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CARBAZOLOQUINONES FROM *MURRAYA KOENIGII*

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Key Word Index—*Murraya koenigii*; Rutaceae; koenigine-quinone A and koenigine-quinone B; carbazole alkaloid.

Abstract—Two new carbazole alkaloids designated as koenigine-quinone A and koenigine-quinone B were isolated from the alcoholic extract of the stem bark of *Murraya koenigii* and their structures were established as 7-methoxy-3-methylcarbazole-1,4-quinone and 6,7-dimethoxy-3-methylcarbazole-1,4-quinone, respectively, from spectral data and synthetic evidences. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Murraya koenigii Spreng is a major source of carbazole alkaloids [1]. We report herein the isolation and characterisation of two new carbazoloquinones from *Murraya koenigii* Spreng. This is the first report of the isolation of carbazoloquinone alkaloids from this plant.

RESULTS AND DISCUSSION

Koenigine-quinone A (**1**) gave a $[M]^+$ ion peak at *m/z* 241 (EIMS) and microanalysis established its molecular formula as $C_{14}H_{11}NO_3$. Its UV spectrum [λ_{max}^{MeOH} 227 (log ε 4.65), 260 (4.51), 286 sh (3.80) and 387 nm (3.72)] was characteristic of a carbazole-1,4-quinone [2]. The IR spectrum showed bands at ν_{max}^{KBr} 3280 (NH), 1652 and 1639 cm^{-1} (carbonyl groups). The ^1H NMR spectrum (300 MHz, $CDCl_3$) showed signals at δ 9.11 (1H, *br s*, NH), 8.03 (1H, *d*, *J* = 8.01 Hz, H-5), 6.93 (1H, *dd*, *J* = 8.0 Hz and 1.8 Hz, H-6), 6.80 (1H, *d*, *J* = 1.8 Hz, H-8), 6.39 (1H, *q*, *J* = 1.3 Hz, H-2), 3.81 (3H, *s*, ArOMe) and 2.09 (3H, *d*, *J* = 1.3 Hz, Me).

In carbazoloquinones H-5 appears at high δ values [2]. The upfield shift of the H-6 and H-8 signals suggested the presence of a methoxy group on the adjacent carbon atom. The methyl group was placed at C-3 on the quinone moiety from biogenetic considerations. From these data the structure of koenigine-quinone A was assigned as 7-methoxy-3-methylcarbazole-1,4-quinone (**1**).

Finally, the assigned structure of koenigine-quinone A (**1**) was confirmed by synthesis as follows (Scheme 1): 2-hydroxymethylene-5-methylcyclohexanone (**3**) [3] on condensation with diazotized 3-methoxyaniline (**4**) under Japp-Klingemann conditions furnished 4-methylcyclohexane-1,2-dione-1-(3-methoxy)phenyl hydrazone (**5**) which on cyclization with a mixture of acetic acid and conc. HCl furnished 2-methoxy-6-methyl-8-oxo-5,6,7,8-tetrahydrocarbazole (**6**). Dehydrogenation of **6** with 5% Pd-C in a sealed tube under vacuum at 170–180° gave 1-hydroxy-7-methoxy-3-methylcarbazole (**7**). Potassium nitrosodisulphonate oxidation [4] of **7** furnished **1** which was found to be identical with natural koenigine-quinone A in all respects (mp, mmp, UV, IR and ^1H NMR).

Koenigine-quinone B (**2**) gave rise to a $[M]^+$ peak at *m/z* 271 (EIMS) and microanalysis established the molecular formula as $C_{15}H_{13}NO_4$. Its UV spectrum [λ_{max}^{MeOH} 225 (log ε 4.61), 263 (4.39), 293 sh (3.21) and 464 nm (3.09)] was characteristic of a carbazole-1,4-quinone [2]. The IR spectrum showed bands at ν_{max}^{KBr} 3284 (NH), 1650 and 1641 cm^{-1} (carbonyl groups). The ^1H NMR (300 MHz, $CDCl_3$) showed signals at δ 9.20 (1H, *br s*, NH), 7.56 (1H, *s*, H-5), 6.84 (1H, *s*, H-8), 6.42 (1H, *q*, *J* = 1.2 Hz, H-2), 3.97 (3H, *s*, ArOMe), 3.94 (3H, *s*, ArOMe) and 2.12 (3H, *d*, *J* = 1.2 Hz, Me). H-5 and H-8 appeared upfield suggesting the presence of the methoxy groups on adjacent carbon atoms. The methyl group was placed at C-3 on biogenetic considerations. From these data, the structure of koenigine-quinone B was assigned as 6,7-dimethoxy-3-methylcarbazole-1,4-quinone (**2**).

Finally, the assigned structure of koenigine-quinone B (**2**) was confirmed by synthesis from 2-hydromethylene-5-methylcycle-hexanone (**3**) [3] and 3,4-dimethoxyaniline (**8**). The product was found to be identical with natural koenigine-quinone B in all respects (mp, mmp, UV, IR and ^1H NMR).

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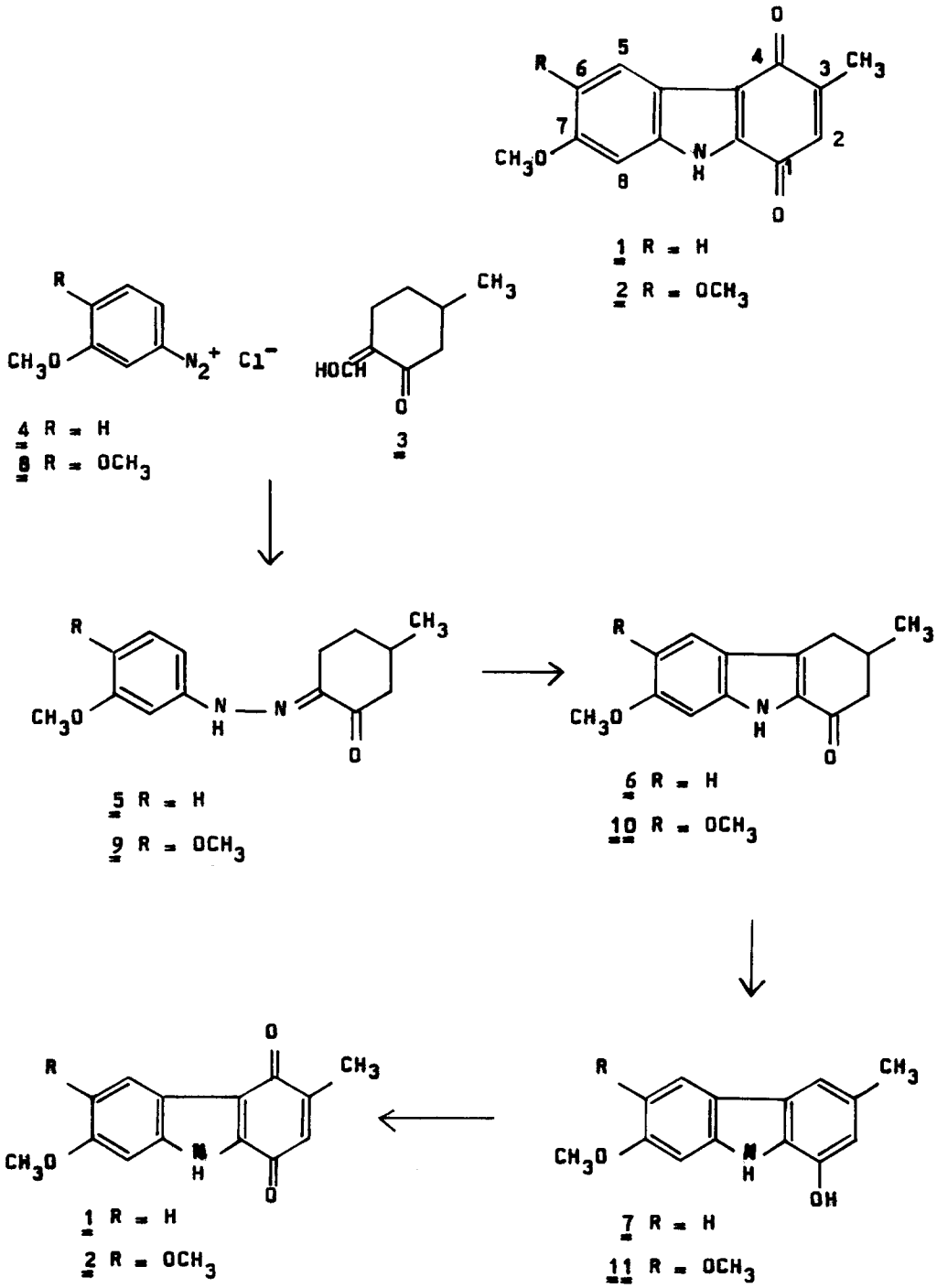

Scheme 1. Chemical synthesis of compounds **1** and **2**.

EXPERIMENTAL

Mps: uncorr; UV and IR: MeOH and KBr pellets, respectively.

Isolation of koenigine-quinone A and koenigine-quinone B

The stem bark of *Murraya koenigii* (1 kg) was first extracted with petrol (60–80°) in a Soxhlet for 36 h. The plant material was then dried and re-extracted with EtOH (95%) in a Soxhlet. From the ethanolic extract, the solvent was removed in a rotary evaporator. The residue was chromatographed over silica gel (200 g), eluting with petrol (60–80°), petrol–CH_2Cl_2 (2:1), petrol–CH_2Cl_2 (1:1) and $CHCl_3$–MeOH (99:1). From the methanolic chloroform eluate a reddish-brown residue (100 mg) was obtained. This residue was again chromatographed over silica gel (10 g) and eluted with the solvent systems as mentioned above. The methanolic chloroform eluates gave, on removal of solvent, a reddish brown solid (55 mg). TLC (silica gel) of the above residue showed the presence of a mixture of two compounds which were separated by prep. TLC (silica gel G, 1 mm, hexane–benzene–EtOAc, 2:2:1). The band at R_f 0.57 was separated and extracted with 5% MeOH in $CHCl_3$. The residue, on removal of solvent, gave a solid, which on recrystallisation from benzene–petrol, furnished koenigine-quinone A (**1**) as red needles (15 mg), mp 240° (dec.). (Found C, 69.58; H, 4.47; N, 5.90%; calculated for $C_{14}H_{11}NO_3$, C 69.71, H 4.56, N 5.81%). The band at R_f 0.51 was also extracted with 5% MeOH in $CHCl_3$. The residue obtained after removal of the solvent was purified by repeated crystallisation from benzene–petrol to furnish reddish brown needles (12 mg), mp 256° (dec.) of koenigine-quinone B (**2**). (Found C 66.50, H 4.69, N 5.21%; calculated for $C_{15}H_{13}NO_4$, C 66.42, H 4.80, N 5.17%).

4 - *Methylcyclohexane* - 1,2 - *dione* - 1 - (3 - *methoxy*) *phenyl hydrazone* (**5**). 2-Hydroxymethylene-5-methylhexanone (**3**, 14 g, 0.1 mol) in MeOH (130 ml) was added to an aq. soln of NaOAc (20 g in 75 ml of H_2O). To this soln was added a soln of 3-methoxyphenyldiazonium chloride (**4**, prepared from 12.3 g, 0.1 mol of *m*-anisidine) over 40 min under mechanical agitation when reddish brown crystals of **5** were obtained. These were removed by filtration and crystallised from EtOH to yield reddish brown crystals (18.5 g, 75%), mp 194–196°. (Found C 68.56, H 7.51, N 11.23%, calculated for $C_{14}H_{18}N_2O_2$, C 68.29, H 7.32, N 11.38%). IR ν_{max}^{KBr} cm^{-1}: 3455 (NH), 1633 (CO) and 1600, 1510 (aromatic).

2 - *Methoxy* - 6 - *methyl* - 8 - *oxo* - 5,6,7,8 - *tetrahydrocarbazole* (**6**). Compound **5** (4.92 g, 0.02 mol) was boiled with glacial HOAc (30 ml) and conc. HCl (7 ml) for 5 min and then diluted with ice water (150 ml). The reaction mixture was extracted with CH_2Cl_2 (3 × 125 ml), and CH_2Cl_2 extract washed with water (2 × 100 ml) and then dried (Na_2SO_4). The solvent was then removed to obtain the crude product. The crude product was chromatographed over a silica gel (150 g) column eluted with petrol, petrol–CH_2Cl_2 (1:1) and CH_2Cl_2. The eluates from the petrol–CH_2Cl_2 (1:1) and CH_2Cl_2 furnished a colourless solid which on crystallisation from benzene–petrol (60–80°) yielded **6** as colourless crystals (3 g, 65.5%) mp 210–211°. (Found C 73.46, H 6.59, N 6.05%; calculated for $C_{14}H_{15}NO_2$, C 73.36, H 6.55, N 6.11%). IR ν_{max}^{KBr} cm^{-1}: 3360 (NH) and 1630 (CO).

1-*Hydroxy*-7-*methoxy*-3-*methylcarbazole* (**7**). A mixture of **6** (458 mg, 2 mmol) and 5% paladised charcoal (750 mg) moistened with EtOH (1 ml) was heated at 170–180° in a sealed tube under vacuum for 4 h. The reaction mixture was extracted with 5% methanolic CH_2Cl_2 (3 × 30 ml) and filtered. After removal of solvent, the residue was crystallised from benzene–petrol to yield **7** (300 mg, 66%), mp 175–178°. (Found C 74.16, H 5.90, N 6.23%; calculated for $C_{14}H_{13}NO_2$, C 74.00, H 5.73, N 6.17%). UV λ_{max}^{MeOH} nm: 241, 300 and 323 with log ε, 4.39, 3.37 and 3.29; IR ν_{max}^{KBr} cm^{-1}: 3390 (NH), 3310 (OH) and 1595 (aromatic).

7 - *Methoxy* - 3 - *methylcarbazole* - 1,4 - *quinone* (*koenigine-quinone A*, **1**). A soln of **7** (100 mg, 0.44 mmol) in Me_2CO (50 ml) was slowly added to a soln of potassium nitrosodisulphonate (240 mg, 0.89 mmol) and KH_2PO_4 (30 mg) in water (30 ml). The mixture was stirred at room temp. for 30 min. The reaction mixture was filtered and washed with Me_2CO. After removing Me_2CO the aq. part was extracted with $CHCl_3$ (3 × 75 ml). The organic layer was washed with water and dried (Na_2SO_4). The product was purified by prep. TLC (silica gel G, 1 mm, hexane–benzene–EtOAc, 4:4:2). The upper red band was extracted with 5% methanolic $CHCl_3$ and the residue thus obtained after removing the organic solvent was crystallised from benzene-petrol to yield **1** (81 mg, 76.5%) mp 241° (dec.). (Found C 69.65, H 4.49, N 5.87%; calculated for $C_{14}H_{11}NO_3$, C 69.71, H 4.56, N 5.81%).

4-*Methylcyclohexane*-1,2-*dione*-1-(3,4-*dimethoxy*) *phenylhydrazone* (**9**). This was prepared from **3** and 3,4-dimethoxy phenyldiazonium chloride (**8**, prepared from 15.4 g, 0.1 mol of 3,4-dimethoxy aniline [5]) in a similar way to that used to prepare **5** (see above), **9** was obtained as brown crystals (19.5 g, 70%), mp 172–173°. (Found C 65.41, H 7.37, N 10.00%; calculated for $C_{15}H_{20}N_2O_3$, C 65.22, H 7.25, N 10.14%). IR ν_{max}^{KBr} cm^{-1}: 3450 (NH), 1635 (CO) and 1600, 1510 (aromatic).

2,3 - *Dimethoxy* - 6 - *methyl* - 8 - *oxo* - 5,6,7,8 - *tetrahydrocarbazole* (**10**). Compound **9** (5.52 g, 0.02 mol) was boiled with glacial HOAc (30 ml) and concentrated HCl (7 ml) for 5 min and then diluted with ice water (150 ml). The solid obtained was filtered, washed with water, dried and crystallised from benzene–petrol (40–60°) mixture when colourless needles (3.9 g, 75%), mp 247–248° of **10** were obtained. (Found C 69.58, H 6.61, N 5.38%; calculated for

$C_{15}H_{17}NO_3$, C 69.50, H 6.56, N 5.40%). IR ν_{max}^{KBr} cm^{-1}: 3355 (NH) and 1635 (CO).

2,3-*Dimethoxy-8-hydroxy-6-methylcarbazole* (**11**). This was prepared from **10** by the same procedure as that used to prepared **7**. Yield **11** (320 mg, 62%), mp 216–217°. (Found: C 70.14, H 5.72, N 5.56%; calculated for $C_{15}H_{15}NO_3$, C 70.04, H 5.84, N 5.45%). UV λ_{max}^{MeOH} nm: 235.6, 304 and 331 (log ε 4.40, 3.23 and 3.21); IR ν_{max}^{KBr} cm^{-1}: 3385 (NH), 3310 (OH) and 1600 (aromatic).

6,7 - *Dimethoxy* - 3 - *methylcarbazole* - 1,4 - *quinone* (*koenigine-quinone B*, **2**). A soln of **11** (150 mg, 0.58 mmol) in Me_2CO (50 ml) was slowly added to a soln of potassium nitrosodisulphonate (350 mg, 1.30 mmol) and KH_2PO_4 (45 mg) in water (40 ml). The mixture was stirred at room temp. for 30 min. The reaction mixture was filtered and washed with Me_2CO. After removing Me_2CO the aq. part was extracted with $CHCl_3$ (4 × 75 ml). The organic layer was washed with water and dried (Na_2SO_4). The product was purified by prep. TLC (silica gel G, 1 mm, hexane–benzene–EtOAc, 4:4:2). The upper red band was extracted with 5% methanolic $CHCl_3$ and the residue thus obtained after removing the organic solvent was crystallised from benzene–petrol to yield **2** (114 mg, 72%) mp 246–247° (dec.). (Found C 66.48, H 4.72, N 5.21%; calculated for $C_{15}H_{13}NO_4$, C 66.42, H 4.80, N 5.17%).

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