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Graphical abstract:

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Qiuya Wang, Zunting Zhang, Xi Zhang, Jin Zhang, Yang Kang and Jufang Peng

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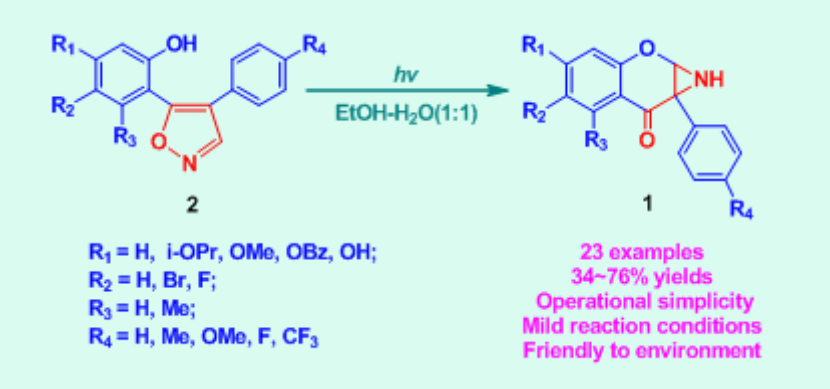

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A novel protocol has been developed for the synthesis of 1a, 7a-dihydro-7a-phenyl-benzopyrano [2,3-*b*]azirin-7-ones *via* the photoisomerization of 4-phenyl-5-(2-hydroxyphenyl)isoxazoles. This procedure involves a photo-catalyzed ring opening of isoxazole and subsequent intramolecular nucleophilic addition between 2*H*-azirine intermediate and phenolic hydroxyl group. The synthetic method offers several notable advantages including the operational simplicity, mild reaction conditions, moderate to high yields and friendly to environment.

Introduction

Organic photochemical reactions play an important role in the context of green chemistry and total synthesis.[1] The photons can be considered as the ideal clean reagent for organic synthesis in contrast to toxic chemical activators.[2] Another big advantage of reactions in the excited state is their applications in the synthesis of polycyclic or highly functionalized molecules which would be difficult to access with standard chemistry reactions in the ground state.[3] Therefore, organic photochemical reactions has received considerable interest in the academic and industry.[4]

Aziridines, the smallest saturated aza-heterocycles, are versatile synthetic intermediates, which have been paid great attentions due to their important and wide applications in organic synthesis and medicinal chemistry.[5] For an instance, natural fused aziridines such as mitomycins,[6] azinomycins,[7] ficellomycin[8] displayed significant antibiotic and antitumor activities (Scheme 1).

Current preparation of aziridines mainly included the cyclization reactions,[9] nitrene addition to olefins,[10] carbene and ylide addition to imines,[11-12] addition of azirines,[13] aza-Darzen approaches[14]

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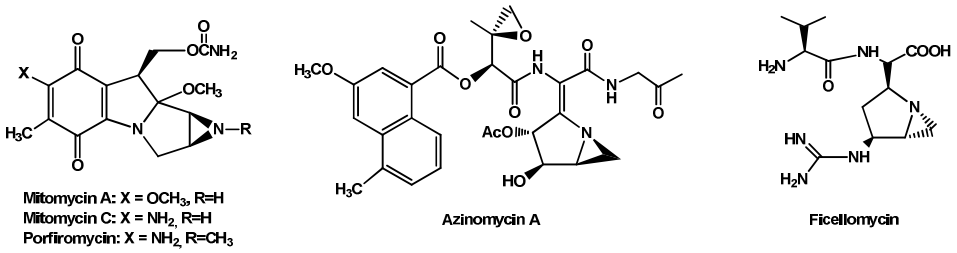
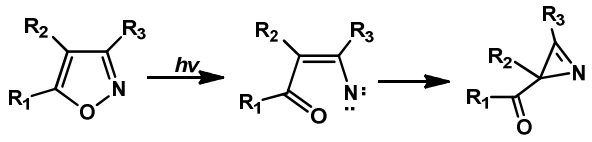
† Electronic supplementary information (ESI) available: Part experimental details, spectroscopic data and CCDC 1017876. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/xxx



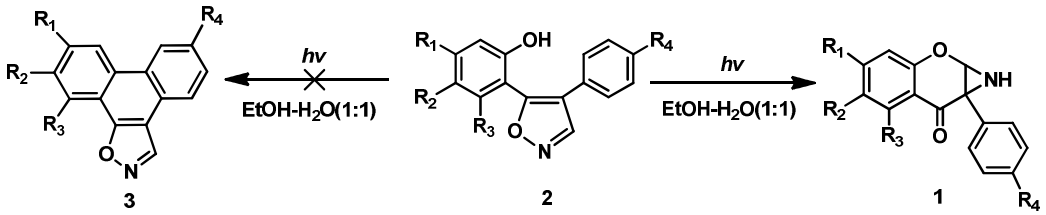
Scheme 1 Fused aziridines in the natural products.

and ring contraction.[15] Another interesting methodology was affording 2*H*-azirines by the photo-cleavage reaction of isoxazoles (Scheme 2).[16] It was known that 2*H*-azirines could be employed to synthesize aziridines by the addition with O-, S-, N-, C-nucleophiles and hydride.[17] Although the synthesis of aziridines and its derivatives have been well developed, the synthesis of fused aziridine derivatives was scarce due to the inconvenience of starting materials, nitrene source, catalysts and the harsh reaction conditions.



Scheme 2 The formation of 2*H*-azirines *via* photo-cleavage of isoxazoles

In the previous work, we have synthesized *2H*-phenanthro[9,10-*c*]pyrazoles by the intra-molecular photocyclization and dehydration of 3,4-diaryl-1*H*-pyrazoles in EtOH-H_2O (1:1, v/v).[18] Following our investigations on the development of new methodologies for the access to novel polyheterocyclic derivatives, we expect to synthesize phenanthro[9,10-*c*]isoxazoles **3** by the photocyclization of 4-phenyl-5-(2-hydroxyphenyl)isoxazoles **2**. Under the same conditions, the unexpected products, 7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-ones **1** were isolated and identified instead of phenanthro[9,10-*c*]isoxazoles **3** (Scheme 3). As yet, only *Buggle* [19] reported the synthesis of 1a,7a-dihydro-7a-phenyl-benzopyrano[2,3-*b*]azirin-7-one as a byproduct



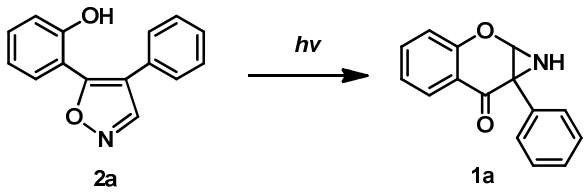
Scheme 3 Irradiation of 4-phenyl-5-(2-hydroxyphenyl)isoxazoles

in 11 % yield. In this paper, a series of 7a-phenyl-1a,7a-dihydro-benzopyrano [2,3-*b*]azirin-7-one analogues were successfully synthesized *via* the photoisomerization reaction of 4-phenyl-5-(2-hydroxyphenyl)isoxazoles **2** in EtOH-H_2O (1:1, v/v).

Results and discussion

Optimization of the photoisomerization conditions

Table 1 Optimization for the photoisomerization conditions of **2a** [a]



2a **1a**

Entry	Solvent	Time (min)	Yield (%) [b]
1	EtOH-H_2O(1:1)	60	56
2	CH_2Cl_2	120	21
3	Me_2CO	120	28
4	MeCN	90	43
5	MeOH	90	34
6	EtOH	90	39
7	MeCN-H_2O(1:1)	60	60
8	MeOH-H_2O(1:1)	60	48

[a] The intermediate **2a** (1 mmol) was dissolved in different solvents (100 mL). The solution was irradiated at λ ≥300 nm with a 500 W medium-pressure mercury lamp under an argon atmosphere at about 20 ℃.

[b] Yield of isolated product after column chromatography based on **2**a.

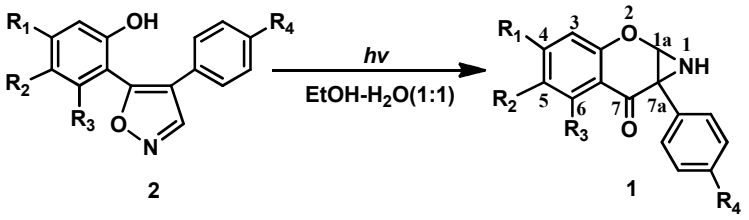
On the basis of the literature,[20] 4-phenyl-5-(2-hydroxyphenyl)isoxazoles **2** were prepared by the condensation of isoflavones and hydroxylamine hydrochloride with Et_3N as a base in refluxing EtOH. The yields of 4-phenyl-5-(2-hydroxyphenyl)isoxazoles **2** are in the range of 72%~90%. Initially, 4-phenyl-5-(2-hydroxyphenyl) isoxazole (**2a**) was irradiated in EtOH-H_2O(1:1, v/v) with a 500 W middle-pressure mercury lamp at about 20 ℃ according to the methods of our previous work.[18] Based on the careful isolation and characterization, it was surprise to find that 7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7- one (**1a**) was obtained in 56 % yield (Entry 1).

Subsequently, other solvents were screened for the photoisomerization reaction. When replacing EtOH-H_2O (1:1, v/v) with organic solvent (CH_2Cl_2, Me_2CO, MeCN, MeOH, and EtOH), the yields of **1a** were decreased (21~43%, Entries 2-6). And using MeCN-H_2O (1:1, v/v) and MeOH-H_2O (1:1, v/v) as solvents, the yields of **1a** were 60% and 48%, respectively (Entries 7-8). Although the yield of **1a** in MeCN-H_2O (1:1, v/v) was slightly higher than that in EtOH-H_2O (1:1, v/v), while from the economical and environmental point of view, EtOH-H_2O(1:1,v/v) was finally chosen as the reaction medium. Ultimately, the optimized conditions involved the irradiation of **2a** (C =10^{-2} mol/L) in EtOH-H_2O (1:1, v/v) with a 500 W medium- pressure mercury lamp ($\lambda \geq 300$ nm) under an argon atmosphere at about 20 □ (Entry 1).

The scope of the substrates

In order to explore the reaction scope, different substituted substrates **2a-w** were irradiated under the optimized reaction conditions, which generated a structurally divergent 7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-ones **1a–w** in moderate to good yields (Table 2). Obviously, the reaction was practicable for substrates bearing either electron-donating or electron-withdrawing substituent. The functionalities such as Me, OMe, i-OPr, OBz, OH, F, Br and CF_3 were all tolerated, leading to the desired products **1a–w**. While the electronic effect of different substituents had an influence on the yields of products **1**. The substrates bearing electron-donating substituents including Me, OMe, *i*-OPr, OBz or OH gave the corresponding product in good yield (60-76%, Entries 2~13), and when electron-withdrawing substituent such as F, Br or CF_3 was present, the corresponding product was obtained in relative lower yields (34-50%, Entries 14~23).

Table 2 Synthesis of 7a-phenyl-1a,7a-dihyd*ro*-benzopyrano[2,3-*b*]azirin-7-ones(**1**) *via* the photoisomerization [a]



Entry	Substrate	R_1	R_2	R_3	R_4	Product	Time (min)	Yield (%) [b]
1	**2a**	H	H	H	H	**1a**	60	56

2	**2b**	i-OPr	H	H	H	**1b**	40	68
3	**2c**	i-OPr	H	H	OMe	**1c**	50	75
4	**2d**	i-OPr	H	H	Me	**1d**	70	71
5	**2e**	OH	H	H	H	**1e**	60	60
6	**2f**	OH	H	H	OMe	**1f**	70	72
7	**2g**	OMe	H	H	OMe	**1g**	70	74
8	**2h**	OBz	H	H	OMe	**1h**	70	70
9	**2i**	OMe	H	H	H	**1i**	50	73
10	**2j**	H	H	H	OMe	**1j**	60	61
11	**2k**	OMe	H	Me	H	**1k**	60	76
12	**2l**	OMe	H	H	Me	**1l**	70	72
13	**2m**	H	H	H	Me	**1m**	80	61
14	**2n**	H	Br	H	H	**1n**	80	44
15	**2o**	H	F	H	H	**1o**	90	35
16	**2p**	H	H	H	F	**1p**	100	39
17	**2q**	i-OPr	H	H	F	**1q**	90	43
18	**2r**	OMe	H	H	F	**1r**	90	46
19	**2s**	H	F	H	OMe	**1s**	80	40
20	**2t**	H	F	H	F	**1t**	120	34
21	**2u**	H	H	H	CF_3	**1u**	120	41
22	**2v**	OMe	H	H	CF_3	**1v**	100	50
23	**2w**	i-OPr	H	H	CF_3	**1w**	100	48

[a]Conditions: **2** (1 mmol) was irradiated at λ ≥300 nm with a 500 W high-pressure mercury lamp in 100 mLEtOH-H_2O (1:1, v/v) under an argon atmosphere at about 20 □ until it was consumed completely indicative by TLC. [b] Isolated yields after silica chromatography.

Characterization of the products

All the products, 7a-Phenyl-1a,7a-dihydro-benzopyrano[2,3-b]azirin-7-ones **1** were characterized by IR, NMR and HRMS. In the ^{1}H NMR (DMSO-d_6) spectra of **1**, two doublets showed up around 4.7 ppm and 5.4 ppm. When one drop of D_2O was added to the DMSO-d_6 solution, a doublet at about 4.7 ppm disappeared completely, and the doublet at 5.4 ppm was replaced by singlet. The results of deuterium (^2H)-exchange showed that two signals around 4.7 ppm and 5.4 ppm belonged to –N**H**- and –C**H**- of aziridine ring. Simultaneously, in the ^{13}C NMR spectra of **1**,

the peak at 188~191 ppm indicated the generation of carbonyl group (-C=O). The appearance of the peaks at about 47 ppm and 70 ppm validated the existence of two saturated carbon atoms (C_{7a} and C_{1a}) in the aziridine ring. In addition, the single crystal of **1k** was obtained from methanol, and single crystal X-ray diffraction analysis also established the postulated structures unequivocally (Figure 1).

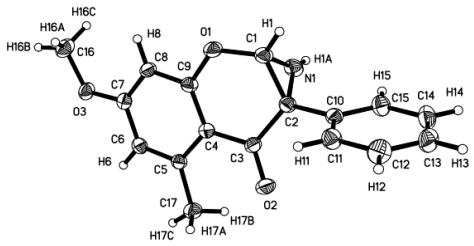
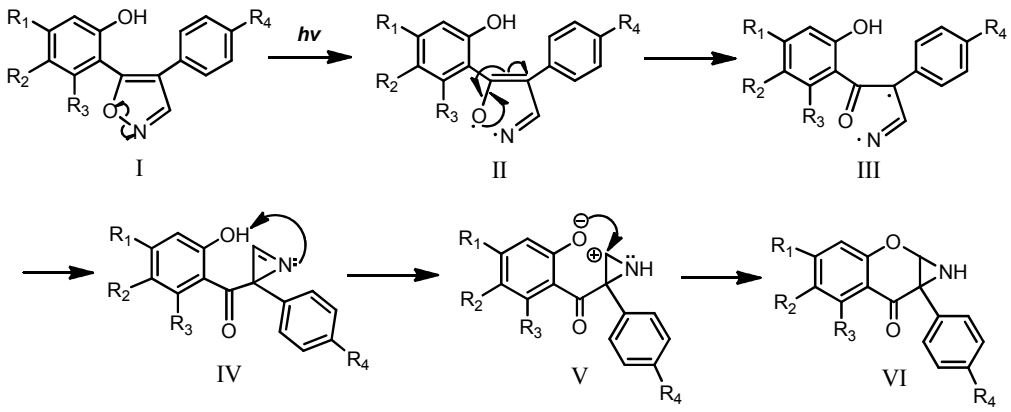


Figure 1 X-ray crystal structure of **1k** showing 30% probability ellipsoids.

Mechanism of the photoisomerization reaction



Scheme 4 Proposed mechanism for the photoisomerization of 4-phenyl-5-(2-hydroxylphenyl)isoxazoles.

A proposed mechanism for the formation of 7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*] azirin-7-one is depicted in scheme 4. According to the photochemical characteristics of substituted isoxazoles,[16] the first step of this photoisomerization reaction has been suggested to occur through homolytic cleavage of the labile N−O bond of isoxazole **I** with the generation of a diradical II, followed by giving a stable benzylic radical III, which then forms a 2*H*-azirine intermediate IV by coupling with the nitrogen centered radical. Second, an intramolecular nucleophilic addition reaction occurs between the phenolic hydroxyl group (-OH) of **IV** and the C=N bond of 2*H*-azirines ring. The N atom of 2*H*-azirine first accepts a proton from the phenolic

hydroxyl group to produce an azirine carbonium ion **V**. Next, the phenoxyl anion attacks the carbonium ion to obtain the target product **VI**. Compared with the irradiation of 3,4-diaryl-1*H*-pyrazoles to synthesize *2H*-phenanthro[9,10-*c*]pyrazoles,[18] 4-phenyl-5- (2-hydroxy phenyl)isoxazoles underwent the photoisomerization to produce the 7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7- ones owning to the labile N-O bonds.

Conclusions

In summary, a simple and efficient protocol has been developed for the synthesis of 7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-ones *via.* the photoisomerization of 4-phenyl-5-(2-hydroxylphenyl)isoxazole in EtOH–H_2O(1:1,v/v) at λ ≥300 nm with a 500 W medium-pressure mercury lamp. This method offers several notable advantages including the operational simplicity, mild reaction conditions, moderate to high yields and friendly to environment. The formation of 7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-b]azirin-7-one involves a photo-catalyzed ring opening of isoxazole and subsequent intramolecular nucleophilic addition between 2*H*-azirine intermediate and phenolic hydroxyl group.

Experimental sections

Melting points were measured by a X-5 micromelting point apparatus and are uncorrected. NMR spectra were recorded on a Bruker AM 300, 400 or 600 instrument using solvent peaks as DMSO-*d6* solutions. High resolution mass spectrometry (HRMS) were recorded using electron-spray ionization (ESI) technique and IR spectra were recorded on a Nicollet 170SX FT-IR spectrophotometer with KBr pellets. The crystal diffraction data were collected on a Bruker Smart-1000 CCD diffractometer. All the irradiation experiments were performed in a BL-GHX-V photochemical reactor equipped with a 500 W medium-pressure mercury lamp. TLC was performed on silica gel 60-GF_{254} plate. The silica gel (size 200-300 mesh) used for the column chromatography was purchased from Qingdao Haiyang Chemistry Plant (China).

General Procedure for Synthesis of 7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-b]azirin-7-one (1a-w).

4-Phenyl-5-(2-hydroxyphenyl)isoxazoles **2a-w** (1 mmol) was dissolved in 50 mL EtOH and 50 ml redistilled water. The solution was contained in 100 mL quartz tubes, deaerated by bubbling Ar

for 30 min and irradiated at λ ≥300 nm with a 500 W medium-pressure mercury lamp, which were cooled to about 20 ℃ with tap water by means of an internal cold finger. The progress of reaction was monitored by TLC at regular intervals until the intermediate **2a-w** has disappeared completely. Then, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel using petroleum ether-ethyl acetate to give the corresponding products (**1a-w**), and they are characterized by ^{1}H NMR, ^{13}C NMR, IR and HRMS spectra.

7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1a): Yield: 56%; Yellow solid; m.p. 80.6~ 81.5 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 4.61(d, 1H, J = 6.6 Hz), 5.44(d, 1H, J = 6.6 Hz), 7.09~7.17(m, 2H), 7.34~7.42(m, 5H), 7.61(m, 1H), 7.80(dd, 1H, J = 7.8, 1.6 Hz); ^{1}H NMR(600 MHz, DMSO-d_6 + D_2O), δ(ppm) 5.40(s, 1H), 7.07(d, 1H, J = 8.4 Hz), 7.12~7.15(m, 1H), 7.32~7.38(m, 5H), 7.58~7.61(m, 1H), 7.76~7.77(m, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 48.3, 70.1, 117.8, 119.5, 122.2, 126.8, 128.0, 128.9, 134.1, 135.8, 155.4, 190.1; IR (KBr), ν (cm^{-1}) 3552, 3476, 3415, 1675, 1614, 1465, 1216, 751, 616; HRMS (m/z) : calc. for $C_{15}H_{11}NO_2$ $[M + Na]^+$ 260.0687, found 260.0675.

4-Isopropoxy-7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1b): Yield: 68%; White solid; m.p. 123.8~124.7 ℃. ^{1}H NMR(300 MHz, DMSO-d_6), δ(ppm) 1.29(d, 6H, J = 6.0 Hz), 4.59(d, 1H, J = 6.6 Hz), 4.75(m, 1H), 5.39(d, 1H, J = 6.6 Hz), 6.58(d, 1H, J = 2.1 Hz), 6.71(dd, 1H, J = 8.8, 2.1 Hz), 7.36~7.40(m, 5H), 7.73(d, 1H, J = 8.8 Hz); ^{1}H NMR(400 MHz, DMSO-d_6 + D_2O), δ(ppm) 1.25(d, 6H, J = 6.0 Hz), 4.67(m, 1H), 5.35(s, 1H), 6.52~6.54(m, 1H), 6.67~6.69(m, 1H), 7.33~7.36(m, 5H), 7.69~7.71(m, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 21.6, 47.3, 70.1, 70.5, 102.2, 111.3, 112.5, 127.9, 128.0, 128.6, 128.8, 134.5, 157.5, 163.7, 188.6; IR (KBr), ν (cm^{-1}) 3473, 3250, 2978, 1651, 1617, 1444, 1381, 1297, 1246, 1113, 946, 853, 768, 691, 611; HRMS (m/z) calc. for $C_{18}H_{17}NO_3$ $[M + H]^+$ 296.1287, found 296.1286.

4-Isopropoxy-7a-(4-methoxyphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1c): Yield: 75%; Yellow solid; m.p. 128.3~ 128.8 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 1.29(d, 6H, J = 6.0 Hz), 3.77(s, 3H), 4.39 (d, J = 6.8 Hz, 1H), 4.74(m,1H), 5.38 (d, J = 6.8 Hz, 1H), 6.57 (d, J = 2.0 Hz, 1H), 6.70(dd, J =8.8, 2.0 Hz, 1H), 6.94(d, J =8.8 Hz , 2H), 6.94(d, J =8.8 Hz , 2H), 7.72(d, J =8.8 Hz , 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 21.6, 46.9, 55.1, 70.1, 70.5,

102.1, 111.2, 112.6, 113.4, 126.4, 128.6, 130.1, 157.5, 158.9, 163.6, 188.8; IR (KBr), ν (cm^{-1}) 3553, 3477, 3415, 3265, 2977, 1649, 1613, 1515, 1448, 1292, 1246, 1188, 1115, 1028, 947, 825, 748, 624; HRMS (ESI) calc. for $C_{19}H_{19}NO_4$ $[M + H]^+$ 326.1392, found 326.1379.

4-Isopropoxy-7a-(4-methylphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1d): Yield: 71%; White solid; m.p. 156.2~157.1 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 1.29(d, 6H, J = 6.0 Hz), 2.32(s, 3H), 4.43(d, J = 6.0 Hz, 1H), 4.74(m,1H), 5.35(d, J = 6.0 Hz, 1H), 6.58((s, 1H), 6.70(d, J =8.8, 1H), 7.19(d, J =6.8 Hz , 2H), 7.28~7.30(m, 2H), 7.72~7.74(m, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 20.7, 21.6, 47.1, 70.1, 70.5, 102.2, 111.3, 112.6, 128.5, 128.6, 128.7, 131.5, 137.1, 157.5, 163.7, 188.7; IR (KBr), ν (cm^{-1}) 3447, 3271, 2978, 2025, 1652, 1613, 1443, 1388, 1247, 1188, 1110, 854, 752, 642; HRMS (ESI) calc. for $C_{19}H_{19}NO_3$[M + Na]$^+$ 332.1263, found 332.1245.

4-Hydroxy-7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1e): Yield: 60%; White solid; m.p. 81.3~82.1 ℃. 1H NMR(600 MHz, DMSO-d6), δ(ppm) 4.38(d, J = 6.0 Hz, 1H), 5.38(d, J = 6.0 Hz, 1H), 6.33(s, 1H), 6.54(d, J = 9.0 Hz, 1H), 7.29~7.34 (m, 5H), 7.62~7.64(m, 1H); 13C NMR(150 MHz, DMSO-d6), δ(ppm) 47.7, 70.9, 102.9, 111.8, 112.3, 128.3, 128.4, 129.3, 129.4, 135.2, 158.0, 164.9, 188.9; IR (KBr), ν (cm-1) 3522, 3444, 3280, 2025, 1679, 1626, 1515, 1484, 1443, 1400, 1265, 1219, 1159, 995, 740, 565; HRMS (ESI) calc. for $C_{15}H_{11}NO_3$ $[M + Na]^+$ 276.0637, found 276.0616.

4-Hydroxy-7a-(4-methoxyphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1f): Yield: 72%; Yellow solid; m.p.109.8~110.7 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 3.76(s, 3H), 4.30(d, J = 6.8 Hz, 1H), 5.32 (d, J = 6.8 Hz, 1H), 6.37(d, J = 2.1 Hz, 1H), 6.58(dd, J = 8.8, 2.1 Hz, 1H), 6.93(d, J = 8.8 Hz, 2H), 7.31(d, J = 8.8 Hz, 2H), 7.66~7.68(m, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 46.8, 55.1, 70.4, 102.4, 111.2, 111.8, 113.4, 126.6, 128.9, 130.1, 157.5, 158.9, 164.3, 188.7; IR (KBr), ν (cm^{-1}) 3553, 3477, 3415, 3239, 2929, 2361, 1616, 1254, 622, 483; HRMS (ESI) calc. for $C_{16}H_{13}NO_4$ $[M + H]^+$ 284.0923, found 284.0909.

4-Methoxy-7a-(4-methoxyphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1g): Yield: 74%; Yellow solid; m.p. 142.7~143.9 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 3.77(s, 3H),

3.84(s, 3H), 4.40(d, J = 6.8 Hz, 1H), 5.40 (d, J = 6.8 Hz, 1H), 6.60(d, J = 2.1 Hz, 1H), 6.94(d, J = 8.8 Hz, 2H), 7.32(dd, J = 8.8, 2.1 Hz, 2H) 7.74(d, J = 8.8 Hz, 2H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 47.0, 55.1, 55.8, 70.5, 100.9, 110.4, 112.8, 113.4, 126.4, 128.5, 130.1, 157.5, 158.9, 165.3, 189.0; IR (KBr), ν (cm^{-1}) 3552, 3476, 3415, 3239, 2926, 2361, 1723, 1617, 1515, 1439, 1247, 1024, 838, 624, 482; HRMS (ESI) calc. for $C_{17}H_{15}NO_4$[M + Na]$^+$ 320.0899, found 320.0880.

4-Benzyloxy-7a-(4-methoxyphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1h) : Yield: 70%; Yellow solid; m.p.101.8~102.7 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 3.77(s, 3H), 4.41(d, J = 6.8 Hz, 1H), 5.20(s, 2H), 5.39 (d, J = 6.8 Hz, 1H), 6.69(d, J = 2.1 Hz, 1H), 6.80~6.82(m, 1H), 6.93~6.95 (m, 2H), 7.32~7.37 (m, 3H), 7.39~7.47 (m, 4H), 7.74(m, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 47.0, 55.1, 69.7, 70.5, 101.9, 110.0, 113.0, 113.4, 126.3, 127.8, 128.1, 128.5, 128.6, 130.1, 136.2, 157.4, 158.9, 164.3, 189.0; IR (KBr), ν (cm^{-1}) 3553, 3476, 3414, 3272, 2926, 1612, 1510, 1444, 1244, 1171, 1026, 835, 624; HRMS (ESI) calc. for $C_{23}H_{19}NO_4$[M + H]$^+$ 374.1392, found 374.1370.

4-Methoxy-7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1i): Yield: 73%; Yellow solid; m.p.103.0~104.1 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 3.84(s, 3H), 4.51(d, J = 6.4 Hz, 1H), 5.42 (d, J = 6.4 Hz, 1H), 6.62 (d, J = 2.1 Hz, 1H), 6.75 (dd, J = 8.8, 2.1Hz, 1H), 7.36~7.41(m, 5H), 7.76 (d, J = 8.8 Hz, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 47.4, 55.8, 70.5, 100.9, 110.5, 112.8, 127.9, 128.0, 128.5, 128.8, 134.4, 157.5, 165.4, 188.7; IR (KBr), ν (cm^{-1}) 3633, 3213, 1656, 1609, 1572, 1493, 1440, 1285, 1244, 1187, 1024, 839, 587; HRMS (ESI) calc. for $C_{16}H_{13}NO_3$[M + H]$^+$ 268.0974, found 268.0974.

7a-(4-Methoxyphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1j): Yield: 61%; Yellow solid; m.p.83.8~84.9 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 3.77(s, 3H), 4.53 (d, J = 6.4 Hz, 1H), 5.44 (d, J = 6.4 Hz, 1H), 6.94~6.96 (m, 2H),7.09~7.18(m, 2H), 7.35(d, J = 8.8 Hz, 2H), 7.61~7.64(m, 1H), 7.80~7.82(m, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 47.9, 55.1, 70.2, 113.5, 117.8, 119.5, 122.2, 126.1, 126.8, 130.2, 135.7, 155.4, 159.0, 190.3; IR (KBr), ν (cm^{-1}) 3552, 3476, 3415, 2922, 1617, 1517, 1464, 1292, 1250, 1027, 825, 752, 623; HRMS (ESI) calc. for $C_{16}H_{13}NO_3$[M +Na]$^+$ 290.0793, found 290.0781.

4-Methoxy-6-methyl-7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1k): Yield: 76%; Yellow solid; m.p. 132.1~132.9 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 2.51(s, 3H), 3.81(s, 3H), 4.37(d, J = 6.4 Hz, 1H), 5.40(d, J = 6.4 Hz, 1H), 6.47~6.56(m, 2H), 7.35~7.40(m, 5H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 22.0, 49.6, 55.6, 69.7, 99.5, 112.5, 112.9, 127.8, 127.9, 129.1, 134.7, 142.6, 158.4, 163.5, 190.6; IR (KBr), ν (cm^{-1}) 3479, 3247, 3056, 2924, 1665, 1610, 1573, 1446, 1356, 1281, 1245, 1205, 1142, 1045, 885, 840, 751, 698, 594; HRMS (ESI) calc. for $C_{17}H_{15}NO_3$[M + H]$^+$ 282.1130, found 282.1131.

4-Methoxy-7a-(4-methylphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1l): Yield: 72%; Yellow solid; m.p. 135.7~136.5 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 2.32(s, 3H), 3.84(s, 3H), 4.46(d, J = 6.0 Hz, 1H), 5.38 (d, J = 6.0 Hz, 1H), 6.61(s, 1H), 6.73~6.75(m, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.28~7.30(m, 2H), 7.75 (dd, J = 8.8, 2.1 Hz, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 20.7, 47.2, 55.8, 70.5, 101.0,110.4, 112.9, 128.5, 128.7, 131.4, 137.2, 157.5, 165.3, 188.8; IR (KBr), ν (cm^{-1}) 3520, 3443, 3278, 2930, 2025, 1670, 1609, 1513, 1443, 1386, 1245, 1189, 1107, 836, 570; HRMS (ESI) calc. for $C_{17}H_{15}NO_3$[M+Na]$^+$ 304.0950, found 304.0934.

7a-(4-Methylphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1m): Yield: 61%; Yellow solid; m.p. 83.8~84.9 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 2.32(s, 3H), 4.58(d, J = 6.4 Hz, 1H), 5.43(d, J = 6.4 Hz, 1H), 7.10~7.21(m, 4H), 7.30~7.32(m, 2H), 7.61~ 7.65(m, 1H), 7.82 (d, J = 8.0 Hz, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 20.7, 48.1, 70.2, 117.8, 119.5, 122.2, 126.8, 128.6, 128.8, 131.1, 135.7, 137.3, 155.4, 190.2; IR (KBr), ν (cm^{-1}) 3552, 3415, 3240, 2027, 1616, 1517, 1464, 1395, 1285, 1215, 1143, 986, 812, 752, 6 ; HRMS (ESI) calc. for $C_{16}H_{13}NO_2$[M +H]$^+$ 252.1025, found 252.1013.

5-Bromo-7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1n): Yield: 44%; Yellow solid; m.p.56.5~57.3 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 4.85(d, J = 6.4 Hz, 1H), 5.52(d, J = 6.4 Hz, 1H), 7.13 (d, J = 8.8 Hz, 1H), 7.37~7.45(m, 5H), 7.79 (dd, J = 8.8, 2.1 Hz, 1H), 7.88 (d, J = 2.50 Hz, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 48.2, 70.4, 113.8, 120.6, 121.2, 128.0, 128.1, 128.8, 128.9, 133.6, 138.1, 154.5, 189.0; IR (KBr), ν (cm^{-1}) 3555, 3479, 3414, 3274, 3060, 2922, 2360, 1678, 1597, 1468, 1420, 1262, 1219, 1184, 1126, 982, 817, 746, 694, 587, 501;

HRMS (ESI) calc. for $C_{15}H_{10}BrNO_2[M+H]^+$ 315.9973, found 315.9960.

10-Fluoro-7a-phenyl-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1o): Yield: 35%; Yellow solid; m.p.78.9~80.2 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 4.73(d, J = 6.8 Hz, 1H), 5.50(d, J = 6.8 Hz, 1H), 7.21~7.22(m, 1H), 7.39~7.44(m, 5H), 7.51~7.53(m, 2H); ^{1}H NMR(400 MHz, DMSO-d_6 + D_2O), δ(ppm) 5.46(s, 1H), 7.15~7.19(m, 1H), 7.36~7.40(m, 5H), 7.47~7.52(m, 2H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 48.1, 70.3, 111.7(d, ^2J = 23.6 Hz), 120.0, 120.1, 120.3(d, ^3J = 6.6 Hz), 123.2 (d, ^2J = 24.2 Hz), 128.1(d, ^3J = 5.8 Hz), 128.9, 133.8, 151.7, 157.0 (d, ^1J=238.4 Hz), 189.5; IR (KBr), ν (cm^{-1}) 3479, 3412, 3298, 3080, 1675, 1624, 1483, 1441, 1345, 1264, 1212, 1161, 1125, 1041, 990, 942, 822, 744, 699, 612; HRMS (ESI) calc. for $C_{15}H_{10}FNO_2[M+H]^+$ 256.0774, found 256.0765.

7a-(4-Fluorophenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1p): Yield: 39%; Yellow solid; m.p.104.0~104.9 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 4.65(d, J = 6.8 Hz, 1H), 5.48(d, J = 6.8 Hz, 1H), 7.11~7.25(m, 4H), 7.47~7.51(m, 2H), 7.62~7.66(m, 1H), 7.81~7.83 (m, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 47.7, 70.1, 114.9(d, ^2J = 21.3 Hz), 117.8, 119.4, 122.3, 126.8, 130.4, 131.1(d, ^3J = 8.4 Hz), 135.8, 155.4, 161.8(d, ^1J = 242.9 Hz), 189.9; IR (KBr), ν (cm^{-1}) 3553, 3477, 3414, 3293, 3044, 1662, 1613, 1509, 1470, 1292, 1218, 1155, 1104, 1012, 899, 812, 747, 622; HRMS (ESI) calc. for $C_{15}H_{10}FNO_2[M+Na]^+$ 278.0593, found278.0580.

4-Isopropoxy-7a-(4-fluorophenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1q): Yield: 43%; Yellow solid. m.p.98.8~99.5 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 1.29 (d, 6H, J = 6.0 Hz), 4.52(d, J = 6.0 Hz, 1H), 4.75(m, 1H), 5.41(d, J = 6.0 Hz, 1H), 6.59(s, 1H), 6.70~6.72(m, 1H), 7.19~7.24(m, 2H), 7.45~7.48(m, 2H), 7.73 (dd, J = 8.8, 2.4 Hz, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 21.6, 46.7, 70.1, 70.4, 102.2, 111.3, 112.4, 114.8(d, ^2J = 21.3 Hz), 128.6, 130.7, 131.1(d, ^3J = 8.3 Hz), 157.5, 161.7(d, ^1J = 242.8 Hz), 163.7, 188.4; IR (KBr), ν (cm^{-1}) 3520, 3443, 3277, 2930, 2025, 1670, 1609, 1514, 1443, 1385, 1245, 1189, 1159, 1110, 1017, 836, 769, 680, 570; HRMS (ESI) calc. for $C_{18}H_{16}FNO_3[M+Na]^+$ 336.1012, found 336.0989.

4-Methoxy-7a-(4-fluorophenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1r): Yield: 46%; Yellow solid; m.p.112.8~113.1 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 3.84(s, 3H), 4.54(d, J = 6.0 Hz, 1H), 5.44(d, J = 6.0 Hz, 1H), 6.63(s, 1H), 6.74~6.76(m, 1H), 7.19~ 7.24(m,

2H), 7.46~7.49(m, 2H), 7.74~7.77(m, 1H); ^{13}C NMR(100 MHz, DMSO-d_6), δ(ppm) 46.8, 55.8, 70.4, 101.0, 110.5, 112.7, 114.8(d, ^{2}J = 21.4 Hz), 128.6, 130.7, 131.1(d, ^{3}J = 8.4 Hz), 157.5, 161.8(d, ^{1}J = 242.7 Hz), 165.4, 188.6; IR (KBr), ν (cm^{-1}) 3444, 3255, 2025, 1663, 1613, 1513, 1440, 1403, 1246, 1155, 1101, 1031, 831, 767, 679, 569; HRMS (ESI) calc. for $C_{16}H_{12}FNO_3[M+Na]^+$ 308.0699, found 308.0687.

4-Fluoro-7a-(4-methoxyphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1s): Yield: 40%; Yellow solid; m.p.57.9~58.2 ℃. ^{1}H NMR(600 MHz, DMSO-d_6), δ(ppm) 3.76(s, 3H), 4.60(d, J = 6.6 Hz, 1H), 5.45(d, J = 6.6 Hz, 1H), 6.93~6.94(m, 2H), 7.15~7.18(m, 1H), 7.33~7.34(m, 2H), 7.48~7.51(m, 2H); ^{13}C NMR(150 MHz, DMSO-d_6), δ(ppm) 48.1, 55.6, 70.9, 112.2(d, ^{2}J=23.7 Hz), 114.0, 120.5(d, ^{3}J = 7.6 Hz), 120.8(d, ^{3}J = 6.5 Hz), 123.6 (d, ^{2}J = 24.3 Hz), 126.3, 130.7, 152.2, 157.5(d, ^{1}J = 238.4 Hz), 159.6, 190.2; IR (KBr), ν (cm^{-1}) 3520, 3443, 3279, 2930, 2026, 1670, 1609, 1513, 1443, 1387, 1244, 1189, 1106, 1018, 836, 769, 681, 570; HRMS (ESI) calc. for $C_{16}H_{12}FNO_3[M+Na]^+$ 308.0699, found 308.0684.

4-Fluoro-7a-(4-fluorophenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1t): Yield: 34%; Yellow solid; m.p.139.5~140.1 ℃. ^{1}H NMR(600 MHz, DMSO-d_6), δ(ppm) 4.72 (d, J = 6.60 Hz, 1H), 5.49 (d, J = 6.60 Hz, 1H), 7.17-7.22 (m, 3H), 7.48-7.53 (m, 4H); ^{13}C NMR(150 MHz, DMSO-d_6), δ(ppm) 47.9, 70.8, 112.2 (d, ^{2}J = 23.7 Hz), 115.3(d, ^{2}J = 21.3 Hz), 120.5(d, ^{3}J = 7.6 Hz), 120.7(d, ^{3}J = 6.9 Hz), 123.7(d, ^{2}J = 24.3 Hz), 130.6, 131.6(d, ^{3}J = 8.5 Hz), 152.1, 157.5(d, ^{1}J = 238.5 Hz), 162.4(d, ^{1}J = 243.5 Hz), 189.8. IR (KBr), ν (cm^{-1}) 3612, 3522, 3444, 3281, 2025, 1679, 1626, 1604, 1516, 1484, 1402, 1265, 1219, 1159, 1126, 995, 829, 763, 740, 700, 565; HRMS (ESI) calc. for $C_{15}H_9F_2NO_2[M+Na]^+$ 296.0499, found 296.0482.

7a-(4-Trifluoromethylphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one(1u): Yield: 41%; Yellow solid. m.p.106.1~107.0 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 4.82 (d, J = 6.6 Hz, 1H), 5.51 (d, J = 6.6 Hz, 1H) 7.13~7.21(m, 2H), 7.64~7.70(m, 3H), 7.77 (d, J = 8.4 Hz, 2H), 7.84 (dd, J = 8.0, 2.1 Hz, 1H); ^{13}C NMR(150 MHz, DMSO-d_6), δ(ppm) 47.8, 70.1, 117.9, 119.3, 122.4, 124.2(q, ^{1}J = 270.6 Hz), 124.8(q, ^{3}J = 3.8 Hz), 126.9, 128.5(q, ^{2}J = 31.5 Hz), 129.8, 136.0, 138.7, 155.3, 189.5; IR (KBr), ν (cm^{-1}) 3669, 3284, 3072, 1671, 1610, 1470, 1413, 1331, 1296, 1219, 1164, 1113, 1067, 1010, 903, 858, 815, 752; HRMS (ESI) calc. for $C_{16}H_{10}F_3NO_2[M+Na]^+$

328.0561, found 328.0549.

4-Methoxy-(4-trifluoromethylphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1v): Yield: 50%; Yellow solid; m.p.132.3~133.2 ℃. ^{1}H NMR(400 MHz, DMSO-d_6), δ(ppm) 3.85(s, 3H), 4.72 (d, J = 6.6 Hz, 1H), 5.47 (d, J = 6.6 Hz, 1H), 6.65 (d, J = 2.4 Hz, 1H), 6.76 (dd, J = 8.4, 2.4 Hz, 1H), 7.68 (d, J = 8.4 Hz, 2H), 7.74~7.78(m, 3H); ^{3}C NMR(100 MHz, DMSO-d_6), δ(ppm) 46.9, 55.9, 70.5, 101.0, 110.7, 112.6, 124.2(q, ^{1}J = 270.5 Hz), 124.7(q, ^{3}J = 3.7 Hz), 128.5(q, ^{2}J = 31.6 Hz), 128.9, 129.8, 139.1, 157.5, 165.5, 188.1. IR (KBr), ν (cm^{-1}) 3553, 3476, 3414, 3238, 2361, 1616, 1440, 1325, 1247, 1171, 1134, 1065, 1022, 869, 832, 620, 482 ; HRMS (ESI) calc. for $C_{17}H_{12}F_3NO_3[M+Na]^+$ 358.0667, found 358.0650.

4--Isopropoxy-(4-trifluoromethylphenyl)-1a,7a-dihydro-benzopyrano[2,3-*b*]azirin-7-one (1w) : Yield: 48%; Yellow solid; m.p.107.5~108.9 ℃. ^{1}H NMR(600 MHz, DMSO-d_6), δ(ppm) 1.29 (d, 6H, J = 6.0 Hz), 4.69 (d, J = 6.8 Hz, 1H), 4.76(m, 1H), 5.44(d, J = 6.8 Hz, 1H), 6.61 (d, J = 2.4 Hz, 1H), 6.73 (dd, J = 8.4, 2.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 2H), 7.74~7.76(m, 3H); ^{13}C NMR(150 MHz, DMSO-d_6), δ(ppm) 21.5, 46.8, 70.1, 70.5, 102.2, 111.5, 112.3, 124.2(q, ^{1}J = 270.6 Hz), 124.7 (q, ^{3}J = 3.6 Hz), 128.4(q, ^{2}J = 31.6 Hz), 129.8, 139.1, 128.7, 157.5, 163.9, 188.0; IR (KBr), ν (cm^{-1}) 3553, 3477, 3415, 3290, 2986, 1654, 1617, 1572, 1500, 1445, 1331, 1279, 1248, 1165, 1113, 1066, 1015, 925, 856, 816, 610, 484; HRMS (ESI) calc. for $C_{19}H_{19}F_3NO_3[M+H]^+$ 364.1161, found 364.1147.

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