

## SYNTHESIS OF UNSYMMETRICAL BIFLAVONE

THE Ullmann condensation between 2-hydroxy-4, 6-dimethoxy-3-iodoacetophenone and 2, 4-dibenzoyloxy-3-iodoacetophenone yields a mixture of 2-hydroxy-4, 6-dimethoxy-2', 4'-dibenzoyloxy-3, 3'-diacetyl-biphenyl (1: a), 2, 2'-dihydroxy-4, 4', 6, 6'-tetramethoxy-3, 3'-diacetyl-biphenyl (1: b) and 2, 2', 6, 6'-tetrabenzoyloxy-3, 3'-diacetyl-biphenyl (1: c). Compound 1: a on condensation with benzoic anhydride and sodium benzoate followed by hydrolysis affords the unsymmetrical biflavone (2).

Several symmetrical biflavones have so far been synthesised by the simple or crossed Ullmann reaction of the appropriate iodoflavones<sup>1-3</sup>, the dehydrogenation<sup>4-6</sup> and alkaline hydrogen peroxide oxidation<sup>7</sup> of the corresponding bichalcone, double Baker-Venkataraman transformation of the biphenyl derivatives<sup>8-9</sup> followed by ring closure and the oxidative coupling of the suitable flavone<sup>10</sup>. By Allan-Robinson condensation, the biflavone<sup>11</sup> linked through a methylenedioxy group has been synthesised. Symmetrical biflavans have been synthesised by the reductive dimerization of the flavones<sup>12</sup>. In the present communication, we wish to report our observations on the approach to the synthesis of the unsymmetrical biflavone (2) from the biphenyl derivative (1: a).

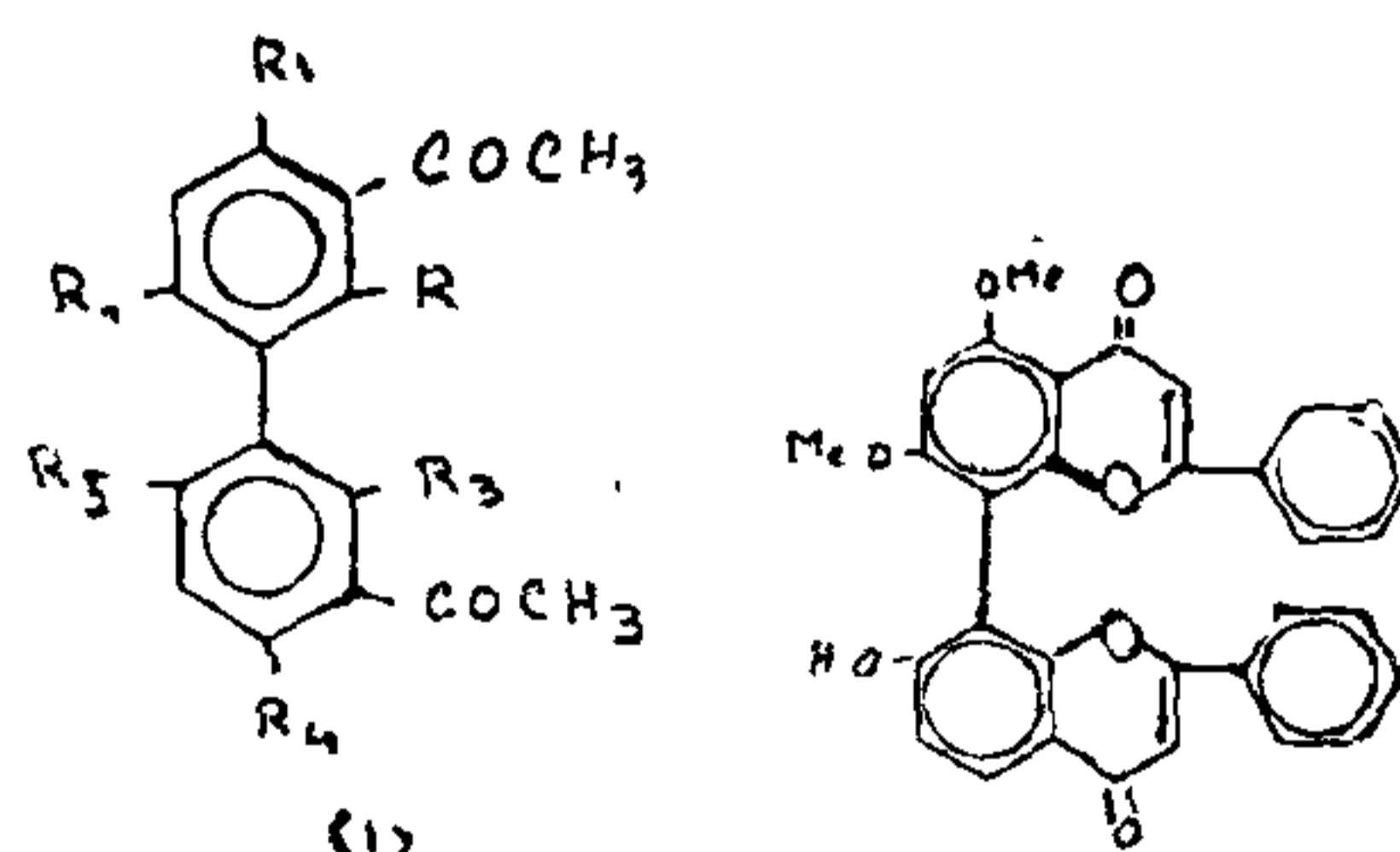
The monoiodination of xanthoxylin gave 2-hydroxy-4, 6-dimethoxy-3-iodoacetophenone<sup>13</sup>. Monoiodination of resacetophenone gave 2, 4-dihydroxy-3-iodoacetophenone which on benzylation gave the dibenzoate<sup>3</sup>. These two iodo derivatives on reaction with copper bronze at 280° gave a mixture of 2-hydroxy-4, 6-dimethoxy-2', 4'-dibenzoyloxy-3, 3'-diacetyl-biphenyl (1: a), 2, 2'-dihydroxy-4, 4', 6, 6'-tetramethoxy-3, 3'-diacetyl-biphenyl (1: b) and 2, 2', 6, 6'-tetrabenzoyloxy-3, 3'-diacetyl-biphenyl (1: c).

Compound (1: a) was separated from the mixture by dissolving in acetone-water (7:3) mixture in which compounds 1: b and 1: c are insoluble. The IR spectrum of compound (1: a) has bands at 2950-3100 (chelated OH), 1690 and 1630 cm<sup>-1</sup> (C=O). Condensation of the compound 1: a with benzoic anhydride and sodium benzoate, followed by hydrolysis gave I-5, I-7-dimethoxy-II-hydroxy- [I-8, II-8] biflavone (2). Its IR spectrum has bands at 3460 (OH) and 1645 cm<sup>-1</sup> (C=O). In the mass spectrum of the biflavone (2) showed a molecular ion at mass 518 having elemental composition C<sub>32</sub>H<sub>22</sub>O<sub>7</sub>. The general fragmentation pattern was typical of a C-C linked biflavone<sup>14,15</sup>.

## Experimental

(A) 2-Hydroxy-4, 6-dimethoxy-2', 4'-dibenzoyloxy-3, 3'-diacetyl-biphenyl (1: a): A mixture of 2-hydroxy-3-iodo-4, 6-dimethoxy acetophenone (6.4 g), 2,

4-dibenzoyloxy-3-iodoacetophenone (9.7 g), copper bronze (30 g) in dimethyl-formamide (150 ml) was refluxed in a metal bath for 4 hours, filtered hot and washed with 20 ml of the solvent. Water (200 ml) was added to the combined filtrate. The precipitate was filtered and dissolved in acetone-water (140:60). The insoluble portion is a mixture of compounds 1: b and 1: c. The acetone-water (7:3) dissolved portion is precipitated by the addition of water. Compound 1: a was crystallised from water-acetone (2:1) mixture as colourless needles, m.p. 206° C. (Found C, 69.5; H, 4.5; Mol. wt. by mass spectrometry, 554; C<sub>32</sub>H<sub>26</sub>O<sub>9</sub> requires: C, 69.3; H, 4.65%; Mol. wt. 554).



	R	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>
a:	OH	OMe	OMe	OBz	H	OBz
b:	OH	OMe	OMe	OH	OMe	OMe
c:	OBz	H	OBz	OBz	H	OBz

(B) I-5, I-7-Dimethoxy-II-7-Hydroxy [I-8, II-8] biflavone (2): A mixture of 2-hydroxy-4, 6-dimethoxy-2', 4'-dibenzoyloxy-3, 3'-diacetyl-biphenyl (5 g), benzoic anhydride (40 g) and sodium benzoate (7 g) was heated at 180-185° C for 4 hours and after cooling, alcohol (150 ml) was added and the mixture was boiled during the gradual addition of potassium hydroxide (18 g dissolved in 150 ml of water) and then refluxed for about 20 minutes. After removal of greater part of alcohol by distillation, the residue was dissolved in water. The filtered solution was saturated with carbon dioxide and the precipitated biflavone (2) was filtered and recrystallised from dilute alcohol as yellow needles, m.p. 219-220° C. (Found C, 73.85; H 4.15; OMe, 11.7; Mol. wt. by mass spectrometry, 518; C<sub>32</sub>H<sub>22</sub>O<sub>7</sub> requires C, 74.00; H, 4.25; 2 OMe, 11.95%, Mol. wt. 518).

The authors are thankful to Dr. (Mrs.) Krishna Misra for the helpful discussions and to Miss T. Suseela for her conscientious efforts in preparing this manuscript. One of the authors (P. G.) is grateful to the C.S.I.R., New Delhi, for financial support.

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June 30, 1977.

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1. Murti, V. V. S., Raman, P. V. and Seshadri, T. R., *Tetrahedron*, 1967, **23**, 397.
2. Nakazawa, K. and Ito, M., *Chem. Pharm. Bull. (Tokyo)*, 1963, **11**, 283.
3. Jurd, L., *Chem. and Ind.*, 1961, p. 322.
4. Mathai, K. P. and Sethna, S., *J. Indian Chem. Soc.*, 1964, **41**, 347.
5. —, Kanakalakshmi, B. and Sethna, S., *Ibid.*, 1967, **44**, 148.
6. Kanakalakshmi, B., *Ibid.*, 1969, **46**, 279.
7. Gandhi, P., *Indian J. Chem.*, 1976, **14B**, 1009.
8. Ahmad, S. and Razaq, S., *Tetrahedron Letters*, 1971, **48**, 4633.
9. Gandhi, P. and Tiwari, R. D., *J. Indian Chem. Soc.*, 1975, **52**, 1111.
10. Molyneux, R. J., Waisé, A. C. and Haddon, W. F., *Tetrahedron*, 1970, **26**, 1409.
11. Gandhi, P. and Tiwari, R. D., *Curr. Sci.* 1976, **45**, 18.
12. — and —, *Indian J. Chem.*, 1976, **14B**, 632.
13. Nakazawa, K., *Chem. Pharm. Bull. (Tokyo)*, 1962, **10**, 1036.
14. Gandhi, P., *D.Phil. Thesis*, Allahabad University, 1974.
15. Natarajan, S., Murti, V. V. S. and Seshadri, T. R., *Indian J. Chem.*, 1969, **7**, 751.

#### SOME NEW HYDROXY SANDARACOPIMAR-15-ENES FROM *PREMNA LATIFOLIA* ROXB.

WE report in this communication the isolation and constitution of four diterpene alcohols from the root-bark of *Premna latifolia* Roxb. (Verbenaceae). The residues obtained from *n*-hexane extracts were chromatographed over silica gel, after removal of latex, when the four compounds A, B, C and D separated out and their properties are recorded below. All these compounds gave red Liebermann-Burchard test.

Compound-A appeared as colourless needles from *n*-hexane, m.p. 42–43° (C<sub>20</sub>H<sub>34</sub>O; m/e M<sup>+</sup>, 290), [α]<sub>D</sub><sup>20</sup> – 6.6° (c, 1.0, CHCl<sub>3</sub>); no absorption in the U.V. above 200 nm; I.R.  $\nu_{\text{max}}^{\text{CCl}_4}$  cm<sup>-1</sup> 3620 (–OH), 3090, 1820, 1640 and 910 (vinyl), 1390, 1370 (gem dimethyl) and <sup>1</sup>H NMR (XL-100 spectrum) CCl<sub>4</sub> (δ) 0.85 (s, 6H, two *t*-CH<sub>3</sub>), 0.97 (s, 3H, *t*-CH<sub>3</sub>), 1.19 (s, 3H, *t*-CH<sub>3</sub>) and an ABX pattern characteristic of vinyl group (4.73, dd, J = 10.5, 1.5 Hz, 1H; 4.77,

dd, J = 17.5, 1.5 Hz, 1H and 5.63, dd, J = 17.5, 10.5 Hz, 1H). The presence of five terminal pendant groups, viz., four *t*-methyls and a vinyl group, besides its molecular formula suggest a pimarane, rosane or cassane type structure for compound-A. A survey of literature reveals that these characteristics are in agreement with those recorded for sandaracopimar-15-en-8β-ol (I) which was isolated by Corbett *et al.*<sup>1</sup> from *Dacrydium colensoi* and Bohlmann *et al.*<sup>2,3</sup> from *Garuleum pinnatifidum* DC., *G. bipinnatum* Less., *Osteospermum fruticosum* (L.) Norl., *O. junceum* Berg., *O. corymbosum* and *O. rotundifolium*.

Compound-B crystallised from *n*-hexane as colourless needles, m.p. 204–206° (C<sub>20</sub>H<sub>32</sub>O<sub>2</sub>; m/e M<sup>+</sup>, 304), [α]<sub>D</sub><sup>20</sup> – 5.5° (c, 1.0, pyridine); no absorption in the U.V. above 200 nm; I.R.  $\nu_{\text{max}}^{\text{KBr}}$  cm<sup>-1</sup> 3370 (–OH), 3080, 1820, 1635 and 915 (vinyl), 1698 (six membered ketone) and 1375, 1395 (gem dimethyl) and <sup>1</sup>H NMR (XL-100 spectrum) CCl<sub>4</sub> (δ) 0.85 (s, 6H, two *t*-CH<sub>3</sub>), 1.22 (s, 3H, *t*-CH<sub>3</sub>), 1.24 (s, 3H, *t*-CH<sub>3</sub>), an ABX pattern of vinyl (4.86, dd, J = 10.5, 1.5 Hz; 1H; 4.90, dd, J = 17.5, 1.5 Hz, 1H and 5.76, dd, J = 17.5, 10.5 Hz, 1H) and 2.08–2.47 (broad, 4H). It did not form a 2, 4-dinitrophenylhydrazone, perhaps, the carbonyl is hindered. Further, it did not yield an acetate with Ac<sub>2</sub>O/pyridine indicating that the hydroxyl is either hindered or tertiary. The presence of five terminal pendant groups, the molecular formula, besides the co-occurrence of I indicates that it could well be considered as sandaracopimar 15-en-8β-ol with a carbonyl function. The position of the carbonyl group could be established by dehydration using *p*-toluenesulphonic acid, when a liquid (C<sub>20</sub>H<sub>30</sub>O) was obtained, U.V.  $\lambda_{\text{max}}^{\text{EtOH}}$  252 nm (log ε, 3.92) indicating α, β-unsaturated ketone further confirmed by I.R.  $\nu_{\text{max}}^{\text{liq. film}}$  1665 cm<sup>-1</sup> and absence of hydroxyl bands. It formed a 2, 4-dinitrophenylhydrazone, m.p. 155–157° (C<sub>20</sub>H<sub>34</sub>O<sub>4</sub>N<sub>4</sub>). The <sup>1</sup>H NMR spectrum in CCl<sub>4</sub> showed no mere olefinic protons besides the three vinylic hydrogens, thereby showing that the double bond formed was tetra-substituted and reasonably assumed to be Δ<sup>8,9</sup>. The carbonyl function could then be present in 7, 11 or 14 positions, and out of these 11 position was preferred in order to account for a single proton signal at 2.73 (δ), dm, J = 13 Hz assignable<sup>17,2</sup> to C1-β H in this anhydro ketone, the constitution of which could be represented as sandaracopimar-8, 15 dien-11-one (II b) and the starting keto alcohol is 8β hydroxysandaracopimar 15-en-11-one (II a). Sodium borohydride reduction of II a gave a diol (II c), m.p. 158–162 (C<sub>20</sub>H<sub>34</sub>O<sub>2</sub>), [α]<sub>D</sub><sup>20</sup> + 21.6° (c, 1.0, CHCl<sub>3</sub>) which neither reacted periodic acid nor could be acetylated with Ac<sub>2</sub>O/pyridine and showed in <sup>1</sup>H NMR spectrum a single proton signal at 4.44 δ, broad w<sub>1</sub> 7 Hz assignable