Benzene derivatives from the marine sponges Cinachyrella

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Abstract. The benzene derivatives from the Spermonde Archipelago sponges Cinachyrella was isolated. 4-hydroxy-benzenepropanoic acid (1) from Cinachyrella australiensis, 4-methyl-benzoic acid (2) and 4-hydroxy-benzonitrile (3) from Cinachyrella sp. The structures of 1, 2, and 3 have been determined by 1H-NMR, 13C-NMR, and HR-MS.

1. Introduction
The benzene derivatives compounds are commonly referred to as aromatic compounds. Some very important compounds that we come across on a daily basis are manufactured from derivatives of benzene. One of the most obvious is polystyrene, manufactured through the polymerisation of styrene.

Some benzene derivatives are reported isolated from Australian marine sponge, Ianthella sp. are 4-hydroxybenzaldehyde, 4-hydroxybenzoic acid, 4-methoxybenzoic acid, and ethyl 4-hydroxybenzoate [1].

The GC/MS analysis revealed that 55 compounds were identified in the supernatant static extract and mycelial extract of the fungus Aspergillus unguis RSPG_204 isolated from the Sponge (Agelas sp.) among others 4-hydroxy-benzenepropanoic acid (1) identified in the supernatant static extract [2].

Isolation of the chemical compounds from marine sponges of Cinachyrella genus reported in this paper, found three known compounds of benzene derivatives; compound 1, 4-methyl-benzoic acid (2), and 4-hydroxy-benzonitrile (3). Compounds 1, 2, and 3 are described for the first time from this genus.

2. Eksperiment

2.1. General
The NMR spectra were recorded on an Agilent 500 MHz. HR-MS spectra were performed with a Waters LCT Premier XE HRMS ESI-TOF.

The specimen of sponges were collected from Spermonde Archipelago, South Sulawesi, Indonesia, by SCUBA, in Sep-Oct 2015. A voucher specimen Cinachyrella australiensis (SVP 01/10/15) and Cinachyrella sp. (SVP 02/10/15) were deposited at the Research Center for Oceanography Indonesian Institute of Sciences in North Jakarta [3].
2.2. Extraction and Isolation
The sponge samples (10 kg, dry wt.), were immersed in methanol. The methanol extracts were collected and dried by rotary evaporator to obtain the crude extracts. The crude methanol extract was partitioned with n-hexane and followed by ethyl acetate. Each fraction was dried to get of n-hexane, ethyl acetate, and methanol extracts from sponges C. autraliensis and Cinachyrella sp. [3].

2.2.1. Isolation compound 1. The ethyl acetate extract sponge C. autraliensis was fractionated using vacuum-liquid column chromatograph (VLC), obtaining 20 fractions. The fractions 18-20 (567,1 mg) were united, then fractionated using Centrifugal Thin-Layer Chromatograph (Chromatotron), obtaining 13 fractions. The fractions 9-11 (27,5 mg) were united, then isolated using Chromatotron, obtaining 6 fractions. The fractions 2-4 (14,7 mg) were united, then purified, is obtained compound 1 (4,6 mg. as a yellowish green gel).

2.2.2. Isolation compounds 2 and 3. The ethyl acetate extract sponge Cinachyrella sp. was fractionated using VLC, obtaining 12 fractions. Fraction 5 (53 mg) is isolated by using Chromatotron, obtaining 10 fraction. Fraction 9 (3,0 mg. as a brown gel) as compound 2 and fraction 7 (2,3 mg. as a brown gel) as compound 3.

2.3. Spectral Data

2.3.1. Compound 1: 1H NMR (CDCl₃, 500 MHz) : δH 2.6639 (2H, t, J = 7.5 ; 15 Hz), 2.8876 (2H, t, J = 7.5 ; 15 Hz), 6.7612 (2H, d, J = 8.2 Hz), 7.0698 (2H, d, J = 8.2 Hz) ; 13C NMR (CDCl₃, 125 MHz) : δC 35.68, 37.11, 115.38, 129.41, 132.23, 154.19, 176.47 ; HR-MS (negative ion mode) for C₉H₆O₃ [M-H] : Calc. Mass 165.0552, Mass 165.0547.

2.3.2. Compound 2 : 1H NMR (CDCl₃, 500 MHz) : δH 2.5614 (3H, s), 6.8930 (2H, d, J = 8.8 Hz), 7.9048 (2H, d, J = 8.8 Hz) ; HR-MS (negative ion mode) for C₈H₇O₂ [M-H] : Calc. Mass 135.0446, Mass 135.0441.

2.3.3. Compound 3 : 1H NMR (CDCl₃, 500 MHz) : δH 5.3659 [1H, bs], 6.9448 (2H, d, J = 8.4 Hz), 7.5356 (2H, d, J = 8.4 Hz) ; HR-MS (negative ion mode) for C₇H₄NO [M-H] : Calc. Mass 118.0293, Mass 118.0298.

3. Discussion

3.1. Compound 1
1H-NMR, shown the doublet signal of the aromatic proton at 6.7612 and 7.0698 on the ortho coupling (J = 8.2 Hz), these data indicates the presence of symmetry in the benzene ring. 13C NMR, shows that there are three aromatic carbon signals at 115.38, 129.41, 132.23, and one aromatic carbon bonded to oxygen at 154.19 ppm. The structure skeleton can be described as

![Figure 1. Compound 1 skeleton structure.](image-url)
The triplet signals at 2.6639 and 2.8876 are the -CH₂ groups adjacent to the carbonyl (δC 176.47) and aromatic groups, aliphatic protons are bound to carbon 37.11 and 35.68 ppm. The presence of vicinal coupling (7.5 Hz) and geminal coupling (15 Hz) indicates that the protons do not rotate because they are flanked by two large groups (the carbonyl and aromatic). Based on NMR data analysis, supported by HR-MS data, the structure of compound 1 is:

![Figure 2. 4-hydroxy-benzenepropanoic acid (1).](image-url)

Confirmation of NMR data of compound 1 with previous research, indicates a conformity that reinforces the estimated structure of compound 1 as follows:

\[ \text{H NMR (CD₃OD, 300 MHz)} \delta: 7.02 (2H, d, J=8.4 Hz), 6.94 (2H, d, J=8.4 Hz), 2.80 (2H, t, J=7.5 Hz), 2.53 (2H, t, J=7.8 Hz); \]

\[ \text{13C NMR (CD₃OD, 75 MHz)} \delta: 177.1, 156.3, 132.9, 130.2, 116.1, 37.0, 31.0 \] [4].

\[ \text{H NMR (400 MHz, CDCl₃)} \delta: 7.07 (2H, d, 8.0 Hz, H-2 and H-6), 6.76 (2H, d, 8.0 Hz, H-3 and H-5), 2.89 (2H, t, 8.0 Hz, H-7), 2.64 (2H, t, 8.0 Hz, H-8); \]

\[ \text{13C NMR (100 MHz, CDCl₃)} \delta: 29.8 (C-7), 115.4 (C-3 and C-5), 129.4 (C-2 and C-6), 131.1 (C-1), 155.6 (C-4), 179.9 (C-9) \] [5].

\[ \text{H NMR (CDCl₃, 500.13 MHz)} \delta: 2.60 (2H, t, CH₂COOH, J = 7.5 Hz); 3.86 (2H, t, ArCH₂, J = 7.5 Hz); 6.67 (2H, d, Ar, J = 8.5 Hz), 7.01 (2H, d, Ar, J = 8.5 Hz) \] [6].

3.2. Compound 2

H NMR, shown the doublet signal of the aromatic proton at 6.8930 and 7.9048 on the *ortho* coupling (J = 8.8 Hz). These data indicate the presence of symmetry in the benzene ring. The singlet signal at 2.5614 indicates that -CH₃ is bound to aromatic.

The HR-MS data shows the molecular formula C₉H₇O₂ [M-H] : Calc. Mass 135.0446, Mass 135.0441. Based on NMR and HR-MS data, the structure of compound 2 is:

![Figure 3. 4-methyl-benoiz acid (2).](image-url)

Confirmation of NMR data of compound 2 with previous research, indicates a conformity that reinforces the estimated structure of compound 2 as follow:

\[ \text{H NMR (400 MHz)} \delta 2.43 (3H, s), 7.28 (2H, d, J = 8.1 Hz), 8.01 (2H, d, J = 8.1 Hz) \] [7].
3.3. Compound 3

$^1$H NMR, shows that the doublet signal of the aromatic proton at 6.9448 and 7.5356 on the ortho coupling ($J = 8.4$ Hz), these data indicate the presence of symmetry in the benzene ring. The broad singlet signal at 5.3659 indicates -OH is bound to aromatic.

The HR-MS data shows the molecular formula C$_7$H$_4$NO [M-H] : Calc. Mass 118.0293, Mass 118.0298. Based on NMR and HR-MS data, the structure of compound 3 is:

![Figure 4. 4-hydroxy-benzonitrile (3).](image)

Confirmation of NMR data of compound 3 with previous research, indicates a conformity that reinforces the estimated structure of compound 3 as follow: $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$: 7.56 (2H, d, $J= 8.6$ Hz), 6.94 (2H, d, $J=8.6$ Hz), 6.79 (1H, bs) [8].

4. Conclusion

Ethyl acetate extracts of sponge C. australiensis and Chynachyrella sp. from the Spermonde Archipelago contain the 4-hydroxy-benzenepropanoic acid (1), 4-methyl-benzoic acid (2), and 4-hydroxy-benzonitrile (3).

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