Phytochemistry, Vol. 20, No. 8, 1877–1881, 1981.
Printed in Great Britain.

0031–9422/81/081877–05 $02.00/0

NEW SESQUITERPENOIDS OF *BOMBAX MALABARICUM**

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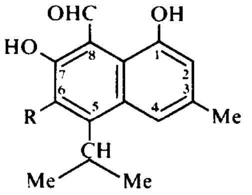
(*Revised received* 2 *December* 1980)

Key Word Index—*Bombax malabaricum*; Bombacaceae; new isohemigossypol derivatives; ^{1}H NMR long range couplings.

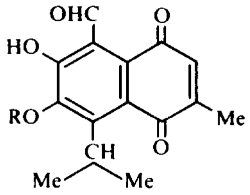
Abstract—Hemigossypol-6-methyl ether, reported to be present in the root bark of *Bombax malabaricum*, has been shown to be isohemigossypol-1-methyl ether. Isohemigossypol-1,2-dimethyl ether, 8-formyl-7-hydroxy-5-isopropyl-2-methoxy-3-methyl-1,4-naphthaquinone, 7-hydroxycadalene and an unidentified phenolic compound have also been isolated. Long range couplings in the ^{1}H NMR spectrum of isohemigossypol-1-methyl ether have been established by decoupling experiments.

INTRODUCTION

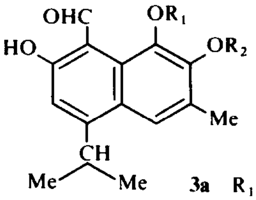
Extracts of the root bark of *Bombax malabaricum* (Bombacaceae) were first studied by Seshadri *et al.* who isolated a naphthol [1] and two naphthaquinones [2] to which they assigned the structures **1b** and **2a** and **2b**, respectively. Hemigossypol (**1a**) and its 6-methyl ether (**1b**) were subsequently isolated from diseased stele tissues of *Gossypium barbadense* by Bell *et al.* [3] who reported that the mp and UV and NMR spectra of their methyl ether were slightly different from those of the methyl ether of Seshadri *et al.* [1]. A compound isolated from a similarly infected *Gossypium* sp. was assigned the isohemigossypol structure **3a** by Sadykov *et al.* [4]. Veech *et al.* [5], however, showed by the use of double resonance experiments that Sadykov's compound was identical with their hemigossypol (**1a**). Subsequently, in another report Bell *et al.* [6] discussed the dissimilarity of terpenoids in *Gossypium* and *Bombax* and suggested that Seshadri's hemigossypol-6-methyl ether (**1b**), hemigossypolone (**2a**) and hemigossypolone-7-methyl ether (**2b**) were probably **3c**, **4a** and **4b**, respectively. They also suggested that the extracts of *Bombax* needed further study before the structures could be definitely assigned. Our continuing research in the chemistry of naturally occurring naphthols and naphthaquinones prompted us



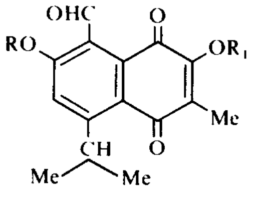
1a R = OH
1b R = OMe
1c R = H



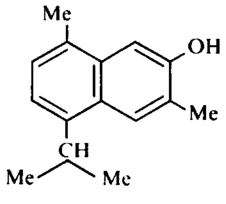
2a R = H
2b R = Me



3a $R_1 = R_2 = H$
3b R_1 = Me. R_2 = H
3c R_1 = H. R_2 = Me
3d R_1 = Me. R_2 = COMe
3e $R_1 = R_2$ = Me



4a $R = R_1 = H$
4b R = H. R_1 = Me
4c $R = R_1$ = Me



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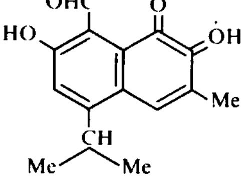

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* Dedicated to Dr. G. S. Sidhu, Director, Regional Research Laboratory, Hyderabad, India, on the occasion of his sixtieth birthday.

to initiate a thorough investigation of the extracts of the root bark of *B. malabaricum*, and from this source we have isolated six phenolic compounds and a naphthaquinone (BM1–BM7), four of which (BM3, BM4, BM5 and BM7) have been characterized.

RESULTS AND DISCUSSION

BM7, a white crystalline solid, mp 153° (petrol, 40–60°), M^+ 274.121, $C_{16}H_{18}O_4$ (calc. 274.1205), was separated from the chloroform extract by repeated column chromatography and preparative TLC. The UV, IR and NMR spectra of BM7 closely resembled that of the naphthol provided by Seshadri *et al.* [1].

The chemical shifts of H-2 and H-4 in hemigossypol-6-methyl ether were at δ 6.68 and 7.49, respectively, and in deoxyhemigossypol (**1c**) they were at δ 6.72 and 7.39, respectively. H-6 in the latter had the chemical shift at δ 6.97 [3]. In the ^{1}H NMR spectrum of BM7, (Fig. 1), the signals of the aromatic protons appeared as a singlet at δ 6.90 and a multiplet at 7.65, in close agreement with the report of Seshadri *et al.* [1]. Since the signal at δ 6.90 was aomewhat downfield for assignment to the H-2 of hemigossypol-6-methyl ether and was closer to the H-6 of deoxyhemigossypol (H-2 of 1-hydroxy-8-methoxy-3-methylnaphthalene (δ 6.74) and 1,8-dimethoxy-3-methylnaphthalene (δ 6.67) [7]), BM7 was either isohemigossypol-1-methyl ether (**3b**) or isohemigossypol-2-methyl ether (**3c**). Significantly, the methyl group of BM7 was a doublet at δ 2.42 ($J = 1$ Hz). This was also in accordance with the earlier observations on the double bond fixation in 2-methylnaphthalene derivatives, since the methyl is split into a doublet in 1-hydroxy-2-methoxy-3-methylnaphthalene derivatives but not in 1-hydroxy-4-methoxy-3-methylnaphthalene derivatives [7] (J = *ca* 1 Hz). The other signals from BM7 at δ 1.35 (*d*, $J = 7$ Hz), 3.65 (*septet*, $J = 7$ Hz), 3.75, 6.23, 11.00 and 13.90 were assigned to isopropyl methyl, isopropyl methine, methoxyl, C2-hydroxyl, aldehyde and C7-hydroxyl protons, respectively (Fig. 1).

Extensive decoupling experiments were carried out and acetylation shifts were studied to distinguish between structures **3b** and **3c**. Irradiation of the aromatic proton at δ 7.65 in BM7 collapsed the doublet aromatic methyl to a sharp singlet. Conversely, irradiation at δ 2.42 sharpened the aromatic proton; the irradiation also partially saturated the dissolved water in $CDCl_3$ (near the isopropyl doublet), and exchange of protons between H_2O and hydroxy groups transferred the saturation to the –OH resonance at δ 6.23 causing a reduction in the –OH proton signal. Irradiation of –OH at δ 6.23 eliminated the water peak in the same way, but only decreased the other hydroxyl peak slightly, since the latter was hydrogen-bonded so strongly that it underwent exchange much more slowly. The other aromatic proton at δ 6.90 coupled with the isopropyl methine proton to give a broadened signal which sharpened on irradiation at δ 3.65 (Fig. 2). The methine proton was also coupled with H-4, and irradiation at δ 3.65 apparently changed the H-4 signal to an unresolved quartet due to the aromatic methyl coupling. Thus the position of the isopropyl CH proton seemed to be maintained favourably for coupling through five bonds to H-4 at δ 7.65.

The reverse decoupling experiment at δ 6.90 sharpened the aldehyde proton. This five-bond coupling could be the cause of the apparent doublet of the aldehyde peak. Irradiation of the aldehyde peak at δ 11.00 sharpened the

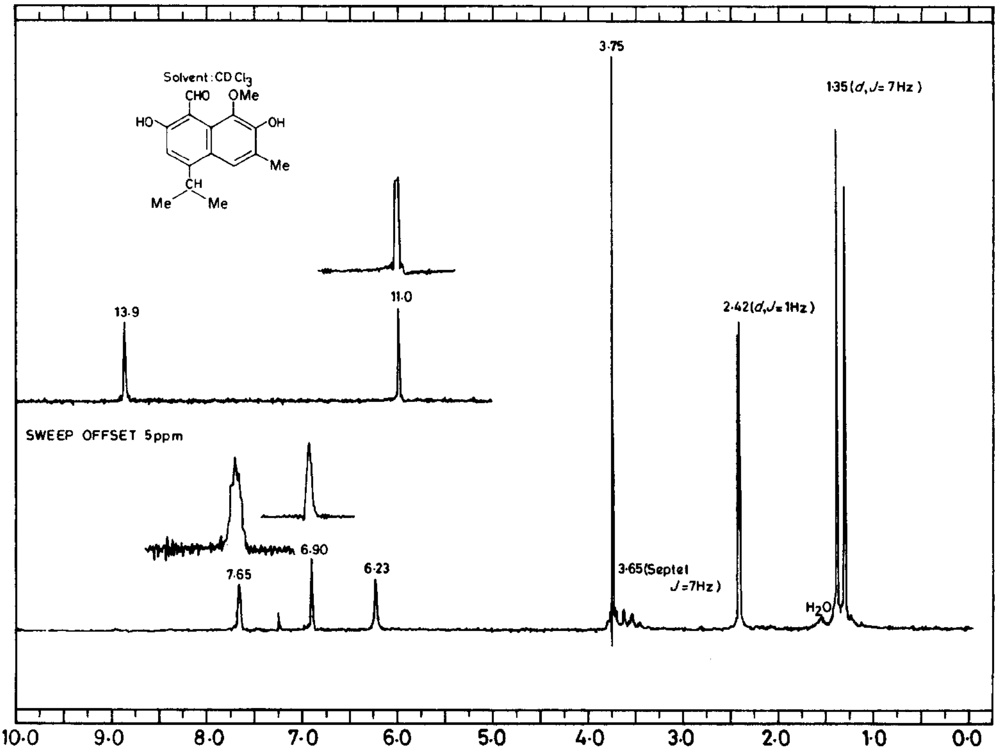

Fig. 1. ^{1}H NMR spectrum of BM7.

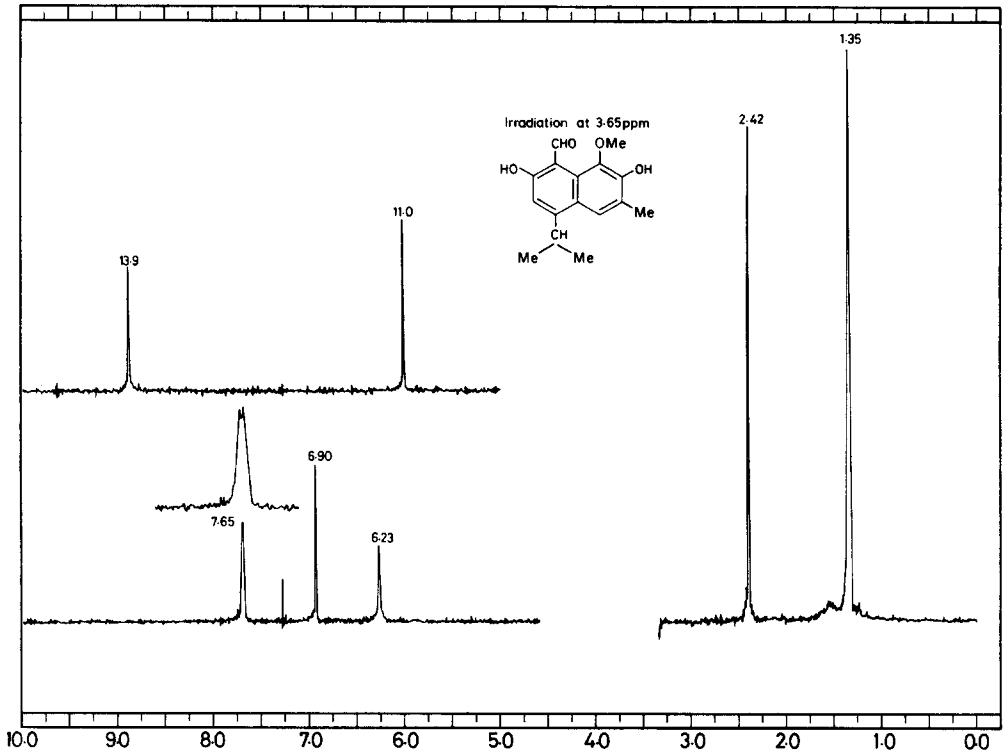

Fig. 2. ^{1}H NMR spectrum of BM7 irradiated at 3.65.

δ 6.90 peak slightly and increased its amplitude relative to the δ 6.23 peak.

Irradiation at δ 2.42 (aromatic methyl) with the use of positive exponential weighting function resulted in a spectrum (Fig. 3) in which the signals of the different protons revealed hidden long range couplings. A doublet for the –OH signal at δ 6.23 ($J = 1$ Hz) was caused by a favoured long range coupling with the proton at δ 7.65 (unresolved triplet) [8] which was also weakly coupled with the isopropyl methine proton at δ 3.65. The signal at δ 6.90 was also seen as a triplet due to coupling with the isopropyl methine proton and the aldehyde proton at δ 11.00. The aldehyde proton was also seen as a triplet due to coupling with the proton at δ 6.90 and the –OH at δ 13.4 (*d*). These decoupling experiments favoured structure **3b** and ruled out **3c** and demonstrated some interesting ^5J couplings in the naphthalene system. The general nature of some of these couplings is under investigation.

In the ^{1}H NMR spectrum of 1-acetoxy-2,8-dimethoxy-3-methylnaphthalene, the H-4 underwent the expected deshielding effect ($\Delta\ \delta = 0.40$) when compared to the corresponding 1-hydroxy derivative [7]. In the case of the isomeric 1,8-dimethoxy-2-acetoxy-3-methylnaphthalene and the corresponding hydroxy derivative, such an acylation shift on H-4 was not to be expected [7]. In the NMR spectrum of BM7 monoacetate (**3d**), the signal assigned to H-4 (δ 7.69) did not undergo a significant acetylation shift ($\Delta\delta = 0.04$), further confirming structure **3b**.

The loss of a molecule of water to give an intense $M^+ - H_2O$ fragment was shown to be diagnostic in the mass spectra of deoxyhemigossypol (**1c**), hemigossypol (**1a**) and hemigossypol-6-methyl ether (**1b**) which possess a hydroxyl *peri* to the aldehyde group [3]. The mass spectrum of BM7 showed a weak $M^+ - H_2O$ fragment (5 %). Thus, the hydroxyl and methoxyl group should be at C-2 and C-1, respectively, supporting structure **3b**. The major fragmentation pattern appeared to be triggered by the methoxyl leading to $M^+ - Me$ (100 %) (**6**), although the loss of the methyl from the isopropyl group cannot be excluded [$M^+ - CH_2O$ (15 %) and $M^+ - OCH_3$ (11 %)] [9].

BM3, a yellow crystalline solid, mp 101–102° (petrol 41°), M^+ 288.1362, $C_{17}H_{20}O_4$ (calc. 288.136160), appeared to be the 2-methyl ether of BM7 (**3e**) (UV, IR and ^{1}H NMR).

BM4, a yellow crystalline solid, mp 82° (methanol), M^+, 288.099765, $C_{16}H_{16}O_5$ (calc. 288.099775), closely resembled the quinone that was isolated from *B. malabaricum* DC and was assigned the structure **2b** by Seshadri *et al.* [2]. The major difference was in its ^{1}H NMR spectrum, wherein the 2-methyl and H-3 were previously reported as a doublet and quartet, respectively. In the ^{1}H NMR spectrum of BM4, the corresponding signals appeared at δ 2.09 (*s*) and δ 7.27 (*d*, $J =$ *ca* 0.5 Hz). The doublet at δ 7.27 could have been due to weak coupling with the isopropyl –CH, and this excluded any allylic coupling between the methyl and adjacent olefinic proton in the quinone ring (2-methyl-1,4-naphthaquinone, $J_{\mathrm{CH3,H}} = 1.5$ Hz). From these considerations, structure **4b** was assigned to BM4 [10]. However, it was not possible for us to obtain an authentic sample from Seshadri for a direct comparison. The ^{1}H NMR spectrum of hemigossypylone-7-methyl ether (**2b**), on the other hand, showed the methyl and vinylic signals at δ 2.14 and 6.60 as broadened singlets, and the UV data were different from those of BM4 [6]. BM4 gave a monomethyl ether, yellow crystalline solid, mp 117–118° (petrol, 40–60°) M^+ 302.115414, $C_{17}H_{18}O_5$ (calc. 302.115425), IR and NMR data consistent with the assigned structure (**4c**). These

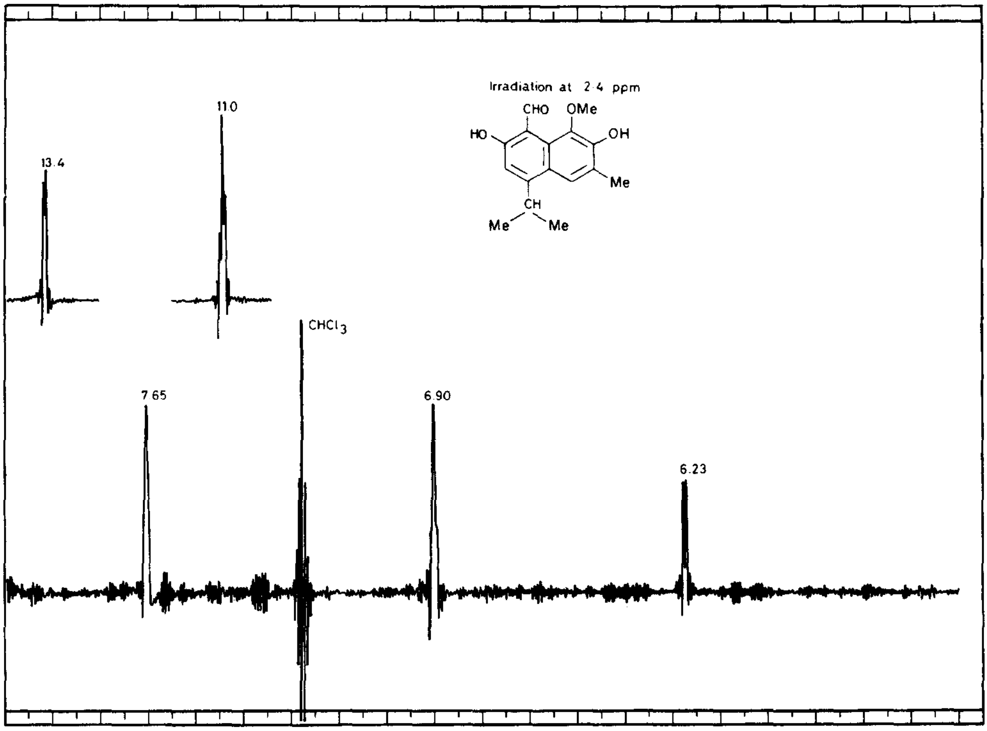

Fig. 3. ^{1}H NMR spectrum of BM7 irradiated at 2.4.

derivatives of isohemigossypol are reported for the first time, although hemigossypol and its derivatives are already known.

BM5, a white crystalline solid, mp 113–114° (petrol 60–80°), M$^+$, 214.13575, $C_{15}H_{18}O$ (requires 214.135765) was identified as 7-hydroxycadalene (**5**) by comparison of its UV, IR and ^{1}H NMR spectra with those of a sample supplied by Dr. Rowe. In its mass spectrum *m/z* 199 (M$^+$ − Me) was the base peak.

EXPERIMENTAL

Isolation of BM3, BM4, BM5 and BM7. Powdered, air-dried root bark (200 g), collected at the Regional Research Laboratory Campus, Hyderabad, was extracted with $CHCl_3$ at room temp. for 24, 32 and 168 hr successively. The extracts were similar by TLC. The solvent was removed, and the residues were dissolved in C_6H_6 and chromatographed over Si gel (< 200 mesh) using C_6H_6 as eluant. This gave some pure BM4 and mixtures. Like fractions were combined and subjected to repetitive column chromatography and prep. TLC (Si gel) to give pure BM3, BM4, BM5, and BM7. BM1 and BM2 were semi-solid in nature, and were not investigated further.

Isohemogossypol-1,2-dimethyl ether (**3e**, *BM3*). BM3 was contaminated with BM2 and BM4. Mixtures of BM2, BM3 and BM4 were separated by prep. TLC (Si gel, C_6H_6–$CHCl_3$, 2:1) followed by column chromatography (gradient elution, petrol, 60–80°, C_6H_6) to give BM3, yellow crystalline solid (69 mg), mp 101–102° (petrol 40°); MS (70 eV, direct inlet), *m/z* (rel. int.): 289 (18), 288 (M$^+$, 100), 274 (15), 273 (M$^+$ − Me, 83), 259 (M$^+$ − CHO, 9), 258 (M$^+$ − CH_2O, 41), 257 (M$^+$ − OMe, 38), 128 (15), 115 (20), 91 (16); UV λ_{max}^{MeOH} nm (log ε): 207 (4.32), 228 (4.74), 250 (4.29), 336–338 (4.02); IR ν_{max}^{KBr} cm^{-1}: 3360–3600 (br, OH); ^{1}H NMR (79.5 MHz, $CDCl_3$): δ 1.42 (*d*, *J* = 7 Hz, –CH (M$\underline{e}$)$_2$), 2.46 (*d*, *J* = 0.9 Hz, Me-3), 3.66 (*septet*, *J* = 7 Hz, –C$\underline{H}$(Me)$_2$, 3.93 and 4.05 (*s*, OMe-1 and OMe-2), 7.01 (H-6), 7.70 (*quintet*, H-4, coupled to Me-3 and –C$\underline{H}$(Me)$_2$) ^{1}H NMR (90 MHz, CCl_4): δ 11.03 (*s*, CHO), 13.84 (*s*, OH-7).

8-Formyl-7-hydroxy-5-isopropyl-2-methoxy-3-methyl-1,4-naphthaquinone (**4b**, *BM4*). The major quantity was obtained pure from column chromatography (Si gel) and was combined with the pure BM4 obtained from separation of its mixture with BM3 and BM5, yellow crystalline solid, mp. 82° (MeOH); MS (70 eV, direct inlet) *m/z* (rel. int.): 289 (21), 288 (M$^+$, 100), 273 (M$^+$ − Me, 47), 271 (M$^+$ − OH, 21), 256 (M$^+$ − MeOH, 15), 245 (25), 217 (18), 213 (24), 201 (15), 200 (21), 199 (21), 185 (15), 145 (15), 141 (15), 131 (15), 128 (24), 127 (15), 115 (32), 91 (21), 77 (27), 65 (15), 63 (21), 51 (21), 39 (23); UV λ_{max}^{MeOH} nm (log ε): 212 (4.26), 252 (4.06), 279 (4.04), 287 (4.05), 312.5 (3.63), 337 (3.49); IR ν_{max}^{KBr} cm^{-1}: 3530–3310 (br, –OH), 1650, 1665 (>C=O); ^{1}H NMR (79.5 MHz, $CDCl_3$): δ 1.29 [*d*, *J* = 7 Hz, –CH(M$\underline{e}$)$_2$], 2.09 (*s*, Me-3), 4.08 (*s*, OMe-2), 4.33 (*septet*, *J* = 7 Hz, –C$\underline{H}$(Me)$_2$), 7.27 (*d*, *J* = *ca.* 0.5 Hz, H-6 coupled to –C$\underline{H}$(Me)$_2$; ^{1}H NMR (60 MHz, CCl_4): δ 10.53 (*s*, –CHO), 12.43 (*s*, OH-7).

7-Hydroxycadalene (**5**, *BM5*). Mixtures of BM4 and BM5 were separated by prep. TLC (Si gel, $CHCl_3$) to give BM5, white crystalline solid (2.1 mg), mp 113–114°, (petrol 60–80°). MS (70 eV, direct inlet) *m/z* (rel. int.): 215 (9), 214 (M$^+$, 50), 200 (18), 199 (M$^+$ − Me, 100), 185 (M$^+$ − CHO, 8), 184 (25), 183 (9), 171 (8), 169 (11), 165 (9), 155 (10), 153 (9), 152 (10), 129 (8), 128 (12), 115 (13), 91 (8), 77 (8), 51 (8), 39 (8); UV λ_{max}^{MeOH} nm (log ε): 235 (4.45), 285 (3.77), 297 (3.73), 319 (3.30), 332.5 (3.40); IR ν_{max}^{KBr} cm^{-1}: 3320 (–OH); ^{1}H NMR (60 MHz, CCl_4): δ 1.38 (*d*, *J* = 7 Hz, –CH (M$\underline{e}$)$_2$, 2.47 (*s*, Ar-M$\underline{e}$), 2.50 (*s*, Ar-M$\underline{e}$), 3.68 (*m*, –C$\underline{H}$(Me)$_2$), 4.97 (*br*, –OH), 7.15 (*s*, H-2 and H-3), 7.19 (*d*, *J* = 1 Hz, H-8), 7.93 (*br*, H-5).

*BM*6. The purification and identification of BM6 is in progress.

*Isohemigossypol-*1*-methyl ether* (**3b**, *BM*7). BM7 was purified by repeated prep. TLC and CC (Si gel) using $CHCl_3$ as the eluant to give a white crystalline solid (7.6 mg), mp 153° (petrol 40–60°). MS (direct inlet 70°) *m/z* (rel. int.): 275 (11), 274 (M^+, 53), 260 (19), 259 (M^+, $-$Me, 100), 256 ($M^+ - H_2O$, 5), 244 ($M^+ - CH_2O$, 15), 243 ($M^+ -$ Me, 11), 242 (5), 241 ($M^+ -$ Me, $-H_2O$, 23), 213 (7), 171 (5), 157 (5), 141 (5), 128 (6), 115 (9), 83 (5), 81 (6), 71 (7), 69 (8), 57 (10), 55 (8), 43 (9), 41 (7); UV λ_{max}^{MeOH} nm ($\log \varepsilon$): 204 (4.08), 232 (4.71), 275.5 (3.81), 363 (3.99); IR ν_{max}^{KBr} cm^{-1}: 3290 (–OH).

2,7*-Dimethoxy-*8*-formyl-*5*-isopropyl-*3*-methyl-*1,4*-naphthaquinone* (**4c**). BM4 (100 mg) in $CHCl_3$ (10 ml), Ag_2O (420 mg) and MeI (0.50 ml) were shaken at room temp. for 8.5 hr. The soln was filtered and concd, leaving a yellow crystalline solid (88 mg), mp 117–118° (petrol 40–60°). MS: M^+, *m/z* 302.115414, $C_{17}H_{18}O_5$ (calc. 302.115425); IR ν_{max}^{KBr} cm^{-1}: 1715, 1665; ^1H NMR (60 MHz, CCl_4): δ 1.27 (*d*, $J = 7$ Hz, $-CH(Me)_2$), 2.02 (*s*, Me-3), 3.96 and 4.10 (*s*, OMe-2 and OMe-7), 4.48 (*septet*, $J = 7$ Hz, $-C\underline{H}(Me)_2$), 7.27 (*s*, H-6), 10.32 (*s*, 1 H, –CHO).

2*-Acetoxy-*8*-formyl-*7*-hydroxy-*5*-isopropyl-*1*-methoxy-*3*-methylnaphthalene* (**3d**). BM7 (17 mg) in dry pyridine (1 ml), and Ac_2O (0.3 ml) were kept for 3 days at room temp. The reaction mixture was worked up to give a brownish, viscous residue. On purification by prep. TLC (Si gel, $CHCl_3$–EtOAc, 60:7), it yielded a brown crystalline solid, mp 133–135° (CH_2Cl_2–petrol 40°). ^1H NMR (79.5 MHz, $CDCl_3$): δ 1.39 (*d*, $J = 7$ Hz, $-CH(\underline{Me})_2$), 2.35 (*d*, $J = 0.9$ Hz, Me-3), 2.45 (*s*, $-OCOC\underline{H}_3$), 3.63 (*septet*, $J = 7$ Hz, $-C\underline{H}(Me)_2$), 3.81 (*s*, OMe-1), 7.05 (*s*, H-6), 7.75 (*quintet*, H-4, coupled to Me-3 and $-C\underline{H}(Me)_2$); ^1H NMR (100 MHz, $CDCl_3$): δ 10.94 (*s*, CHO), 13.84 (*s*, C7–OH).

Acknowledgements—We thank Prof. F. Bohlmann, Organische Chemisches Institut, Technische Universität, Berlin, for high resolution MS; Dr. D. R. Sreedhar, Indian Drugs and Pharmaceuticals Ltd., Hyderabad and Prof. G. Mehta, University of Hyderabad, for the 90 MHz and 100 MHz NMR spectra, respectively; Dr. V. Seshadri, Department of Chemistry, University of Delhi, for the sample of the naphthol derivative from *Bombax malabaricum* DC; Dr. J. W. Rowe, Forest Products Laboratory, Madison, U.S.A., for a sample of 7-hydroxycadalene, and Prof. K. V. N. Rao, Department of Botany, Osmania University, Hyderabad, for the identification of the plant material.

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