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ACETYLENIC THIOPHENE DERIVATIVES FROM *BLUMEA OBLIQUA*

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Key Word Index—*Blumea obliqua*; Asteraceae; acetylenic thiophenes.

Abstract—The phytochemical investigations of *Blumea obliqua* afforded 5′-methyl-[5-(4-acetoxy-1-butynyl)]-2,2′-bithiophene, 5′-methyl-[5-(4-hydroxy-1-butynyl)]-2,2′-bithiophene, 5′-acetoxymethyl-5-(3-butene-1-ynyl)-2,2′-bithiophene and 5′-methyl-[5-(3-hydroxy-4-isovaleroxy-1-butynyl)]-2,2′-bithiophene. The first three thiophenes are known compounds whereas the fourth is a new natural product. The structures of these compounds were elucidated by spectroscopic methods.

INTRODUCTION

Blumea obliqua (Syn. *Erigeron obliquum* L., *Blumea amplectens* DC.) is a member of tribe Inuleae (Asteraceae) and is placed in the *Pluchea* group [1]. We have previously reported two acetylenic thiophenes from this plant [2], but so far only limited literature is available on these types of compounds from *Blumea*. In continuation of our work on the phytochemical investigations of *B. obliqua*, we have isolated four more acetylenic thiophenes (**1**–**4**) from this plant.

RESULTS AND DISCUSSION

The investigations on *Blumea obliqua* were carried out on aerial parts. The hexane soluble part of the methanolic extract was chromatographed on a silica gel column and then on preparative TLC to afford 5′-methyl-[5-(3-hydroxy-4-isovoleroxy-1-butynyl)]-2,2′-bithiophene] (**4**) along with three known dithienyl derivatives 5′-methyl-[5-(4-acetoxy-1-butynyl)]-2,2′-bithiophene (**1**) [3], 5′-methyl-[5-(4-hydroxy-1-butynyl)]-2,2′-bithiophene (**2**) [3] and 5′-acetoxymethyl-5-(3-butene-1-ynyl)-2,2′-bithiophene (**3**) [4].

The new dithienyl derivative was obtained as yellow oil and its structure was established by 1D and 2D NMR techniques. Peak matching of its molecular ion peak $[M]^+$ at *m/z*: 348 resulted in the exact value of 348.08519 which was analyzed for the molecular formula $C_{18}H_{20}O_3S_2$. ^1H NMR spectrum of compound **4** showed a 6H doublet at δ 0.96 ($J = 6.5$ Hz), a 1H multiplet at δ 2.15 and a 2H doublet at δ 2.26 ($J = 6.5$ Hz). This confirmed the presence of an isovaleroxy moiety. A two proton doublet at δ 4.29 ($J = 2.3$ Hz) and a one proton broad triplet at δ 4.82 (unresolved) were assigned to 4″ and 3″ protons respectively. The signals at δ 6.66 (*dq*, $J = 3.5$ and 1.0 Hz), 6.91 (*d*, $J = 3.8$ Hz), 6.97 (*d*, $J = 3.5$ Hz) and 7.08 (*d*, $J = 3.8$ Hz) were attributed to H-4′, H-3, H-3′ and H-4 thiophenic protons respectively. The ring methyl protons resonated as a doublet of three protons at δ 2.46 ($J = 1.0$ Hz). The assignments were made with the help of COSY-45° spectrum in which H-4 showed correlation with H-3, H-4′ with H-3′ and H-3″ with H-4″ respectively. H-3a also showed interactions with H-2a and H-4a. The ring methyl protons exhibited correlation with H-4′ thiophenic proton which is due to allylic coupling. The structure of compound **4** was also supported by the ^{13}C NMR spectral data (see Experimental). The chemical shift assignments for various carbons were made by comparing the ^{13}C NMR data of the similar compounds reported in the literature [5].

The structures of **1**–**3** were established by comparing their HRMS and ^1H NMR spectral data with the literature values. Structures of **1** and **3** were also confirmed by 2D NMR techniques such as HMBC and HMQC. Table 1 summarizes the ^{13}C NMR assignments of **1** and **3** which has not been reported in the literature.

EXPERIMENTAL

NMR spectra were recorded on 500 and 300 MHz instruments and measured in $CDCl_3$ using TMS as internal standard. Silica gel (Merck 70-230 mesh) was used for CC and silica gel 60 F_{254}, 0.25 mm precoated plates (Merck) were used for TLC and preparative TLC.

Plant material. Aerial parts of *B. obliqua* were collected from Karachi (May, 1991). A voucher specimen remains in the herbarium at the Botany Department, University of Karachi (Voucher No. 63484).

Extraction and isolation. The fresh plant (20 kg) was chopped and macerated twice for 10 day periods each time with MeOH. The combined extract was

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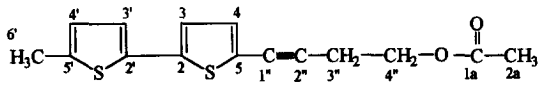

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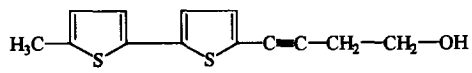

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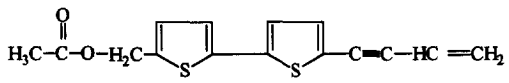

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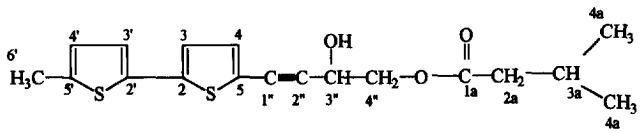

4

filtered and evaporated under reduced pressure to a viscous mass (480 g) which was partitioned between methanol–water (9:1) and hexane. The hexane soluble portion was evaporated under reduced pressure to an oily paste (57 g) which was chromatographed on a silica gel column and eluted with hexane, hexane–

Table 1. ^{13}C NMR data and $^{1}H/^{13}C$ connectivities (HMQC) for **1** and **3** in $CDCl_3$

	1			3		
Carbon no.	Chemical shift (δ)	Multiplicity (DEPT)	$^{1}H/^{13}C$ Connectivity (J = Hz)	Chemical shift (δ)	Multiplicity (DEPT)	$^{1}H/^{13}C$ Connectivity (J = Hz)
2	*	–C–	—	138.1	–C–	—
3	122.5	CH	6.88 (*d*, J = 3.7)	123.7	CH	7.00 (*d*, J = 3.8)
4	132.5	CH	6.99 (*d*, J = 3.9)	132.8	CH	7.07 (*d*, J = 3.8)
5	121.1	–C–	—	122.2	–C–	—
2′	*	—	—	138.6	–C–	—
3′	124.0	CH	6.93 (*d*, J = 3.5)	123.7	CH	7.02 (*d*, J = 3.6)
4′	126.0	CH	6.64 (*dq*, J = 3.5, 1.0)	129.0	CH	6.97 (*d*, J = 3.6)
5′	140.0	–C–	—	137.6	–C–	—
6′	14.1	CH_3	2.48 (*d*, J = 0.8)	60.5	CH_2	5.19 (*s*)
1″	77.5	–C–	—	83.0	–C–	—
2″	90.5	–C–	—	93.1	–C–	—
3″	22.7	CH_2	2.76 (*t*, J = 6.9)	116.8	CH	6.01 (*dd*, J = 17.5, 11.3)
4″	62.1	CH_2	4.22 (*t*, J = 6.9)	127.1	CH_2	5.54 (*dd*, J = 11.3, 1.9) *cis*
4″	—	—	—	127.1	CH_2	5.72 (*dd*, J = 17.5, 1.9) *trans*
1a	*	—	—	172.0	–C–	—
2a	20.9	CH_3	2.08 (*s*)	20.9	CH_3	2.08 (*s*)

*Carbon did not appear.

chloroform and chloroform. The fractions obtained with 10% chloroform in hexane were combined. Repeated CC and finally preparative TLC on silica gel yielded compounds **1**, **2**, **3** and **4**.

5′-Methyl-[5-(4-acetoxy-1-butynyl)]-2,2′-bi-thiophene (**1**). Purified as yellow oil (4 mg) by prep. TLC using hexane–Et_2O (9:1, R_f 0.3). FD-MS *m/z*: 290 $[M]^+$; Peak matching *m/z*: 290.0429 $[M]^+$ ($C_{15}H_{14}O_2S_2$, requires 290.0435); ^1H and ^{13}C NMR (500 MHz and 125 MHz): see Table 1.

5′-Methyl-[5-(4-hydroxy-1-butynyl)]-2,2′-bi-thiophene (**2**). Purified as yellow oil (3 mg) by prep. TLC using hexane–chloroform (1:1, R_f 0.5); FD-MS *m/z*: 247.8 $[M]^+$; Peak matching *m/z*: 248.0324 $[M]^+$ ($C_{13}H_{12}OS_2$, requires 248.0329); ^1H NMR (500 MHz, $CDCl_3$): δ 2.24 (3H, *d*, $J = 1.1$ Hz, H-6′), 2.70 (2H, *t*, $J = 6.2$ Hz, H-3″), 3.80 (2H, *t*, $J = 6.2$ Hz, H-4″), 6.64 (1H, *dq*, $J = 1.1$ and 3.8 Hz, H-4′), 6.89 (1H, *d*, $J = 3.5$ Hz, H-3), 6.93 (1H, *d*, $J = 3.8$ Hz, H-3′), 7.01 (1H, *d*, $J = 3.5$ Hz, H-4).

5′-Acetomethyl-5-(3-butene-1-ynyl)-2,2′-bi-thiophene (**3**). Purified by prep. TLC using hexane–Et_2O (9:1, R_f 0.5); EI-MS *m/z* (rel. int.): 287.8 $[M]^+$ (62), 228.8 $[M-OAc]^+$ (100); HR-EI-MS *m/z*: 288.0277 $[M]^+$ ($C_{15}H_{14}O_2S_2$, requires 288.0278); ^1H and ^{13}C NMR (500 MHz and 125 MHz): see Table 1.

5′-Methyl-[5-(3-hydroxy-4-isovaleroxy-1-butynyl)]-2,2′-bithiophene (**4**). Purified as yellow oil (4 mg) by prep. TLC using hexane–chloroform (1:1, R_f 0.4); FD-MS *m/z*: 348 $[M]^+$; Peak matching *m/z*: 348.08519 $[M]^+$ ($C_{18}H_{20}O_3S_2$, requires 348.0853); ^1H NMR (300 MHz): δ 0.96 (6H, *d*, $J = 6.5$ Hz, H-4a), 2.15 (1H, *m*, H-3a), 2.26 (2H, *d*, $J = 6.5$ Hz, H-2a), 2.46 (3H, *d*, $J = 1.0$ Hz, H-6′), 4.29 (2H, *d*, $J = 2.3$ Hz, H-4″), 4.82 (1H, *t* (broad), H-3″), 6.66 (1H, *dq*, $J = 3.5$ and 1.0 Hz, H-4′), 6.91 (1H, *d*, $J = 3.8$ Hz, H-3), 6.97 (1H, *d*, $J = 3.5$ Hz, H-3′), 7.08 (1H, *d*, $J = 3.8$ Hz, H-4); ^{13}C NMR (75 MHz): δ 14.0 (C-6′), 22.3 (2 × C-4a), 24.8 (C-3a), 43.2 (C-2a), 61.8 (C-4″), 65.0 (C-3″), 79.7 (C-1″), 90.4 (C-2″), 122.1 (C-5), 122.6 (C-3), 124.4 (C-3′), 126.2 (C-4′), 133.6 (C-4), 140.0 (C-2′)[a], 140.2 (C-5′)[a], 139.4 (C-2)[a], 173.0 (C-1a) (a = assignments may be interchanged).

REFERENCES

1. Merxmuller, H., Leins, P. and Roessler, H. (1977) in *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds), p. 579. Academic Press, London.
2. Ahmad, V.U. and Alam, N. (1995). *J. Nat. Prod.* **58**, 1426.
3. Bohlmann, F. and Zdero, C. (1976) *Chem. Ber.* **109**, 901.
4. Bohlmann, F. and Kleine, K.-M. (1963) *Chem. Ber.* **96**, 1229.
5. Zeisberg, R. and Bohlmann, F. (1975) *Chem. Ber.* **108**, 1040.