1, 3-Dipolar Cycloaddition of Nitrones with Electron-rich Alkenes Catalyzed by $Yb(OTf)_3$

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1,3-Dipolar cycloaddition of nitrones with ethyl vinyl ether or 2, 3-dihydrofuran proceeds smoothly in the presence of a catalytic amount (10 mol%) of ytterbium triflate to afford isoxazolidines and dicyclic isoxazolidine respectively with good yields and high stereoselectivity.

Keywords 1, 3-Dipolar cycloaddition, nitrone, ethyl vinyl ether, 2,3-dihydrofuran, ytterbium triflate

Introduction

The 1,3-dipolar cycloaddition (1,3-DC) reaction between nitrones and alkenes is an extremely powerful synthetic method for the creation of isoxazolidines, which have long been regarded as important intermediates to synthesize a wide variety of natural products and related molecules, particularly alkaloids, β-amino acids and amino-sugars.[1] Deshong[2] has extensively studied the 1, 3-dipolar cycloaddition of α-phenyl-*N*-alkyl nitrones with ethyl vinyl ether under thermal and high-pressure conditions. Since many nitrones are not stable under the prolong heating (72 h at 80℃), which is requirement for realizing cycloaddition with electron-rich olefins, resulting in a very low yield and stereoselectivity of cycloaddition. Application of high pressure (6 h, 200 MPa, 50℃, no solvent, 35 equiv. ethyl vinyl ether) afforded the cycloadduct in 83% chemical yield but without any stereoselectivity (*cis* : *trans* = 50 : 50). Scheeren[3] has also reported the 1, 3-dipolar cycloaddition reaction of nitrones with ethyl vinyl ether catalyzed by 20 mol% chiral oxazaborolidines under high pressure (18 h at 200 MPa) to furnish the cycloadducts in 84% chemical yields with poor stereoselectivity.

Rare earth metal triflates are one of the strongest Lewis acids because of the electron-withdrawing trifluoromethanesulfonyl group. Moreover, it was stable in water and easily recovered from an aqueous layer after the reaction was complete, and could be reused. We have reported the smooth reaction of glyoxylates with alkenes in the presence of ytterbium triflate,[4] one pot synthesis of amino phosphonates from aldehydes using ytterbium triflate as the catalyst,[5] catalytic synthesis of furo[3, 2-*c*] and pyrano[3, 2-*c*]quinolines by ytterbium triflate[6] and lanthanide chloride,[7] lanthanide triflate catalyzed Biginelli reaction, one-pot synthesis of dihydropyrimidiones under solvent-free conditions,[8] as well as addition of silyl ketene adducts to nitrones catalyzed by lanthanide triflates.[9] To our knowledge, the 1,3-dipolar cycloaddition of nitrone with electron-rich alkenes catalyzed by lanthanide triflates has not been reported. The 1,3-DC reaction of nitrones with alkenes involves a dominant interaction of the $LUMO_{nitrone}$ and the $HOMO_{alkene}$.[1d] Lanthanide compounds have strong affinity to coordinate with nitrones, which could significantly decrease the energy level of $LUMO_{nitrone}$, therefore, accelerate the 1,3-DC reaction. Herein, we describe the 1,3-DC reaction of nitrones with ethyl vinyl-ether catalyzed by $Yb(OTf)_3$ for the first time.

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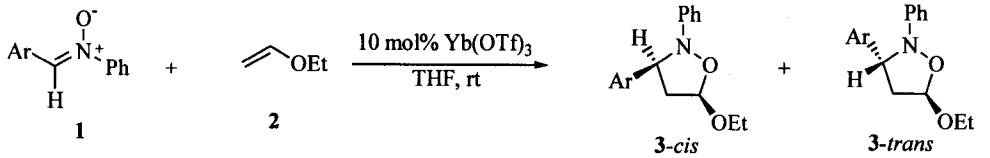
Results and discussion

N, α-Diphenylnitrone was added into the solution of $Yb(OTf)_3$(10 mol%) in dichloromethane. After stirring at room temperature for 10 min, ethyl vinyl ether was added. The conversion could be easily determined following by TLC (Scheme 1). The relative stereochemistry of the isolated *cis* and *trans* isomer was assigned by analysis of ^1H NMR coupling constants and correlation with the known ^1H NMR data of *cis*-2-phenyl-3-phenyl-5-ethoxy isoxazolidine and the corresponding *trans* isomer.[3] The acetal proton H-5 in *cis*-isoxazolidine displayed a doublet of doublets at δ 5.37 (J = 2.14 and 6.08 Hz), and *trans*-isoxazolidine displayed a doublet at δ 5.34 (J = 4.49 Hz).

Scheme 1



1a Ar = 4-$MeOC_6H_4$ **1b** Ar = 4-MeC_6H_4
1c Ar = 4-ClC_6H_4 **1d** Ar = C_6H_4
1e Ar = 2-furfuryl **1f** Ar = 4-$NO_2C_6H_4$

The 1, 3-dipolar cycloaddition reaction of nitrone **1d** with ethyl vinyl ether **2** has been investigated as a model reaction using ytterbium triflate as catalyst at room temperature. Firstly, we investigated the effect of different solvent on the 1, 3-DC reaction. The results are summarized in Table 1.

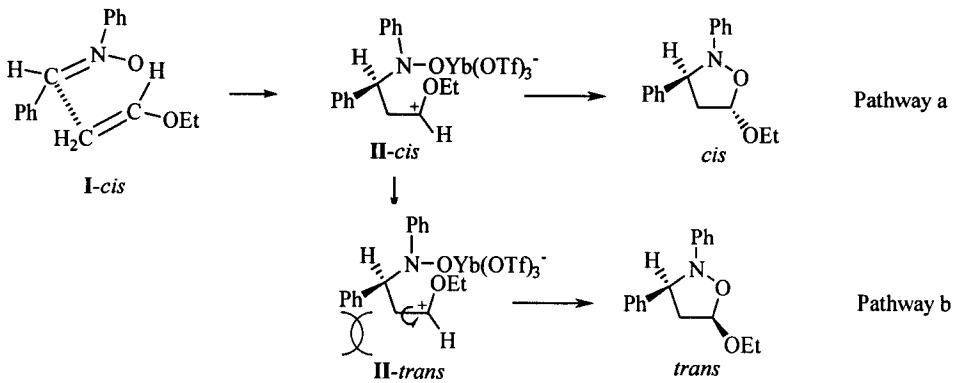
Table 1 Effect of solvent on the 1, 3-DC reaction between nitrone **1d** and ethyl vinyl ether **2**[a]

Entry	Solvent	Time (min)	*cis*: *trans*	Yield (%)
1	Et_2O	100	45:55	10
2	THF	30	1:99	74
3	CH_3CN	30	2:98	70
4	$C_6H_5CH_3$	30	36:63	89
5	*n*-C_6H_{14}	30	62:38	89

[a] Reaction conditions: room temperature, 10 mol% of $Yb(OTf)_3$.

The reaction proceeds smoothly in the presence of 10 mol% $Yb(OTf)_3$ with all the solvents examined except Et_2O to give the mixtures of *cis* and *trans* isomers respectively in good to excellent yield. It was found that solvent has obvious effect on the ratio of stereoisomers. In tetrahydrofuran (THF), the stereoselectivity (1/99 *cis*/*trans*) is the highest, and the *trans*-2-phenyl-3-phenyl-5-ethoxy isoxazolidine was obtained as the major stereoisomer. On the contrary, the *cis*-2-phenyl-3-phenyl-5-ethoxy isoxazolidine was formed as the main stereoisomer in *n*-hexane. This result could be explained as described in Scheme 2: In polar solvent such as THF, the intermediate **II**-*cis* could exist in enough time, which allows it to adopt the more stable form of **II**-*trans* with the smaller repellent action through the rotation of the C_4—C_5 bond. Therefore the isomer produced is mainly *trans via* the reaction pathway b. The nonpo-

Scheme 2



lar solvent such as *n*-hexane could not stabilize the intermediate II-*cis*, which hinders the rotation of C_4—C_5 bond, so the *cis*-2-phenyl-3-phenyl-5-ethoxy isoxazolidine was formed as the main stereoisomer through the reaction pathway a.

The 1,3-DC reactions of the various nitrones **1a—f** proceed well with the different aryl substituents on the nitrone carbon atom, and the results are presented in Table 2. We found that the reaction of different *N*-phenyl nitrones with ethyl vinyl ether (5 equiv.) was effectively catalyzed by 10 mol% $Yb(OTf)_3$ in THF at room temperature giving the corresponding desired product in good yields after 30 min. The ratio of stereoisomers varied with different nitrones examined, however, *trans*-isoxazolidines were obtained as the major isomer in all cases.

Table 2 1,3-DC reaction of nitrones **1a—f** with ethyl vinyl ether **2** by $Yb(OTf)_3$(10 mol%)[a]

Entry	Nitrone (Ar)	Product (*cis*:*trans*)	Yield (%)
1	**1a** (4-$MeOC_6H_4$)	**3a**-*c*, **3a**-*t* (32:68)	68
2	**1b** (4-MeC_6H_4)	**3b**-*c*, **3b**-*t* (30:70)	74
3	**1c** (4-Cl C_6H_4)	**3c**-*c*, **3c**-*t* (37:63)	83
4	**1d** (Ph)	**3d**-*c*, **3d**-*t* (1:99)	74
5	**1e** (2-furfuryl)	**3e**-*c*, **3e**-*t* (28:72)	60
6	**1f** (4-$NO_2C_6H_4$)	**3f**-*c*, **3f**-*t* (28:72)	75

[a] Reaction conditions: room temperature, 30 min, THF as the solvent.

The reaction has also been conducted with the electron-rich alkene 2,3-dihydrofuran **4**, a rigid *Z*-alkyl vinyl ether, in the presence of a catalytic amount of $Yb(OTf)_3$ (10 mol%) in THF at room temperature (Scheme 3). The dicyclic isoxazolidines were obtained as the mixture of *cis* and *trans* isomers in good yields after 30 min, in which the *trans* isomer was the main product (Table 3). Some of the isomers could be separated by flash column chromatography on silica gel, the *cis* to *trans* ratio could be determined by ^1H NMR spectroscopy of the product.

Table 3 1,3-DC reaction of nitrones **1a—f** with 2,3-dihydrofuran **4** catalyzed by 10 mol% $Yb(OTf)_3$[a]

Entry	Nitrone (Ar)	Product (*cis*:*trans*)	Yield (%)
1	**1a** (4-$MeOC_6H_4$)	**3a**-*c*, **3a**-*t* (23:77)	73
2	**1b** (4-MeC_6H_4)	**3b**-*c*, **3b**-*t* (26:74)	78
3	**1c** (4-ClC_6H_4)	**3c**-*c*, **3c**-*t* (8:92)	73
4	**1d** (Ph)	**3d**-*c*, **3d**-*t* (22:78)	78
5	**1e** (2-furfuryl)	**3e**-*c*, **3e**-*t* (25:75)	53
6	**1f** (4-$NO_2C_6H_4$)	**5f**-*c*, **5f**-*t* (30:70)	72

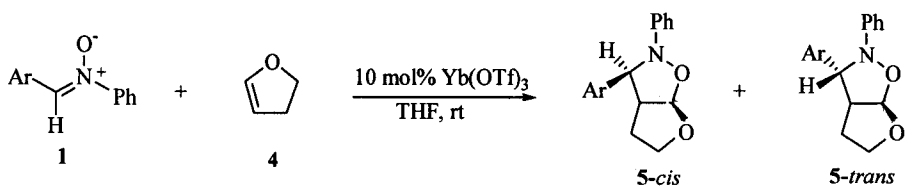
[a] Reaction conditions: room temperature, 30 min, THF as the solvent.

In conclusion, ytterbium triflate (10 mol%) is an efficient catalyst in the reaction of nitrones with ethyl vinyl ether or 2,3-dihydrofuran to afford the isoxazolidines and dicyclic isoxazolidine, respectively, with good yields and high stereoselectivity under mild reaction conditions. Further synthetic application of these reactions is in progress.

Experimental

Nitrones were prepared by the condensation reaction of different substituted benzaldehyde with *N*-phenyl-hydroxylamine,[3] respectively. ^1H NMR spectra were recorded as $CDCl_3$ solutions on a VXL-300 instrument. Infrared spectra were recorded on a Perkin-Elmer 983 FT-IR spectrometer as liquid forms on potassium bromide plates unless otherwise noted. Mass spectra were recorded on a HP5989A spectrometer and Elemental analysis was carried out on a MOD-1106 elemental analyzer.

Scheme 3



1a Ar = 4-$MeOC_6H_4$ **1b** Ar = 4-MeC_6H_4
1c Ar = 4-ClC_6H_4 **1d** Ar = C_6H_4
1e Ar = 2-furfuryl **1f** Ar = 4-$NO_2C_6H_4$

A typical procedure for the reaction of nitrones with ethyl vinyl ether

$Yb(OTf)_3$ (18 mg, 0.03 mmol) was dissolved in 1 mL of THF at room temperature and stirred for 5 min, *N*, α-diphenyl nitrone **1d** (60 mg, 0.3 mmol) was added and stirred for further 10 min, then ethyl vinyl ether **2** (110 mg, 1.5 mmol) was added. After appropriate reaction time, 10 mL of EtOAc and 1 mL of water were then added, the organic layer was separated, dried over anhydrous Na_2SO_4 and evaporated to give the crude product. Analytical pure products were then obtained (61 mg, overall yields 74%) by column chromatography. *cis* and *trans* isomers were determined by ^1H NMR.

3a-*c* and **3a**-*t*: known compounds,[10] could be seperated by flash column chromatography, *cis*: *trans* = 32:68.

3a-*c*: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.44—6.87 (m, 9H), 5.35 (dd, J = 2.21, 6.10 Hz, 1H), 4.24 (dd, J = 6.96, 9.33 Hz, 1H), 3.99 (dq, J = 7.08, 9.66 Hz, 1H), 3.80 (s, 3H), 3.62 (q, J = 7.06, 9.66 Hz, 1H), 2.99 (ddd, J = 6.11, 9.39, 13.21 Hz, 1H), 2.35 (ddd, J = 2.21, 6.93, 9.14 Hz, 1H), 1.30 (t, J = 7.06 Hz, 3H); IR (KBr) ν: 3060, 2971, 2931, 2871, 1610, 1596, 1510, 1489, 1301, 1253, 1174, 1095, 1040, 1000, 978, 848, 759 cm^{-1}; MS (70 eV) *m/z* (%): 299 (M^+, 12.04), 254 (7.06), 191 (100), 163 (27.50), 135 (24.25), 91 (63.27), 77 (42.40); Anal. calcd. for $C_{18}H_{21}NO_3$: C 72.21, H 7.07, N 4.68; found C 71.91, H 7.03, N 4.47.

3a-*t*: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.41—6.87 (m, 9H), 5.33 (d, J = 4.47 Hz, 1H), 4.75 (dd, J = 6.98, 10.11 Hz, 1H), 3.84 (dq, J = 7.07, 9.45 Hz, 1H), 3.78 (s, 3H), 3.54 (dq, J = 7.02, 9.42 Hz, 1H), 2.73 (dd, J = 6.98, 12.40 Hz, 1H), 2.43 (ddd, J = 4.47, 10.11, 12.40 Hz, 1H), 1.06 (t, J = 7.07 Hz, 3H); IR (KBr) ν: 3056, 2972, 2834 , 1596, 1508, 1488, 1249, 1094, 1037, 950, 834, 760, 698 cm^{-1}; MS (70 eV) *m/z* (%): 300 (M^+ + 1, 5.64), 299 (M^+, 21.87), 254 (9.13), 192 (14.47), 191 (100), 163 (22.38), 135 (24.57), 91 (58.85), 77 (49.88); Anal. calcd. for $C_{18}H_{21}NO_3$: C 72.21, H 7.07, N 4.68; found C 72.04, H 7.08, N 4.49.

3b-*c* and **3b**-*t*: known compounds,[10] could not be seperated by flash column chromatography, *cis*: *trans* = 30:70.

3b-*c*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.39—6.87 (m, 9H), 5.36 (d, J = 2.23 Hz, 1H), 4.26 (dd, J = 6.98, 9.35 Hz, 1H), 3.99 (dq, J = 7.10, 9.67 Hz, 1H), 3.64 (dq, J = 7.10, 9.67 Hz, 1H), 2.99 (ddd, J = 3.33, 6.09, 9.35 Hz, 1H), 2.43 (ddd, J = 2.23, 6.98, 9.21 Hz, 1H), 2.34 (s, 3H), 1.30 (t, J = 7.07 Hz, 3H).

3b-*t*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.39—6.87 (m, 9H), 5.33 (d, J = 4.35 Hz, 1H), 4.77 (dd, J = 7.04, 10.11 Hz, 1H), 3.84 (dq, J = 7.12, 9.43 Hz, 1H), 3.54 (dq, J = 7.12, 9.43 Hz, 1H), 2.76 (dd, J = 6.99, 12.44 Hz, 1H), 2.43 (ddd, J = 4.46, 10.11, 12.44 Hz, 1H), 2.34 (s, 3H), 1.05 (t, J = 7.12 Hz, 3H).

3c-*c* and **3c**-*t*: known compounds,[10] could not be seperated by flash column chromatography, *cis*: *trans* = 37:63.

3c-*c*: ^1H NMR δ: 7.48—6.89 (m, 9H), 5.36 (dd, J = 1.87, 6.00 Hz, 1H), 4.30 (dd, J = 7.14, 9.95 Hz, 1H), 4.01 (dq, J = 7.20, 9.90 Hz, 1H), 3.64 (dq, J = 7.20, 9.90 Hz, 1H), 3.00 (ddd, J = 6.00, 9.90, 13.20 Hz, 1H), 2.34 (ddd, J = 1.87, 7.14, 13.20 Hz, 1H), 1.28 (t, J = 7.20 Hz, 3H); MS (70 eV) *m/z* (%): 303 (M^+, 17.07), 258 (14.52), 197 (34.22), 195 (base), 167 (40.13), 91 (45.25), 77 (63.84).

3c-*t*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.48—6.89 (m, 9H), 5.33 (d, J = 4.43 Hz, 1H), 4.78 (dd, J = 7.14, 9.95 Hz, 1H), 3.84 (dq, J = 7.13, 9.41 Hz, 1H), 3.57 (dq, J = 7.13, 9.41 Hz, 1H), 2.77 (dd, J = 7.09, 12.38 Hz, 1H), 2.40 (ddd, J = 4.45, 10.07, 12.39 Hz, 1H), 1.05 (t, J = 7.07 Hz, 3H).

3d-*c* and **3d**-*t*: known compounds,[3] could not be seperated by flash column chromatography, *cis*: *trans* = 1:99.

3d-*c*: ^1H NMR ($CDCl_3$, 300 MHz,) δ: 7.53—7.16 (m, 7H), 6.96—6.92 (m, 3H), 5.37 (dd, J = 2.14, 6.08 Hz, 1H), 4.31 (dd, J = 6.69, 9.54 Hz, 1H), 3.99 (dq, J = 7.08, 9.69 Hz, 1H), 3.62 (dq, J = 7.08, 9.69 Hz, 1H), 3.02 (ddd, J = 6.08, 9.54, 13.18 Hz, 1H), 2.39 (ddd, J = 2.15, 6.50, 13.09 Hz, 1H), 1.24 (t, J = 7.08 Hz, 3H).

3d-*t*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.52—7.16 (m, 7H), 6.95—6.85 (m, 3H), 5.34(d, J =

4.49 Hz, 1H), 4.81 (dd, J = 7.11, 9.93 Hz, 1H), 3.84 (dq, J = 7.10, 9.05 Hz, 1H), 3.55 (dq, J = 7.10, 9.05 Hz, 1H), 2.78 (dd, J = 7.07, 12.40 Hz, 1H), 2.45 (ddd, J = 4.47, 10.09, 12.39 Hz, 1H), 1.05 (dt, J = 1.47, 7.10 Hz, 3 H); IR (KBr) ν: 3060, 3027, 2973, 1597, 1488, 1450, 1341, 1264, 1213, 1195, 1098, 1098, 1035, 969, 950, 914, 873, 750, 700 cm^{-1}.

3e-*c* and **3e**-*t*: unknown compounds, could be seperated by flash column chromatography, *cis*: *trans* = 28:72.

3e-*c*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.42—6.98 (m, 6H), 6.36—6.33 (m, 2H), 5.42 (dd, J = 2.46, 6.14 Hz, 1H), 4.40 (dd, J = 6.65, 8.93 Hz, 1H), 3.95 (dq, J = 7.07, 9.66 Hz, 1H), 3.60 (dq, J = 7.07, 9.66 Hz, 1H), 2.85 (ddd, J = 6.14, 8.96, 13.17 Hz, 1H), 2.62 (ddd, J = 2.47, 6.65, 9.12 Hz, 1H), 1.27 (t, J = 7.07 Hz, 3H); IR (KBr) ν: 3030, 2973, 2925, 1596, 1489, 1449, 1374, 1341, 1202, 1151, 1100, 1035, 759, 698, 600 cm^{-1}; MS (70 eV) m/z (%): 260 (M^+ + 1, 12.03), 259 (M^+, 41.26), 214 (17.33), 186 (9.66), 151 (100), 123 (25.64), 95 (23.33), 91 (30.20), 77 (33.21), 67 (15.67); Anal. calcd. for $C_{15}H_{17}NO_3$: C 69.48, H 6.61, N 5.40; found C 69.72, H 6.70, N 5.51.

3e-*t*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.39—6.90 (m, 6 H), 6.34—6.30 (m, 2 H), 5.41—5.39 (m,1 H), 4.92 (t, J = 7.90 Hz, 1H), 3.83 (dq, J = 7.07, 9.47 Hz, 1H), 3.55 (dq, J = 7.07, 9.47 Hz, 1H), 2.75—2.67 (m, 2H), 1.05 (t, J = 7.07 Hz, 3H); IR (KBr) ν: 2974, 2904, 1597, 1488, 1449, 1374, 1344, 1203, 1147, 1103, 1044, 997, 806, 760, 698, 601 cm^{-1}; MS (70 eV) m/z (%): 260 (M^+ + 1, 4.03), 259 (M^+, 18.01), 151 (100), 123 (49.56), 95 (35.02), 91 (55.45), 77 (45.4); Anal. calcd. for $C_{18}H_{21}NO_3$: C 69.48, H 6.61, N 5.40; found C 69.64, H 6.68, N 5.49.

3f-*c* and **3f**-*t*: unknown compounds, could not be seperated by flash column chromatography, *cis*: *trans* = 28:72.

3f-*c*: ^1H NMR ($CDCl_3$,300 MHz) δ: 8.18 (d, J = 8.65 Hz, 2H), 7.64 (d, J = 8.65 Hz, 2H), 7.25—7.17 (m, 2H), 6.97—6.87 (m, 3H), 5.41 (dd, J = 1.45, 5.80 Hz, 1H), 4.49 (dd, J = 4.94, 10.18 Hz, 1 H), 3.95 (dq, J = 7.07, 9.64 Hz, 1H), 3.64 (dq, J = 7.07, 9.64 Hz, 1H), 3.00 (ddd, J = 5.80, 10.18, 13.02 Hz, 1H), 2.31 (ddd, J = 1.45, 5.66, 7.11 Hz, 1H), 1.24 (t, J = 7.06 Hz, 3H).

3f-*t*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 8.18 (d, J = 8.65 Hz, 2H), 7.64 (d, J = 8.65 Hz, 2H), 7.22—7.17 (m, 2H), 6.93—6.87 (m, 3H), 5.36 (d, J = 4.49 Hz, 1H), 4.92 (dd, J = 7.42, 9.52 Hz, 1H), 3.83 (dq, J = 7.12, 9.44 Hz, 1H), 3.52 (dq, J = 7.12, 9.44 Hz, 1H), 2.84 (dd, J = 7.30, 12.02 Hz, 1H), 2.40 (ddd, J = 4.48, 9.68, 12.36 Hz, 1H), 1.03 (t, J = 7.06 Hz, 3H); IR (KBr) ν: 3071, 2977, 2908, 1597, 1515, 1487, 1344, 1317, 1258, 1093, 1042, 968, 869, 836, 757, 699 cm^{-1}; MS (70 eV) m/z (%): 314 (M^+, 9.25), 269 (3.91), 207 (15.4), 206 (100), 178 (69.55), 150 (9.12), 132 (27.17), 104 (21.52), 91 (36.71), 77 (53.91); Anal. calcd. for $C_{17}H_{18}N_2O_4$: C 64.96, H 5.77, N 8.91; found C 64.86, H 5.95, N 8.56.

5a-*c* and **5a**-*t*: known compounds,[10] could not be seperated by flash column chromatography, *cis*: *trans* = 23:77.

5a-*c*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.25—6.84 (m, 9H), 5.99 (d, J = 5.28 Hz, 1H), 4.39 (d, J = 3.71 Hz, 1H), 3.95—3.79 (m, 2H), 3.77 (s, 3H), 3.28—3.20 (m, 1H), 2.12—2.02 (m, 2H).

5a-*t*: ^1H NMR ($CDCl_3$, 300 MHz) ν: 7.25—6.84 (m, 9H), 5.88(d, J = 5.52 Hz, 1H), 4.45 (d, J = 8.06, 1H), 4.08 (ddd, J = 5.52, 8.06, 11.32 Hz, 1H), 3.92 (ddd, J = 1.43, 7.91, 9.49 Hz, 1H), 3.80 (s, 3H), 3.42 (ddd, J = 1.30, 8.96, 14.93 Hz, 1H), 1.78—1.54 (m,1 H), 1.57 (dd, J = 5.49, 13.17 Hz, 1H).

5b-*c* and **5b**-*t*: known compounds[10], could not be seperated by flash column chromatography, *cis*: *trans* = 26:74.

5b-*c*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.24—6.86 (m, 9H), 5.99 (d, J = 5.28 Hz, 1H), 4.43 (d, J = 3.70 Hz, 1H), 3.86—3.78 (m, 2H), 3.54—3.39 (m, 1H), 2.32 (s, 3H), 2.16—1.97 (m, 2H).

5b-*t*: ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.25—6.95 (m, 9H), 5.89 (d, J = 5.47 Hz, 1H), 4.48 (d, J = 8.08 Hz, 1H), 4.13—4.05 (m, 1H), 3.94—3.89 (m, 1H), 3.48—3.40 (m, 1H), 2.35 (s, 3H) 1.74—1.52 (m, 2H).

5c-*c* and **5c**-*t*: unknown compounds, could not be seperated by flash column chromatography, *cis*: *trans* = 8:92.

5c-*c*: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.35—6.89 (m, 9H), 6.02 (d, J = 5.26 Hz, 1H), 4.51 (d, J = 3.27 Hz, 1H), 4.00—3.82 (m, 2H), 3.27 (dd, J = 3.14, 5.17 Hz, 1H), 2.17—2.13 (m, 1H), 2.07—2.03 (m, 1H).

5c-*t*: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.36—7.00 (m, 9H), 5.94 (d, J = 5.46 Hz, 1H), 4.53 (d, J = 8.08 Hz, 1H), 4.08 (m, 1H), 3.95 (dt, J = 1.62, 6.16 Hz, 1H), 3.48 (m, 1H), 1.74 (m, 1H), 1.52 (dd, J = 5.45, 13.26 Hz, 1H); IR (KBr): 2971, 2891, 1596, 1487, 1259, 1078, 1024, 923, 787, 754, 697 cm^{-1}; MS (70 eV) *m/z* (%): 310 (M^+, 6.7), 195 (32.42), 193 (100), 216 (13.6), 165 (10.0), 91 (61.17), 77 (75.94); Anal. calcd. for $C_{17}H_{16}ClNO_2$: C 67.66, H 5.34, N 4.64; found C 67.68, H 5.31, N 4.71.

5d-*c* and **5d**-*t*: known compounds,[10] could not be seperated by flash column chromatography, *cis*: *trans* = 22:73.

5d-*c*: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.35—6.80 (m, 10H), 6.03 (d, J = 5.47 Hz, 1H), 4.48 (d, J = 3.59 Hz, 1H), 3.97—3.66 (m, 2H), 3.34—3.27 (m, 1H), 2.29—1.86 (m, 1H), 1.84—1.63 (m, 1H).

5d-*t*: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.35—6.94 (m, 10H), 5.91 (d, J = 5.47 Hz, 1H), 4.52 (d, J = 8.11 Hz, 1H), 4.14—4.05 (m, 1H), 3.97—3.88 (m, 1H), 3.51—3.43 (m, 1H), 1.78—1.50 (m, 2H); IR (KBr) ν: 3058, 3026, 2972, 1715, 1597, 1490, 1450, 1254, 1078, 1021, 923, 762, 700 cm^{-1}; MS (70 eV) *m/z* (%): 268 (M^+ + 1, 23.23), 267 (M^+, 48.06), 250 (7.92), 180 (8.78), 160 (12.35), 159 (100), 131 (11.32), 91 (10.50), 77 (19.06).

5e-*c* and **5e**-*t*: unknown compounds, could not be seperated by flash column chromatography, *cis*: *trans* = 25:75.

5e-*c*: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.45—6.88 (m, 6H), 6.36 (dd, J = 1.85, 3.24 Hz, 1H), 6.28 (d, J = 3.26 Hz, 1H), 5.95 (d, J = 5.43 Hz, 1H), 4.51 (d, J = 8.04 Hz, 1H), 4.18 (ddd, J = 2.29, 7.95, 13.44 Hz, 1H), 4.03—3.91 (m, 1H), 3.53—3.45 (m, 1H), 1.95—1.64 (m, 2H).

5e-*t*: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.45—6.88 (m, 6H), 6.24 (dd, J = 1.85, 3.26 Hz, 1H), 6.14 (d, J = 3.26 Hz, 1H), 6.05 (d, J = 5.35 Hz, 1H), 4.69 (d, J = 2.33 Hz, 1H), 4.03—3.88 (m, 2H), 3.55—3.47 (m, 1H), 2.28—2.14 (m, 1H), 2.06—1.99 (m, 1H); IR (KBr) ν: 3100, 2956, 2898, 1594, 1488, 1330, 1260, 1150, 1074, 1016, 930, 804, 756, 738, 696 cm^{-1}; MS (70 eV) *m/z* (%): 257 (M^+, 9.06), 239 (3.10), 210 (25.13), 149 (100), 91 (45.31), 77 (45.31); Anal. calcd. for: $C_{15}H_{15}NO_3$: C 70.02, H 5.87, N 5.44; found C 70.08, H 5.87, N 5.52.

5f-*c* and **5f**-*t*: unknown compounds, could not be seperated by flash column chromatography, *cis*: *trans* = 30:70.

5f-*c*: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.10 (d, J = 8.78 Hz, 2H), 7.49 (d, J = 8.78 Hz, 2H), 7.22—7.16 (m, 2 H), 7.05—6.89 (m, 3H), 5.96 (d, J = 5.25 Hz, 1H), 4.63 (d, J = 2.91 Hz, 1H), 3.76—3.52 (m, 2H), 3.25—3.15 (m, 1H), 2.23—1.88 (m, 2H).

5f-*t*: ^{1}H NMR ($CDCl_3$, 300 MHz) ν: 8.24 (d, J = 8.64 Hz, 2H), 7.55 (d, J = 8.64 Hz, 2H), 7.22—7.16 (m, 2H), 7.05—6.89 (m, 3H), 5.95 (d, J = 5.38 Hz, 1H), 4.66 (d, J = 8.16 Hz, 1H), 4.06 (ddd, J = 5.53, 8.22, 11.17 Hz, 1H), 3.98—3.93 (m, 1H), 3.56 (dd, J = 8.37, 14.28 Hz, 1H), 1.90—1.70 (m, 1H), 1.42 (dd, J = 5.68, 13.37 Hz, 1H); IR (KBr) ν: 3065, 2957, 2889, 1596, 1523, 1491, 1348, 1254, 1106, 1079, 1020, 924, 844, 759, 745, 696 cm^{-1}; MS (70 eV) *m/z* (%): 312 (M^+, 15.86), 205 (15.43), 204 (base), 130 (20.81), 91 (26.85), 77 (50.46); Anal. calcd. for: $C_{17}H_{16}N_2O_4$: C 64.14, H 5.07, N 8.80; found C 64.08, H 5.35, N 8.50.

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