Titanocene(III) chloride mediated radical-induced synthesis of 3,4-disubstituted tetrahydrofurans: Formal synthesis of (±)-burseran and (±)-dehydrocubebin

S Jana, M Paira & S C Roy*
Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700 032, India
E-mail: ocscr@iacs.res.in

Received 5 October 2007; accepted (revised) 14 February 2008

Synthesis of 3,4-disubstituted tetrahydrofurans has been achieved via radical cyclization of epoxides using titanocene(III) chloride (Cp₂TiCl) as a transition-metal radical source. The radical initiator (Cp₂TiCl) is generated in situ from commercially available titanocene dichloride (Cp₂TiCl₂) and zinc dust in THF under argon. Formal synthesis of two bioactive lignans, burseran and dehydrocubebin has also been accomplished through the radical technology.

Keywords: Radical cyclization, epoxides, titanocene(III) chloride, burseran, dehydrocubebin

Substituted tetrahydrofurans are widely distributed among various types of naturally occurring lignans, which are known to exhibit interesting biological properties. In this broad lignan family, 3,4-diaryl tetrahydrofurans lignans burseran 1 and dehydrocubebin 2 belong to a class of anti-tumor agents called spindle poisons. This class of compounds interacts with the tubulin-microtubule systems, the precursors for spindle formation. Besides the anti-tumor activity, they also exhibit platelet activity-factor antagonism and diuretic properties. Due to their widespread occurrence in nature and broad range of biological activity, these types of lignans are much popular target compounds in synthetic organic chemistry. Synthetic procedures reported in the literature mainly involved Michael addition, dehydration of substituted 1,4-diols or alkylation methodologies. Only one report by Hanessian and his co-worker reported tin hydride mediated radical cyclization as the key step. Previously, from this laboratory, the syntheses of tri-substituted tetrahydrofuran lignans were achieved using radical cyclization reactions. Herein is now described a radial mediated route towards the synthesis 3,4-disubstituted tetrahydrofurans using titanocene(III) chloride as the radical initiator and formal synthesis of (±)-burseran 1 and (±)-dehydrocubebin 2.

Results and Discussion

The key concept applied in this approach relies on the formation of tetrahydrofuran rings by radical cyclization of appropriate epoxy olefinic compounds. Thus, readily available ketal 3 was subjected to O-alkylation reaction with cinnamyl bromides to afford compounds 4a in excellent yield (Scheme I). Deketalization of 4a by treatment with 80% aqueous acetic acid at RT followed by selective tosylation of primary hydroxyl group with tosyl chloride and pyridine furnished monotosylate 5a in moderate yield. Treatment of the tosylate 5a with sodium hydride at 0°C afforded the desired terminal epoxides 6a in almost quantitative yield. Radical cyclization of epoxy olefinic compound 6a using titanocene(III) chloride (Cp₂TiCl) at RT under argon yielded the cyclized product 7a as a mixture of cis and trans isomers in 1:1 ratio. Since 1H NMR shows no distinguishable signals for the isomers, the ratio was determined by GC (Column: ZB5, oven temperature: 150°C). Similarly, compounds 7b,c were prepared from 3 following the identical sequence as described for 7a. The substituted tetrahydrofuran 7c has already been employed as the synthetic intermediate by Balme and his co-workers for the total synthesis of burseran 1.

Note

Taking into account the context and the content of the paper, it seems like a laboratory study focused on the synthesis of specific compounds using a particular method. The paper is structured to detail the experimental procedures, results, and discussion in a clear and logical manner, allowing readers to understand the methodology and conclusions drawn from the research. The use of keywords such as radical cyclization, epoxides, titanocene(III) chloride, burseran, and dehydrocubebin highlights the specific focus areas of the study. The results are presented in a way that shows the progression from initial reactions to the final compounds synthesized, demonstrating the effectiveness of the methods used.

The paper concludes with a discussion of the broader implications of the research, mentioning the biological properties and therapeutic potential of the synthesized compounds. This highlights the significance of the work in the field of synthetic organic chemistry and the potential applications of the developed methodologies.

In summary, the paper provides a detailed account of a successful laboratory study, which not only contributes to the field of synthetic chemistry but also opens avenues for further research and applications in medicinal chemistry.
The alcohol 7a was subjected to oxidation with PDC in dry dichloromethane to furnish the aldehyde 8a in 80% yield as a mixture of cis and trans isomers in 1:1 ratio (Scheme II). This ratio was determined from the signal of aldehyde proton in $^1$H NMR spectrum, which appeared at $\delta$ 9.47 for the trans isomer and at $\delta$ 9.82 for the cis-isomer. When the mixture of aldehydes 8a was treated with DBU in dichloromethane at RT only the trans aldehyde 9a was obtained as a sole product in 95% yield. Hanessian has already synthesized $^5b$ (±)-burseran and (±)-dehydrocubebin from the aldehyde 9a. All the compounds were characterized by IR, $^1$H and $^{13}$C NMR and HRMS studies. Therefore, the formal synthesis of (±)-burseran and (±)-dehydrocubebin has now been completed.

In conclusion, the radical cyclization reaction of suitable epoxy olefinic compounds for the synthesis of 3,4-disubstituted tetrahydrofurans and formal synthesis of two bioactive lignans, burseran and dehydrocubebin in racemic form has been demonstrated.

**Experimental Section**

$^1$H and $^{13}$C NMR were recorded in CDCl$_3$ using TMS as an internal standard on 300 and 75 MHz spectrometer (Bruker) respectively and IR were recorded using a Shimadzu FT IR-8300 instrument. High-resolution mass spectra were obtained using a Qtof Micro YA263 instrument. Diethyl ether, tetrahydrofuran and toluene were dried over sodium. DMSO was dried over sodium hydride. Dichloromethane was freshly distilled from phophorus pentoxide. Pyridine was distilled over potassium hydroxide prior to use. Tosyl chloride was freshly crystallized from benzene prior to use.
Petroleum ether of boiling range 60-80°C and silica gel of 60-120 mesh were used for column chromatography.

**Preparation of compound 4**

To a magnetically stirred suspension of NaH (50% dispersion, 306 mg, 6.39 mmol) in dry THF (1 mL) was added drop-wise, a solution of alcohol 3 (1.0 g, 5.81 mmol) in dry THF:DMSO (10 mL, 10:1) at 0°C under N₂ over 30 min. Then it was stirred at RT for further 30 min. After the evolution of H₂ ceased (1 hr) a solution of appropriate cinnamyl bromide (1.54 g, 6.39 mmol) in dry THF (7 mL) was added drop-wise at 0°C over 30 min. The reaction mixture was then stirred at RT for 8 hr and carefully decomplexed with ice-cold water. After removal of most of the solvent under reduced pressure, the resulting residue was extracted with diethyl ether (4 × 25 mL). The combined ether extract was washed with water (2 × 10 mL), brine (1 × 10 mL) and finally dried (anhyd. Na₂SO₄). The solvent was removed under reduced pressure and the residual crude material on being subjected to column chromatography (10% ethyl acetate in petroleum ether) yielded the corresponding cinnamyl derivative 4a (1.73 g, 90%) as a viscous liquid. IR (neat): 2935, 2860, 1564, 1606, 1504, 1488, 1446, 1365, 1350, 1251 cm; ¹H NMR (CDCl₃): δ 1.30-1.58 (m, 10H), 3.40 (dd, J = 5.7, 9.6 Hz, 1H), 3.50 (dd, J = 5.7, 9.9 Hz, 1H), 3.68 (dd, J = 6.3, 8.1 Hz, 1H), 4.00 (dd, J = 6.3, 8.1 Hz, 1H), 4.09 (d, J = 6.0 Hz, 2H), 4.10-4.25 (m, 1H), 5.87 (s, 2H), 6.31 (td, J = 6.0, 15.9 Hz, 1H), 6.44 (d, J = 15.6 Hz, 1H), 6.68 (d, J = 8.1 Hz, 1H), 6.74 (dd, J = 1.2, 7.8 Hz, 1H), 6.86 (d, J = 1.2 Hz, 1H); ¹³C NMR (CDCl₃): δ 24.2, 24.4, 25.6, 27.3, 35.3, 36.9, 66.9, 71.7, 72.5, 74.8, 101.5, 106.1, 108.6, 110.3, 121.6, 124.4, 131.5, 132.8, 147.7, 148.4; HRMS: Calcd. for C₁₀H₁₄O₃Na (M+Na): m/z 355.1514. Found 355.1543.

Similarly, compound 4b (1.56 g, 95%) was obtained from the alcohol 3 (1.0 g) following the same procedure as described for compound 4a. IR (neat): 2935, 2860, 1448, 1365, 1280, 1163, 1103 cm; ¹H NMR (CDCl₃): δ 1.28-1.55 (m, 10H), 3.39 (dd, J = 5.7, 9.8 Hz, 1H), 3.49 (dd, J = 5.7, 9.8 Hz, 1H), 3.66 (dd, J = 6.1, 8.2 Hz, 1H), 3.97 (dd, J = 6.4, 8.1 Hz, 1H), 4.10 (d, J = 6.0 Hz, 2H), 4.21 (quintet, J = 6.2 Hz, 1H), 6.06 (td, J = 6.0, 15.9 Hz, 1H), 6.51 (d, J = 15.9 Hz, 1H), 7.11-7.30 (m, 5H); ¹³C NMR (CDCl₃): δ 23.7, 23.9, 25.0, 34.8, 36.3, 66.4, 71.2, 71.9, 74.3, 109.9, 125.7, 126.3, 127.6, 128.4, 128.5, 132.5; HRMS: Calcd. for C₁₈H₂₅O₄Na (M+Na): m/z 311.1615. Found 311.1648.

Similarly, compound 4c (1.75 g, 80%) was obtained from the alcohol 3 (1.0 g) following the same procedure as described for compound 4a. IR (neat): 2935, 2860, 1583, 106, 1450, 1417, 1334, 1240 cm; ¹H NMR (CDCl₃): δ 1.33-1.39 (m, 2H), 1.44-1.60 (m, 8H), 3.47 (dd, J = 5.6, 9.8 Hz, 1H), 3.55 (dd, J = 5.6, 9.8 Hz, 1H), 3.72 (dd, J = 6.4, 7.9 Hz, 1H), 3.81 (s, 3H), 3.84 (s, 6H), 4.04 (dd, J = 6.2, 7.9 Hz, 1H), 4.16 (d, J = 6.0 Hz, 2H), 4.26-4.32 (m, 1H), 6.16 (td, J = 6.0, 15.8 Hz, 1H), 6.50 (d, J = 15.8 Hz, 1H), 6.58 (s, 2H); ¹³C NMR (CDCl₃): δ 24.1 24.4, 25.5, 35.2, 36.8, 56.4, 61.3, 63.5, 65.7, 66.9, 71.8, 72.4, 74.7, 76.1, 103.9, 110.4, 125.7, 132.7, 132.9, 153.6; HRMS: Calcd. for C₁₂H₁₆O₃Na (M+Na): m/z 401.1940. Found 401.1944.

**Preparation of compound 5**

The compound 4a (1.00 g, 3.01 mmol) was stirred overnight with 80% aqueous acetic acid (15 mL) at 25°C (monitored by TLC). Removal of acetic acid on a rotary evaporator (temperature 40°C) using dry toluene (3 × 25 mL) afforded the intermediate diol as a highly viscous oil. This was dissolved in dry CH₂Cl₂ (10 mL) and then pyridine (238 mg, 3.01 mmol) and p-toluene sulphonyl chloride (630 mg, 3.31 mmol) was added and stirred overnight at RT. The reaction mixture was decomposed with 5% hydrochloric acid (5 mL) and was extracted with diethyl ether (4 × 25 mL). The combined ether extract was successively washed with water (2 × 10 mL), brine (1 × 10 mL) and finally dried over anhyd. Na₂SO₄. The solvent was removed under reduced pressure and the residual crude material on being subjected to column chromatography (25% ethyl acetate in petroleum ether) yielded the corresponding monotosyl derivative 5a (770 mg, 63%) as a gummy material. IR (neat): 3402, 2898, 1487, 1444, 1359, 1274 cm; ¹H NMR (CDCl₃): δ 2.34 (s, 3H), 3.40-3.45 (m, 1H), 3.90-4.10 (m, 6H), 5.86 (s, 2H), 5.94 (td, J = 6.1, 15.8 Hz, 1H), 6.19 (d, J = 15.5 Hz, 1H), 6.66 (d, J = 7.9 Hz, 1H), 6.71 (d, J = 7.9 Hz, 1H), 6.82 (s, 1H), 7.24 (d, J = 7.9 Hz, 2H), 7.71 (d, J = 8.1 Hz, 2H); ¹³C NMR (CDCl₃): δ 21.5, 68.3, 69.8, 70.6, 71.9, 101.0, 105.7, 108.2, 121.2, 123.3, 127.8, 129.9, 130.0, 130.8, 132.6, 144.9, 147.4, 147.9; HRMS: Calcd. for C₁₉H₁₈O₄SNa (M+Na): m/z 429.0984. Found 429.0948.

Similarly, compound 5b (817 mg, 65%) was obtained from the compound 4b (1.0 g) following the
same procedure as described for compound 5a. IR (neat): 3425, 2864, 1596, 1492, 1452, 1359, 1174 cm; $^1$H NMR (CDCl$_3$): $\delta$ 2.44 (s, 3H), 3.53-3.56 (m, 1H), 4.01-4.16 (m, 6H), 6.22 (td, $J = 6.1$, 15.9 Hz, 1H), 6.57 (d, $J = 15.9$ Hz, 1H), 7.28-7.40 (m, 7H), 7.60 (d, $J = 8.3$ Hz, 2H); $^{13}$C NMR (CDCl$_3$): $\delta$ 21.4, 68.1, 69.4, 69.9, 70.6, 125.1, 126.3, 127.7, 128.7, 128.8, 129.8, 132.7, 136.3, 144.9; HRMS: Calcd. for C$_{19}$H$_{22}$O$_3$Na (M+Na): $m/z$ 385.1078. Found 385.1054.

Similarly, compound 5c (717 mg, 60%) was obtained from the compound 4c (1.0 g) following the same procedure as described for compound 5a. IR (neat): 3490, 2939, 2877, 1583, 1506, 1461, 1357, 1336, 1242, 1176, 1124 cm; $^1$H NMR (CDCl$_3$): $\delta$ 2.33 (s, 3H), 3.44-3.49 (m, 1H), 3.76 (s, 3H), 3.78 (s, 6H), 3.93-4.11 (m, 6H), 6.06 (td, $J = 5.9$, 15.6 Hz, 1H), 6.41 (d, $J = 16.1$ Hz, 1H), 6.53 (s, 2H), 7.23 (d, $J = 7.1$ Hz, 2H), 7.69 (d, $J = 8.1$ Hz, 2H); $^{13}$C NMR (CDCl$_3$): $\delta$ 21.9, 56.5, 61.3, 68.7, 70.4, 71.1, 72.3, 104.0, 125.2, 128.3, 130.3, 132.6, 133.3, 145.5, 153.7; HRMS: Calcd. for C$_{25}$H$_{28}$O$_3$Na (M+Na): $m/z$ 475.1403. Found 475.1400.

Preparation of epoxy olefin compound 6

To a magnetically stirred solution of NaH (50% dispersion, 59 mg, 1.23 mmol) in dry THF (1 mL) was added dropwise a solution of compound 5a (500 mg, 1.23 mmol) in dry THF:DMSO (10 mL, 10:1) at 0°C under N$_2$. After the evolution of H$_2$ ceased, the reaction mass was stirred at RT for 3 hr and then carefully decomposed with ice-cold water. After removal of most of the solvent under reduced pressure, the resulting residue was extracted with diethyl ether (3 × 25 mL). The combined ether extract was successively washed with water (2 × 10 mL), brine (1 × 10 mL) and finally dried over anhyd. Na$_2$SO$_4$. The solvent was removed under reduced pressure and the residual crude material on purification by column chromatography over silica gel (20% ethyl acetate in petroleum ether) afforded pure terminal epoxide 6a (274 mg, 95%) in quantitative yield. IR (neat): 2986, 1504, 1488, 1444, 1249 cm; $^1$H NMR (CDCl$_3$): $\delta$ 2.62 (dd, $J = 2.7$, 5.0 Hz, 1H), 2.80 (t, $J = 5.0$ Hz, 1H), 3.15-3.20 (m, 1H), 3.42 (dd, $J = 5.8$, 11.4 Hz, 1H), 3.75 (dd, $J = 3.0$, 11.4 Hz, 1H), 4.14-4.18 (m, 2H), 3.85 (s, 2H), 6.10 (td, $J = 6.1$, 15.8 Hz, 1H), 6.51 (d, $J = 15.8$ Hz, 1H), 6.73 (d, $J = 8.0$ Hz, 1H), 6.81 (dd, $J = 1.6$, 8.0 Hz, 1H), 6.91 (d, $J = 1.6$ Hz, 1H); $^{13}$C NMR (CDCl$_3$): $\delta$ 44.7, 51.3, 71.2, 72.3, 126.0, 126.9, 128.2, 133.2, 137.0; HRMS: Calcd. for C$_{19}$H$_{22}$O$_3$Na (M+Na): $m/z$ 257.0782. Found 257.0724.

Similarly, compound 6b (260 mg, 99%) was obtained from compound 5b (500 mg) following the same procedure as described for compound 6a. IR (neat): 3003, 2925, 2854, 1496, 1448, 1363, 1251, 1114 cm; $^1$H NMR (CDCl$_3$): $\delta$ 2.54 (dd, $J = 2.7$, 4.9 Hz, 1H), 2.72 (dd, $J = 4.5$, 4.7 Hz, 1H), 3.08-3.12 (m, 1H), 3.35 (dd, $J = 5.8$, 11.4 Hz, 1H), 3.69 (dd, $J = 2.9$, 11.4 Hz, 1H), 4.10-4.14 (m, 2H), 6.20 (td, $J = 6.0$, 16.0 Hz, 1H), 6.53 (d, $J = 15.9$ Hz, 1H), 7.12-7.32 (m, 5H); $^{13}$C NMR (CDCl$_3$): $\delta$ 44.7, 51.3, 71.2, 72.3, 126.0, 126.9, 128.2, 133.2, 137.0; HRMS: Calcd. for C$_{19}$H$_{22}$O$_3$Na (M+Na): $m/z$ 213.0884. Found 213.0899.

Similarly, compound 6c (300 mg, 97%) was obtained from compound 5c (500 mg) following the same procedure as described for compound 6a. IR (neat): 2995, 2939, 2639, 1674, 1583, 1506, 1456, 1419 cm; $^1$H NMR (CDCl$_3$): $\delta$ 2.61-2.64 (m, 1H), 2.81 (t, $J = 4.6$ Hz, 1H), 3.19 (m, 1H), 3.47 (dd, $J = 5.9$, 11.4 Hz, 1H), 3.83 (s, 3H), 3.85 (s, 6H), 4.18-4.23 (m, 2H), 6.19 (td, $J = 6.1$, 15.7 Hz, 1H), 6.53 (d, $J = 15.7$ Hz, 1H), 6.60 (s, 2H); $^{13}$C NMR (CDCl$_3$): $\delta$ 44.4, 50.9, 56.2, 60.9, 69.6, 70.8, 71.8, 103.6, 125.2, 132.8, 153.4; HRMS: Calcd. for C$_{19}$H$_{22}$O$_3$Na (M+Na): $m/z$ 303.1208. Found 303.1209.

Preparation of compound 7

A red solution of Cp$_2$TiCl$_3$ (214 mg, 0.86 mmol) in deoxygenated THF (11 mL) was stirred with activated zinc dust (85 mg, 1.29 mmol) under argon until it turned green. Then the resulting green solution was added dropwise to a stirred solution of the epoxy-olefin 6a (100 mg, 0.43 mmol) in dry THF (11 mL) during 1.5 hr at RT under argon. It was further stirred for an additional 30 min and then decomposed with saturated aqueous sodium dihydrogen phosphate (10 mL). After removal of most of the THF under reduced pressure, the crude material obtained was extracted with diethyl ether (3 × 25 mL). The combined ether extract was successively washed with water (10 mL), brine (10 mL) and finally dried over anhyd. Na$_2$SO$_4$. After removal of the volatiles the crude material obtained was purified by column chromatography over silica gel to furnish compound 7a (79 mg, 78%). IR (neat): 3396, 2883, 1504, 1487, 1440, 1247 cm; $^1$H NMR (CDCl$_3$): $\delta$ 2.43-2.54 (m, 4H), 2.59-2.68 (m, 2H), 2.81 (dd, $J = 5.2$, 13.1 Hz, 2H), 3.45-3.58 (m, 4H), 3.66-3.97 (m, 8H), 5.93 (s, 4H), 6.62-6.75 (m,
6H); $^{13}$C NMR (CDCl$_3$): $\delta$ 33.7, 39.6, 43.1, 44.1, 44.3, 47.6, 61.9, 65.0, 71.3, 72.8, 73.7, 95.3, 101.2, 101.5, 108.6, 109.2, 109.4, 121.7, 121.9, 134.8, 146.3 and 148.1. HRMS: Calcd. for C$_{13}$H$_{16}$O$_5$Na (M+Na): $m/z$ 259.0939. Found 259.1024.

Similarly, compound 7b (76 mg, 75%) was obtained from compound 6b (100 mg) following the same procedure as described for compound 7a. IR (neat): 3388, 2933, 2856, 1521, 1452, 1365 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta$ 2.36-2.67 (m, 3H), 2.82 (dd, $J = 5.1, 13.2$ Hz, 1H), 2.46-2.55 (m, 2H), 2.68-2.70 (m, 2H), 2.74 (dd, $J = 7.2, 14.0$ Hz, 1H), 2.85 (dd, $J = 5.1, 13.2$ Hz, 1H), 3.47-3.56 (m, 2H), 3.58-3.63 (m, 2H), 3.65-3.76 (m, 2H), 3.79-3.90 (m, 22H), 3.93-4.01 (m, 2H), 6.39 (s, 2H), 6.40 (s, 2H); HRMS: Calcd. for C$_{13}$H$_{16}$O$_5$Na (M+Na): $m/z$ 215.1048. Found 215.0101.

Similarly, compound 7c (Ref 5e) (70 mg, 70%) was obtained from compound 6c (100 mg) following the same procedure as described for compound 7a. IR (neat): 3444, 2927, 2850, 1589, 1506, 1461, 1421, 1308, 1238, 1126 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta$ 2.17 (m, 2H), 2.47-2.55 (m, 2H), 2.64-2.70 (m, 2H), 2.74 (dd, $J = 7.2, 14.0$ Hz, 1H), 2.85 (dd, $J = 5.1, 13.2$ Hz, 1H), 3.47-3.56 (m, 2H), 3.58-3.63 (m, 2H), 3.65-3.76 (m, 2H), 3.79-3.90 (m, 22H), 3.93-4.01 (m, 2H), 6.39 (s, 2H), 6.40 (s, 2H); HRMS: Calcd. for C$_{13}$H$_{16}$O$_5$Na (M+Na): $m/z$ 305.1365. Found 305.1364.

**Preparation of compound 8a**

To a stirred solution of compound 7a (100 mg, 0.42 mmol) in dry dichloromethane (10 mL) was added pyridinium dichromate (239 mg, 0.63 mmol) in a single lot at RT. The reaction mixture was then stirred for 24 hr in the dark. After this, most of the solvent was removed under reduced pressure and the residue obtained was filtered through a bed of silica gel using ethyl acetate as eluent. The solvent was removed under reduced pressure to obtain the residue. It was stirred for further 16 hr at the same condition. Then reaction mixture was diluted with dichloromethane and was filtered through a bed of silica gel. The solvent was removed and the crude residue obtained was purified by column chromatography over silica gel to afford the pure trans aldehyde 9a (47 mg, 95%) as a sole product. IR (neat): 2923, 2856, 2781, 1722, 1608, 1504, 1488 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta$ 2.16 (dd, $J = 8.7, 15.8$ Hz, 1H), 2.46-2.55 (m, 1H), 2.68-2.74 (m, 2H), 3.43-3.47 (m, 1H), 3.83-3.94 (m, 2H), 4.00-4.04 (m, 1H), 5.87 (s, 2H), 6.50-6.59 (m, 2H), 6.67 (d, $J = 7.8$ Hz, 1H), 9.41 (d, $J = 1.9$ Hz, 1H); $^{13}$C NMR (CDCl$_3$): $\delta$ 38.4, 43.2, 57.2, 67.5, 70.3, 73.3, 74.8, 101.1, 108.5, 109.2, 121.8, 133.1, 200.5; HRMS: Calcd. for C$_{13}$H$_{16}$O$_5$Na (M+Na): $m/z$ 257.0782. Found 257.0781.

**Acknowledgements**

The authors thank the Department of Science and Technology, New Delhi for financial assistance. SJ and MP thank CSIR, New Delhi for awarding their research fellowships.

**References**

1. (a) MacRae W D & Towers G H N, *Phytochemistry*, 23, 1984, 1207;
