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AN EFFICIENT SYNTHESIS OF BENZOPYRANO-2-ISOXAZOLINES

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ABSTRACT : A series of benzopyrano-2-isoxazoline compounds have been prepared efficiently by three-step synthesis from corresponding salicylaldehyde derivatives.

Intramolecular dipolar cycloaddition[1] provides an efficient route for fused ring heterocyclic compounds. Very recently, Masamune and coworkers[2] prepared benzopyranoisoxazolidines, new chiral auxiliaries for asymmetric alkylations using an intramolecular dipolar cycloaddition as the key reaction. Thus, optically active benzopyranoisoxazolidines **1** and **2** were obtained by intramolecular nitrone cycloadditions[3] followed by

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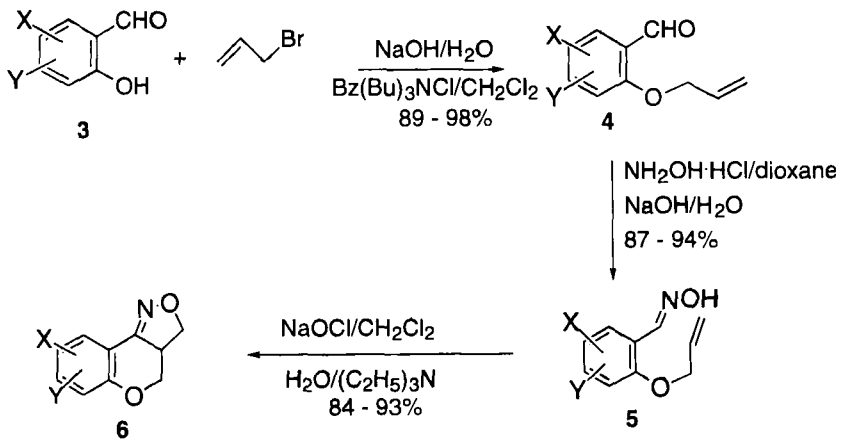
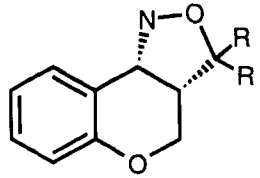


Scheme 1

resolutions with (+)-10-camphorsulfonic acid or L-dibenzoyltartaric anhydride. Benzopyrano-2-isoxazolines can be readily reduced by reducing agent such as $BH_3{\cdot}SMe_2$[4] to afford benzopyranoisoxazolidines and can be converted to synthetically useful compounds including γ-hydroxy-α-amino acids.[5]



1, R=H
2, R = CH_3

Here we report an efficient three-step synthesis for benzopyrano-2-isoxazoline. As starting materials, commercially available salicylaldehyde derivatives were employed. Phase transfer catalyzed allylation of starting materials provided *o*- allyloxybenzaldehydes **4** in good yields. Oxime formation followed by intramolecular nitrile oxide cycloaddition[6] afforded the desired benzopyrano-2-isoxazolines **6**(Scheme 1).

Table. Isolated Yields of Reaction Intermediates and Benzopyrano-2-isoxazolines

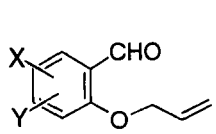
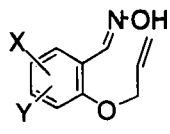
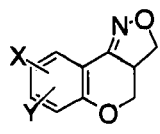
 **4**	 **5**	 **6**
X=H Y=H	**4a**,98%	**5a**,91%	**6a**,93%
X=H Y=3-Methoxy	**4b**,98%	**5b**,91%	**6b**,91%
X=5-Bromo Y=H	**4c**,95%	**5c**,90%	**6c**,90%
X=5-Chloro Y=H	**4d**,95%	**5d**,89%	**6d**,92%
X=H Y=4-Methoxy	**4e**,98%	**5e**,90%	**6e**,90%
X=5-Methoxy Y=H	**4f**,96%	**5f**,93%	**6f**,92%
X=5-Chloro Y=3-Chloro	**4g**,89%	**5g**,87%	**6g**,84%
X=5-Bromo Y=3-Bromo	**4h**,96%	**5h**,93%	**6h**,90%
X=5-Iodo Y=3-Iodo	**4i**,98%	**5i**,92%	**6i**,88%

Table summerizes the experimental results. In most cases, the reaction yields of each step were excellent(89-98% for allylation, 87-93% for oxime formation, and 84-93% for the final cycloaddition) and three-step overall yields from starting salicylaldehyde derivatives were in the range of 65-83%. Thus, this reaction sequence represents one of most

efficient synthetic routes for the preparation of benzopyrano-2-isoxazolines, which have great versatility and utility in organic synthesis.

EXPERIMENTAL

Most reagents in reactions were purchased from Aldrich and Janssen and used without further purification. Anhydrous solvents were obtained as followed: diethyl ether,distillation from sodium/benzophenone; triethyl amine, distillation from calcuim hydride. ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker Aspect 3000. IR spectra were obtained with BOMEM model FT-IR M100-C15 and Mass spectra with Kratos 25 RFA(70eV,EI). Elemental analyses were performed by Galbraith Laboratories, Inc. and melting points were determined by using Haake Buchler apparatus and are uncorrected. Flash column chromatography was carried out with Merck silica gel 60(230-400 mesh).

General Method 1 : Preparation of *o*-allyloxybenzaldehydes

To a solution of the corresponding salicylaldehyde derivatives(10.0mmol) in CH_2Cl_2(50mL) was added allyl bromide(2.17mL, 25mmol), NaOH(0.65g, 15mmol), distilled water(50mL) and catalytic amount of benzyltributylammonium chloride(0.31g, 1mmol). After being stirred at room temperature for 1-2h, the mixture was extracted by ethyl acetate. Combined organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo to give the corresponding allyl ethers. The allyl ethers were purified by column chromatography and/or recrystallization.

2-Allyloxybenzaldehyde (4a)

The crude product was synthesized according to the general method 1 and purified by flash column chromatography on silica gel to give a yellowish liquid(yield 98%). ^{1}H NMR($CDCl_3$) δ 10.54(s, 1H), 7.85-7.82(m,1H),7.55-7.49(m, 1H), 7.26-6.97(m, 2H), 6.14-6.02(m,1H), 5.45(dd, J=17.3,1.2Hz,1H), 5.33(dd,J=10.6,1.2Hz,1H), 4.68-4.65(m, 2H); ^{13}C NMR ($CDCl_3$) δ 190.0, 161.3, 136.3, 132.8, 128.7, 125.4, 121.2, 118.4, 113.2, 69.5.

2-Allyloxy-3-methoxybenzaldehyde (4b)

The crude product was synthesized according to the general method 1 and purified by flash column chromatography on silica gel to give a yellowish liquid(yield 98%). ^{1}H NMR($CDCl_3$) δ 10.44(s, 1H), 7.43-7.40(m, 1H), 7.16-7.11(m, 2H), 6.12-6.03(m, 1H), 5.35(m,1H), 5.26(dd,J=10.6, 1.2Hz,1H), 4.68-4.65(m, 2H), 3.90(s, 3H),; MS(EI, m/e) 192(M^+), 163, 151, 136, 131, 122, 108, 95, 93, 85, 83, 81,77.

2-Allyloxy-5-bromobenzaldehyde(4c)

The crude product was synthesized according to the general method 1 and purified by flash column chromatography on silica gel to give a yellowish liquid(yield 95%). ^{1}H NMR($CDCl_3$) δ 10.44(s, 1H), 7.93(d,J=2.5Hz,1H), 7.60(m, 1H), 6.88(d,J=8.7Hz, 1H), 6.10-5.99(m, 1H), 5.44(m, 1H), 5.35(m,1H), 4.66-4.64(m, 2H) ; ^{13}C NMR($CDCl_3$) δ 188.6, 160.1, 138.6, 132.3, 131.1, 126.5, 118.9, 115.4, 113.9, 69.8; IR($CHCl_3$, cm^{-1}) 1683, 1590, 1477, 1394, 1254, 1180, 1000, 813, 651, 428; MS(EI, m/e) 240(M^+), 225, 213, 199, 190, 170, 143, 132, 115, 105, 77.

2-Allyloxy-5-chlorobenzaldehyde(4d)

The crude product was synthesized according to the general method 1 and purified by flash column chromatography on silica gel to give a white solid(yield 95%). mp 100.7-101.7°C; ^{1}H NMR($CDCl_3$) δ 10.45(s, 1H), 7.78(d,J=2.5Hz,1H) 7.47-7.43(m, 1H), 6.94(d,J=8.7Hz,1H), 6.10-6.02 (m, 1H), 5.44(dd,J=18.7,1.3Hz,1H), 5.35(dd,J=11.9,1.3Hz,1H), 4.66-4.63(m, 2H) ; ^{13}C NMR($CDCl_3$) δ 196.3, 195.9, 160.5, 137.3, 132.9, 126.3, 125.0, 121.5, 119.8, 64.8; IR($CHCl_3$, cm^{-1}) 1683, 1471, 1377, 1276, 1163.

2-Allyloxy-4-methoxybenzaldehyde(4e)

The crude product was synthesized according to the general method 1 and purified by flash column chromatography on silica gel to give a white solid(yield 98%). mp 37.9-38.1°C; ^{1}H NMR($CDCl_3$) δ 10.35(s, 1H), 7.82(d, J=8.7Hz, 1H), 6.55(m, 1H), 6.44(d,J=2.5Hz, 1H), 6.13-6.01 (m, 1H), 5.45(m, 1H), 5.34(dd,J=10.6,1.3Hz,1H), 4.64-4.62(m, 2H), 3.83(s, 3H) ; ^{13}C NMR($CDCl_3$) δ 188.0, 165.9, 162.6, 132.2, 130.4, 119.4, 118.0, 106.1, 99.1, 69.2, 55.5; IR($CHCl_3$, cm^{-1}) 2879, 1677, 1599, 1502, 1436, 1294, 1262, 1202, 1169, 1110, 1015, 932, 827; MS(EI, m/e) 192(M^+), 163, 151, 135, 119, 108, 103, 95, 88, 86, 84, 82, 79.

2-Allyloxy-5-methoxybenzaldehyde(4f)

The crude product was synthesized according to the general method 1 and purified by flash column chromatography on silica gel to give a yellowish liquid(yield 93%). ^{1}H NMR($CDCl_3$) δ 10.49(s, 1H), 7.32(d,J=3.1Hz, 1H), 7.10(m,1H), 6.93(d,J=9.4Hz, 1H), 6.12-5.99(m, 1H), 5.42(m, 1H), 5.32(m,1H), 4.62-4.60(m, 2H),3.79(s, 3H); ^{13}C NMR($CDCl_3$) δ

189.2, 156.7, 153.8, 132.6, 125.5, 123.2, 117.8, 114.9, 110.4, 70.0, 55.6; MS(EI, m/e) 192(M^+), 163, 151, 137, 123, 108, 95, 93, 86, 84, 79, 77, 65.

2-Allyloxy-3,5-dichlorobenzaldehyde (4g)

The crude product was synthesized according to the general method 1 and purified by flash column chromatography on silica gel to give a white solid(yield 96%). mp 44.8- 45.8°C; ^{1}H NMR($CDCl_3$) δ 10.27(s,1H), 7.69(d,J=2.5Hz,1H), 7.61(d,J=2.5Hz,1H), 6.08-6.05(m,1H), 5.38(dd,J=16.1,1.3Hz,1H),5.34(dd,J=10.6,1.3Hz,1H), 4.63-4.60(m,2H).

2-Allyloxy-3,5-dibromobenzaldehyde (4h)

The product was synthesized according to the general method 1 and recrystallized from methylene chloride-hexane to give a white solid(yield 98%). mp 171.6-172.4°C; ^{1}H NMR($CDCl_3$) δ 10.24 (s,1H), 7.92(d,J=2.5Hz,1H),7.88(d,J=2.5Hz,1H), 6.08-6.03(m,1H), 5.39(dd,J=16.8, 1.3Hz, 1H), 5.33(d,J=9.9Hz,1H), 4.60-4.58(d,J=6.2Hz,2H)

2-Allyloxy-3,5-diiodobenzaldehyde (4i)

The product was synthesized according to the general method 1 and recrystallized from ethyl acetate-hexane to give a white solid(yield 96%). mp 117.4-118.4°C; ^{1}H NMR($CDCl_3$) δ 10.16(s,1H), 8.32(d, J=2.5Hz, 1H),8.07(d,J=1.9Hz, 1H), 6.11-6.06(m,1H), 5.41(dd,J=16.8,1.3Hz,1H), 5.33(d, J=10.6Hz,1H), 4.54-4.52(d,J=6.2Hz, 2H).

General Method 2 : Preparation of *o*- allyloxybenzaldoximes.

To a solution of allyl ether(9.25mmol) in dioxane(75mL) was added $NH_2OH{\cdot}HCl$ (11.3mmol), NaOH (19.3mmol), in distilled water(75mL).

After being stirred for 2-3h at room temperature, the mixture was concentrated to a quarter of the original volume. The mixture was extracted ethyl acetate and dried over $MgSO_4$, filtered and concentrated in vacuo to the corresponding oximes. The oximes were purified by column chromatography and/or recrystallization.

2-Allyloxybenzaldoxime (5a)

The crude product was synthesized according to the general method 2 and purified by flash column chromatography on silica gel to give a yellowish liquid(yield 91%). ^{1}H NMR($CDCl_3$) δ 9.35(s, 1H), 8.55(s,1H), 7.74-7.70(m, 1H), 7.34-7.25(m, 1H), 6.98-6.88(m, 2H), 6.11-5.99 (m, 1H), 5.39(dd,J=17.3,1.2Hz,1H), 5.28(dd,J=10.5,1.2Hz,1H), 4.57(d, J=5.1Hz, 2H); IR($CHCl_3$, cm^{-1}) 2927, 2828, 1601, 1491, 1454, 1370, 1288, 1237, 1073, 976, 756; MS(EI, m/e) 177(M^+), 160, 145, 132, 120, 105, 91, 887, 85, 83, 77.

2-Allyloxy-3-methoxybenzaldoxime (5b)

The crude product was synthesized according to the general method 2 and purified by flash column chromatography on silica gel to give a white solid(yield 91%). mp 47.9-49.5°C; ^{1}H NMR($CDCl_3$) δ 8.48(s, 1H), 7.37-7.34(m, 1H),7.07-6.91(m, 2H), 6.11-6.00(m, 1H), 5.34(m,1H), 5.23(dd,J=10.0,1.3Hz,1H), 4.52(dd,J=4.4,1.2Hz, 2H), 3.86(s,3H); MS(EI, m/e) 207(M^+), 190, 175, 166, 163, 151, 121, 108, 103, 93, 80, 77.

2-Allyloxy-5-bromobenzaldoxime(5c)

The product was synthesized according to the general method 2 and recrystallized from ethyl acetate to give a white solid(yield 90%). mp

87.0-88.5°C; ^{1}H NMR($CDCl_3$) δ 8.72(br,1H), 8.46(s, 1H), 7.83(s, 1H), 7.38(m, 1H),6.75(d, J=8.7Hz, 1H), 6.06-5.97(m,1H), 5.38(dd,J=17.4,1.2Hz,1H), 5.29(dd,J=10.6,1.2Hz,1H), 4.57-4.54(m, 2H); ^{13}C NMR($CDCl_3$) δ 156.3, 146.0, 134.2, 133.1, 129.9, 123.5, 118.8, 114.9, 114.1,70.2; IR($CHCl_3$, cm^{-1}) 3301, 1483, 1412, 1256, 1129, 959; MS(EI, m/e) 255(M^+), 238, 197, 169, 149, 135, 105, 91, 77, 69, 63; Elemental Analysis calcd. for $C_{19}H_{21}O_5N$ C, 66.46; H, 6.16; N, 4.08. Found C, 66.50; H, 6.06; N, 4.07.

2-Allyloxy-5-chlorobenzaldoxime(5d)

The product was synthesized according to the general method 2 and recrystallized from ethyl acetate to give a white solid(yield 90%). mp 100.7-101.7°C; ^{1}H NMR($CDCl_3$) δ 8.48(s, 1H), 8.30(s, 1H), 7.70(s, 1H), 7.26(m, 1H), 6.82(d,J=8.7Hz, 1H), 6.01-5.98(m, 1H), 5.40(dd,J=16.8,1.2Hz, 1H), 5.30(dd,J=10.6,1.3Hz,1H), 4.58-4.55(m, 2H); ^{13}C NMR($CDCl_3$) δ 155.8,146.2, 133.1,131.3,127.0, 123.1, 118.8,, 114.5, 70.3 ; IR($CHCl_3$, cm^{-1}) 3303, 2897, 1485, 1414, 1256, 1229, 1184, 1132, 955, 772; MS(EI, m/e) 210(M^+), 193, 178, 163, 153, 130, 124, 115, 98, 89,75.

2-Allyloxy-4-methoxybenzaldoxime(5e)

The crude product was synthesized according to the general method 2 and purified by flash column chromatography on silica gel to give a white solid(yield 90%). mp 61.1-62.7°C; ^{1}H NMR($CDCl_3$) δ 8.45(s, 1H), 7.62(d,J=8.7Hz, 1H), 6.48(m, 1H), 6.42(d,J=2.5Hz,1H), 6.06-5.98(m, 1H), 5.39(dd,J=17.4,1.3Hz,1H), 5.28(dd,J=10.6,1.3Hz,1H), 4.54(m, 2H), 3.78(s, 3H); ^{13}C NMR($CDCl_3$) δ 163.0, 158.6, 146.9, 133.4, 128.5, 118.4, 114.7, 106.5, 100.3, 69.9, 56.0; IR($CHCl_3$, cm^{-1}) 3293, 3002, 1609, 1575, 1507, 1462,

1422, 1284, 1201, 1168, 1120, 949, 858, 830; MS(EI, m/e) 207(M^+), 198, 190, 175, 160, 149, 104, 91, 83, 78, 69, 65, 60.

2-Allyloxy-5-methoxybenzaldoxime(5f)

The crude product was synthesized according to the general method 2 and purified by flash column chromatography on silica gel to give a yellowish solid(yield 93%). mp 57.8-59.3°C; ^{1}H NMR($CDCl_3$) δ 8.46(s, 1H), 7.63(d,J=8.7Hz, 1H), 6.51-6.43(m, 2H), 6.08-5.98(m, 1H), 5.40(dd,J=17.4,1.2Hz,1H),5.28(dd,J=10.6,1.2Hz,1H), 4.55-4.53(m, 2H),3.77(s, 3H); ^{13}C NMR($CDCl_3$) δ 154.5, 151.8, 147.1, 133.8, 122.3, 118.3, 115.2, 111.0, 70.9, 56.4 MS(EI, m/e) 207(M^+), 190, 175, 166, 149, 134, 111, 106, 91, 83, 78, 65.

2-Allyloxy-3,5-dichlorobenzaldoxime (5g)

The crude product was synthesized according to the general method 2 and purified by flash column chromatography on silica gel to give a white solid(yield 93%). mp 86.2-86.8°C ^{1}H NMR($CDCl_3$) δ 8.36(s,1H), 7.71(d,J=2.5Hz,1H), 7.64(s,1H), 7.43(d,J=2.5Hz,1H),6.16-6.03(m, 1H), 5.43(dd,J=17.2,1.4Hz,1H),5.34(dd,J=10.3,1.4Hz,1H), 4.51(d,J=5.9Hz, 1H).

2-Allyloxy-3,5-dibromobenzaldoxime (5h)

The product was synthesized according to the general method 2 and recrystallized from ethyl acetate to give a white solid(yield 93%). mp 108.7-109.7°C; ^{1}H NMR($CDCl_3$) δ 8.31(s,1H), 8.10(s,1H), 7.85(d, J=2.6Hz, 1H),7.70(d,J=2.6Hz, 1H), 6.11-6.00(m,1H), 5.39(dd,J=17.7,1.3Hz,1H),

5.30(d,J=11.1Hz,1H), 4.45(d,J= 5.9Hz,2H); ^{13}C NMR($CDCl_3$) δ 152.9, 145.7, 137.6, 132.9, 129.8, 129.2, 120.0, 119.5, 118.4, 76.4.

2-Allyloxy-3,5-diiodobenzaldoxime (5i)

The product was synthesized according to the general method 2 and recrystallized from ethyl acetate to give a white solid(yield 94%). mp 145.3-145.8°C; ^1H NMR($CDCl_3$) δ 8.25(s,1H), 8.10(d,J=2.0Hz,1H), 8.05(d,J=2.0Hz,1H) 7.60 (s,1H), 6.15-6.02(m,1H), 5.42(d,J=17.0Hz,1H), 5.30(d,J=11.2Hz,1H), 4.38(d,J= 5.9Hz,2H).

General Method 3 : Preparation of benzopyrano-2-isoxazoline

To a precooled(0°C) solution of the oxime(6.5mmol) in CH_2Cl_2(25mL) was added catalytic amount of triethyl amine(0.18mmol) and dropwise 4% NaOCl aqueous solution(12mmol) over 1h. After stirring for 2 h, the mixture was extracted with ethyl acetate and dried over MgSO4, filtered and concentrated in vacuo to give the corresponding isoxazolines. The isoxazolines were purified by column chromatography and/or recrystallization.

4H-[1]benzopyrano[4,3-c]-2-isoxazoline (6a)

The crude product was synthesized according to the general method 3 and purified by flash column chromatography on silica gel to give a yellowish solid(yield 93%). mp 59.0-61.0°C; ^1H NMR($CDCl_3$) δ 7.79(dd,J=7.7,1.6Hz,1H), 7.36-7.26(m, 1H), 7.02-6.93(m, 2H), 4.71-4.65(m, 2H), 4.12-4.05(m, 1H), 4.00-3.66(m, 2H); ^{13}C NMR($CDCl_3$) δ 156.2, 153.4, 133.1, 126.3, 122.5, 118.0, 113.7, 71.2, 69.9, 46.5; IR($CHCl_3$, cm^{-1}) 1610, 1484,

1311, 1229, 1035, 999, 860, 826, 751; MS(EI, m/e) 175(M^+), 167, 161, 149, 145, 129, 121, 115, 111, 97, 93, 91, 83, 73, 71.

8'-Methoxy-4H-[1]benzopyrano[4,3-c]-2-isoxazoline (6b)

The crude product was synthesized according to the general method 3 and purified by flash column chromatography on silica gel to give a white solid(yield 91%). mp 95.8-96.3°C; ^{1}H NMR($CDCl_3$) δ 7.41(dd,J=7.3,2.5Hz, 1H), 6.98-6.91(m, 2H), 4.84-4.79(m, 1H), 4.72-4.70(m, 1H), 4.16-4.08(m, 1H), 3.97-3.91(m,2H), 3.89(s,3H) ; ^{13}C NMR($CDCl_3$) δ 153.0, 149.0, 145.6, 126.3, 122.0, 117.6, 114.1, 71.1, 70.1, 56.4, 46.1; IR($CHCl_3$, cm^{-1}) 2933, 1577, 1491, 1448, 1383, 1267, 1233, 1130, 1055, 1001, 903, 835, 734; MS(EI, m/e) 205(M^+), 175, 149, 118, 102, 97, 92, 87, 84, 77, 71; Elemental Analysis calcd. for $C_{11}H_{11}O_3N$ C, 64.38; H, 5.40; N, 6.82. Found C, 64.44; H, 5.53; N, 6.73.

6'-Bromo-4H-[1]benzopyrano[4,3-c]-2-isoxazoline(6c)

The crude product was synthesized according to the general method 3 and purified by flash column chromatography on silica gel to give a brown solid(yield 91%). mp 127.0-128.1°C; ^{1}H NMR($CDCl_3$) δ 7.91(s, 1H), 7.40(dd,J=8.7,2.5Hz,1H), 6.83(d, J=9.3Hz, 1H), 4.71-4.70(m, 2H), 4.10-4.02(m, 1H), 3.96-3.87(m, 2H); ^{13}C NMR($CDCl_3$) δ 155.1, 152.4, 135.8, 128.7, 120.0, 115.4, 114.8, 71.5, 70.0, 46.0; IR($CHCl_3$, cm^{-1}) 2988, 2879, 1609, 1474, 1439, 1299, 1275, 1226, 1132, 820; MS(EI, m/e) 252(M^+), 224, 196, 143, 115, 89, 83, 75, 71; Elemental Analysis calcd. for $C_{10}H_8O_2NBr$ C, 47.27; H, 3.17; N, 5.51. Found C, 47.39; H, 3.28; N, 5.43.

6'-Chloro-4H-[1]benzopyrano[4,3-c]-2-isoxazoline(6d)

The crude product was synthesized according to the general method 3 and purified by flash column chromatography on silica gel to give a yellowish solid(yield 92%). mp 130.3-131.3°C; ^{1}H NMR($CDCl_3$) δ 7.72(d,J=2.6, 1H), 7.25(dd,J=9.2,2.6Hz, 1H), 6.89(d,J=8.5Hz, 1H), 4.71-4.66(m, 2H), 4.10-4.02(m, 1H), 3.92-3.87(m, 2H); ^{13}C NMR($CDCl_3$) δ 154.6, 152.4, 132.9, 127.5, 125.5, 119.5, 114.8, 71.5, 69.9, 46.0; IR($CHCl_3$, cm^{-1}) 3649, 2931, 1476, 1223, 1133, 1009, 831; MS(EI, m/e) 209(M^+), 198, 179, 153, 125, 115, 105, 98, 91, 83, 81, 77, 75; Elemental Analysis calcd. for $C_{10}H_8O_2NCl$ C, 57.30; H, 3.85; N, 6.68. Found C, 57.37; H, 4.01; N, 6.55.

7'-Methoxy-4H-[1]benzopyrano[4,3-c]-2-isoxazoline(6e)

The crude product was synthesized according to the general method 3 and purified by flash column chromatography on silica gel to give a yellowish solid(yield 85%). mp 132.5-134.0°C ; ^{1}H NMR($CDCl_3$) δ 7.70(d,J=8.7Hz, 1H), 6.60(dd,J=8.7,2.5Hz, 1H), 6.46(d,J=2.5Hz, 1H), 4.68-4.65(m, 2H), 4.07-4.03(m,1H), 3.92-3.84(m,2H), 3.82(s,3H); ^{13}C NMR($CDCl_3$) δ 163.3, 157.1, 152.5, 126.9, 109.8, 105.9, 101.5, 70.2, 69.4, 55.4, 46.2; IR($CHCl_3$, cm^{-1}) 1619, 1506, 1435, 1243, 1016, 809 MS(EI, m/e) 205(M^+), 175, 160, 149, 132, 121, 115, 106, 91, 82, 77; Elemental Analysis calcd. for $C_{11}H_{11}O_3N$ C, 64.38; H, 5.40; N, 6.82. Found C, 64.56; H, 5.46; N, 6.70.

6'-Methoxy-4H-[1]benzopyrano[4,3-c]-2-isoxazoline(6f)

The crude product was synthesized according to the general method 3 and purified by flash column chromatography on silica gel to give a white solid(yield 92%). mp 62.0-63.5°C; ^{1}H NMR($CDCl_3$) δ

7.24(d,J=2.5Hz, 1H), 6.92-6.86(m, 2H), 4.70-4.63(m, 2H), 4.08-4.03(m, 1H), 3.91-3.89(m, 2H), 3.78(s, 3H); ^{13}C NMR($CDCl_3$) δ 154.9, 153.8, 150.7, 121.6, 119.2, 113.5, 107.9, 71.4, 69.9, 56.4, 46.6; MS(EI, m/e) 205(M^+), 189, 175, 160, 149, 132, 119, 106, 91, 82, 77; Elemental Analysis calcd. for $C_{11}H_{11}O_3N$ C, 64.38; H, 5.40; N, 6.82. Found C, 64.37; H, 5.49; N, 6.70.

6',8'-Dichloro-4H-[1]benzopyrano[4,3-c]-2-isoxazoline (6g)

The product was synthesized according to the general method 3 and recrystallized from ethyl acetate to give a yellowish solid(yield 90%). mp 144.7-148.0°C; ^{1}H NMR ($CDCl_3$) δ 7.72(d,J=2.5Hz,1H), 7.43(d, J=2.5Hz, 1H), 4.90-4.85(m,1H), 4.81-4.76(m,1H), 4.22-4.12(m,1H), 4.04-3.89 (m,2H); MS(EI,m/e) 243(M+), 213, 149, 123, 115, 91, 88, 83, 77, 71.

6',8'-Dibromo-4H-[1]benzopyrano[4,3-c]-2-isoxazoline (6h)

The crude product was synthesized according to the general method 3 and purified by flash column chromatography on silica gel to give a white solid(yield 88%). mp 157.4-158.3°C; ^{1}H NMR ($CDCl_3$) δ 7.86(d, J=2.5Hz,1H), 7.68(d,J=2.5Hz,1H), 4.82(dd,J=10.6,5.6Hz, 1H), 4.73(m, 1H), 4.15-4.07(m, 1H), 3.95-3.92(m,2H); ^{13}C NMR ($CDCl_3$) δ 151.8, 138.3, 135.0 127.8, 116.4, 114.7, 113.0, 71.0, 70.6, 45.7.

6',8'-Diiodo-4H-[1]benzopyrano[4,3-c]-2-isoxazoline (6i)

The product was synthesized according to the general method 3 and recrystallized from ethyl acetate to give a yellowish solid(yield 85%). mp 198.9-200.3°C; ^{1}H NMR ($CDCl_3$) δ 8.10(s,2H), 4.87-4.75(m,2H), 4.18-4.11(m,1H),4.02-3.92(m,2H) ; MS(EI, m/e) 427(M+) 279, 167, 149, 127, 97, 85, 71.

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References

1. Padwa, A. "1,3-Dipolar Cycloaddition Chemistry", John Wiley & Sons, New York, **1984**, vol.2, pp. 277-466.
2. Abiko, A. ; Moriya, O. ; Masamune,S. *Angew.Chem.Int.Ed.Engl.* **1995**, *34*, 793.
3. Tufariello,J.J. "1,3-Dipolar Cycloaddition Chemistry",John Wiley & Sons, New York, **1984**, vol.2, pp.116-122.
4. Bolm, C. ; Felder, M. *Synlett* . **1994**, 655.
5. Barett, A. G. M. ; Dhanak, D. ; Lebold, S. A. ; Russell, M. A. ; *J. Org. Chem.* **1991**,*56*, 1894.
6. a)Garanti,L.;Sala,A.;Zecchi,G. *J.Org.Chem.* **1975**,*40*, 2403.
   b)Lee,G.A. *Synthesis*, **1982**, 508.
   c)Jung,M.E.;Vu,B.T. *Tetrahedron Lett.* **1996**,*37*, 451.

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