), 5.09 (d, *J* = 16.8 Hz, 1H), 4.96 (d, *J* = 10.2 Hz, 1H), 1.96 (d, *J* = 7.2 Hz, 2H), 1.32-1.22 (m, 12H), 0.89 (t, *J* = 7.2 Hz, 3H), 0.84 (s, 6H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 137.4, 133.0, 132.5, 114.6, 45.2, 42.0, 33.7, 31.9, 30.5, 27.1, 24.0, 22.7, 14.1. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{15}H_{29}$): m/z 209.2264; found: 209.2266.

4.2.27 (E)-3,3-Dimethylocta-5,7-dien-1-yl 4-methylbenzene sulfonate (19)

According to *method B*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 70% yield (64.8 mg, 0.210 mmol) as colorless oil.

IR (KBr) *v* = 3384, 2958, 2928, 1719, 1600, 1453, 1173, 1125, 1037, 1003, 816, 680, 562. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 6.27 (dt, *J* = 17.4, 10.2 Hz, 1H), 5.97 (dd, *J* = 15.6, 10.2 Hz, 1H), 5.62-5.57 (m, 1H), 5.08 (d, *J* = 16.8 Hz, 1H), 4.98 (d, *J* = 10.2 Hz, 1H), 4.08 (t, *J* = 7.8 Hz, 2H), 2.45 (s, 3H), 1.92 (d, *J* = 7.8 Hz, 2H), 1.57 (t, *J* = 7.8 Hz, 2H), 0.85 (s, 6H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 144.7, 136.9, 133.8, 133.1, 130.6, 129.8, 127.8, 115.4, 67.9, 45.3, 39.6, 33.0, 27.0, 21.6. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{17}H_{25}O_3S$): m/z 309.1519; found: 309.1529.

4.2.28 (E)-3,3-Dimethylocta-5,7-dien-1-yl 6-bromohexanoate (20)

According to *method B*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 47% yield (46.7 mg, 0.141 mmol) as colorless oil.

IR (KBr) *v* = 2951, 2866, 1730, 1460, 1362, 1258, 1178, 978, 732, 650. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 6.32 (dt, *J* = 17.4, 10.2 Hz, 1H), 6.04 (dd, *J* = 15.0, 10.2 Hz, 1H), 5.72-5.67 (m, 1H), 5.10 (d, *J* = 16.8 Hz, 1H), 4.98 (d, *J* = 10.2 Hz, 1H), 4.12 (t, *J* = 7.8 Hz, 2H), 3.53 (t, *J* = 6.6 Hz, 2H), 2.30 (t, *J* = 7.8 Hz, 2H), 2.00 (d, *J* = 7.8 Hz, 2H), 1.78 (t, *J* = 7.8 Hz, 2H), 1.64 (t, *J* = 7.8 Hz, 2H), 1.55 (t, *J* = 7.8 Hz, 2H), 1.48-1.45 (m, 2H), 0.91 (s, 6H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 173.5, 137.1, 133.6, 131.2, 115.2, 61.6, 45.5, 44.7, 39.6, 34.2, 33.0, 32.2, 27.1, 26.4, 24.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{16}H_{28}BrO_2$): m/z 331.1267; found: 331.2363.

4.2.29 Di-*tert*-butyl (3aS)-3a-((E)-penta-2,4-dien-1-yl)-2,3,3a,8a-tetrahydropyrrolo[2,3-*b*] indole-1,8-dicarboxylate (21)

According to *method B*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 67% yield (85.7 mg, 0.201 mmol) as foam solid.

IR (KBr) *v* = 2978, 2929, 1703, 1482, 1398, 1364, 1172, 1007, 893, 746. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.58 (bs, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.09 (d, *J* = 7.2 Hz, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.20 (dt, *J* = 17.4, 10.2 Hz, 1H), 6.07-6.02 (m, 2H), 5.51-5.46 (m, 1H), 5.08 (d, *J* = 16.8 Hz, 1H), 4.96 (d, *J* = 10.2 Hz, 1H)，3.73 (dd, *J* = 11.4, 7.8 Hz, 1H), 2.84 (td, *J* = 12.0, 5.4 Hz, 1H), 2.55-2.52 (m, 1H), 2.44 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.04-1.95 (m, 2H), 1.55 (s, 9H), 1.47 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 153.9, 152.4, 142.9, 136.6, 134.7, 128.7, 128.2, 123.1, 122.9, 116.2, 81.3, 79.9, 65.3, 45.8, 42.0, 41.3, 28.4, 28.3. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{25}H_{35}N_2O_4$): m/z 427.2591; found: 427.2606.

4.2.30 Di-*tert*-butyl (3aS)-5-chloro-3a-((E)-penta-2,4-dien-1-yl)-2,3,3a,8a-tetrahydro pyrrolo[2,3-*b*] indole-1,8-dicarboxylate (22)

According to *method B*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 45% yield (62.2 mg, 0.135 mmol) as foam solid. mp: 89-91 ^{o}C.

IR (KBr) *v* = 2976, 2927, 1711, 1480, 1396, 1316, 1250, 1160, 1020, 891, 754. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.53 (bs, 1H), 7.16 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.05 (d, *J* = 1.8 Hz, 1H), 6.20 (dt, *J* = 16.8, 10.2 Hz, 1H), 6.08-6.03 (m, 2H), 5.46-5.41 (m, 1H), 5.10 (d, *J* = 16.8 Hz, 1H), 4.98 (d, *J* = 10.2 Hz, 1H)，3.75 (dd, *J* = 11.4, 7.2 Hz, 1H), 2.85 (td, *J* = 12.0, 5.4 Hz, 1H), 2.55-2.52 (m, 1H), 2.43 (dd, *J* = 13.8, 8.4 Hz, 1H), 1.99-1.96 (m, 2H), 1.54 (s, 9H), 1.46 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 153.8, 152.1, 141.6, 136.4, 135.1, 128.2, 123.1, 116.6, 81.7, 80.1, 56.4, 55.9, 45.8, 41.2, 28.4, 28.3. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{25}H_{34}ClN_2O_4$): m/z 461.2202; found: 461.2213.

4.2.31 8-(*Tert*-butyl) 1-methyl (3aS)-3a-((E)-penta-2,4-dien-1-yl)-2,3,3a,8a-tetrahydro pyrrolo[2,3-*b*] indole-1,8-dicarboxylate (23)

According to *method B*, flash column chromatography (SiO_2: 5% ethyl acetate in petroleum ether) provided this compound in 49% yield (56.5 mg, 0.147 mmol) as foam solid. mp: 55-56 ^{o}C.

IR (KBr) *v* = 2924, 2858, 1707, 1450, 1394, 1156, 1011, 752. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.61 (bs, 1H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 1.2 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 6.20 (dt, *J* = 16.8, 10.2 Hz, 1H), 6.06 (dd, *J* = 15.0, 10.8 Hz, 1H), 5.96 (s, 1H), 5.47-5.42 (m, 1H), 5.10 (d, *J* = 17.4 Hz, 1H), 4.98 (d, *J* = 10.2 Hz, 1H)，3.75 (dd, *J* = 10.2, 8.4 Hz, 1H), 3.71 (s, 3H), 2.90 (td, *J* = 12.0, 5.4 Hz, 1H), 2.52 (dd, *J* = 13.8, 7.2 Hz, 1H), 2.44 (dd, *J* = 14.4, 8.4 Hz, 1H), 2.12 (dd, *J* = 6.6, 5.4 Hz, 1H), 2.04-1.99 (m, 1H), 1.55 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 155.1, 152.3, 142.7, 136.5, 134.9, 134.5, 128.5, 128.4, 123.4, 122.7, 116.8, 116.5, 81.3, 79.8, 56.6, 52.4, 45.8, 41.2, 28.3. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{22}H_{29}N_2O_4$): m/z 385.2122; found: 385.2142.

4.2.32 1,8-di-tert-butyl 2-methyl (2S,3aS,8aR)-3a-((E)-penta-2,4-dien-1-yl)-2,3,3a,8a- tetrahydropyrrolo[2,3-b] indole-1,2,8-tricarboxylate (24)

According to *method B*, flash column chromatography (SiO_2: 10% ethyl acetate in petroleum ether) provided this compound in 58% yield (84.3 mg, 0.174 mmol) as foam solid. mp: 73-75 ^{o}C.

IR (KBr) *v* = 2973, 2925, 2856, 1749, 1711, 1335, 1158, 1011, 900, 749. **^{1}H NMR (600 MHz, Chloroform-*d*):** δ 7.62 (bs, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 7.10 (d, *J* = 6.6 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 6.22-6.15 (m, 1H), 6.02-5.98 (m, 2H), 5.44-5.39 (m, 1H), 5.08 (d, *J* = 17.4 Hz, 1H), 4.97 (d, *J* = 10.2 Hz, 1H), 3.89 (dd, *J* = 10.8, 6.6 Hz, 1H), 3.71 (s, 3H), 2.53 (dd, *J* = 12.6, 6.6 Hz, 1H), 2.46-2.37 (m, 2H), 2.10 (dd, *J* = 12.6, 10.2 Hz, 1H), 1.55 (s, 9H), 1,39 (s, 9H). **^{13}C NMR (150 MHz, Chloroform-*d*):** δ 173.1, 152.3, 142.2, 136.5, 135.0, 132.6, 128.5, 127.8, 122.7, 118.6, 116.6, 81.4, 80.3, 59.3, 52.1, 40.7, 35.2, 28.2. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{27}H_{37}N_2O_6$): m/z 485.2646; found: 485.2674.

4.2.33 Methyl 1-(2-phenylallyl) cyclopropane-1-carboxylate (25)

According to *method A*, flash column chromatography (SiO_2: 1% ethyl acetate in petroleum ether) provided this compound in 52% yield (33.7 mg, 0.156 mmol) as colorless oil.

IR (KBr) *v* = 2941, 1766, 1723, 1445, 1355, 1212, 1152, 756, 701. **^{1}H NMR (500 MHz, Chloroform-*d*):** δ 7.44-7.42 (m, 2H), 7.36-7.33 (m, 2H), 7.31-7.29 (m, 1H), 5.37 (d, *J* = 1.0 Hz, 1H), 5.16 (d, *J* = 1.5 Hz, 1H), 3.66 (s, 3H), 2.86 (s, 2H), 1.30 (q, *J* = 7.0 Hz, 2H), 0.79 (q, *J* = 7.0 Hz, 2H). **^{13}C NMR (125 MHz, Chloroform-*d*):** δ 175.5, 145.7, 141.9, 128.2, 127.4, 126.0, 113.1, 51.9, 37.6, 22.0, 15.4. **HRMS** (ESI) exact mass calculated for [M+H$^+$] ($C_{14}H_{17}O_2$): m/z 217.1223; found: 217.1225.

Acknowledgments

Financial support was provided by the Chinese NSF (Nos. 21572140 and 21372151).
Ms Yanhong Song was thanked for use of NMR facility.

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