Synthesis and antifungal activities of Schiff bases derived from 3-amino-2H-pyrano[2,3-b]quinolin-2-ones.

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Received 18 January 2000; accepted (revised) 9 February 2001

2-Chloro-3-formylquinolines 1a-e have been reacted with ethyl glycinate hydrochloride in pyridine to afford 3-amino-2H-pyrano[2,3-b]quinolin-2-ones 2a-e. Reaction of 2a-e with benzaldehyde in presence of glacial acetic acid yields the corresponding Schiff bases 3a-e. Structures of all the products have been established by spectral and elemental analysis data. The activity of Schiff bases against the fungal strains Aspergillus niger and Fusarium sp. have been tested in vitro.

Pyranoinelines constitute the parent ring structure of pyranoineline alkaloids which occur in the plant family Rutaceae. These pyranoineline alkaloids have gained considerable importance in recent years due to their pharmacological activities like anticoagulant, coronary constricting, optically brightening and antifungal activity. Pyran[2,3-b]quinoline alkaloids have also been reported to be associated with interesting pharmacological properties.

Based on the above facts, some unknown 3-amino-2H-pyrano[2,3-b]quinolin-2-ones were derived from 2-chloro-3-formylquinolines (Scheme 1). 1a was reacted with ethyl glycinate hydrochloride in pyridine at 120°C for 6 hr. After work up, the reaction mixture yielded a crude product which was purified by column chromatography.

The absence of bands at 1680 and 1040 cm⁻¹ corresponding to an aldehydic group and C-Cl bond respectively and the presence of bands corresponding to the pyrone system and the NH₂ bonds respectively given in the experimental together with ¹H NMR and mass spectral data confirm the structure of 2a. The generality of the reaction was tested with 1b-e.

It is a well known fact that the presence of azomethine linkage in the compound is found to exhibit biological activity particularly antifungal activity. With this view in mind, we prepared Schiff bases by refluxing 2a-e with benzaldehyde in methanol in the presence of glacial acetic acid (Scheme 1).

![Scheme 1](image-url)
The structures of all the compounds prepared above were confirmed from their elemental analyses and spectral data.

**Antifungal activity**

The antifungal activity of Schiff bases 3a-e were checked by the Agar plate technique. Six days old cultures of *Aspergillus niger* and *Fusarium sp.* were used as test organisms which were grown on a potato dextrose agar medium. 200μg/L solutions of 3a-e in DMSO were used for studies. The percentage inhibition was calculated as 100(C-T)/C, where C is the average diameter of fungal growth on the control plate and T is the average diameter of fungal growth on the test plate. The results (Table I) showed that the Schiff bases 3a-e are active against the fungus species. But it could not reach the effectiveness of the conventional fungicide, Bavistin.

**Experimental Section**

Melting points were determined on the Mettler FP 51 apparatus and are uncorrected. IR spectra (KBr) were recorded on a Perkin Elmer 598 spectrophotometer ($\nu_{\text{max}}$ in cm$^{-1}$). $^1$H NMR spectrum was taken on a Varian AMX-400 spectrometer using TMS as internal standard (chemical shifts in $\delta$, ppm) and mass spectra on a Jeol JMS D-300 mass spectrometer. Micro analyses were performed on a Perkin Elmer 24 B CHN analyser and values are within the permissible limits ($\pm$ 0.5).

The 2-chloro-3-formylquinolines$^9$ and ethyl glycinate hydrochloride$^10$ have been prepared by known procedures.

**8-Methyl-3-amino-2H-pyano[2,3-b]quinolin-2-one 2a$^{11}$**. It was prepared by a reported procedure. IR(KBr): 1730 (C=O), 1630 (C=C) and 3300-3400 cm$^{-1}$(N-H stretching); $^1$H NMR spectrum of (CDCl$_3$): $\delta$ 2.56 (s, 3H, 8-CH$_3$), 4.5 (s, 2H, NH$_2$, D$_2$O exchangeable), 7.03-7.89 (m, 4H, C$_6$H, C$_7$H, C$_8$H and C$_9$H), 9.16 (d, 1H, C$_9$-H); MS (m/z): 226 (M$^+$). Melting points of compounds 2a-e are 121, 107, 188, 134, 155°C respectively and their yields are 80, 77, 80, 74,79% respectively.

Compounds 2b-e were prepared similarly.

**Schiff bases 3a-e**. A mixture of 2c (0.01 mole) and benzaldehyde (0.01 mole) in dry methanol with a few drops of glacial acetic acid was refluxed on a water bath for 9 hr. Methanol was then removed by in vacuo and the resulting solid was recrystallised from chloroform to give 3c: IR(KBr): 1620 (C=O) and 1710 cm$^{-1}$(C=O); $^1$H NMR spectrum of (CDCl$_3$): $\delta$ 1.25 (s, 3H, 9-CH$_3$), 7.2 - 7.9 (m, 10H, C$_6$H, C$_7$H, C$_8$H, C$_9$H, C$_{10}$H and 5Ar-H), 8.6 (s, 1H, -N=CH-); MS (m/z): 314(M$^+$). Melting points of compounds 3a-e are 69, 124, 130, 98°C respectively and their yields are 67, 64, 65, 62% respectively.

Compounds 3a, 3b, 3d and 3e were prepared as above.

**Antifungal activity**$^{12}$

Potato dextrose agar medium (20 cm$^3$) (prepared from potato 150 g, dextrose 5.0 g and agar 2.0 g in 200 cm$^3$ distilled water) was poured into the sterilised petriplates and allowed to solidify. The plates were inoculated with spore suspension of either *Aspergillus niger* or *Fusarium sp.* (10$^6$ spores cm$^{-3}$ of medium). By using a sterilised cork borer (9 cm dia), wells were dug in the centre of the culture plates. The test solutions in DMSO were added (0.5 cm$^3$) to these wells, and the plates were incubated at 37°C for four days. After four days, the inhibition zone appearing around the wells in each plate was measured. To avoid the activity of the solvent that is used in the test solutions, a solvent only treated plate was maintained. An untreated control plate was also maintained in order to calculate the percentage inhibition. Bavistin was used as a standard to compare the antifungal activity of the compounds 3a-e.

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**Table 1 — Antifungal activity data**

<table>
<thead>
<tr>
<th>Compd</th>
<th><em>Aspergillus niger</em></th>
<th><em>Fusarium sp.</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>3b</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>3c</td>
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</tr>
<tr>
<td>3d</td>
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<td>Bavistin</td>
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**References**