Rapid Communication

Novel conversion of some E-3-benzylideneflavanones to 3-benzoylchromones under a Schmidt rearrangement condition

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On treatment with NaN₃/TFA, some E-3-benzylideneflavanones yield 3-benzoylchromones with the loss of 2-ary group as the corresponding aniline, a plausible mechanistic path for which has been delineated. An acid-catalysed skeletal rearrangement of some E-3-benzylideneflavanones also takes place.

The most interesting feature of the Schmidt reaction with 4-chromanones is that owing to preferential alkyl migration it yields a different type of products from that with 1-tetralones. Thus, the structure of the major product obtained from flavanone had to be revised as 1. A very simple synthesis of E-3-benzylideneflavanones, recently developed by us, has grown our interest in studying various reactions of these compounds. Hence, we undertook an investigation of the Schmidt reaction of 2 considering that this might produce some interesting results as the migratory aptitude of the substituted β-styryl moiety of these compounds would be different from that of the 3-CH₂ of flavanones, and this property could be varied by variation of the substituent in the aromatic ring. Moreover, migration of the β-styryl moiety would produce flavonoid derived enamides which might show interesting biological activities. In the very first round of this investigation, some novel observations have been obtained, which are presented in this communication.

Among the reaction conditions known for effecting Schmidt rearrangement of chromanones, NaN₃/TFA at rt was first applied on 2a. After 4 days the starting material was found to undergo almost complete conversion yielding a product which, to our surprise, was a smaller molecule than the starting material and having no nitrogen. Analytical and spectral data confirmed it to be 3-benzoylchromone 4a. The study was extended to other benzylideneflavanones, and the results obtained are presented in Table I.

The results given in Table I show the following interesting features:
(i) The E-3-benzylideneflavanones 2f and 2g, both bearing a 2-(p-methoxyphenyl) group, underwent complete isomerisation through an acid-catalysed skeletal rearrangement and one of the isomerised products suffered loss of its 2-ary group. In case of 2c, however, such rearrangement was only partial.

![Chemical structures](image)
Table I — Results of Schmidt reaction on 2 (\(\text{NaN}_3\), TFA, room temperature, 4 days)

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product(s)* (Yield, %)</th>
<th>Starting material recovered (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>4a(30)</td>
<td>Trace</td>
</tr>
<tr>
<td>2b</td>
<td>4b(15)</td>
<td>35</td>
</tr>
<tr>
<td>2c</td>
<td>4c(21) + 2j(5)</td>
<td>31</td>
</tr>
<tr>
<td>2d</td>
<td>4d(12)</td>
<td>38</td>
</tr>
<tr>
<td>2e</td>
<td>4b(16)</td>
<td>41</td>
</tr>
<tr>
<td>2f</td>
<td>2k(92)</td>
<td></td>
</tr>
<tr>
<td>2g</td>
<td>4b(13) + 2b(42)</td>
<td>–</td>
</tr>
<tr>
<td>2h</td>
<td>No reaction</td>
<td>95</td>
</tr>
<tr>
<td>2i</td>
<td>No reaction</td>
<td>98</td>
</tr>
</tbody>
</table>

(ii) A 2-(p-chlorophenyl) group was not lost, possibly due to the reduced migratory aptitude of this group.

In search of the product generated from the missing 2-aryl group, the aqueous solution left after extraction of the diluted reaction mixture with ether was made alkaline and re-extracted with the same solvent. The second extraction afforded an aniline with the missing 2-aryl group (characterised individually and also by converting to the corresponding N-acetyl derivative). This proved that the 2-aryl group migrated to an electron-deficient nitrogen and the anilino moiety generated thereby was eliminated subsequently.

The observed skeletal rearrangement of several \(E\)-3-benzylideneflavanones may be considered as the result of successive occurrence of the steps: protonation at 1-position, 2-aryl-assisted heterocyclic ring opening, and recyclisation (Scheme I). The stability difference between the isomeric compounds appears to be the driving force for the process.

The mechanistic aspect of the conversion of 2 to 4 appears somewhat complicated. In TFA \(E\)-3-benzylideneflavanones do not isomerise to 3-benzylflavones, eliminating possibility of the intermediacy of...
the latter. The observed acid-catalysed skeletal rearrangement of several E-3-benzylideneflavanones (Table I, Scheme I) suggests the formation of an intermediate like 5, at least in low concentration. If such an intermediate is attacked by \( \text{HIN}_3 \), the changes shown in Scheme II may lead to the product 4. Involvement of aerial oxygen in the process was evident from the fact that when the reaction was carried out in nitrogen atmosphere even traces of 4 could not be obtained. However, in this path there is a strong possibility for the formation of a second 3-benzoylchromone, at least in low yield, through the attack of I-\( \text{IN}_3 \) at the other electron-deficient centre (marked with asterisk) of 5, which was not observed in any one of the cases. On the other hand, consideration of the attack of \( \text{HIN}_3 \) at either C-4 or C-\( \beta \) of 9 (formed by protonation of substrate at the carbonyl oxygen) requires a much unexpected 1,4(C=\( \rightarrow \)N) aryl migration to generate 6. We are now in the pursuit of settling the actual mechanism by carrying out properly designed experiments.

The reaction of 2a performed with Na\( \text{N}_2/\text{Conc.} H_2\text{SO}_4\cdot\text{HIOAc} \), however, yielded the desired product 3 (R=I, Ar=Ar\( ^\gamma =\text{Ph} \)) (32%). Interestingly, in an extension of this study to several substituted compounds, the reaction was found to follow some more unusual courses, the details of which will be published soon.

In summary, we report a novel result originating from a simple reaction of E-3-benzylideneflavanones 2. The mechanistic aspect of this reaction appears very interesting.

Acknowledgement

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References and Notes

11. Typical experimental procedure. An appropriate E-3-benzylideneflavanone (1 mmole) was dissolved in TFA (3 mL) at 5 °C and to the cold solution sodium azide (1.5 mmoles) was added in three portions at 5 min intervals. The resulting mixture was kept at room temperature for 4 days and then diluted with water 150 mL and extracted with ether (3 x 25 mL). The concentrate of the ether extract was chromatographed over silica gel to get pure product.
13. All the products gave satisfactory analytical and spectral data.

Supplementary Data

4a: mp 128-129 °C (lit\(^{12} \) 130°). Anal. Caled for C\(_{18}\)H\(_{18}\)O\(_2\): C, 76.79; H, 4.03%. Found: C, 76.52; H, 3.88%; UV (EtOH): 245.6, 293.5 and 338.4 nm (Absorbance: 1.8, 0.70 and 0.23) [Lit.\(^{12} \) 240 (log ε 4.1) and 290 (3.65)]; IR (KBr): \( \nu \text{cm}^{-1} \) (C=O) = 1670 (C=O) and 1650 (C=O); \( ^1\text{H NMR} \) (300 MHz, CDCl\(_3\)) \( \delta \) 7.47 - 7.63 (5H, m, Ar-H), 7.75 (1H, s, H-2), 7.85 - 7.88 (2H, m, H-2', 6'), 8.27 (1H dd, J = 7.8 and 1.5 Hz, H-5) and 8.31 (1H, s, H-2') [Lit.\(^{12} \) 8.3 (H, s, H-2'), 8.2 (d, H-5) and 7.5 (m, other protons)]; EI-MS: \( m/z \) 250 (M\(^+\)).
4b: mp 149-150 °C. Anal. Caled for C\(_{18}\)H\(_{18}\)O\(_2\): C, 72.85; H, 4.32%. Found: C, 72.56; H, 4.19%; IR (KBr): 1660 (C=O) and 1640 cm\(^{-1} \) (C=O); \( ^1\text{H NMR} \) (300 MHz, CDCl\(_3\)) \( \delta \) 3.88 (3H, s, OCH\(_3\)), 6.95 (2H, pattern resembles a pair of triplets, J = 7.8 and 3 or 2 Hz, H-3', 5'), 7.48 (1H, dt, J = 8.1 and 1.5 Hz, H-6), 7.54 (1H, dd, J = 8.4 and 1.3 Hz, H-8), 7.75 (1H, dd, J = 8.4, 7.8 and 1.5 Hz, H-7), 7.87 (2H pattern resembles a pair of triplets, J = 7.8 and 2 or 3 Hz, H-2', 6'), 8.27 (1H, dd, J = 8.4 and 1.5 Hz, H-5) and 8.27 (1H, s, H-2'); \( ^1\text{C NMR} \) (75 MHz, CDCl\(_3\)) \( \delta \) 55.86 (OCH\(_3\)), 114.09 (C-3', 5').
118.66 (C-8), 125.37 (C-3), 126.02 (C-4a), 126.38 (C-6), 126.89 (C-5), 130.42 (C-1'), 132.57 (C-2', 6'), 134.65 (C-7), 156.48 (C-8a), 158.40 (C-2), 164.41 (C-4'), 175.16 (C-4) and 190.36 (C=O); EIMS: m/z 280 (M+).

4c: mp 160 - 161 °C. Anal. Calcd for C_{16}H_{9}O_{3}: C, 67.51; H, 3.18%. Found: C, 67.48; H, 3.14%; IR (KBr): 1655 (C=O) and 1645 cm^{-1} (C=O); ^1H NMR (300 MHz, CDCl3): δ 7.42 (2H, pattern resembles a pair of triplets, J = 8.4 and 2.1 or 3.1 Hz, H-2', 6'), 8.24 (1H, dd, J = 7.8 and 1.4 Hz, H-5) and 8.34 (1H, s, H-2).

4d: mp 139 - 140 °C. Anal. Calcd for C_{17}H_{12}O_{4}: C, 72.85; H, 4.19%. Found: C, 72.81; H, 4.41%; IR (KBr): 1658 (C=O) and 1648 cm^{-1} (C=O); ^1H NMR (300 MHz, CDCl3): δ 3.83 (3H, s, OCH3), 6.92 (1H, d, J = 2.4 Hz, H-8), 7.03 (1H, dd, J = 8.7 and 2.4 Hz, H-6), 7.46 (2H, t, J = 7.5 Hz, H-3', 5'); 7.56-7.61 (1H, m, H-4'); 7.86 (2H, dd, J = 7.5 and 1.5 Hz, H-2', 6'), 8.15 (1H, d, J = 8.7 Hz, H-5), and 8.22 (1H, s, H-2).