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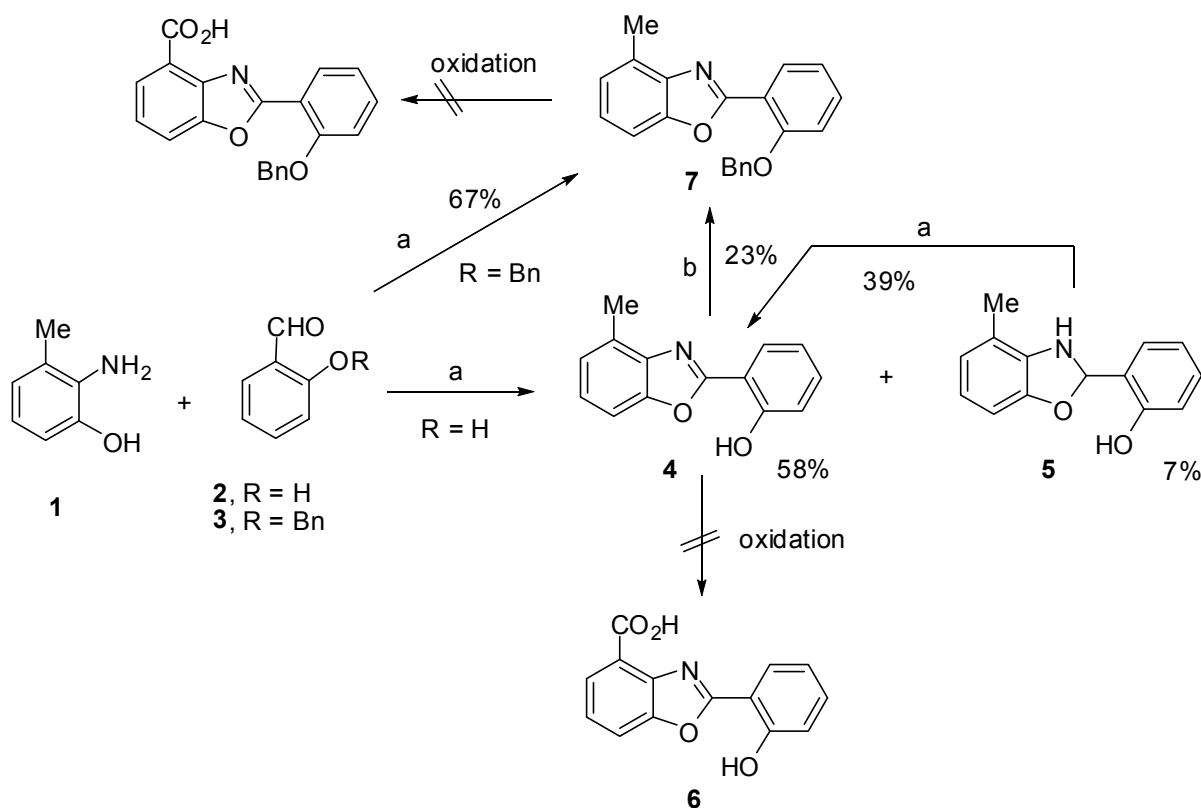
SYNTHESIS OF CABOXAMYCIN AND ITS DERIVATIVES USING ECO-FRIENDLY OXIDATION

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Abstract – The reaction of 3-hydroxyanthranilic acid or methyl 3-hydroxyanthranilate with *O*-benzylsalicylaldehyde in xylenes gave benzoxazole derivatives, which lead to a novel benzoxazole antibiotic, caboxamycin *via* debenzylation or demethylation in good yield, in the presence of dry activated carbon and bubbling molecular oxygen. The present reaction involves the simple procedure, easy workup and environmentally benign materials such as reusable activated carbon and molecular oxygen.

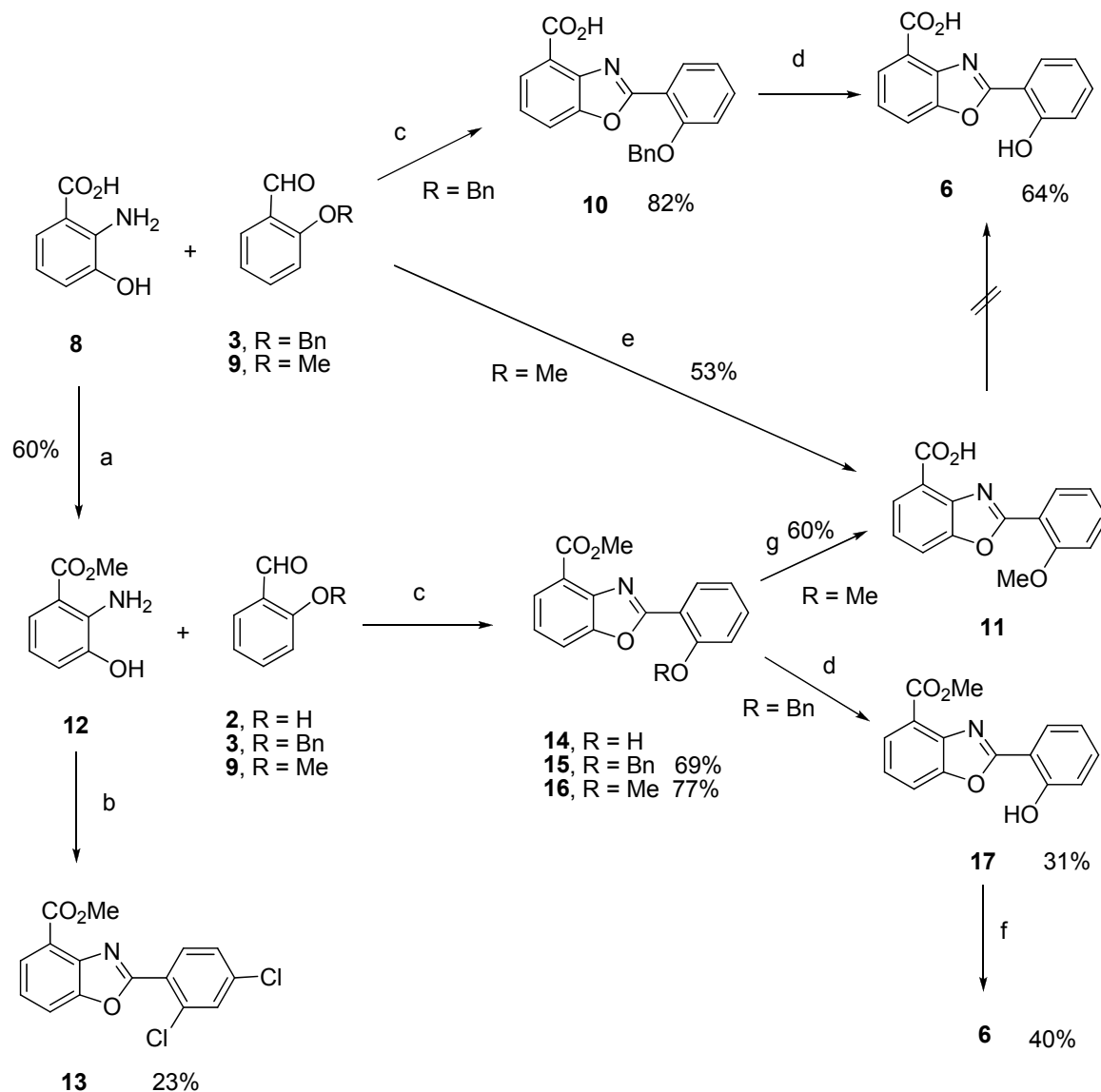
Caboxamycin is a new antibiotic of the benzoxazole family isolated from deep-sea sediment in Canary Basin.¹ It showed inhibitory activity against Gram-positive bacteria, selected human tumor cell lines and enzyme phosphodiesterase. The structure of caboxamycin was determined by the various spectral data and x-ray analysis, but the synthesis is officially still not reported.^{1,2} It is of great interest to prepare caboxamycin and the derivatives to examine various biological activities. We have already reported the preparation of benzimidazole derivatives by eco-friendly oxidation of 1,2-phenylenediamine with a variety of aromatic aldehydes in the presence of environmentally benign materials, dry activated carbon and bubbling molecular oxygen.³ Applying this synthetic method, we investigated the preparation of caboxamycin and its derivatives, and finally obtained caboxamycin and its derivatives in satisfactory yields. At the first stage we have tried the direct reaction of 3-hydroxyanthranilic acid with salicyl aldehyde in xylenes in the presence of activated carbon and molecular oxygen to obtain caboxamycin in one step reaction, but no reaction proceeded. The reaction of 2-amino-*m*-cresol (**1**) with salicyl aldehyde (**2**) in xylenes in the presence of activated carbon and molecular oxygen gave compounds (**4**) and (**5**) in 58% and 7% yields, respectively. Compound **5** was oxidized to **4** in 39% yield under the same reaction conditions above mentioned. The oxidation of methyl group on **4** to carboxylic acid will give caboxamycin (**6**). So, a variety of oxidations, *i.e.*, *t*-BuOK/O₂/DMF,⁴ crown ether/KMnO₄/PhH,⁵ Co(OAc)₂/NHPI/O₂/AcOH,⁶ Ni(bpy)₂Cl₂/NaOCl/MeCN,⁷ KMnO₄/H₂O,⁸ in order to oxidize methyl group on **4** to carboxylic acid was examined to proceed in vain. The compound (**7**) prepared from **4** also showed the resistance to oxidation of methyl group to carboxylic acid by Co(OAc)₂/NHPI/O₂/AcOH⁶ (Scheme 1).



Scheme 1 Reagents and conditions: (a) activated carbon (A.C.), O₂, xylenes, 110-115 °C, 3 h ; (b) BnBr, K₂CO₃, Me₂CO, reflux, 4 h

Reaction of 3-hydroxyanthranilic acid⁹ (**8**), which was prepared *via* 5 step reactions from *m*-cresol, with 2-benzyloxybenzaldehyde¹⁰ (**3**) or *o*-anisaldehyde¹¹ (**9**) in xylenes in the presence of activated carbon and molecular oxygen gave benzyloxyphenyl benzoxazole derivative (**10**) or methoxyphenyl benzoxazole derivative (**11**) in 82% or 53% yields, respectively. Compound **10** was reductively debenzylated by Pd/C/H₂¹² to give **6** in 64% yield, whose spectral data such as ¹H and ¹³C-NMR spectra were completely coincided with those reported on the original journal.¹ On the other hand, **11** was not demethylated by Pd/C/H₂, *p*-TsOH/PhMe¹² or piperazine/DMA¹³ to give **6** (Scheme 2).

Methyl 3-hydroxyanthranilate¹⁴ (**12**) reacted with 2,4-dichlorobenzaldehyde in xylenes in the presence of activated carbon and molecular oxygen to give dichlorophenyl benzoxazole ester (**13**) in 23% yield, but reaction of **12** with **2** did not proceed to the desired cyclic compound (**14**). So, we carried out the reaction of **12** with **3** and **9**, which have no phenolic hydroxygroup, under the same reaction conditions aforementioned to give benzyloxyphenyl benzoxazole ester (**15**) and methoxyphenyl benzoxazole ester (**16**) in 69% and 77% yields, respectively. While **15** was debenzylated by Pd/C/H₂ to result in hydroxyphenyl benzoxazole ester (**17**) in 31% yield, which was hydrolyzed with 5N-NaOH aqueous solution¹² to give **6** in 40% yield, **16** was hydrolyzed with 5N-NaOH aqueous solution to give **11** in 60% yield (Scheme 2).



Scheme 2 Reagents and conditions: (a) MeOH, c-H₂SO₄; (b) activated carbon (A.C.), O₂, 2,4-dichlorobenzaldehyde, xylenes, 110-115 °C, 1 h; (c) A.C., O₂, xylenes, 110-115 °C, 3 h; (d) Pd/C/H₂, rt, 3 h; (e) A.C., O₂, xylenes, 110-115 °C, 1 h; (f) 5N-NaOH, THF, reflux, 6.5 h; (g) 5N-NaOH, THF, reflux, 2 h

In conclusion, we synthesized caboxamycin with 2 routes *via* debezylation and demethylation under eco-friendly and simple reaction conditions composed of activated carbon and molecular oxygen in moderate yield, and the present report is officially the first synthesis of caboxamycin. It is possible to prepare a variety of derivatives of caboxamycin by changing functional group and functional group position or using various aromatic benzaldehydes. From these standpoints, our investigation is currently under way to prepare such derivatives of caboxamycin which are expected to have any valuable biological activities.

EXPERIMENTAL

Melting points were measured on a Yanagimoto micro melting points apparatus and are uncorrected. Spectral data were recorded on the following spectrometers: IR spectra, JASCO FT/IR-4100; ^1H NMR spectra, JEOL GX-400 (400 MHz) and JEOL A-500 (500 MHz); ^{13}C NMR spectra, JEOL GX-400 (100 MHz) and JEOL A-500 (125 MHz); mass spectra, JEOL JMS-DX300 for EI-ms and JMS-HX110 for FAB-ms. The HH-COSY, CH-COSY, and DEPT experiments were also used for the assignments of the structures. The chemical shifts are given on the δ scale (ppm) using TMS as the internal standard. Elemental analyses were performed on Yanaco MT-6 instrument. Medium pressure liquid chromatography (mplc) was carried out with a Yamazen 540 FMI-C pump and Wakogel FC-40 (20-40 μm , Wako). Column chromatography was carried out with Kieselgel 60 (70-230 mesh, Merck). Activated carbon (Darco[®] KB) was purchased from Aldrich Chemical Company and used after drying *in vacuo* with heating.

General Procedure for reaction of 2-aminophenol derivatives with aromatic aldehyde in the presence of activated carbon and molecular oxygen

A mixture of 2-aminophenol derivative (5.00 mmol), aromatic aldehyde (5.00 mmol) and activated carbon (50 weight% of 2-aminophenol derivative) was heated at 110-115 $^{\circ}\text{C}$ for the time shown in Schemes 1 and 2 in xylenes (40 mL) with stirring under bubbling of molecular oxygen into xylenes. The resulting solution was filtered and the activated carbon was washed with MeOH. After removal of the solvent, the residue was worked up in the manner as shown below.

The residue of the reaction of **1** with **2** was chromatographed with chloroform to give 0.65 g (58%) of **4** and 0.08 g (7%) of **5**, respectively.

2-(4-Methylbenzo[d]oxazol-2-yl)phenol (**4**)

This compound was recrystallized from 99% EtOH to give colorless prisms, mp 113-114 $^{\circ}\text{C}$.

^1H NMR(CDCl_3) δ (ppm): 2.62 (3H, s, Me), 6.98-7.01 (1H, m), 7.10-7.12 (1H, m), 7.15 -7.17 (1H, m), 7.24-7.27 (1H, m), 7.40-7.44 (2H, m), 8.00 (1H, dd, $J=7.6$ and 1.5 Hz), 11.55 (1H, s, OH). ^{13}C NMR(CDCl_3) δ (ppm): 16.4 (q, CH_3), 107.9 (d), 110.8 (s), 117.4 (d), 119.5 (d), 125.1 (d), 125.5 (d), 127.0 (d), 129.8 (s), 133.3 (d), 139.3 (s), 148.9 (s), 158.7 (s), 162.2 (s). MS (FAB) m/z 226 (MH^+). *Anal.* Calcd for $\text{C}_{14}\text{H}_{11}\text{NO}_2$: C, 74.65; H, 4.92; N, 6.22. Found: C 74.68 ; H, 5.00 ; N, 6.20. IR (KBr, cm^{-1}): 3030, 1629, 1591, 1549, 1488, 1417, 1249, 1071, 753, 714.

2-(4-Methyl-2,3-dihydrobenzo[d]oxazol-2-yl)phenol (**5**)

This compound was recrystallized from 99% EtOH to give pale yellow prisms, mp 215-217 $^{\circ}\text{C}$.

^1H NMR($\text{DMSO}-d_6$) δ (ppm): 2.22 (3H, s, Me), 6.75 (1H, d, $J=7.3$ Hz), 6.84 (1H, d, $J=8.2$ Hz), 6.93-6.98 (3H, m), 7.39-7.42 (1H, m), 7.57 (1H, dd, $J=7.9$ and 1.8 Hz), 8.95 (1H, s, NHCH), 9.65 (1H, s, NH), 13.52 (1H, s, OH). ^{13}C NMR($\text{DMSO}-d_6$) δ (ppm): 18.3 (q, CH_3), 114.3 (d), 116.6 (d), 118.9 (d), 119.3 (s), 121.1 (d), 126.0 (d), 132.1 (s), 132.3 (d), 132.8 (d), 134.4 (s), 148.5 (s), 160.5 (s), 167.1 (d, NH-CH). MS (FAB)

m/z 228 (MH^+). *Anal.* Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.94; H, 5.89; N, 6.13. IR (KBr, cm^{-1}): 1615, 1536, 1456, 1382, 1272, 1218, 1140, 1111, 561, 490.

Transformation of **5** into **4**

A mixture of **5** (0.15 g, 0.66 mmol) and activated carbon (0.075 g) was heated at 110–115 °C for 3 h in xylenes (30 mL) with stirring under bubbling of molecular oxygen into xylenes. The resulting solution was filtered and the activated carbon was washed with MeOH. After removal of the solvent, the residue was chromatographed with chloroform to give 0.058 g (39%) of **4**.

2-(2-(Benzyloxy)phenyl)-4-methylbenzo[d]oxazole (**7**)

The residue was chromatographed with $CHCl_3$ to give 1.06 g (67%) of **7**. This compound was recrystallized from 95% EtOH to give colorless needles, mp 92–93 °C. 1H NMR($CDCl_3$) δ (ppm): 2.71 (3H, s, Me), 5.28 (2H, s, CH_2), 7.10–7.15 (3H, m), 7.23 (1H, dd, $J=8.1$ and 8.1 Hz), 7.29–7.32 (1H, m), 7.37–7.40 (3H, m), 7.45–7.49 (1H, m), 7.67–7.69 (2H, m), 8.17 (1H, dd, $J=7.6$ and 1.8 Hz).

^{13}C NMR($CDCl_3$) δ (ppm): 16.6 (q, CH_3), 70.7 (t, CH_2), 107.7 (d), 113.9 (d), 117.4 (s), 121.2 (d), 124.6 (d), 124.8 (d), 126.8 (d), 127.7 (d), 128.4 (d), 130.6 (s), 131.4 (d), 132.4 (d), 136.9 (s), 141.5 (s), 150.3 (s), 157.5 (s), 160.9 (s). MS (FAB) m/z 316 (MH^+). *Anal.* Calcd for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found: C, 80.16; H, 5.57; N, 4.44. IR (KBr, cm^{-1}): 1610, 1499, 1443, 1292, 1266, 1239, 1022, 744, 730, 696.

Preparation¹⁰ of **7** from **4**

To a solution of **4** (0.3 g, 1.33 mmol) in dry acetone (30 mL) was added anhydrous K_2CO_3 (0.28 g, 2 mmol) and benzyl bromide (0.26 g, 1.53 mmol), and the resulting mixture was refluxed for 4 h. After removal of the solvent, the residue was extracted with EtOAc. After evaporation of the solvent, the residue was purified by mpc (hexane : EtOAc = 10 : 1) to give 0.1 g (23%) of **7**.

2-(2-(Benzyloxy)phenyl)benzo[d]oxazole-4-carboxylic acid (**10**)

The residue was chromatographed with $CHCl_3$ to give 1.41 g (82%) of **10**. This compound was recrystallized from 2-propanol – H_2O to give colorless prisms, mp 68–69 °C. 1H NMR($CDCl_3$) δ (ppm): 5.29 (2H, s, CH_2), 7.15 (1H, dd, $J=7.5$ and 7.5 Hz), 7.18 (1H, d, $J=8.2$ Hz), 7.35 (1H, dd, $J=7.3$ and 7.3 Hz), 7.42 (1H, dd, $J=7.5$ and 7.9 Hz), 7.48 (1H, dd, $J=7.9$ and 7.9 Hz), 7.51–7.59 (4H, m), 7.76 (1H, dd, $J=7.9$ and 0.9 Hz), 8.13 (1H, dd, $J=7.6$ and 0.9 Hz), 8.21 (1H, dd, $J=7.9$ and 1.4 Hz), 11.83 (1H, brs, CO_2H). ^{13}C NMR($CDCl_3$) δ (ppm): 71.0 (t, CH_2), 113.8 (d, Ar), 114.8 (s, Ar), 115.1 (d, Ar), 120.2 (s, Ar), 121.2 (d, Ar), 125.4 (d, Ar), 127.0 (d, Ar), 127.2 (d, Ar), 128.3 (d, Ar), 128.8 (d, Ar), 131.6 (d, Ar), 134.3 (d, Ar), 136.0 (s, Ar), 141.1 (s, Ar), 149.9 (s, Ar), 158.2 (s, Ar), 163.1 (s, Ar), 164.8 (s, $C=O$). MS (FAB) m/z 346 (MH^+). *Anal.* Calcd for $C_{21}H_{15}NO_4 + 1.2 H_2O$: C, 68.73; H, 4.78; N, 3.82. Found: C, 68.71; H, 4.73; N, 3.79. IR (KBr, cm^{-1}): 3421, 1747, 1704, 1605, 1541, 1496, 1432, 1290, 1253, 751, 697.

2-(2-Methoxyphenyl)benzo[d]oxazole-4-carboxylic acid (**11**)

The residue was chromatographed with $CHCl_3$ to give 0.71 g (53%) of **11**. This compound was

recrystallized from 2-propanol to give pale yellow cottony crystals, mp 192-194 °C. ^1H NMR(CDCl_3) δ (ppm): 4.03 (3H, s, Me), 7.11-7.16 (2H, m), 7.50 (1H, dd, $J=8.2$ and 7.9 Hz), 7.57-7.60 (1H, m), 7.82 (1H, d, $J=8.2$ Hz), 8.14 (1H, d, $J=7.9$ Hz), 8.19 (1H, dd, $J=7.9$ and 1.8 Hz), 11.97 (1H, brs, CO_2H). ^{13}C NMR(CDCl_3) δ (ppm): 56.1 (q, CH_3), 112.4 (d), 114.3 (s), 115.2 (d), 120.1 (s), 120.9 (d), 125.3 (d), 127.0 (d), 131.5 (d), 134.3 (d), 141.1 (s), 149.9 (s), 159.2 (s), 163.2 (s), 164.8 (s, $\text{C}=\text{O}$). MS (FAB) m/z 270(MH^+). *Anal.* Calcd for $\text{C}_{15}\text{H}_{11}\text{NO}_4$: C, 66.91; H, 4.12; N, 5.20. Found: C, 66.86; H, 4.22; N, 5.23. IR (KBr, cm^{-1}): 3211, 1753, 1604, 1529, 1477, 1430, 1404, 1267, 1250, 1168, 754.

Methyl 2-(2,4-dichlorophenyl)benzo[d]oxazole-4-carboxylate (13)

The residue was purified by mple (hexane : EtOAc = 10 : 1) to give 0.37 g (23%) of **13**.

This compound was recrystallized from hexane to give yellow curdy (cotton) crystal, mp 129-130 °C.

^1H NMR(CDCl_3) δ (ppm): 4.05 (3H, s, Me), 7.41 (1H, dd, $J=8.4$ and 2.0 Hz), 7.47 (1H, dd, $J=7.9$ and 7.9 Hz), 7.59 (1H, d, $J=2.1$ Hz), 7.81 (1H, dd, $J=8.2$ and 0.9 Hz), 8.07 (1H, dd, $J=7.8$ and 1.1 Hz), 8.22 (1H, d, $J=8.5$ Hz). ^{13}C NMR(CDCl_3) δ (ppm): 52.5 (q, CH_3), 115.1 (d), 122.7 (s), 124.5 (s), 125.1 (d), 127.3 (d), 127.4 (d), 131.3 (d), 133.2 (d), 134.7 (s), 138.1 (s), 141.0 (s), 151.4 (s), 162.0 (s), 165.6 (s, $\text{C}=\text{O}$). MS (FAB) m/z 322(MH^+). *Anal.* Calcd for $\text{C}_{15}\text{H}_9\text{NO}_3\text{Cl}_2$: C, 55.93; H, 2.82; N, 4.35. Found: C, 55.96; H, 2.87; N, 4.32. IR (KBr, cm^{-1}): 1710, 1561, 1460, 1392, 1308, 1291, 1137, 1098, 788, 754.

Methyl 2-(2-(benzyloxy)phenyl)benzo[d]oxazole-4-carboxylate (15)

The residue was chromatographed with CH_2Cl_2 to give 1.24 g (69%) of **15**.

This compound was recrystallized from hexane to give colorless prisms, mp 106-107 °C.

^1H NMR(CDCl_3) δ (ppm): 4.01 (3H, s, Me), 5.30 (2H, s, CH_2), 7.11-7.14 (2H, m), 7.30-7.33 (1H, m), 7.38-7.41 (3H, m), 7.48-7.51 (1H, m), 7.63-7.65 (2H, m), 7.74 (1H, dd, $J=8.2$ and 1.1 Hz), 8.03 (1H, dd, $J=7.9$ and 1.1 Hz), 8.27 (1H, dd, $J=7.6$ and 1.8 Hz). ^{13}C NMR(CDCl_3) δ (ppm): 52.4 (q, CH_3), 70.8 (t, CH_2), 113.9 (d), 114.7 (d), 116.6 (s), 121.1 (d), 122.2 (s), 124.1 (d), 126.8 (d), 126.9 (d), 127.7 (d), 128.5 (d), 132.0 (d), 133.2 (d), 136.8 (s), 141.6 (s), 151.4 (s), 157.9 (s), 163.7 (s), 166.0 (s, $\text{C}=\text{O}$). MS (FAB) m/z 360(MH^+). *Anal.* Calcd for $\text{C}_{22}\text{H}_{17}\text{NO}_4$: C, 73.53; H, 4.77; N, 3.90. Found: C, 73.75; H, 4.92; N, 3.91. IR (KBr, cm^{-1}): 1705, 1603, 1533, 1449, 1421, 1318, 1293, 1269, 1242, 1126, 752.

Methyl 2-(2-methoxyphenyl)benzo[d]oxazole-4-carboxylate (16)

The residue was purified by mple (hexane : EtOAc = 10 : 1) to give 1.09 g (77%) of **16**.

This compound was recrystallized from hexane to give pale yellow crystals, mp 110-111 °C.

^1H NMR(CDCl_3) δ (ppm): 4.02 (3H, s, OMe), 4.06 (3H, s, COOMe), 7.07-7.12 (2H, m), 7.40 (1H, dd, $J=7.9$ and 7.9 Hz), 7.50-7.53 (1H, m), 7.78 (1H, dd, $J=8.1$ and 1.1 Hz), 8.03 (1H, dd, $J=7.9$ and 1.2 Hz), 8.24 (1H, dd, $J=7.9$ and 1.8 Hz). ^{13}C NMR(CDCl_3) δ (ppm): 52.4 (q, COOMe), 56.1 (q, OMe), 112.1 (d), 114.8 (d), 115.9 (s), 120.7 (d), 122.1 (s), 124.2 (d), 126.9 (d), 131.9 (d), 133.3 (d), 141.6 (s), 151.3 (s), 158.9 (s), 163.7 (s), 166.0 (s, $\text{C}=\text{O}$). MS (FAB) m/z 284(MH^+). *Anal.* Calcd for $\text{C}_{16}\text{H}_{13}\text{NO}_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.82; H, 4.68; N, 4.89. IR (KBr, cm^{-1}): 1706, 1607, 1482, 1422, 1314, 1302, 1271, 1239, 1196, 739.

General Procedure for reduction of compounds 10 and 15 by hydrogenation on Pd/C

A mixture of **10** or **15** (0.5 mmol) and Pd/C (20 mg, 10% of Pd on charcoal) in MeOH (30 mL) under hydrogen atmosphere (3.3 kgf/cm²) was hydrogenated for 3 h. After the catalyst was removed by filtration, the filtrate was worked up in the manner as shown below.

2-(2-Hydroxyphenyl)benzo[d]oxazole-4-carboxylic acid (Caboxamycin) (6)

The residue was recrystallized from 2-propanol to give white powder. Yield 64%. mp 237-239 °C.

¹H NMR(DMSO-*d*₆) δ(ppm): 0.50-2.00 (0.5H, brs, OH), 7.10-7.16 (2H, m), 7.55-7.60 (2H, m), 8.00 (1H, dd, *J*=7.8 and 1.1 Hz), 8.05 (1H, dd, *J*=7.9 and 1.5 Hz), 8.10 (1H, dd, *J*=8.2 and 0.9 Hz), 11.79 (1H, s, COOH). ¹³C NMR(DMSO-*d*₆) δ(ppm): 109.7 (s), 115.3 (d), 117.3 (d), 120.0 (d), 121.8 (s), 125.3 (d), 127.1 (d), 127.4 (d), 134.4 (d), 138.7 (s), 149.5 (s), 158.4 (s), 163.6 (s), 165.5 (s, C=O). MS (FAB) *m/z* 256(MH⁺). *Anal.* Calcd for C₁₄H₉NO₄: C, 65.88; H, 3.55; N, 5.49. Found: C, 65.86; H, 3.71; N, 5.48. IR (KBr, cm⁻¹): 3011, 1703, 1631, 1546, 1484, 1432, 1302, 1258, 1245, 755.

Methyl 2-(2-hydroxyphenyl)benzo[d]oxazole-4-carboxylate (17)

The residue was chromatographed with CHCl₃ to give 0.04 g (31%) of **17**.

This compound was recrystallized from hexane to give colorless crystals, mp 136 °C.

¹H NMR(CDCl₃) δ(ppm): 1.66 (1H, brs, OH), 4.06 (3H, s, Me), 7.02 (1H, dd, *J*=7.5 and 7.5 Hz), 7.15 (1H, d, *J*=8.5 Hz), 7.43-7.49 (2H, m), 7.80 (1H, d, *J*=7.6 Hz), 8.03 (1H, dd, *J*=7.6 and 1.5 Hz), 8.07 (1H, d, *J*=7.6 Hz). ¹³C NMR(CDCl₃) δ(ppm): 52.4 (q, CH₃), 110.0 (s), 114.9 (d), 117.8 (d), 119.6 (d), 121.5 (s), 124.8 (d), 127.2 (d), 127.5 (d), 134.3 (d), 139.5 (s), 149.8 (s), 159.5 (s), 164.4 (s), 165.6 (s, C=O). MS (FAB) *m/z* 270(MH⁺). *Anal.* Calcd for C₁₅H₁₁NO₄ + 0.2 H₂O: C, 66.03; H, 4.21; N, 5.13. Found: C, 66.00; H, 4.06; N, 5.11. IR (KBr, cm⁻¹): 1718, 1633, 1550, 1489, 1422, 1304, 1244, 1061, 748, 708.

General Procedure for saponification of compounds 16 and 17 by NaOH

To a solution of compounds **16** or **17** (0.5 mmol) in THF (10 mL) was added 5 N NaOH solution (10 mL), and the solution was refluxed for 6.5 h. After removal of the solvent, the residue was acidified by 10% HCl solution and resulting solution was extracted with CHCl₃ or EtOAc. The CHCl₃ or EtOAc solution was worked up in the manner as shown below.

2-(2-Hydroxyphenyl)benzo[d]oxazole-4-carboxylic acid (Caboxamycin) (6)

After removal of the solvent, the residue was recrystallized from 2-propanol to give 0.05 g (40%) of **6**.

2-(2-Methoxyphenyl)benzo[d]oxazole-4-carboxylic acid (11)

After removal of the solvent, the residue was recrystallized from 2-propanol to give pale yellow cottony crystals, 0.08 g (60%).

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