Pergamon

Tetrahedron 58 (2002) 6615–6620

TETRAHEDRON

Total synthesis of (±)-brasiliquinone B

Mahesh L. Patil, Hanumant B. Borate, Datta E. Ponde and Vishnu H. Deshpande*

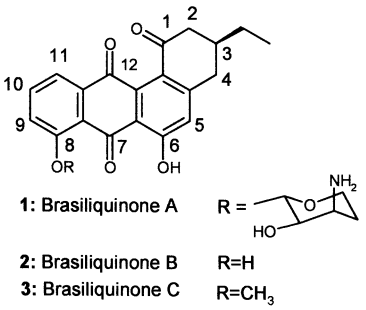
National Chemical Laboratory, Dr Homi Bhabha Road, Pune 411 008, India

Received 15 January 2002; revised 5 June 2002; accepted 27 June 2002

Abstract—The total synthesis of (±)-brasiliquinone B has been achieved via a Friedel–Crafts alkylation approach. In contrast, a Friedel–Crafts acylation approach for the synthesis of (±)-brasiliquinone B resulted in formation of A ring aromatized tetracyclic products. © 2002 Published by Elsevier Science Ltd.

1. Introduction

Brasiliquinones A–C[1,2] are cytotoxic benz[*a*]anthraquinone antibiotics isolated from the pathogenic species of *Nocardia* of the strain IFM 0089. Brasiliquinones belong to a large group of antibiotics commonly called angucyclines. As a special feature, brasiliquinones A–C possess an ethyl group at C-3 whereas all other angucyclines reported possess a methyl group at C-3.



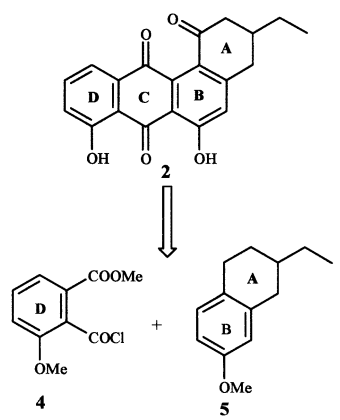
Brasiliquinones A–C showed a remarkable antitumour activity along with very good antiviral and antimicrobial activities. In vitro antitumor activity of brasiliquinones against L1210 and P388 proved brasiliquinones B (**2**) and C (**3**) more effective than brasiliquinone A (**1**). Previously we have reported the first total synthesis of (±)-brasiliquinone B (**2**)[3] using a Friedel–Crafts alkylation as the key step. Subsequently Mal et al.[4] reported syntheses of (±)-brasiliquinone B (**2**) and C (**3**) involving phthalide annulation and photooxygenation as the key steps. Krohn et al.[5] used a boron triacetate mediated Diels–Alder reaction for the synthesis of (±)-6-deoxybrasiliquinone B. We describe herein our synthesis of (±)-brasiliquinone B (**2**) via Friedel–Crafts alkylation and Friedel–Crafts acylation approaches.

2. Results and discussion

Our synthetic route for the synthesis of (±)-brasiliquinone B (**2**) was based on the Friedel–Crafts acylation of functionalised AB ring synthon **5** and its condensation with D ring synthon **4** for the construction of ring C as shown in Scheme 1. The most appropriate D ring synthon was considered to be acid chloride **4**,[6] which has been widely used in the syntheses of anthracyclines.

Although the key intermediate tetralin **5** looked structurally simple it has not been reported in literature. We undertook synthesis of this substituted tetralin **5** starting from commercially available 7-methoxy-1-tetralone (Scheme 2).

7-Methoxy-1-tetralone (**6**) was acylated using acetic anhydride and boron trifluoride etherate at room temperature followed by treatment with sodium acetate in refluxing methanol to give 2-acetyl-7-methoxy-1-tetralone (**7**) in 65%

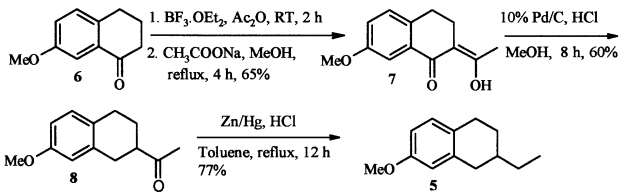


Scheme 1. Retrosynthetic plan for brasiliquinone B (**2**).

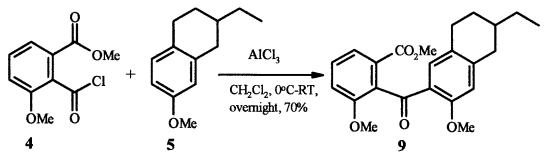
Keywords: antitumor; antibiotics; Friedel–Crafts reaction; regiospecificity.

* Corresponding author. Tel.: +91-20-5893300x2284; fax: +91-20-5893614; e-mail: vhdesh@dalton.ncl.res.in

0040–4020/02/$ - see front matter © 2002 Published by Elsevier Science Ltd.
PII: S0040-4020(02)00740-8



Scheme 2. Synthesis of tetralin derivative **5**.



Scheme 3. Acylation of tetralin derivative **5.**

yield. Hydrogenation of the compound **7** using 10% Pd/C and HCl in methanol followed by Clemmensen's reduction afforded desired tetralin derivative **5**.

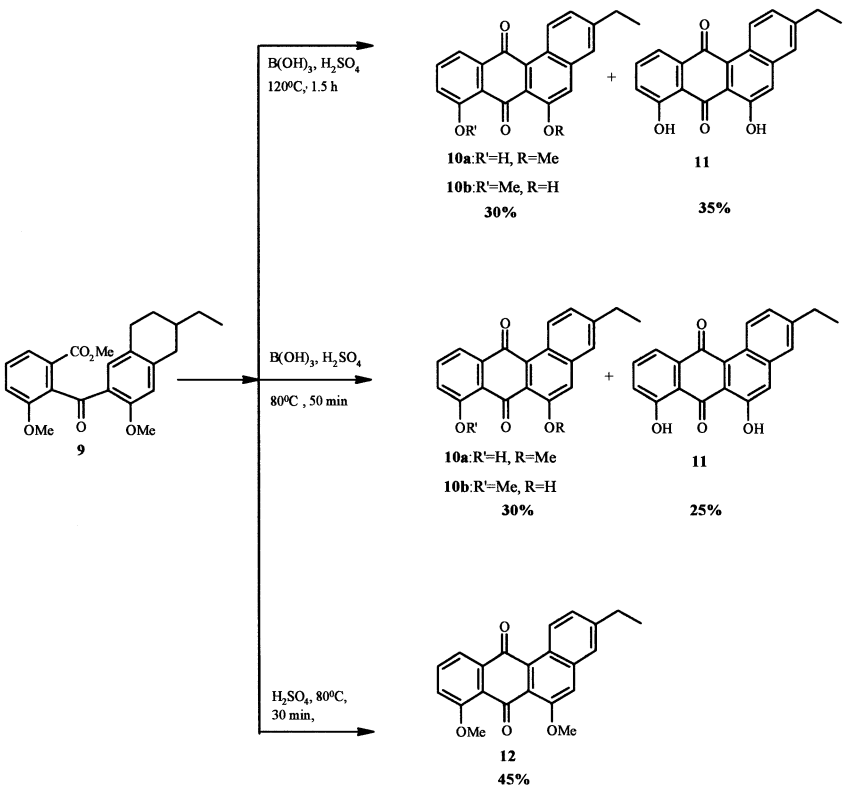
2.1. Friedel–Crafts acylation approach for the synthesis of (±)-brasiliquinone B

After synthesis of the AB ring synthon, we explored the use of a Friedel–Crafts acylation approach for the construction of the C ring of the angularly fused tetracyclic skeleton. The tetralin derivative **5** on Friedel–Crafts acylation with benzoyl chloride **4** in the presence of aluminium chloride yielded acylated product **9** in 70% yield as shown in Scheme 3.

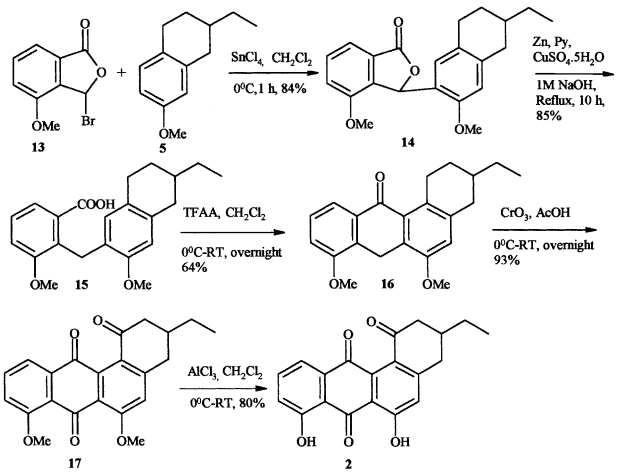
The ^{1}H NMR spectrum of **9** revealed two singlets, each integrating for one proton at δ 6.58 and 7.68 indicating regioselectivity in the acylation reaction. Our immediate aim was to cyclize the compound **9** and further oxidize it to give the desired dimethyl ether of brasiliquinone B.

Accordingly cyclization of the compound **9** was attempted using boric acid and sulfuric acid[7] but surprisingly it resulted in formation of A ring aromatized tetracyclic products, the members of tetrangulol group of angucycline antibiotics[8] (Scheme 4). Careful examination of the ^{1}H NMR spectrum of the reaction product suggested formation of the mixture of regioisomers **10a**+**10b** possessing one methoxy group and one hydroxyl group which could not be separated while compound **11** had hydroxyl groups at C-6 and C-8 positions. Decreasing the temperature and time of the reaction also resulted in the same products. Cyclization was also attempted with sulfuric acid alone at 80°C, which resulted in the cyclized and aromatized product **12** having both methoxy groups intact. The structure of compound **11** was established with the help of spectral data. Shifting of the triplet of methyl protons from δ 0.97–1.39 and appearance of a quartet at δ 2.82 indicated the presence of an aromatic ethyl group as well as singlets at δ 12.20 and 12.38 suggested the presence of chelated –OH groups.

In the literature, angucyclines possessing aromatic A rings have been reported. Tetrangulol, an angucycline antibiotic possessing an aromatic A ring was isolated by Kunstman[8–9] and synthesized by Brown and Thomson[10] using a Michael reaction. The compounds obtained in the present work are novel analogues of brasiliquinone B belonging to the tetrangulol type of angucyclines. Although the attempted Friedel–Crafts acylation approach to brasiliquinone B resulted in the synthesis of new tetrangulol type of the angucyclines, the synthesis of natural product remained as a challenge.



Scheme 4. Cyclization of the compound **9**.



Scheme 5. Friedel–Crafts alkylation approach for (±)-brasiliquinone B.

2.2. Friedel–Crafts alkylation approach for the synthesis of (±)-brasiliquinone B

Johnson et al.[11] introduced a phthalido-residue into the aromatic nucleus by a Friedel–Crafts reaction of an appropriate AB ring synthon with 3-bromo-4-methoxyphthalide (**13**)[11] in the presence of stannic chloride. It was thought to utilize this approach for the construction of the benz[*a*]anthraquinone structural framework. Friedel–Crafts alkylation of tetralin **5** with 3-bromo-4-methoxyphthalide (**13**) in the presence of stannic chloride in dichloromethane at 0°C afforded regiospecifically the lactone **14** in 84% yield as shown in Scheme 5. The lactone **14** underwent smooth reductive opening[12] with zinc in 1 M sodium hydroxide, pyridine, and cupric sulfate under reflux for 10 h to give acid **15** in 85% yield. Cyclization of the acid **15** to the anthrone **16** was achieved effectively under mild conditions using trifluoroacetic anhydride in dichloromethane. Our next target was to oxidize the anthrone **16** to the dimethyl ether of brasiliquinone B (**17**). The desired oxidation was carried out under chromium trioxide–acetic acid conditions to afford the compound **17** in 93% yield. Finally the desired synthesis of (±)-brasiliquinone B (**2**) was achieved by demethylating the dimethyl ether of brasiliquinone B (**17**) using aluminum chloride in 80% yield. This compound was characterized by IR, ^{1}H NMR and mass spectra. All spectral data for compound **2** were in good agreement with the values reported in literature.[1–2]

3. Conclusion

Thus a short, simple and regioselective methodology has been developed for the total synthesis of (±)-brasiliquinone B using a Friedel–Crafts alkylation approach. Although the Friedel–Crafts acylation approach failed to give brasiliquinone B, it can be utilized for the synthesis of tetrangulol analogues. This method of synthesis of the angucyclines is regioselective and would prove to be a convenient route towards the synthesis of other angucycline antibiotics, especially angucyclines possessing a hydroxy group at C-6 position.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-200 spectrometer in $CDCl_3$ containing TMS as an internal standard. Infrared spectra (ν_{max} in cm^{-1}) were recorded as either nujol mull or in $CHCl_3$ on Perkin–Elmer Infra-red 683 B or 160S FT-IR spectrometer with sodium chloride optics. All solvents and reagents were purified and dried by standard procedures. TLC was carried out on silica gel plates prepared by spreading the slurry (in CCl_4) and drying at room temperature. The plates were analyzed by keeping in iodine chamber. Column chromatography was performed on silica gel (60–120 mesh). Petroleum ether refers to the fraction boiling in the range of 60–80°C.

4.1.1. 2-Acetyl-7-methoxy-1-tetralone (7). BF_3-etherate (7.5 mL) was added dropwise to a stirred mixture of 7-methoxy-1-tetralone (2.5 g, 0.014 mol) in acetic anhydride (25 mL). The dark brown solution was then stirred at room temperature for 2 h. It was then poured into ice-water (250 mL), stirred for 1 h, filtered and the residue was dissolved in methanol (150 mL). A saturated solution of sodium acetate (100 mL) was added to it, followed by refluxing for 4 h. The methanol was removed by distillation and the solution was extracted with chloroform (3×50 mL). The chloroform layer was washed successively with water (50 mL) and brine (50 mL) and dried over sodium sulfate. Evaporation of the solvent followed by purification by column chromatography (20% EtOAc/petroleum ether) afforded **7** as yellow solid (2 g, 65%); mp 60–62°C. IR ($CHCl_3$): 3300, 1640 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.25 (s, 3H, CO*CH*$_3$), 2.55–2.65 (m, 2H), 2.75–2.90 (m, 2H), 3.85 (s, 3H, –OMe), 6.92–7.20 (m, 2H, aromatic), 7.45 (s, 1H, aromatic), 16.45 (s, 1H, enolic –OH). Mass (*m*/*z*): 218 (M^+). Anal. calcd for $C_{13}H_{14}O_3$: C 71.55, H 6.42; Found C 71.35, H 6.60.

4.1.2. 2-Acetyl-7-methoxytetralin (8). 2-Acetyl-7-methoxy-1-tetralone (2.2 g, 10 mmol) was dissolved in methanol (50 mL), followed by addition of conc. HCl (1 mL) and water (1 mL). 10% Pd/C (0.5 g) was then added to it and the mixture was subjected to hydrogenation at 50 psi pressure for 8 h. The mixture was filtered through Celite and methanol was removed from the filtrate under reduced pressure. The oily residue obtained was extracted with chloroform (3×25 mL). The combined organic layer was washed with water (30 mL), brine (30 mL) and dried over sodium sulfate. Evaporation of the solvent and purification of the residue by column chromatography (15% EtOAc/petroleum ether) yielded compound **8** as a colourless liquid (1.2 g, 60%). IR ($CHCl_3$): 1690 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.60–1.78 (m, 2H), 2.15–2.22 (m, 1H), 2.25 (s, 3H, CO*CH*$_3$), 2.70–2.80 (m, 2H), 2.90–2.98 (m, 2H), 3.79 (s, 3H, –*OMe*), 6.61 (s, 1H, aromatic), 6.70 (d, *J*=8 Hz, 1H, aromatic), 7.00 (d, *J*=8 Hz, 1H, aromatic). Mass (*m*/*z*): 204 (M^+). Anal. calcd for $C_{13}H_{16}O_2$: C 76.47, H 7.84; Found C 76.23, H 7.95.

4.1.3. 2-Ethyl-7-methoxy-1,2,3,4-tetrahydronaphthalene (5). Zinc wool (7 g), mercuric chloride (0.7 g), conc. HCl (2 mL) and water (10 mL) were mixed together with stirring

for 10 min. The aqueous layer was decanted and the residue was washed with water (2×50 mL). 2-Acetyl-7-methoxy tetralin (2.3 g, 14.70 mmol) in toluene (20 mL) was added to above prepared zinc amalgam, followed by concentrated HCl (5 mL). After cooling, water (5 mL) was added and the mixture was refluxed for 12 h. Then the mixture was filtered through Celite, the toluene layer was separated and washed with water (25 mL), brine (25 mL) and dried over sodium sulfate. Removal of the toluene under reduced pressure and purification of the residue by column chromatography (10% EtOAc/petroleum ether) afforded compound **5** as colourless liquid (2.1 g, 77%). IR ($CHCl_3$): 1608 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 1.00 (t, J=7.3 Hz, 3H), 1.35–1.50 (m, 3H), 1.52–1.75 (m, 1H), 1.80–2.05 (m, 1H), 2.15–2.55 (m, 2H), 2.65–2.95 (m, 2H), 3.90 (s, 3H, –OMe), 6.55–6.80 (m, 2H, aromatic), 7.00 (d, J=7.8 Hz, 1H, aromatic). Mass (m/z): 190 (M^+). Anal. calcd for $C_{13}H_{18}O$: C 82.10, H 9.47; Found C 82.00, H 9.52.

4.1.4. 3-Ethyl-6-methoxy-7-(2′-carbomethoxy-6′-methoxybenzoyl)-1,2,3,4-tetrahydronaphthalene (9). The compound **5** (380 mg, 2 mmol) in dry dichloromethane (5 mL) under a nitrogen atmosphere, was cooled to 0°C. Anhydrous aluminum chloride (400 mg, 3 mmol) was added to it slowly and allowed to stir for 15 min. The acid chloride 4 (456 mg, 2 mmol) in dry dichloromethane (5 mL) was added dropwise to the above reaction mixture at 0°C. The resulting mixture was allowed to stir at 0°C for 30 min and at room temperature overnight. After completion of reaction (TLC), the reaction mixture was poured on the mixture of crushed ice (5 g) and conc. HCl (2 mL), allowed to stir for 10 min and extracted with dichloromethane (3×20 mL). The combined organic layer was washed with water (20 mL), brine (20 mL) and dried over sodium sulfate. Evaporation of the solvent followed by column chromatographic purification (20% EtOAc/petroleum ether) yielded compound **9** as a colourless semisolid (535 mg, 70%). IR ($CHCl_3$): 1700, 1750 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 0.99 (t, J=7.0 Hz, 3H), 1.30–1.50 (m, 3H), 1.51–1.80 (m, 2H), 1.89–2.00 (m, 1H), 2.30–2.55 (m, 1H), 2.65–2.97 (m, 2H), 3.50 (s, 3H, –OMe), 3.72 (s, 3H, –OMe), 3.75 (s, 3H, $-CO_2Me$), 6.58 (s, 1H, aromatic), 7.10 (d, J=8.1 Hz, 1H, aromatic), 7.40 (t, J=8.1 Hz, 1H, aromatic), 7.62 (d, J=8.1 Hz, 1H, aromatic), 7.68 (s, 1H, aromatic). Mass (m/z): 382 (M^+). Anal. calcd for $C_{23}H_{26}O_5$: C 72.23, H 6.85; Found C 72.27, H 6.92.

4.2. Cyclization of compound 9

A mixture of ester **9** (382 mg, 1 mmol), conc. H_2SO_4 (2 mL) and boric acid (100 mg) was heated at 120°C for 1.5 h with stirring. The reaction mixture was cooled and poured over crushed ice (5 g). The dark brown aqueous part was extracted with chloroform (3×20 mL) and the chloroform layer was washed successively with saturated solution of sodium bicarbonate (20 mL), water (20 mL), brine (20 mL) and dried over sodium sulfate followed by column chromatographic purification (5–10% EtOAc/petroleum ether) to afford compounds (**10a**+**10b**) and **11** as reddish foam.

4.2.1. Compound 11. Yield: 111 mg (35%). ^1H NMR ($CDCl_3$, 200 MHz): δ 1.39 (t, J=7.8 Hz, 3H, $-CH_2CH_3$), 2.82 (q, J=7.8 Hz, 2H, $-CH_2CH_3$), 7.30 (s, 1H, aromatic), 7.38 (t, J=7.8 Hz, 1H, aromatic), 7.47 (d, J=7.8 Hz, 1H, aromatic), 7.61 (s, 1H, aromatic), 7.68 (d, J=7.8 Hz, 1H, aromatic), 7.85 (d, J=7.8 Hz, 1H, aromatic), 9.50 (d, J=7.8 Hz, 1H, aromatic), 12.20 (s, 1H, –OH), 12.38 (s, 1H, –OH). Mass (m/z): 318 (M^+).

4.2.2. Compound 10a+10b. Yield: 97 mg (30%). ^1H NMR showed inseparable mixture of regioisomers **10a** and **10b**. ^1H NMR ($CDCl_3$, 200 MHz): δ 1.30–1.45 (m, 6H, $-CH_3$), 2.70–2.90 (m, 4H, $-CH_2CH_3$), 4.08 (s, 3H, –OMe), 4.10 (s, 3H, –OMe), 7.20–7.80 (m, 11H, aromatic), 7.95 (d, J=7.8 Hz, 1H, aromatic), 9.00 (d, J=7.8 Hz, 1H, aromatic), 9.45 (d, J=7.8 Hz, 1H, aromatic), 12.20 (s, 1H, –OH), 12.70 (s, 1H, –OH). Mass (m/z): 332 (M^+).

4.2.3. Compound 12. A mixture of ester **9** (382 mg, 1 mmol) and conc. H_2SO_4 (2 mL) was heated at 80°C for 30 min with stirring. The reaction mixture was cooled and poured over crushed ice (5 g). The dark brown aqueous part was extracted with chloroform (3×20 mL) and chloroform layer was washed successively with saturated solution of sodium bicarbonate (10 mL), water (10 mL), brine (10 mL) and dried over sodium sulfate followed by column chromatographic purification (10% EtOAc/petroleum ether) to afford **12** (155 mg, 45%) as reddish foam. ^1H NMR ($CDCl_3$, 200 MHz): δ 1.38 (t, J=7.5 Hz, 3H, $-CH_3$), 2.75–2.95 (m, 2H, $-CH_2CH_3$), 4.05 (s, 3H, –OMe), 4.08 (s, 3H, –OMe), 7.25 (d, J=7.6 Hz, 1H, aromatic), 7.48 (s, 1H, aromatic), 7.52 (d, J=7.6 Hz, 1H, aromatic), 7.58 (s, 1H, aromatic), 7.65 (t, J=7.6 Hz, 1H, aromatic), 7.78 (d, J=7.6 Hz, 1H, aromatic), 8.95 (d, J=7.6 Hz, 1H, aromatic). Mass (m/z): 346 (M^+).

4.2.4. 3-(6-Ethyl-3-methoxy-5,6,7,8-tetrahydro-2-napthalenyl)-4-methoxy-1 (3*H*)-isobenzofuranone (14). The tetralin derivative **5** (570 mg, 3 mmol) was added to a stirred solution of 3-bromo-4-methoxyphthalide (1.1 g, 45 mmol) in dichloromethane (10 mL) at 0°C. Stannic chloride (6.5 g, 0.252 mol) was then introduced and the resulting mixture was stirred at 0°C for 1 h. It was then poured on the mixture of crushed ice (10 g) and conc. HCl (3 mL), stirred for 30 min and extracted with dichloromethane (25 mL). The combined dichloromethane layer was washed with water (20 mL), brine (20 mL) and dried over sodium sulfate. Evaporation of the solvent and purification by column chromatography (30% EtOAc/petroleum ether) afforded compound **14** (887 mg, 84%) as a white solid; mp 132–133°C. IR (Nujol): 1745 (lactone), 1596 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 0.99 (t, J=7.3 Hz, 3H), 1.22–1.49 (m, 3H), 1.50–1.65 (m, 1H), 1.80–1.99 (m, 1H), 2.30–2.51 (m, 1H), 2.55–2.65 (m, 2H), 2.75–2.92 (m, 1H), 3.75 (s, 3H, –OMe), 3.80 (s, 3H, –OMe), 6.50 (s, 1H, aromatic), 6.62 (s, 1H, phthalide), 6.75 (s, 1H, aromatic), 7.00–7.15 (m, 1H, aromatic), 7.45–7.58 (m, 2H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 11.94, 28.81, 29.69 (2C), 36.31 (2C), 36.79, 56.27, 56.42, 112.32, 115.93, 117.47, 121.59, 128.94, 129.45, 131.44, 137.80, 139.86 (2C), 155.11, 156.43, 171.36. Mass (m/z): 352 (M^+). Analysis calculated for $C_{22}H_{24}O_4$: C 75.00, H 6.81; Found C 74.52, H 6.36.

4.2.5. 2-{(6-Ethyl-3-methoxy-5,6,7,8-tetrahydro-2-naphthalenyl)methyl}-3-methoxybenzoic acid (15). The

lactone **14** (704 mg, 2 mmol) was reductively opened by heating with 1 M solution of NaOH (40 mL), activated zinc (3.7 g, 58 mmol), $CuSO_4{\cdot}5H_2O$ (50 mg, 0.2 mmol) and pyridine (10 mL) at 125°C for 10 h under a nitrogen atmosphere. The mixture was then allowed to cool and filtered through a pad of Celite. Acidification of the filtrate with concentrated HCl (15 mL) afforded the corresponding acid 15 (600 mg, 85%) as a white solid; mp 198–200°C. IR (Nujol): 3450, 1609 cm^{-1}. ^1H NMR (acetone-d_6, 200 MHz): δ 0.86 (t, J=7.3 Hz, 3H), 1.11–1.36 (m, 3H), 1.37–1.56 (m, 1H), 1.62–1.86 (m, 1H), 2.16–2.38 (m, 1H), 2.44–2.56 (m, 2H), 2.58–2.64 (br s, 1 H), 2.66–2.68 (m, 1H), 3.71 (s, 6H, 2×OMe), 4.26 (s, 2H benzylic), 6.38 (s, 1H aromatic), 6.44 (s, 1H aromatic), 6.96 (d, J=8.1 Hz, 1H aromatic), 7.21 (t, J=8.1 Hz, 1H aromatic), 7.42 (d, J=8.1 Hz, 1H aromatic). ^{13}C NMR (acetone-d_6, 50 MHz): δ 11.87, 25.96, 28.53, 29.19, 36.06, 40.95, 41.36, 55.65, 56.35, 110.83, 114.32, 122.00, 126.78, 127.70, 128.58, 134.65 (2C), 155.45, 158.57, 164.19, 170.92, 175.96. Mass (*m*/*z*): 354 (M^+). Anal. calcd for $C_{22}H_{26}O_4$: C 74.57, H 7.34; Found C 74.20, H 7.17.

4.2.6. 6,8-Dimethoxy-3-ethyl-1,2,3,4,7-pentahydrobenz[*a*]-anthracene-12(1*H*)-one (16). The acid **15** (495 mg, 14 mmol) in dry dichloromethane (15 mL) was cooled to 0°C, and freshly distilled trifluoroacetic anhydride (5 mL) was added to it under a nitrogen atmosphere. The mixture was allowed to stir at 0°C for 30 min and the stirring was continued overnight at room temperature. The trifluoroacetic anhydride and dichloromethane were removed under reduced pressure and saturated solution of potassium carbonate (20 mL) was added to it. This mixture was extracted with chloroform (3×30 mL). The combined chloroform layer was washed with water (20 mL) and brine (20 mL), followed by drying over sodium sulfate and evaporation of the chloroform to yield yellow coloured crude anthrone **16**. Its purification by column chromatography (18% EtOAc/petroleum ether) yielded anthrone 16 (300 g, 64%) as a pale yellow solid; mp 220–222°C. IR (Nujol): 1660 (ketone), 1597 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 1.02 (t, J=7.3 Hz, 3H), 1.21–1.50 (m, 2H), 1.51–1.78 (m, 1H), 1.99–2.12 (m, 1H), 2.40–2.60 (m, 1H), 2.95–3.00 (m, 2H), 3.12–3.35 (m, 1H), 3.43–3.62 (m, 1H), 3.78–4.18 (m, 2H, benzylic), 3.90 (s, 3H, OMe), 3.95 (s, 3H, –OMe), 6.80 (s, 1H, aromatic), 7.05 (d, J=8.1 Hz, 1H, aromatic), 7.40 (t, J=8.1 Hz, 1H, aromatic), 7.85 (d, J=8.1 Hz, 1H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 11.80, 22.50, 28.80, 30.00 (2C), 34.90, 36.95, 55.50 (2C), 111.80, 114.00, 118.50, 126.80, 128.80, 129.00, 130.90, 132.80, 135.00, 136.90, 153.50, 156.50, 186.90. Mass (*m*/*z*): 336 (M^+, 100), 332 (15), 321 (30), 307 (40). Anal. calcd for $C_{22}H_{24}O_3$: C 78.52, H 7.19; Found C 78.60, H 7.17.

4.2.7. Dimethyl ether of brasiliquinone B (17). Chromium trioxide (150 mg, 1.5 mmol) in 80% acetic acid (3 mL) was added slowly to the mixture of compound **16** (37 mg, 0.11 mmol) in glacial acetic acid (2 mL) at 0°C. The reaction mixture was allowed to stir at 0°C for 15 min and overnight at room temperature. After this, reaction mixture was poured into the ice-cold water (10 mL), stirred for 10 min and then extracted with chloroform (3×20 mL). The combined organic layer was washed with water (10 mL), brine (10 mL) and dried over sodium sulfate. Evaporation of the solvent under reduced pressure followed by column chromatographic purification (20% EtOAc/petroleum ether) afforded compound **17** (37 mg, 93%) as a yellow coloured semisolid. IR (nujol): 1705 (ketone), 1675 (quinone), 1595 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 1.00 (t, J=7.3 Hz, 3H), 1.40–1.65 (m, 3H), 2.35- 2.75 (m, 2H), 2.85–3.05 (m, 2H), 3.97 (s, 3H, –OMe), 4.00 (s, 3H, –OMe), 6.90 (s, 1H, aromatic), 7.20–7.32 (m, 1H, aromatic), 7.60–7.75 (m, 2H, aromatic). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 11.64, 29.18, 37.26, 37.52, 45.98, 56.97, 57.19, 115.15, 117.69, 118.90, 124.45, 127.87, 134.86, 137.47, 139.97, 151.32, 159.26, 161.51, 117.64, 182.35, 186.83, 198.63. Mass (*m*/*z*): 364 (M^+, 12), 350 (20), 335 (55), 321 (22), 306 (25). Anal. calcd for $C_{22}H_{20}O_5$: C 72.52, H 5.49; Found C 72.70, H 5.20.

4.2.8. (±)-Brasiliquinone B (2). To the solution of brasiliquinone dimethyl ether (**17**) (36 mg, 0.098 mmol) in dichloromethane (5 mL) was added anhydrous aluminum chloride (50 mg, 0.38 mmol) at 0°C. The mixture was stirred for 2 h and allowed to warm up to room temperature. The reaction mixture was stirred at room temperature for 12 h. It was then poured into a mixture of crushed ice (3 g) and conc. HCl (2 mL) and digested on water bath for 20 min. After cooling to room temperature, it was extracted with dichloromethane (3×20 mL). The combined dichloromethane part was dried over sodium sulfate and concentrated to afford a residue which on column chromatographic purification (25% EtOAc/petroleum ether) yielded (±)-brasiliquinone B (**2**) (26 mg, 80%) as a yellow solid; mp 187–191°C. IR ($CHCl_3$): 3435, 1980, 1690, 1640 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 1.00 (t, J=7.3 Hz, 3H), 1.40–1.80 (m, 2H), 2.00–2.20 (m, 1H), 2.35–2.70 (m, 2H), 2.90–3.08 (m, 2H), 7.02 (s, 1H, aromatic), 7.22–7.32 (m, 1H, aromatic), 7.60–7.7.75 (m, 2H, aromatic), 11.70 (s, 1H, chelated –OH), 12.30 (s, 1H, chelated –OH). Mass (*m*/*z*): 337 (M+1, 26), 336 (M^+, 38), 308 (55), 280 (100). Anal. calcd for $C_{20}H_{16}O_5$: C 71.42, H 4.76; Found C 71.50, H 5.00.

Acknowledgments

M. L. P. thanks CSIR, New Delhi for the award of senior research fellowship.

References

1. Tsuda, M.; Sato, H.; Tanaka, Y.; Yazawa, K.; Mikami, Y.; Sasaki, T.; Kobayashi, J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1773.
2. (a) Nemoto, A.; Tanaka, Y.; Karasaki, Y.; Komaki, H.; Yazawa, K.; Mikami, Y.; Tojo, T.; Kodawaki, K.; Tsuda, M.; Kobayashi, J. *J. Antibiotics* **1997**, *50*, 18. (b) For correction see: *J. Antibiotics* **1997**, *50*, C-1.
3. Patil, M.; Borate, H.; Ponde, D.; Bhawal, B.; Deshpande, V. *Tetrahedron Lett.* **1999**, *40*, 4437.
4. Mal, D.; Roy, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3167.
5. Krohn, K.; Micheel, J.; Zukowski, M. *Tetrahedron* **2000**, *56*, 4753.

6. Miller, D.; Trenbeath, S.; Sih, C. *Tetrahedron Lett.* **1976**, 1637.
7. Graves, G.; Adams, R. *J. Am. Chem. Soc.* **1923**, *45*, 2439.
8. Kunstmann, M.; Mitscher, L. *J. Org. Chem.* **1966**, *31*, 2920.
9. Dann, M.; Lefemine, D.; Barbatschi, P.; Shu, P.; Kunstmann, M.; Mitscher, L.; Bohonos, N. *Antimicrob. Agents Chemother.* **1965**, 832.
10. Brown, P.; Thomson, R. *J. Chem. Soc., Perkin Trans. 1* **1976**, 997.
11. Kim, K.; Suarato, A.; Johnson, F. *J. Am. Chem. Soc.* **1979**, *101*, 2483.
12. Newman, M.; Sankaran, V.; Olson, D. *J. Am. Chem. Soc.* **1976**, *98*, 3237.