

The First Occurrence in Nature of Two Compounds from Hops

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Z. Naturforsch. **58c**, 640–642 (2003); received February 28/April 8, 2003

Two compounds, (*p*-methoxyphenyl) diphenylmethanol (**1**) and tribenzylamine (**2**), were isolated from *Humulus lupulus*. Their structures were established on the basis of spectral evidence (MS, IR, NMR, HMBC, HMQC, ^1H - ^1H COSY experiments). Compounds **1** and **2** were found as natural products at the first time.

Key words: *Humulus lupulus*, (*p*-Methoxyphenyl) diphenylmethanol, Tribenzylamine

Introduction

The hop plant (*Humulus lupulus* L., Cannabina-ceae) is a dioecious twining perennial which is cultivated widely throughout the temperate zones of the world. The inflorescences (hop cones or ‘hops’) are used in the brewing industry to give beer its characteristic flavour and aroma. The prenylated chalcones including xanthohumol from hops have been found to inhibit bone resorption activity (Tobe *et al.*, 1997), antioxidant activity by inhibiting oxidation of human low-density lipoprotein (Miranda *et al.*, 2000), significant competitive binding to estrogen receptors (Liu *et al.*, 2001), and antiproliferative and cytotoxic effects in human cancer cell lines (Miranda *et al.*, 1999). In the present study we have indentified two compounds: (*p*-methoxyphenyl) diphenylmethanol (**1**) and tribenzylamine (**2**) from hops. They are reported here as natural products at the first time even they have been synthesized previously (Winkler and Wittig, 1963; Eisch *et al.*, 1994).

Results and Discussion

Compound **1** was obtained as white solids. With the aid of the DEPT spectrum (Table I), the ten signals in the ^{13}C NMR spectrum of **1** could be attributed to one methoxy [$\delta_{\text{H}} = 3.74$ (s, 3H); $\delta_{\text{C}} = 55.7$], aromatic methine groups [$\delta_{\text{H}} = 7.21 \sim 7.26$ (m), 6.81 (d, $J = 8.8$), 7.10 (d, $J = 8.8$); $\delta_{\text{C}} = 127.9$, 128.6, 129.2, 113.9, 130.5] and four quaternary carbon atoms ($\delta_{\text{C}} = 82.6$, 141.0, 149.0, 160.1). EIMS ($[\text{M}]^+$: 290) and NMR data (Table I) revealed a symmetrical structure and led to the de-

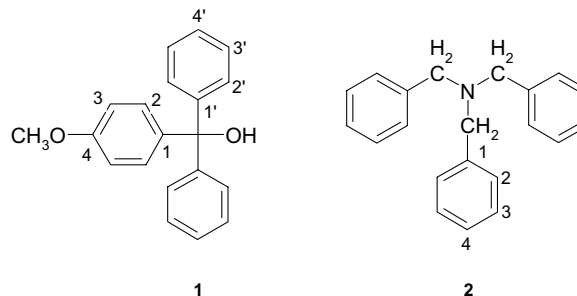


Fig. 1. The structures of (*p*-methoxyphenyl) diphenylmethanol (**1**) and tribenzylamine (**2**).

duction of its molecular formula to be $\text{C}_{20}\text{H}_{18}\text{O}_2$, indicating the presence of three benzene rings in the structure. The presence of the *p*-methoxybenzene moiety is indicated by observation of ^1H - ^1H COSY couplings between H-2, 6 (δ 7.10) and H-3, 5 (δ 6.81) and ^{13}C - ^1H long-range couplings from H-2, 6 to C- α (δ 82.6) and C-4 (δ 160.1), from H-3, 5 to C-1 (δ 141.0) in the HMBC spectrum. The structure was suggested to be (*p*-methoxyphenyl) diphenylmethanol by taking the degrees of unsaturation and other spectral data into account. This was confirmed by HMQC experiments and the correlations of H-2, 6, H-2', 6' with C- α ; H-3, 5 with C-1, OCH₃, H-2, 6 with C-4, H-3', 5' with C-1' in the HMBC spectrum of compound **1** (Table I).

Compound **2** was obtained also as white solids. Five signals in the ^{13}C NMR (DEPT) spectrum of **2** were recognized (CH_2 , 3CH, C), which were assigned to a methylene (δ 57.9), and aromatic methine groups (δ 126.8, 128.2, 128.7), and an aro-

	Position	δ_{H}	δ_{C}	HMBC (selected)
A	α		82.6 (C)	
	1		141.0 (C)	
	2, 6	7.10 (d, $J = 8.8$)	130.5 (CH)	H-2, 6, H-2', 6'
	3, 5	6.81 (d, $J = 8.8$)	113.9 (CH)	H-3, 5
	4		160.1 (C)	
	1'		149.0 (C)	
	2', 6'	7.21 ~ 7.26 (m)	129.2 (CH)	OCH ₃ , H-2, 6
	3', 5'	7.21 ~ 7.26 (m)	128.6 (CH)	H-3', 5'
	4'	7.21 ~ 7.26 (m)	127.9 (CH)	
	-OCH ₃	3.74 (s)	55.7 (CH ₃)	
B	1		139.6 (C)	
	2, 6	7.39 (d, $J = 7.4$)	128.7 (CH)	
	3, 5	7.30 (dd, $J = 7.4, 7.7$)	128.2 (CH)	
	4	7.22 (m)	126.8 (CH)	
	7	3.54 (s)	57.9 (CH ₂)	

Table I. The ^1H and ^{13}C NMR spectral data of compound **1** (A: δ in ppm, J in Hz, CD_3OD) and **2** (B: δ in ppm, J in Hz, CDCl_3).

matic quaternary carbon atom (139.6). The four signals in the ^1H NMR spectrum at δ 3.54 (s), 7.22 (m), 7.30 (dd, $J = 7.4, 7.7$), 7.39 (d, $J = 7.4$) indicated the presence of a highly symmetrical structure and led to structure **2**.

Experimental

General

IR: Perkin-Elmer 577 spectrometer. 1D, 2D NMR: Bruker DRX-500 spectrometer; TMS internal standard. MS: VG Autospec-3000 spectrometer.

Plant material

Hop cones were grown in Northwest of China (Xinjiang) and harvested in 2001. The material was supplied by Kunming Kiss Beer Co. (Kunming).

Extraction and isolation

Hop cones (10 kg fresh wt.) were exhaustively extracted with 70 % ethanol ($5 \times$) at room temperature. The combined filtrations were evaporated *in vacuo* to afford a residue, which was suspended in water and extracted with EtOAc (5×3 l). The EtOAc extracts were evaporated under reduced

pressure and dissolved in petroleum ether. The insoluble residue in petroleum ether was subjected to a silica gel column chromatography using chloroform-methanol gradient elution. The fraction eluting with chloroform-methanol (98:2, v/v) was purified by repeated column chromatography (petroleum ether:acetone, 90:10, v/v) and preparative TLC (petroleum ether:acetone, 90:10, 95:5, v/v, respectively) to afford compound **1** (22 mg) and **2** (42 mg).

(*p*-Methoxyphenyl) diphenylmethanol (**1**), white solids: IR (KBr pellets): $\nu = 3444$ (br. OH), 2364, 1606, 1507, 1445, 1264, 829, 699 cm^{-1} . – EIMS: m/z (rel. %) = 290 (20, $[\text{M}]^+$), 274 (40), 258 (50), 243 (8), 229 (33), 213 (90), 197 (27), 165 (34), 105 (85), 77 (100). – ^1H , ^{13}C NMR: see Table I.

Tribenzylamine (**2**), white solids. IR (KBr pellets): $\nu = 3447, 1605, 1506, 1445, 1241, 1000, 829, 762 \text{ cm}^{-1}$. – EIMS: m/z (rel. %) = 287 (51, $[\text{M}]^+$), 210 (60), 196 (50), 181 (16), 118 (18), 91 (100), 77 (12), 65 (54). – ^1H , ^{13}C NMR: see Table II.

Acknowledgements

We wish to acknowledge the financial support from National Natural Science Foundation of China (30225048).

- Eisch J. J., McNulty J. F., and Shi X. (1994), Synthesis of amines via carbon-sulfur bond cleavages of substituted aminomethyl sulfides with organolithium reagents: aminocarbene route to enamines and sterically hindered amines. *J. Org. Chem.* **59**, 7–9.
- Liu J., Burdette J. E., Xu H., Gu C., Breemen R. B., Bhat K. P. L., Booth N., Constantinou A. I., Pezzuto J. M., Fong H. H. S., Farnsworth N. R., and Bolton J. L. (2001), Evaluation of estrogenic activity of plant extracts for the potential treatment of menopausal symptoms. *J. Agric. Food Chem.* **49**, 2472–2479.
- Miranda C. L., Stevens J. F., Helmrich A., Henderson M. C., Rodrig R. J., Yang Y. H., Denzer M. L., Barnes D. W., and Buhler D. R. (1999), Antiproliferative and cytotoxic effects of prenylated flavonoids from hops in human cancer cell lines. *Food Chem. Toxicol.* **37**, 271–285.
- Miranda C. L., Stevens J. F., Ivanov V., McCall M., Frei B., Deinzer M. L., and Buhler D. R. (2000), Antioxidant and prooxidant actions of prenylated and non-prenylated chalcones and flavanones *in vitro*. *J. Agric. Food Chem.* **48**, 3876–3884.
- Tobe H., Muraki Y., Kitamura K., Komiyama O., Sato Y., Sugioka T., Maruyama H. B., Matsuda E., and Nagai M. (1997), Bone resorption inhibitors from hop extract. *Biosci. Biotech. Biochem.* **61**, 158–159.
- Winkler H. J. S. and Wittig G. (1963), Preparation and reaction of *o*-dilithiobenzene. *J. Org. Chem.* **28**, 1733–1740.