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Note

Total synthesis of antibacterial dibromotyrosine derived alkaloid purpuramine-K[#]

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The first total synthesis of a dibromotyrosine derived alkaloid purpuramine K **1** reported for possible anti-bacterial activity against gram-positive bacteria *viz:* S*taphylococcus aureus*, *Bacillus subtilis*, *Bacillus sphaericus* and gram-negative bacteria like *Chromobacterium violaceum*, *Klebsiella aerogenes*, and *Pseudomonas aeruginosa* has been achieved. The synthesis involves preparation of methyl-3-bromopropyl carbamate **6**, and Boc protected 2-[3,5-dibromo, 4-hydroxy phenyl] ethyl amine **13** which is followed by coupling of these two structural fragments to give corresponding ether **14**. After deprotection of Boc group in compound **14**, it is reacted with 4-hydroxyphenyl pyruvic acid oxime derivative **17** using EDCI/HOBT to give compound **18**, which is further transformed to purpuramine K.

Keywords: Antibacterial activity, purpuramines, methyl carbamate, THP protected hydroxyl amine

IPC: Int.Cl.[8] C07C

Purpuramines, the dibromo tyrosine derived alkaloids which have been isolated from marine sponges, are known to possess significant anti-bacterial activity against *Staphylococcus aureus*[1]. Even though marine sponges are a source of this type of secondary metabolite, the possibility for obtaining the same natural product consistently is remote. This is even more so when the said natural product has been isolated from an unidentified sponge. Purpuramines are among such natural products from marine sources. Previously, two new bromo tyrosine derived metabolites, purpuramine K **1**, and purpuramine L **2** have been isolated from the sponge *Psammaplysilla purpurea*[2] (**Figure 1**). These compounds exhibited significant anti-bacterial activity against gram +ve bacteria *viz*: *Staphylococcus aureus*, *Bacillus subtilis* and *Bacillus sphaericus*, and gram -ve bacteria like *Chromobacterium violaceum*, *Klebsiella aerogenes* and *Pseudomonas aeruginosa*[2].

To confirm the structure derived from the NMR assignment of purpuramine K as well as to scale-up availability and to prepare its analogues, which can be helpful for further activity studies, the total synthesis of purpuramine K has been undertaken and achieved by using simple starting materials and using lucid chemical transformations.

Results and Discussion

The retrosynthetic analysis of purpuramine K **1** revealed that it could be disconnected into three units: the western propyl amine **6**, the central dibromotyramine unit **13**, and the eastern unit, monobromo oxime acid chain **17**. The synthesis of western part originated from 3-amino-1-propanol **3**, which was reacted with ethyl formate to give *N*-formyl alcohol[3], followed by reduction with lithium aluminum hydride in dry THF to give the corresponding *N*-methyl alcohol[3] **4**. Compound **4** was further converted into 3-hydroxypropyl methyl carbamate **5** by reaction with methyl chloroformate in the presence of K_2CO_3 in dry acetone[4]. The alcohol **5** was treated with PBr_3 to give the corresponding bromo compound **6** (**Scheme I**)[5].

For the synthesis of the central unit **13**, the methyl ester of 4-hydroxyphenyl acetic acid **7** was di-brominated[6] by using 2 equivalents of NBS in dry THF to give the dibromo compound **8**. The phenolic group of compound **8** was protected as its TBDMS ether[7] **9**. The ester group in compound **9** was reduced

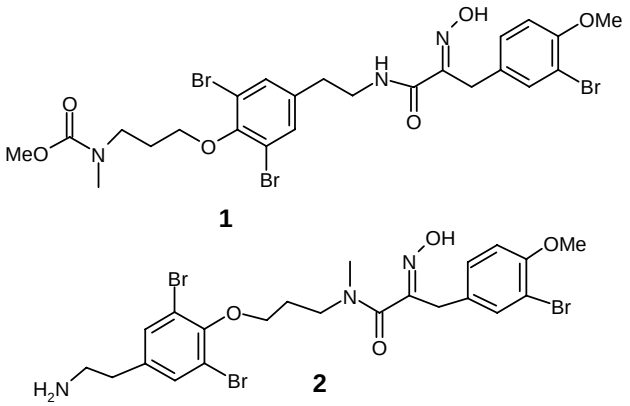

Figure 1

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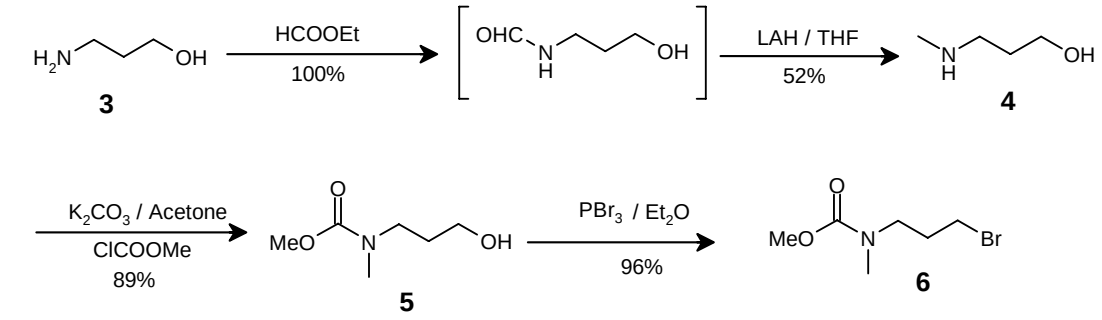
with LAH to yield the corresponding alcohol[8] **10**, which was converted to the Boc protected 3,5-dibromotyramine **13** *via* four conventional steps[9] with an overall yield of 83% (**Scheme II**).

The eastern unit **17** (Ref. 10) was synthesized in good yield by treating 4-hydroxyphenyl pyruvic acid **16**, with *O*-tetrahydropyranyl oxime in ethanol at reflux temperature.

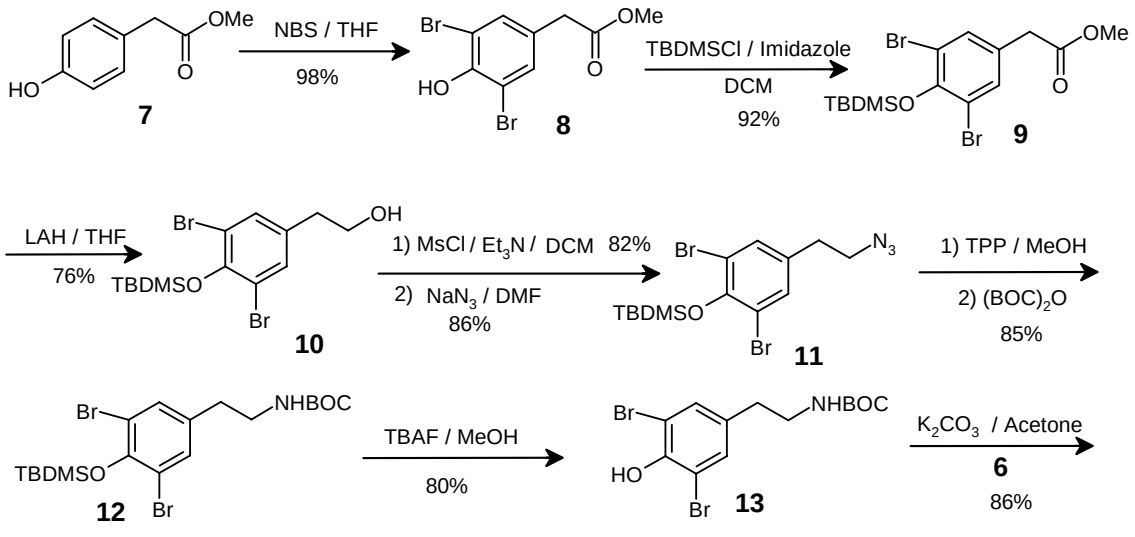
Finally, the western **6** and central **13** units were coupled using K_2CO_3 in acetone at reflux temperature to obtain compound **14**. After deprotection of the Boc group in compound **14**, it was coupled with the eastern unit 4-hydroxyphenylpyruvic acid oxime **17** (Ref. 10), using EDCI/HOBT[10] to give compound **18**. This was then subjected to careful mono bromination using one equivalent of NBS in dry THF followed by *O*-methylation of the phenolic hydroxyl group to get the target molecule purpuramine K as the THP ether **19** (**Scheme III**).

Experimental Section

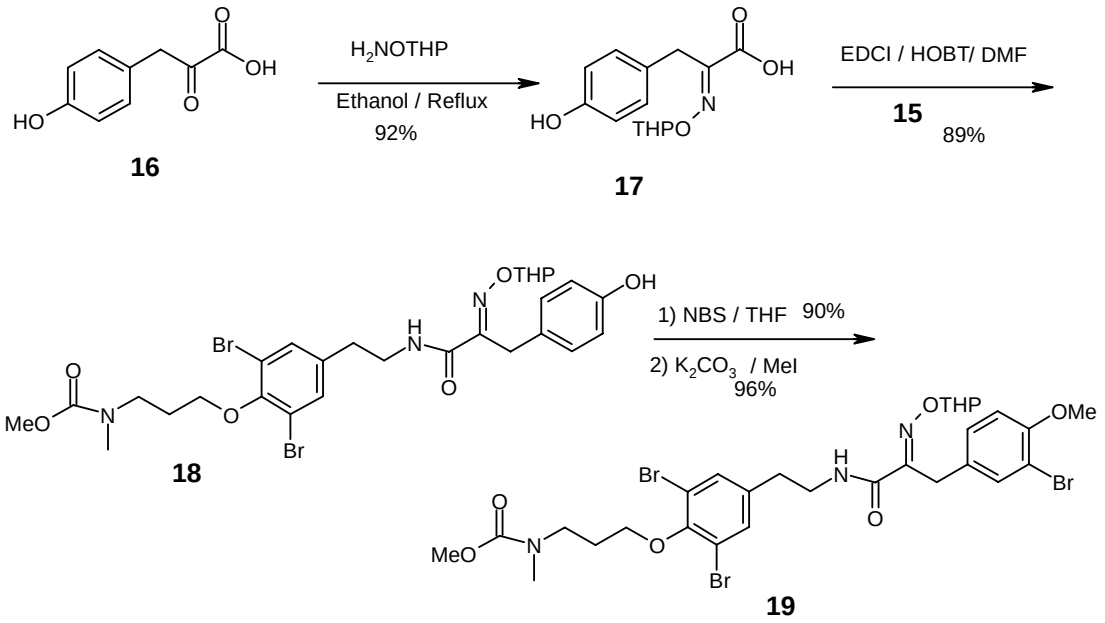
All air or moisture sensitive reactions were carried out under nitrogen atmosphere. Solvents were freshly distilled before use. THF and ether were dried over Na/benzophenone, DCM over P_2O_5 followed by CaH_2, and DMF and DIPA (Diisopropylamine) over



Scheme I



Scheme II



Scheme III

CaH_2. Thin layer chromatography was performed with pre-coated silica gel plates. Column chromatography was carried out over silica gel (100-200 mesh) and hexane and ethyl acetate mixtures as eluent, unless otherwise mentioned. Melting points were determined on a Mel-Temp apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer 240-C instrument, the ^1H and ^{13}C NMR spectra were recorded on 300 MHz (Bruker), and 200 MHz (Varian) instruments using TMS as internal standard. Chemical shifts are reported in δ (ppm) and coupling constants (*J*) are expressed in Hertz. The MS were recorded on a VG Auto Spec-M instrument.

Methyl 3-hydroxypropyl methyl carbamate (5): A mixture of compound **4** (800 mg, 9 mmoles), methyl cloroformate (2.8 mL, 36 mmoles), and K_2CO_3 (7.45 g, 54 mmoles) was taken in dry acetone (100 mL) and refluxed for 12 hr. After completion of the reaction, the solvent was removed under reduced pressure, water was added (20 mL) and extracted into ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give crude product, which was subjected to silica gel column chromatography using hexane:ethyl acetate (25:75) as eluent to give yellowish gummy liquid **5** (1.175 g, 7.99 mmoles) in 89% yield. IR (KBr): 3414, 2951, 1689, 1491, 1398, 1264, 1215, 1151, 1061 and 772 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.69 (3H, s, OMe), 3.53 (2H, t, J = 7.1 Hz), 3.40 (2H, t, J = 6.4 Hz, N-CH_2), 2.89 (3H, s, N-Me), 1.70 (2H, quintet); LCMS: m/z 148 (M^++H), 143, 134, 130, 116, 102, 88, 73 and 59.

Methyl 3-bromopropyl methyl carbamate, 6: To a cooled (0°C) solution of compound **5** (300 mg, 2.04 mmoles) in dry ether (20 mL) was added phosphorus tri-bromide (PBr_3) (0.09 mL, 0.9 mmoles). The reaction was stirred for 30 min at RT. After completion of the reaction, saturated potassium bromide solution was added dropwise at 0°C, and the mass extracted with ether to give crude product **6**. The crude product was chromatographed over silica-gel using hexane and ethyl acetate as eluent to afford pure compound **6** (411 mg, 1.96 mmoles) in 96% yield.

Methyl 2-(3,5-dibromo-4-hydroxyphenyl) acetate, 8: To a solution of compound **7** (2.6 g, 15.66 mmoles) in dry tetrahydrofuran (THF) (100 mL), *N*-bromo succinamide (NBS) (5.6 g, 31.28 mmoles) was added and stirred for 30 min. After completion of the reaction, the reaction was quenched with saturated $Na_2S_2O_3$ solution, and the solvent removed under reduced pressure. The reaction mass was then extracted into ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give crude dibromo compound **8**. The crude product was chromatographed over silica gel column using hexane : ethyl acetate mixture as eluent to afford pure dibromo-compound **8** (4.97 g, 15.34 mmoles) in 98% yield. IR (KBr): 3364, 3018, 2957, 1720, 1553, 1481, 1410, 1288, 1235, 1142, 999, 906 and 753 cm^{-1}; ^1H NMR

($CDCl_3$): δ 7.38 (2H, s), 5.80 (1H, s), 3.65 (3H, s) and 3.42 (2H, s); LCMS: m/z 324, 323, 322, 283, 266, 264, 262, 243, 199, 163, and 113.

3,5-Dibromo-4-(*tert*-butyl-dimethyl-silanyloxy)-phenyl acetic acid methyl ester, 9: To a solution of compound **8** (947 mg, 2.92 mmoles) in dry dichloromethane (DCM, 50 mL) was added imidazole (399.9 mg, 5.88 mmoles) and the mixture stirred for 15 min. To this was then added *tert*-butyl-dimethylsilyl chloride (TBDMS chloride) (534 mg, 3.52 mmoles) and the stirring continued at RT for 90 min. After completion of the reaction, the solvent was evaporated under reduced pressure, water was added (10 mL) and the mass extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give the crude product, which was chromatographed over silica gel column using hexane-ethyl acetate mixture as eluent to give corresponding pure compound **9** (1.17 g, 2.69 mmoles) in 92% yield. IR (KBr): 2922, 1719, 1555, 1481, 1346, 1285, 1219, 1139 and 752 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.40 (2H, s), 3.70 (3H, s), 3.48 (2H, s), 1.06 (9H, s) and 0.35 (6H, s); FABMS: m/z 437, 439, 441 (1: 2: 1 ratio) (M^++H), 379, 381, 383 (1: 2:1 ratio due to M^++ H - ^{t}Bu), 319, 321, 323, 299, 267, 243, 207, and 73.

2-[3,5-dibromo-4-(*tert*-butyl-dimethyl-silanyloxy)-ethanol, 10: To a cooled (0^oC) suspension of lithium aluminium hydride (LAH) (82 mg, 2.28 mmoles) in dry tetrahydrofuran (THF, 75 mL) was added a solution of compound **9** (1 g, 2.28 mmoles) in dry THF (5 mL) and stirred for 12 hr at RT. After completion of the reaction, the reaction was quenched with saturated sodium sulfate solution, filtered over celite, the solvent evaporated under reduced pressure and the mass extracted with ethyl acetate. The organic layer was concentrated under reduced pressure to give crude alcohol **10**, which was chromatographed over silica-gel column by using hexane and ethyl acetate mixture as eluent to afford compound **10** (711 mg, 1.7 mmoles) in 76% yield. IR (KBr): 3368, 2951, 2858, 1463, 1401, 1248.6, 1076, 1044, 918, 879, 836, 759 and 673 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.31 (2H, s), 3.80 (2H, t, J = 6.8 Hz), 2.72 (2H, t, J = 6.8 Hz), 1.40 (1H, br s, OH), 1.06 (9H, s) and 0.38 (6H, s); LCMS: m/z 411 (M^++ H).

[4-(2-Azido-ethyl)-2,6-dibromo-phenoxyl]-*tert*-butyl-dimethyl-silane, 11: To a cooled (0^oC) mixture of compound **10** (916 mg, 2.23 mmoles) and methanesulfonyl chloride (MsCl) (0.21 mL, 2.69 mmoles) was added triethylamine (Et_3N) (0.93 mL, 6.70 mmoles) and the mixture stirred for 3 h. After completion of the reaction, the solvent was evaporated under reduced pressure, water (15 mL) was added, and the mass extracted with ethyl acetate. The organic layer was concentrated under reduced pressure to give mesylated product, which was chromatographed over silica-gel column to give pure mesylated product (894 mg, 1.8 mmoles) in 82% yield. To a solution of mesylated compound (894 mg, 1.8 mmoles) in dry DMF (25 mL) was added sodium azide (NaN_3) (119 mg, 1.8 mmoles) and the mass refluxed under nitrogen. After 4 hr, the reaction mass was cooled to RT and water was added (15 mL). The mixture was extracted with ethylacetate. The organic layer was concentrated to give crude azide **11**, which was purified over silica gel column to afford pure compound **11** (685 mg, 1.57 mmoles) in 86% yield. IR (KBr): 3492, 2932, 2861, 2102, 1729, 1553, 1475, 1361, 1252, 1163, 1067, 972, 825, 739 and 702 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.30 (2H, s), 3.49 (2H, t, J = 7.0 Hz), 2.78 (2H, t, J = 7.0 Hz), 0.10 (6H, s) and 0.92 (9H, s); LCMS: m/z 438 (M^++ H).

[4-(2-*tert*-butyloxycarbonylamino-ethyl)-2,6-dibromo-phenoxyl]-*tert*-butyl-dimethyl-silane, 12: To a solution of azido compound **11** (850 mg, 2.09 mmoles) in methanol (25 mL) was added triphenylphosphine (TPP) (0.55 g, 2.1 mmoles). The reaction mixture was stirred for 4 hr at RT, after which was added Boc anhydride [$(BOC)_2O$] (0.5 mL, 2.3 mmoles) and the stirring continued for another 4 hr. After completion of the reaction, the solvent was evaporated under reduced pressure, water (15 mL) was added, and the mass extracted into dichloromethane (DCM) to give the corresponding crude Boc protected amine, which was purified over silica gel column to give pure Boc protected amino compound **12** (9.3 g, 1.77 mmoles) in 85% yield. IR (neat): 3450, 3361, 2933, 2860, 1704, 1509, 1465, 1394, 1366, 1280, 1255, 1169, 919, 842 and 759 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.30 (2H, s); 4.60 (1H, br s, NH), 3.30 (2H, t, J = 6.8 Hz), 2.68 (2H, t, J = 6.8 Hz), 1.42 (9H, s), 1.04 (9H, s), and 0.32 (6H, s); LCMS: m/z 508, 510, 512 (1: 2: 1 ratio) (M^++H), 475, 453, 279 and 227.

Compound 13: To a solution of compound **12** (100 mg, 0.19 mmoles) in methanol (15 mL), tetra-butylammonium fluoride (TBAF) (62 mg, 0.19 mmoles) was added and the mass stirred for 3 hr. After completion of the reaction, methanol was

evaporated under reduced pressure, water was added, and the mass extracted with ethyl acetate. The organic layer was concentrated under reduced pressure to give crude phenolic compound **13**, which upon silica gel column chromatography afforded pure compound **13** (62 mg, 0.15 mmoles) in 80% yield. m.p. 114.8-115.7°C; ^{1}H NMR ($CDCl_3$): δ 1.45 (9H, s), 2.70 (2H, t, *J* = 7.0 Hz), 3.30 (2H, quartet, *J* = 7.0, 6.2 Hz), 4.55 (1H, t, *J* = 6.2 Hz, NH), 5.95 (1H, brs, OH), and 7.24 (2H, s); FABMS: m/z 398, 396, 394, 342, 340, 338, 296, 279, 265, 215, 198, 154, 137, 121, 107, 89, 77, and 57.

Compound 14: To a mixture of compound **13** (68 mg, 0.17 mmoles) and compound **6** (56 mg, 0.26 mmoles) in dry acetone (20 mL), was added K_2CO_3 (35 mg, 0.26 mmoles) and refluxed for 12 hr. After completion of the reaction, acetone was evaporated under reduced pressure, water (10 mL) was added, and the mass extracted with ethyl acetate. The organic layer was concentrated under vacuum to give corresponding ether **14**, which upon column chromatography over silica gel with hexane and ethyl acetate mixture as eluent afforded pure compound **14** (77 mg, 0.15 mmoles) in 86% yield as a viscous liquid. IR (neat): 3346.3, 2976.3, 2880.9, 1694.2, 1519.9, 1456.5, 1394.0, 1366.0, 1253.7, 1217.2, 1167.5, 1038.4, and 772 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.45 (9H, s), 2.06 (2H, m), 2.71 (2H, t, *J* = 7.2 Hz), 2.97 (3H, s, N-Me), 3.32 (2H, quartet, *J* = 7.2, 6.7 Hz), 3.52 (2H, dd, *J* = 7.1, 6.2 Hz), 3.70 (3H, s, OMe), 4.00 (2H, t, *J* = 6.4, 5.6 Hz), 4.60 (1H, br t, NH), 7.30 (2H, s); ^{13}C NMR ($CDCl_3$): δ 156.4, 154.8, 151.6, 137.5, 132.25 (2 carbons), 117.4 (2 carbons), 79.0, 70.08, 52.0, 46.0, 45.5, 41.0, 34.5, 29.0, and 28.0 (3 carbons); FABMS: m/z 527, 525, 523 (M^++1), 511, 469, 130, 116, 102, 71, and 57.

Compound 15: Compound **14** (100 mg, 0.19 mmoles) was taken in 10 mL of dichloromethane (DCM): trifloroacetic acid (TFA), (1:1) mixture at RT and stirred for 0.5 hr. The reaction was quenched with diisopropylethylamine (2.5 mL), water added (10 mL), and the mass extracted with dichloromethane. The organic layer was concentrated under reduced pressure to get free amine **15**, which was purified over silica-gel column using chloroform and methanol as eluent to afford pure amine **15** (76 mg, 0.18 mmoles) in 94% yield. IR (neat): 3418, 2924, 2362, 1683, 1457, 1397, 1218, and 772 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.36 (2H, s), 4.00 (2H, t, *J* = 6.4, 5.6 Hz), 3.70 (3H, s, OMe), 3.50 (2H, t, *J* = 7.1, 6.2 Hz), 3.20 (2H, m), 2.98 (3H, s, N-Me), 2.80 (2H, m), and 2.06 (2H, m); FABMS: m/z 427, 425, 423 (1:2:1) (M^++ H), 216, 195, 154, 145, 130, 119, 109, 95, 81, 69 and 55.

Compound 18: To a solution of compound **17** (58 mg, 0.2 mmoles) in dry dimethyl formamide (DMF, 10 mL), *N*-hydroxybenzotriazole (HOBT) (56 mg, 0.4 mmoles) was added and the reaction mixture stirred for 15 min at RT. The reaction mixture was then cooled to 0°C, and 1-[3-(dimethylamino) propyl] 3-ethyl carbodiimide (EDCI) (80 mg, 0.4 mmoles) was added and the stirring continued for 30 min at 0°C. To this stirred mass was then added compound **15** (88 mg, 0.2 mmoles). The reaction mass was stirred at RT for 1 hr. After completion of the reaction, water was added (10 mL), and the mass extracted with diethyl ether. The organic layer was concentrated under reduced pressure to give crude product **18**, which was then purified over silica gel column using hexane and ethyl acetate mixture as eluent to afford corresponding pure compound **18** (126 mg, 0.18 mmoles) in 89% yield. Colourless crystalline compound; m.p. 186-88°C; IR (KBr): 3352.1, 3013.8, 2949.7, 2877.8, 1676.3, 1615.6, 1514.4, 1454.3, 1396.0, 1217.0, 1036.8, 970.0, 903.6, and 764.6 cm^{-1}; ^{1}H NMR (methanol-d_4): δ 7.37 (2H, s), 7.01 (2H, d, *J* = 8.018 Hz), 6.64 (2H, d, *J* = 8.82 Hz), 5.32 (1H, t, *J* = 3.0 Hz), 3.93 (2H, t, *J* = 6.41, 5.61 Hz), 3.77 (2H, d, *J* = 4.0 Hz), 3.63 (3H, s), 3.47 to 3.54 (4H, m), 3.39 (2H, dd, *J* = 6.41, 7.21 Hz), 2.91 (3H, s), 2.69 (2H, dd, *J* = 7.21, 6.41 Hz), 2.03 (2H, quintet), and 1.50 to 1.80 (6H, m); ^{13}C NMR (methanol-d_4): δ 165.0, 158.5, 156.4, 154.5, 152.2, 138.6, 133.90 (2 carbons), 131.0 (2 carbons), 128.0, 118.4 (2 carbons), 115.8 (2 carbons), 102.0, 72.0, 62.94, 52.5, 48.2, 41.8, 34.4, 30.3, 29.2, 26.02, and 20.0; LCMS: m/z 709 (M^++ Na), 708, 707, 685, 684, 683, 602, 601, 600, and 543.

Purpuramine K as THP ether, 19: A mixture of compound **18** (50 mg, 0.07 mmoles) and *N*-bromo succinamide (NBS, 13 mg, 0.07 mmoles) in dry tetrahydrofuran (THF, 20 mL) was stirred at RT for 0.5 hr. After completion of the reaction, the reaction mass was quenched with saturated sodium thiosulfate solution. The solvent was removed under reduced pressure, and the mass extracted with ethyl acetate. The organic layer was concentrated under vacuum to give corresponding crude monobromo compound, which was purified over silica gel column to get pure monobromo compound (50 mg, 0.06 mmoles) in 90% yield. To a cooled (0°C) solution of the above monobromo compound (20 mg, 0.02 mmoles) methyl

iodide (MeI, 0.02 mL, 0.10 mmoles) in dry acetone (15 mL), K_2CO_3 (21 mg, 0.15 mmoles) was added. The reaction mixture was refluxed for 12 hr. After completion of the reaction, the solvent was evaporated under reduced pressure and then water was added (10 mL). The mass was extracted with ethyl acetate. The organic layer was concentrated under vacuum to give crude compound **19**, which was further purified over silica gel column to afford pure compound **19** (20.4 mg, 0.02 mmoles) in 96% yield. Colourless solid; m.p. 162.4-164.3°C; IR (KBr): 2948.7, 2853.2, 1679.5, 1512.1, 1457.2, 1396.0, 1254.5, 1216.1, 1037.7, 968.5, and 770.8 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.34 (2H, s), 7.28 (1H, d, *J* = 2.2 Hz), 6.96 (1H, br t, NH), 6.83 (1H, d, *J* = 8.3 Hz), 6.81 (1H, d, *J* = 2.2 Hz), 5.38 (1H, t, *J* = 3.02), 4.02 (2H, t, *J* = 6.04 Hz), 3.93 (1H, dd, *J* = 7.55, 2.26 Hz), 3.87 (1H, s), 3.78 (2H, s), 3.71 (3H, s), 3.4 to 3.70 (6H, m), 2.98 (3H, s), 2.75 (2H, ddd, *J* = 3.02, 7.55, 10.57 Hz), 2.10 (2H, m), and 1.73 to 1.82 (6H, m); FABMS: m/z 804, 802, 800, 798, (M^++ Na), 722, 614, 500, 393, 330, 294, 237, 128, and 74.

Conclusion

To conclude, the first total synthesis of purpuramine K with commercially available simple starting materials using lucid chemical transformations has been achieved. The ^1H and ^{13}C NMR spectral data of the THP protected purpuramine K **19** are in full agreement with the corresponding signals obtained for purpuramine K **1**. This constitutes the first reported total synthesis of purpuramine K, and provides a reliable and versatile method for the synthesis of related compounds, which may act as potent anti-bacterial agents. Further activity studies of purpuramine K, and synthesis of its analogues are under progress.

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References

1 Yagi H, Matsunaga S & Fusetani N, *Tetrahedron*, 49, **1993**, 3749.

2 Goud T V, Srinivasulu M, Reddy V L N, Reddy A V, Rao T P, Kumar D S, Murthy U S N & Venkateswarlu Y, *Chem Pharm Bull*, 51, **2003**, 990.

3 Koepke S R, Kupper R & Michejda C J, *J Org Chem*, 44, **1979**, 2718.

4 Corey E J, Bock M G, Kozikowski A P, Ramarao A V, Floyd D & Lipshutz B, *Tetrahedron Lett*, 19, **1978**, 1051.

5 Amat M, Pchenichnyi G, Bosch J, Molins E & Miravitlles C, *Tetrahedron Asymmetry*, 7, **1996**, 3091.

6 a) Boehlow T R, Harburn J J & Spilling C D, *J Org Chem*, 66, **2001**, 3111; b) Ferrester A R, Thomson R T & Woo S, *J Chem Soc Perkin Trans-I*, **1975,** 2340.

7 Yadav J S & Srihari P, *Tetrahedron Asymmetry*, 15, **2004**, 81.

8 a) Tripathi R P, Tiwari V K, Tewari N, Katiyar N, Saxena N, Sinha S, Gaikwad A, Srivastava A, Chaturvedi V & Manju Y K, *Bio Org Med Chem*, 13, **2005**, 5668; b) Katiyar D, Tiwari V K, Tewari N, Verma S S, Sinha S, Gaikwad A, Srivastava A, Chaturvedi V, Srivastava R, Srivastava B S & Tripathi R P, *Eur J Med Chem*, 40, **2005**, 351.

9 Chakraborti T K, Ghosh S, Jayaprakash S, Sharma J A R P, Ravikanth V, Diwan P V, Nagaraj R & Kunwar A C, *J Org Chem*, 65, **2000**, 6441.

10 Kende A S, Lan J & Fan J, *Tetrahedron Lett*, 45, **2004**, 133.