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AN ANTHRAQUINONE FROM *HEDYOTIS DIFFUSA**

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Key Word Index—*Hedyotis diffusa*; Rubiaceae; anthraquinone.

Abstract—A new anthraquinone, 2,3-dimethoxy-6-methylanthraquinone, has been isolated from *Hedyotis diffusa*.

INTRODUCTION

Hedyotis diffusa and *H. corymbosa* are common medicinal plants growing throughout India and China. The former has been shown to contain oleanolic acid, ursolic acid, sitosterol, stigmasterol and asperglaucide [1] while the latter contains 2-methyl-3-hydroxy-, 2-methyl-3-methoxy-, 2-methyl-3-hydroxy-4-methoxyanthraquinone and an unknown yellow compound A, $C_{17}H_{14}O_4$, mp 238–239° [2].

RESULTS AND DISCUSSION

The ^{1}H NMR spectrum of compound A showed signals for two aromatic methoxyl groups (δ4.00, 6H *s*), a methyl group (δ2.50, 3H, *s*), two isolated aromatic protons (δ7.70, 2H, *s*) and an ABX pattern for three aromatic protons (δ7.55, 1H, *dd*, J = 10 and 1.5 Hz, 8.05 1H, *d*, J = 1.5 Hz and 8.15, 1H, *d*, J = 10 Hz) indicating that compound A was 2,6-dimethoxy-3-methyl-, 3,6-dimethoxy-2-methyl- or 2,3-dimethoxy-6-methyl-9,10-anthraquinone (**1**). As the last structure seemed to be the most likely one for compound A, it was synthesized by the route depicted in Scheme 1. Diels–Alder reaction of *p*-benzoquinone with isoprene gave 6-methyl-5,8,9,10-tetrahydro-1,4-naphthoquinone (**2**) [3], which on dehydrogenation with chloranil, followed by Diels–Alder reaction with 2,3-dimethoxy-1,3-butadiene [4, 5] in the presence of ammonium dihydrogen phosphate gave the anthraquinone **1** which was identical in all respects (IR, UV, NMR and MS) with compound A. Thus, it was established that compound A is 2,3-dimethoxy-6-methylanthraquinone.

EXPERIMENTAL

Extraction of H. diffusa. Air dried whole herb (5 kg) of *Hedyotis diffusa* Willd., purchased by courtesy of Professor Y. P. Chen, the Brion Laboratory at Taipei in 1978, was powdered and extracted exhaustively with MeOH (80 l.) at room temp. The MeOH extract was concd *in vacuo* to 300 ml diluted with H_2O (300 ml), then extracted with *n*-hexane.

CC of the *n*-hexane soluble part on silica gel gave long chain alkanes, fatty acids, stigmasterol, sitosterol, ursolic acid, oleanolic acid and a yellow fraction, which was subjected to repeated CC on silica gel to give 2-methyl-3-hydroxy-, 2-methyl-3-methoxy-, 2-methyl-3-hydroxy-4-methoxyanthraquinone and a yellow compound A each in 0.0001% yield [1]. The spectroscopic data (UV, IR, NMR and MS) indicated that compound A was 2,3-dimethoxy-6-methyl-9,10-anthraquinone (**1**). This was confirmed by chemical synthesis of **1** by the pathway shown in Scheme 1.

6-Methyl-5,8,9,10-tetrahydro-1,4-naphthoquinone (**2**). *p*-Benzoquinone (1.08 g; 0.01 mol), EtOH (1 ml) and isoprene (0.68 g; 0.01 mol) were heated in a sealed tube at 100° for 8 hr to give yellow needles of **2** (1.5 g, 85%), mp 64–65° (EtOH). IR ν_{max}^{KBr} cm^{-1}: 3040, 2980, 1670, 1590, 840; ^{1}H NMR ($CDCl_3$): δ1.68 (3H, *s*), 1.80–2.68 (4H, *br d*), 2.80–3.38 (2H, *m*), 5.30–5.47 (1H, *m*) and 6.64 (2H, *s*).

6-Methyl-1,4-naphthoquinone (**3**). A mixture of **2** (1.76 g; 0.01 mol), chloranil (4.92 g; 0.01 mol) and C_6H_6 (30 ml) was refluxed for 30 hr. CC of the crude product on a column of silica gel using *n*-hexane–EtOAc (6:1) to elute **3**, yellow crystals (0.78 g, 45%), mp 90–91° (EtOAc) (lit. [3] mp 85–86°; [6, 7] mp 90–91°). IR ν_{max}^{KBr} cm^{-1}: 1660, 1600, 1365, 817; ^{1}H NMR ($CDCl_3$) [8]: δ2.45 (3H, *s*), 6.90 (2H, *s*), 7.50 (1H, *dd*, J = 8 and 1.5 Hz), 7.82 (1H, *d*, J = 1.5 Hz), 7.95 (1H, *d*, J = 8 Hz); MS *m/z* (rel. int.): 172 $[M]^+$ (100), 144 $[M-CO]^+$ (47), 116 $[M-2CO]^+$ (72), 90 (59), 89 (78), 63 (66).

2,3-Dimethoxy-6-methylanthraquinone (**1**). A mixture of **3** (200 mg; 1.1 mmol), 2,3-dimethoxy-1,3-butadiene (0.17 g; 1.6 mmol), $NH_4 \cdot H_2PO_4$ (10 mg) in C_6H_6 (3 ml) was refluxed for 48 hr. CC of the crude product on silica gel using *n*-hexane–EtOAc (7:1) to elute **1**, yellow crystals (123 mg, 38%), mp 237–238° ($CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3080, 2920, 1670, 1520, 875; ^{1}H NMR ($CDCl_3$): δ2.50 (3H, *s*), 4.00 (6H, *s*), 7.55 (1H, *dd*, J = 10 and 1.5 Hz), 7.70 (2H, *s*), 8.05 (1H, *d*, J = 1.5 Hz), 8.15 (1H, *d*, J = 10 Hz); MS *m/z* (rel. int.): 282 $[M]^+$ (100), 267 $[M-Me]^+$ (13), 239 $[267-CO]^+$ (17), 211 $[239-CO]^+$ (31), 168 (17), 139 (16).

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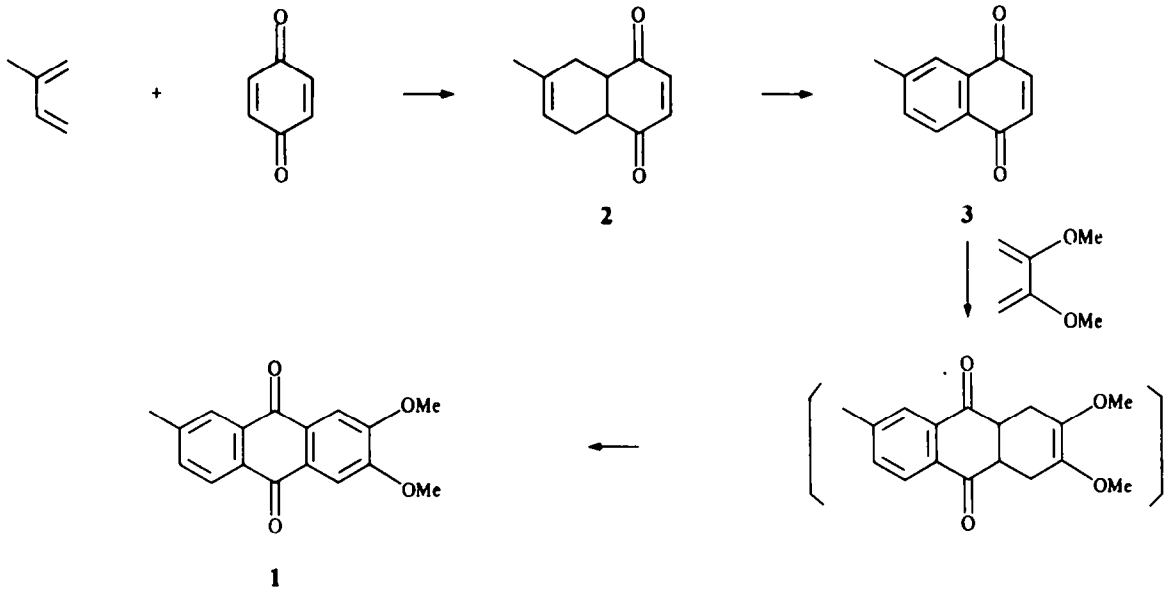

2 3 1

Scheme 1.

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