

## LETTERS TO THE EDITOR

## SYNTHESIS OF SOME NEW SCHIFF BASES DERIVED FROM CAMPHOR AND THEIR BIOLOGICAL ACTIVITIES

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A LARGE number of Schiff bases are known to possess useful biological activities like fungicidal<sup>1</sup>, bactericidal<sup>2</sup>, insecticidal<sup>3</sup> and tuberculostatic<sup>4</sup> activities. The medicinal importance of camphor has been well established for a long time.

In continuation of our studies on potential pesticides<sup>5-8</sup> we have carried out in the present work the synthesis of some new Schiff bases derived from camphor and screened them for antifungal and antibacterial activities.

Due to the fact that C-2 carbonyl of camphor is less reactive, El Ashray *et al.*<sup>9</sup> prepared camphor benzoylhydrazone by the condensation of camphor with benzoylhydrazine in a high boiling protic solvent (isopropanol) and have concluded that it may be due to the steric hindrance of the methyl group at C-1. In the present investigation, different experimental conditions were tried and 2-(*p*-substituted phenyl)imino-borane was obtained in varying yields. It was finally observed that when camphor was subjected to Schiff

condensation with different *p*-substituted primary aromatic amines, in the presence of traces of mineral acids (preferably conc. H<sub>2</sub>SO<sub>4</sub>) gave better yields of the imino-boranes (I to IV). In the synthesis of Schiff bases of camphor, it was found that best yields were obtained by refluxing with absolute ethanol under anhydrous conditions. The yields of Schiff bases in this system varied from 52-82% whereas under other conditions the yields were very low (15-25%). All the compounds have adequately been characterised by their correct elemental analysis and spectral data (IR and PMR).

The IR spectra of Schiff bases have been assigned by comparison with those of the corresponding amines and camphor. The absence of —NH stretching band and the presence of a band in the vicinity of 1600 cm<sup>-1</sup> (—N = C) confirmed the assigned structure. Further, all the compounds showed bands around 1385 and 1365 cm<sup>-1</sup> which can be assigned to the symmetric and asymmetric gem methyl stretching mode of terpene nucleus<sup>10,11</sup> and this impression is reinforced by the PMR spectra. For compounds (nos. I, III and IIIb) strong intense band around 1680-1700 cm<sup>-1</sup> may be

TABLE 1

Physical properties of camphor derived Schiff bases (I-IVd)

Compd.	M.P.	Yield %	Molecular formula*
I	132	76	C <sub>21</sub> H <sub>30</sub> N <sub>2</sub> O
IIa	138-9	54	C <sub>26</sub> H <sub>33</sub> N <sub>3</sub>
IIb	143	56	C <sub>27</sub> H <sub>35</sub> N <sub>3</sub>
IIc	173-4	62	C <sub>27</sub> H <sub>35</sub> N <sub>3</sub>
IId	163	47	C <sub>27</sub> H <sub>35</sub> N <sub>3</sub>
IIIa	154	77	C <sub>27</sub> H <sub>33</sub> N <sub>3</sub> O
IIIb	198	79	C <sub>28</sub> H <sub>35</sub> N <sub>3</sub> O
IVa	185	82	C <sub>17</sub> H <sub>24</sub> N <sub>4</sub> SO <sub>2</sub>
IVb	110	73	C <sub>22</sub> H <sub>28</sub> N <sub>4</sub> SO <sub>2</sub>
IVc	175-6	75	C <sub>25</sub> H <sub>28</sub> N <sub>4</sub> SO <sub>2</sub>
IVd	281	68	C <sub>20</sub> H <sub>24</sub> N <sub>4</sub> SO <sub>2</sub>

\*The observed elemental analyses of C, H and N agreed with the theoretical values within the limits of experimental error.

TABLE 2

PMR (CDCl<sub>3</sub>) data of Schiff bases

Compd	Chemical shift (δ)
I	1.35 (s, 6H, geminal dimethyl group), 1.63 (m, 9H, CH <sub>3</sub> × 3); 2.72 (m, 4H, $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{N}-\begin{array}{l} \text{CH}_2 \\ \text{CH}_2 \end{array} \end{array}$ 3.27 (m, 6H, CH <sub>2</sub> × 3); 7.00-7.45 (m, 4H, ArH).
IIa	1.38 (s, 6H, geminal dimethyl group); 1.72 (s, 3H, CH <sub>3</sub> ); 3.45 (m, 6H, CH <sub>2</sub> × 3), 2.98 (m, 8H, —N— $\begin{array}{l} \text{CH}_2 \\ \text{CH}_2 \end{array}$ × 2) and; 7.05-7.54 (m, 9H, Ar-H).
IIIb	1.36 (s, 6H, geminal dimethyl group); 1.68 (s, 3H, CH <sub>3</sub> ); 2.30 (s, 3H, CH <sub>3</sub> ); 3.80 (m, 6H, CH <sub>2</sub> × 3); 2.70 (m, 4H, $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{N}-\begin{array}{l} \text{CH}_2 \\ \text{CH}_2 \end{array} \end{array}$ ); 3.25 (m, 4H, —N— $\begin{array}{l} \text{CH}_2 \\ \text{CH}_2 \end{array}$ ); 7.00-7.40 (m, 8H, Ar-H).

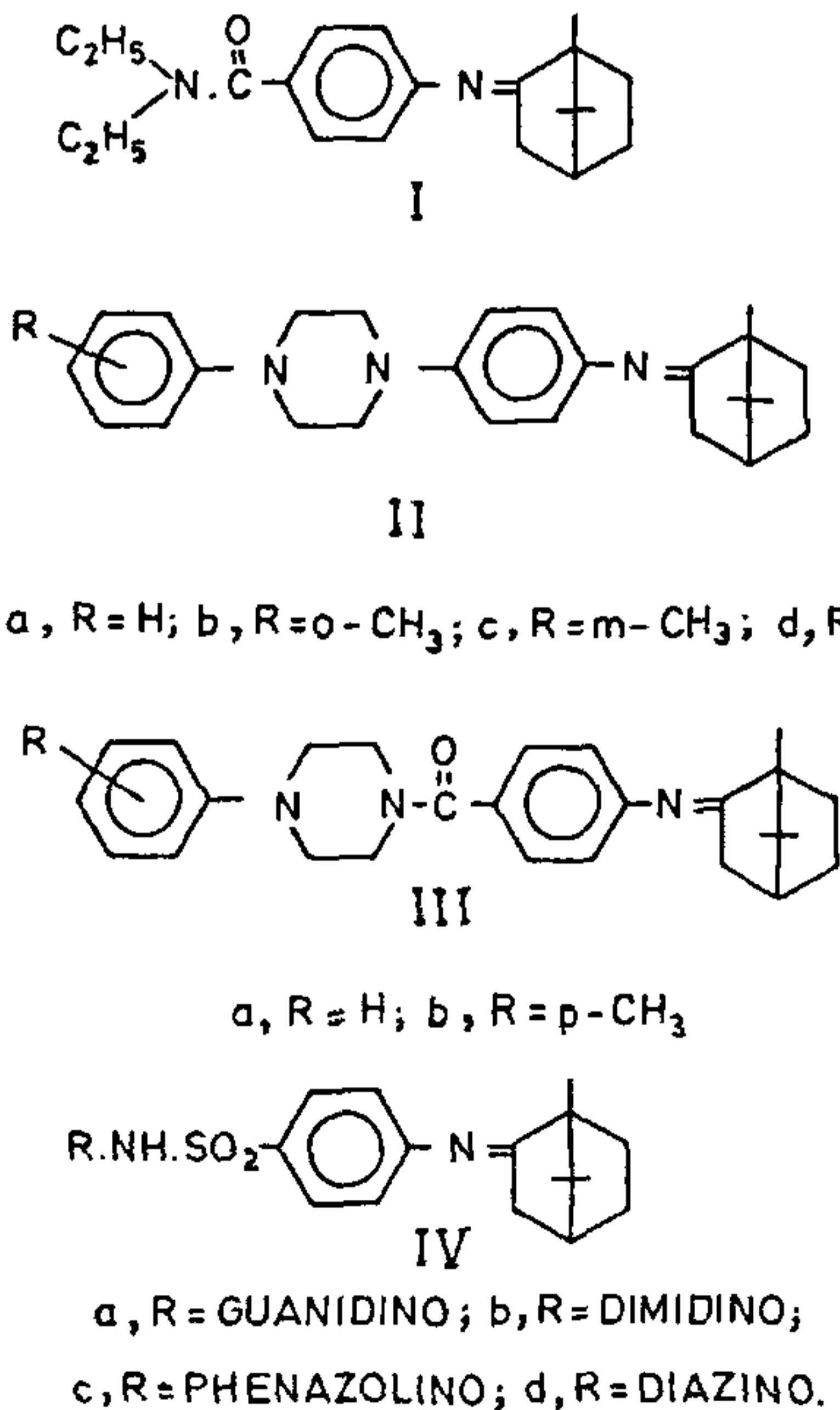
associated with the carbonyl absorption. In addition to these, the Schiff's bases of sulphonamide (IVa-d) showed additional absorption band around  $1380\text{ cm}^{-1}$  and in this region the sulphonamide group frequently is expected to be observed. The PMR data of these Schiff's bases were compatible with the structure assigned (table 2).

#### Biological screening results:

The synthesised Schiff's bases were tested for their antifungal activity against *Aspergillus niger*, *A. terreus* and *Helminthosporium sativum* using agar plate diffusion technique<sup>12</sup> and for antibacterial activity against *Bacillus pumilus*, *B. subtilis*, *B. megaterium*, *B. polymyxa*, *B. cereus* and *Staphylococcus aureus* using the method of Varma *et al.*<sup>13</sup>

Camphor, the parent compound of this series, was inactive at any of the three concentrations with the fungi tested. It was found that compounds IIa and IVc were active against *H. sativum* and *A. terreus* even at low concentrations whereas compound IIb was active only at 1000 ppm concentration and the activity decreased markedly on dilution. However, none of the other compounds was strong enough to merit follow-up studies.

#### SCHEME - I



Most of the Schiff bases were active against all the bacteria tested and the compounds I, IIc and d and IVc and d possessed high antibacterial activity, the activity of I, IIc and IVc against *B. polymyxa* and *B. megaterium* is noteworthy. Here it is again interesting to note that parent camphor has apparently no bacterial interaction as compared to the Schiff bases derived from it. The introduction of carbonyl function between the phenyl ring and piperazine moiety (IIIa and b) decreased the activity.

Compounds were checked by TLC, IR and PMR spectra. IR spectra (KBr) were recorded on a Perkin Elmer infracord 137 ( $\nu$  max in  $\text{cm}^{-1}$ ) and PMR spectra in  $\text{CDCl}_3$  on a Varian A-60D spectrometer using TMS as the internal standard (chemical shift in  $\delta$ -scale). TLC was performed on silica gel layers and spots were visualised by exposing the developed and dried plates to  $\text{I}_2$  vapours.

*p*-(N,N-Diethyl carbamoyl)aniline, *p*-(4-aryl-1-piperazino)aniline and *p*-(4-aryl-1-piperazine carbamoyl)aniline were prepared following the literature methods<sup>14,15</sup>.

#### Synthesis of Schiff bases of Camphor:

The following general method was adopted for the synthesis of such compounds.

A mixture of camphor (0.01 mol) and the respective *p*-substituted primary aromatic amine (0.01 mol) in absolute ethanol (20 ml) containing traces of conc.  $\text{H}_2\text{SO}_4$  was refluxed for about 15-20 hr under anhydrous conditions. On chilling, the crystals of the imino compounds were separated out and these were crystallised from chloroform-pet. ether. Physical properties and PMR data are reported in tables 1 and 2 respectively.

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### A NOTE ON THE CHEMOTAXONOMY OF THE MENISPERMACEAE

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THE Menispermaceae are variously placed under Berberidales, Menispermiales, Ranales or Ranunculales by different taxonomists. But for the alkaloids, the chemotaxonomy of this family is little known<sup>1</sup>. The present study on the chemotaxonomy of the two taxa viz. *Cocculus hirsutus* (L.) Diels and *Tinospora cordifolia* Miers representing the Cocculaceae and the Tinosporaceae tribes respectively, is taken up to fill up the gap.

The results of the standard tests with the fresh material and 80% methanolic extracts of the shade-dried material of the above two taxa, along with those

TABLE I

S. No.	Test/Taxon	<i>Cocculus hirsutus</i>	<i>Tinospora cordifolia</i>	Other Menispermaceae <sup>1</sup>
1.	Alkaloids	+	+	+ 40 genera
2.	Anthroquinones	-	-	..
3.	Cigarette test	+	+	..
4.	Ehrlich test	-	-	- 2 genera/3 species
5.	HCL/methanol test	-	-	- 1/2
6.	HCN test 'A'	+	-	- 5/6
7.	Hot water test	-	+	+ 5.6
8.	Hydroxyquinones	+	-	..
9.	Indoles	-	-	..
10.	Juglone test 'A'	-	-	- 1/1
11.	Labat test	-	-	..
12.	Leucoanthocyanins	-	-	- 2/2
13.	Leucoanthocyanin test 'A'	-	-	- 2/2
14.	Liebermann-Burchard test	+	+	..
15.	Lignans	-	-	..
16.	Maule test	-	-	..
17.	Phenols	+	+	+
18.	Raphides	-	-	-
19.	Salkowski test	+	+	..
20.	Saponins	-	-	+ 4/4; 15/17
21.	Saponin test 'A'	-	-	? 1/1; 1/1
22.	Shinoda test	-	-	..
23.	Syringin test	-	-	- 2/2
24.	Tannins	+ stem ? leaves	-	+ 3/3; 3/5

Positive; + Negative; ? doubtful; ... no record