Microwave-induced, solvent-free transformations of benzoheteracyclanones by HTIB (Koser’s reagent)

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Dedicated to Professor Sándor Antus on the occasion of his 60th birthday
(received 15 Jan 04; accepted 06 Apr 04; published on the web 07 Apr 04)

Abstract
The microwave-activated reactions of [hydroxy(tosyloxy)iodo]benzene (HTIB) with various chromanones, thiochromanones and dihydroquinolones under solvent-free conditions have been studied. In addition to the common dehydrogenation reaction, 2,3-migration also has been observed in the case of flavanone and 2,2-disubstituted chromanones. 3-Tosyloxychromanones were isolated from the reaction of chromanone and 2-methylchromanone for the first time. Substrates with nucleophilic heteroatoms such as thiochromanones and 2-phenyl-2,3-dihydro-4-quinolone reacted by electrophilic attack of the heteroatom.

Keywords: Chromanones, 2,3-dihydro-4-quinolones, hypervalent iodine reagent, microwave irradiation, thiochromanones, tosyloxylation

Introduction

[Hydroxy(tosyloxy)iodo]benzene1 (HTIB, Koser's reagent) and related hypervalent iodine derivatives have become widely used reagents for synthetic organic chemistry during the last decades, and excellent overviews of their chemistry have been forthcoming in several papers.2 The most frequently exploited reactions of HTIB and the other [(arylsulfonyloxy)(hydroxy)iodo]benzene analogues are the α-sulfonyloxylation of ketones (or their enol derivatives), sulfonyloxylation of double bonds, phenyliodination and oxidation, and all of these approaches have been utilized in the synthesis of various heterocyclic systems2. A survey of the literature reveals continuous efforts to develop these reagents and the conditions for their use. Some recent examples are preparation of isoflavones from 2'-hydroxychalcones by
means of a polymer-supported reagent, a-tosyloxylation in ionic liquids, a-hydroxylation of ketones by HTIB in DMSO-water mixtures, oxidative a-tosyloxylation of alcohols into a-tosyloxy aldehydes and ketones or the use of [hydroxy(2,4-dinitrobenzenesulfonfonyloxy)iodo]benzene (HDNIB).

Microwave (MW) irradiation is an efficient and environmentally-benign method to activate various organic transformations to afford products in higher yields in shorter reaction periods. In this class of MW-assisted reactions, solvent-free syntheses are of particular interest and importance in view of their simplicity, tunability and ease of work-up. MW activation was utilized advantageously in the a-tosyloxylation of acetophenones by HTIB in the presence of K10 clay and the generated tosylates were successfully transformed into thiazoles and imidazo[2,1-b]thiazoles.

In continuation of our studies in the field of cyclic a-(arylsulfonyloxy)ketones and oxygen-containing heterocycles, we decided to investigate the reaction of various chromanone derivatives and their sulfur or nitrogen-containing analogues with HTIB under MW irradiation and solvent-free conditions, and the most characteristic results are presented here.

**Results and Discussion**

First, we searched for the most efficient MW-inactive support for use of the highly sensitive 2,2-dimethyl-7-methoxychromanone (5b) as a test molecule. MW irradiation and subsequent work-up afforded the expected 2,3-dimethyl-7-methoxychromone (6b) in addition to some unidentified, highly polar products which could be removed easily by filtration through a short pad of silica or by short-column chromatography (Scheme 1, Table 1). The structure of the product was in accordance with literature data, Prakash and his coworkers have observed the same 2,3-methyl migration and dehydrogenation in refluxing acetonitrile using ultrasound activation.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Support</th>
<th>MW Irradiation (min)</th>
<th>Conversion (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>4x1</td>
<td>80</td>
<td>41</td>
</tr>
<tr>
<td>2</td>
<td>Montmorillonite K-10</td>
<td>20x1</td>
<td>29</td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td>Al2O3 (neutral)</td>
<td>20x1 + 15x2</td>
<td>57</td>
<td>53</td>
</tr>
<tr>
<td>4</td>
<td>CaCO3</td>
<td>20x1 + 5x2</td>
<td>80</td>
<td>59</td>
</tr>
<tr>
<td>5</td>
<td>Na2SO4</td>
<td>12x1</td>
<td>88</td>
<td>61</td>
</tr>
</tbody>
</table>

*According to the General Procedure (Experimental Part) by treating 1.00 mmol of 5b with 1.20 mmol of HTIB, elution with hexane-ethyl acetate (1:1, v/v). Calculated on the basis of the recovered starting material. Refers to pure isolated products, the values are normalized to 100% conversion.
The results summarized in Table 1 reveal a decisive role for the support. Surprisingly, poor conversion and low yield was found using Montmorillonite K10 and neutral alumina. Inorganic salts such as CaCO₃ or Na₂SO₄ gave much better conversions. Good conversions also have been achieved without any support, but the yield was lower due to secondary reactions causing the decomposition of the product. Taking the length of the irradiation period, conversions and yields into consideration, we chose Na₂SO₄ as the carrier for further experiments.

Scheme 1

The reactions of chromanone (1a) and 2-methylchromanone (1b) afforded a mixture of the 3-tosyloxychromanones 2a,b and the corresponding chromones 3a,b under the optimized conditions (Table 2, Scheme 1). It was noteworthy that, in the case of 1b the oxidative
sulfonyloxylation took place with complete diastereoselectivity; only the cis diastereomer could be detected and isolated. The relative configuration of the obtained cis-2-methyl-3-tosyloxychromanone (2b) has been determined on the basis of the small value for the $^3J_{2H,3H}$ coupling constant (3.7 Hz). Earlier, Liebscher and coworkers have reported values of $^3J_{2H,3H} = 12.4$ Hz for trans-3-hydroxy-2-propylchromanone and $^3J_{2H,3H} = 6.0$ Hz for cis-3-hydroxy-2-methylchromanone. The stereochemistry of the cis-3-hydroxy-2-methyl-2,3-dihydro-4H-naphto[2,3-b]pyran-4-one also has been proven by X-ray crystallography. In spite of the low yields of tosylates 2a,b, the method has some synthetic value since 3-arylsulfonyloxychromanones were practically unknown. The only exception, 3-[(4-nitrobenzenesulfonyl)oxy]chromanone, was obtained from 4-acetoxy-2H-1-chromene with bis(4-nitrobenzenesulfonyl) peroxide. Further, no tosylates 2a,b have been isolated previously from the reaction of substrates 1a,b and HTIB in hot acetonitrile with or without sonication, proving again the beneficial effect of MW irradiation.

On the contrary, when flavanone (1c) was treated with HTIB no tosylate 2c was obtained and the reaction yielded a mixture of flavone (3c) and isoflavone (4c) (Table 2, Scheme 1). This result is in accordance with the literature data. According to Prakash et al., 3-tosyloxyflavanone was never observed using classical heating and the product ratio depended strongly on the conditions. In boiling acetonitrile or propionitrile, isoflavone (4c) was the major product accompanied with a small amount of flavone (3c) and methyl 2-phenyl-2,3-dihydrobenzofuran-3-carboxylate. The change of the solvent to methanol resulted in a dramatic shift as flavone (3c) became the major product, accompanied by some cis-3-methoxyflavanone and methyl 2-phenyl-2,3-dihydrobenzofuran-3-carboxylate. The oxidative rearrangement of flavanone (1c) also has been performed using other reagents such as iodosobenzene diacetate/p-toluenesulfonic acid in acetonitrile, iodosobenzene/methanesulfonic acid in methylene chloride or acetonitrile or various thallium(III) reagents.

### Table 2. Reaction of chromanones 1a-c with HTIB under MW irradiation using Na2SO4 support

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>HTIB (equiv.)</th>
<th>MW irradiation (min)</th>
<th>Eluent</th>
<th>Conversion (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>1.2</td>
<td>6x1</td>
<td>A</td>
<td>70</td>
<td>6.1 45 0</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>2.4</td>
<td>8x1</td>
<td>B</td>
<td>63</td>
<td>12 62 0</td>
</tr>
<tr>
<td>3</td>
<td>1b</td>
<td>1.2</td>
<td>3x1</td>
<td>B</td>
<td>85</td>
<td>32 28 0</td>
</tr>
<tr>
<td>4</td>
<td>1b</td>
<td>2.4</td>
<td>3x1</td>
<td>B</td>
<td>100</td>
<td>25 19 0</td>
</tr>
<tr>
<td>5</td>
<td>1c</td>
<td>1.2</td>
<td>4x1</td>
<td>A</td>
<td>100</td>
<td>0 25 20</td>
</tr>
<tr>
<td>6</td>
<td>1c</td>
<td>2.4</td>
<td>2x1</td>
<td>B</td>
<td>95</td>
<td>0 13 47</td>
</tr>
</tbody>
</table>

a: dichloromethane, B: dichloromethane, components of low Rf were eluted by ethyl acetate and re-chromatographed using hexane-ethyl acetate (1:1, v/v).

b: Calculated on the basis of the recovered starting material. c: Refers to pure isolated products, the values are normalized to 100% conversion.
The treatment of various substituted 2,2-dimethylchromanones 5a-c,e-g with HTIB under our MW conditions afforded the corresponding 2,3-dimethylchromones 6a-c,e-g (Table 3, Scheme 1). The use of higher amounts of HTIB resulted in an increase in the conversion in all cases, but the yields were significantly lower due to the decomposition of the primary products formed. This tendency is quite conspicuous in the case of 7-benzyloxy-2,2,5-trimethylchromanone (5g) where the aromatic ring is highly activated and, therefore, sensitive to the competitive attack of the electrophilic reagent (Table 3, Entries 9,10). For the same reason, the reaction of 2,2-dimethyl-7-hydroxychromanone (5d) failed to give any desired rearranged product 6d. The latter was prepared by the acid-catalyzed debenzylation of the protected derivative 6c.

Table 3. Reaction of 2,2-disubstituted chromanones 5a-c,e-g, 8a-c with HTIB under MW irradiation using Na2SO4 support

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>HTIB (equiv.)</th>
<th>MW irradiation (min)</th>
<th>Eluent</th>
<th>Conversion (%)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>1.2</td>
<td>8x1</td>
<td>A</td>
<td>64</td>
<td>6a</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>2.4</td>
<td>6x1</td>
<td>C</td>
<td>100</td>
<td></td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>5b</td>
<td>1.2</td>
<td>6x1</td>
<td>C</td>
<td>65</td>
<td>6b</td>
<td>60</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>2.4</td>
<td>6x1</td>
<td>C</td>
<td>89</td>
<td></td>
<td>37</td>
</tr>
<tr>
<td>5</td>
<td>5c</td>
<td>1.2</td>
<td>5x1</td>
<td>D</td>
<td>80</td>
<td>6c</td>
<td>80</td>
</tr>
<tr>
<td>6</td>
<td>5e</td>
<td>1.2</td>
<td>6x1</td>
<td>C</td>
<td>81</td>
<td>6e</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>5f</td>
<td>1.2</td>
<td>6x1</td>
<td>A</td>
<td>52</td>
<td>6f</td>
<td>84</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>2.4</td>
<td>6x1</td>
<td>C</td>
<td>93</td>
<td></td>
<td>71</td>
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<td>9</td>
<td>5g</td>
<td>1.2</td>
<td>8x1</td>
<td>D</td>
<td>64</td>
<td>6g</td>
<td>28</td>
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<td>10</td>
<td></td>
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<td>D</td>
<td>92</td>
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<td>3.7</td>
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<td>11</td>
<td>8a</td>
<td>1.2</td>
<td>6x1</td>
<td>D</td>
<td>82</td>
<td>9a</td>
<td>82</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>2.4</td>
<td>6x1</td>
<td>D</td>
<td>100</td>
<td></td>
<td>73</td>
</tr>
<tr>
<td>13</td>
<td>8b</td>
<td>1.2</td>
<td>3x1</td>
<td>A</td>
<td>75</td>
<td>9b</td>
<td>97</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>2.4</td>
<td>2x1</td>
<td>A</td>
<td>100</td>
<td></td>
<td>76</td>
</tr>
<tr>
<td>15</td>
<td>8c</td>
<td>1.2</td>
<td>4x1</td>
<td>D</td>
<td>63</td>
<td>9c</td>
<td>80</td>
</tr>
<tr>
<td>16</td>
<td></td>
<td>2.4</td>
<td>2x1</td>
<td>D</td>
<td>100</td>
<td></td>
<td>57</td>
</tr>
</tbody>
</table>

a A: dichloromethane, C: dichloromethane-acetone (10:1, v/v), D: 1,2-dichloroethane.
b Calculated on the basis of the recovered starting material. c Refers to pure isolated products, the values are normalized to 100% conversion.

The 2,3-alkyl migration and dehydrogenation also was observed in the reaction of the 2-spirochromanones 8a-c to give the corresponding tricyclic products 9a-c in good-to-excellent yields. The same reaction had been observed previously from the treatment of the spirochromanones with HTIB in hot acetonitrile, with or without ultrasound activation,10 or with thallium(III) trinitrate in hot acetonitrile.16 Based on the results, we can conclude that the
rearrangement is expected only with 2,2-disubstituted chromanones or 2-substituted chromanones containing a group of high migrating capability (e.g. aryl). HTIB-induced dehydrogenation and migration of spirochromanones offers a useful method for the synthesis of various naturally-occurring and/or biologically active targets and some such molecules containing a tetrahydroxanthone moiety are shown in Figure 1. To the best of our knowledge, the only exploitation of this approach has been presented by Gabutt et al.\textsuperscript{21} who accomplished the synthesis of the rotenoid core.

![Figure 1](image1.png)

**Figure 1**

The obtained results can be integrated in a single mechanism. According to the literature,\textsuperscript{2} the reacting species in the HTIB-mediated reactions is the 3-phenyliodonio intermediate 11 which has a trans relative configuration in the case of 2-substituted chromanones. The preferred formation of this diastereomer can be rationalized in terms of the optimized\textsuperscript{22} conformation of the enol of the chromanone (see Figure 2) which allows attack of the HTIB only from the opposite side. S\textsubscript{N}2 attack of the tosylate anion results in the stereoselective formation of chromanone 2 (arrow (a), Scheme 2) while the migration of the antiperiplanar alkyl or alkylene group by the loss of iodobenzene (arrow (b), Scheme 2) results in the formation of the resonance-stabilized cation 12b.

![Figure 2](image2.png)
The lack of an electron-donating 2-alkyl substituent in cation 12a makes it more unstable and hinders the migration in the case of 2-methylchromanone (1b). On the other hand, it seems very likely that the migration in the flavanone (1c) takes place via the phenonium intermediate 12c.

We have investigated also some heteroanologs of chromanones. Treatment of 1-thiochromanone 13a with HTIB under MW irradiation afforded the corresponding sulfoxide 14a, accompanied by a small amount of 1-thiochrome 15a. Surprisingly, the same product 14a was obtained in nearly the same yield without any MW activation simply by intimately mixing the reagents and the support. 2-Substituted-1-thiochromanones 13b,c gave similar results, affording the sulfoxides 14b,c with low-to moderate diastereoselectivity (Scheme 3, Table 4).
Oxidation of sulfides to sulfoxides without apparent overoxidation to sulfones by [methoxy(tosyloxy)iodo]benzene (MTIB), obtained from HTIB and trimethyl orthoformate,\(^2\) or by HTIB or HCIB in methylene chloride,\(^3\) or by in situ generated HTIB in acetonitrile\(^5\) has been reported, but this is the first case where a heterogenous, solid-phase reaction has been observed. Our finding offers a new and easy entry to heterocyclic sulfoxides.

### Table 4. Reaction of thiochromanones 13a-c and dihydroquinolones 16,18 with HTIB under MW irradiation using Na\(_2\)SO\(_4\) support

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>HTIB (equiv.)</th>
<th>MW irradiation (min)</th>
<th>Eluent*</th>
<th>Conversionb</th>
<th>Yieldd (%)</th>
<th>14 (trans/cis)</th>
<th>15/17</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13a</td>
<td>1.2</td>
<td>2x1</td>
<td>E</td>
<td>84</td>
<td>39 (-)</td>
<td>11</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>13a</td>
<td>2.4</td>
<td>2x1</td>
<td>E</td>
<td>100</td>
<td>12 (-)</td>
<td>9.9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>13a</td>
<td>2.4</td>
<td>none</td>
<td>E</td>
<td>95</td>
<td>37 (-)</td>
<td>traces</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>13b</td>
<td>2.4</td>
<td>none</td>
<td>F</td>
<td>100</td>
<td>38 (79:21)</td>
<td>9.1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>13c</td>
<td>2.4</td>
<td>none</td>
<td>F</td>
<td>56</td>
<td>66 (59:41)</td>
<td>traces</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
<td>2.4</td>
<td>2x1</td>
<td>E</td>
<td>55</td>
<td>-</td>
<td>12</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>18</td>
<td>2.4</td>
<td>3x1</td>
<td>G</td>
<td>74</td>
<td>-</td>
<td>-</td>
<td>19:15</td>
<td>-</td>
</tr>
</tbody>
</table>

*E: ethyl acetate, F: toluene-ethyl acetate (4:1, v/v), G: ethyl acetate-hexane (8:1, v/v)

b Calculated on the basis of the recovered starting material. c Refers to pure isolated products, the values are normalized to 100% conversion.

Finally, the reactivity of 2,3-dihydro-4-quinonolones 16, 18 was tested since previously very little had been published on the reaction of dihydroquinolones with hypervalent iodine reagents. 2-Aryl-2,3-dihydro-4-quinolones were reported to afford 4-alkoxy-2-arylquinolines in the presence of HTIB, trialkyl orthoformate and perchloric acid,\(^26\) and 2-aryl-4-quinolones upon treatment with iodosobenzene diacetate and potassium hydroxide in methanolic solution.\(^27\) Under our conditions, both substrates reacted sluggishly and low conversions were found even by using higher amounts of HTIB. The substitution on the nitrogen plays a decisive role since 2-phenyl-2,3-dihydro-4-quinolone (16) gave the dehydrogenated 2-phenyl-4-quinolone (17) as the sole product while 1-acetyl-2-phenyl-2,3-dihydro-4-quinolone (18) yielded the migrated 3-phenyl-4-quinolone (19) (Scheme 3, Table 4). Neither of these reactions has considerable synthetic value but each provides important mechanistic information. Similarly to the sulfur-containing substrates where the sulfoxidation proceeds by an electrophilic attack on the sulfur atom and runs via the intermediate 20, HTIB attacks the nucleophilic nitrogen atom in the dihydroquinolone 16 giving the phenyliodonium intermediate 21 and then finally the quinolone 22. This latter intermediate transforms into the final product, either by a hydrogen shift or by a protonation-deprotonation sequence (Scheme 3). The acylation of the nitrogen in compound 18 stops its nucleophilic character and directs the transformation to the enol mechanism shown in Scheme 2. This duality proves for the higher reactivity of nucleophilic heteroatoms toward HTIB in comparison with double bonds.
In conclusion, the reaction of 2-unsubstituted and 2-alkylchromanones with HTIB was found to give the corresponding, hitherto unknown 3-tosyloxy derivatives, in addition to dehydrogenation, whereas dehydrogenation and/or 2,3-migration was observed with other chromanones. Attack at the nucleophilic hetero atom was observed in the reactions of 1-thiochromanones or 2-phenyl-2,3-dihydro-4-quinolone, giving the corresponding sulfoxides or the dehydrogenated product, respectively.

Experimental Section

General Procedures. Column chromatography was performed on Kieselgel 60 or Kieselgel 40. – Melting points: Boetius hot-stage, uncorrected values. – IR: Perkin Elmer 16 PC-FT-IR; KBr pellets unless otherwise stated. – NMR: Bruker WP 200 SY, Bruker AM 360 (200 or 360 MHz for $^1$H; 50 or 90 MHz for $^{13}$C). Recorded in CDCl$_3$ solution unless otherwise stated. Chemical shifts are given in $\delta$ relative to an internal standard TMS ($\delta = 0$) or to the residual CHCl$_3$ ($\delta = 7.26$ for $^1$H NMR and $\delta = 77.0$ for $^{13}$C NMR). – Elemental analysis: Carlo Erba EA 1106 CHN analyzer. Starting materials 1a and 13a were purchased while 1b,c, 5a-g, 8a-c, 16 and 18 were synthesized according to literature methods.

General procedure for the microwave-induced reactions
Benzoheteracyclanone 1a-c, 5a-c,e-g, 8a-c, 16, or 18 (1 mmol), HTIB (1.2 or 2.4 mmol) and anhydrous sodium sulfate (5 g) were mixed thoroughly and irradiated in a household microwave oven (2.45 GHz, 700 W) with a one-minute break between two exposures (for details see Tables 1-4). The mixture was washed with dichloromethane (4x30 mL), concentrated in vacuo and the residue was submitted to short-column chromatography. Conversion and yields are shown in the Tables. Known products 3a-c, 4c were identified by TLC comparison, m.p. and $^1$H NMR spectra.

3-Tosyloxychromanone (2a). For the conditions see Table 2. Mp 125-128 °C (hexane-EtOAc). IR: 1690 (C=O), 1606, 1478, 1466, 1364 (SO$_2$), 1314, 1218, 1192, 1174 (SO$_2$), 1008, 942, 908, 852, 814, 774, 738 cm$^{-1}$. $^1$H NMR: 2.48 (s, 3H, 4′-Me), 4.55 (dd, $J = 10.0$, 11.0 Hz, 1H, 2-Hax), 4.66 (dd, $J = 5.1$, 11.0 Hz, 1H, 2-Heq), 5.17 (dd, $J = 5.1$, 10.0 Hz, 1H, 3-H), 7.04 (d, $J = 8.4$ Hz, 1H, 8-H), 7.11 (m, 1H, 6-H), 7.50 (d, $J = 8.4$ Hz, 2H, 3′,5′-H), 7.61 (m, 1H, 7-H), 7.75 (d, $J = 9.0$ Hz, 1H, 5-H), 7.90 (d, $J = 8.4$ Hz, 1H, 2′,6′-H). $^{13}$C NMR: 21.6 (4′-Me), 69.8 (C-2), 75.5 (C-3), 118.7 (C-8), 122.9 (C-6), 128.1 (C-5), 129.0 (C-2′,6′), 130.9 (C-3′,5′), 134.2 (C-1′), 137.6 (C-7), 146.5 (C-4′), 162.0 (C-8a), 185.5 (C-4). Anal. Calcd. for C$_{16}$H$_{14}$O$_5$S (318.34): C, 60.37; H, 4.43. Found: C, 60.11; H, 4.59.

cis-2-Methyl-3-tosyloxychromanone (2b). For the conditions see Table 2. Mp 104-105 °C (hexane-ads. EtOH). IR: 1694 (C=O), 1610, 1466, 1370, 1364 (SO$_2$), 1312, 1188, 1178 (SO$_2$), 972, 948, 846, 684 cm$^{-1}$. $^1$H NMR: 1.50 (d, $J = 7.0$ Hz, 3H, 2-Me), 2.45 (s, 3H, 4′-Me), 4.75 (m, 1H, 2-H), 5.10 (d, $J = 3.7$ Hz, 1H, 3-H), 6.96 (d, $J = 8.4$ Hz, 1H, 8-H), 7.0 (m, 1H, 6-H), 7.34 (d, $J = 8.4$ Hz, 2H, 3′,5′-H), 7.50 (m, 1H, 7-H, ), 7.72 (dd, $J = 1.8$, 8.0 Hz, 1H, 5-H), 7.84 (d, $J = 8.4$ Hz...
Hz, 2H, 2′,6′-H). 13C NMR: 14.5 (2-Me), 21.6 (4′-Me), 75.3 (C-3), 77.5 (C-2), 118.1 (C-8), 119.0 (C-4a), 121.8 (C-6), 127.3 (C-5), 128.0 (C-3′,5′), 129.7 (C-3′,5′), 133.0 (C-1′), 136.8 (C-7), 145.2 (C-4′), 159.8 (C-8a), 185.1 (C-4). Anal. Calcd. for C17H16O5S (332.37): C, 61.43; H, 4.85. Found: C, 61.70; H, 4.69.

2,3-Dimethylchromone (6a). For the conditions see Table 3. Mp 93-94 °C (hexane) (Lit.28 97-99 °C, lit.29 91-93 °C). IR: 1632 (C=O), 1609 (C=C), 1470, 1400, 1173, 772 cm-1. 1H NMR: 2.06 (s, 3H, 2-Me), 2.42 (s, 3H, 3-Me), 7.32-7.39 (m, 2H, 6,8-H), 7.60 (m, 1H, 7-H), 8.20 (dd, J = 1.3, 7.9 Hz, 1H, 5-H). 13C NMR: 9.8 (3-Me), 18.3 (2-Me), 116.9 (C-3), 117.6 (C-8), 122.7 (C-4a), 124.5, 125.9 (C-5, C-6), 133.0 (C-7), 156.0 (C-8a), 162.0 (C-2), 178.1 (C-4).

2,3-Dimethyl-7-methoxychromone (6b). For the conditions see Table 3. Mp 122-123 °C (hexane-EtOAc). (Lit.30 127 oC). IR: 1640 (C=O), 1618 (C=C), 1604, 1574, 1442, 1040, 1352, 1246 (C-O-C), 1204, 826 cm-1. 1H NMR: 2.03 (s, 3H, 2-Me), 2.37 (s, 3H, 3-Me), 3.87 (s, 3H, 7-OMe), 6.75 (d, J = 1.3 Hz, 1H, 8-H), 6.91 (dd, J = 1.3, 9.6 Hz, 1H, 6-H), 8.09 (d, J = 9.6 Hz, 1H, 5-H). 13 C NMR: 9.9 (3-Me), 18.4 (2-Me), 55.6 (7-OMe ), 99.6 (C-8), 113.8 (C-6), 116.4 (C-3), 127.1 (C-5), 157.4 (C-8a), 161.2 (C-2), 163.4 (C-7), 177.3 (C-4).

7-Benzylxoxy-2,3-dimethylchromone (6c). For the conditions see Table 3. Mp 92.5-93.5 oC (hexane). IR: 1644 (C=O), 1610 (C=C), 1442, 1398, 1344, 1244 (C-O-C), 1182, 1098, 746, 708 cm-1. 1H NMR: 2.02 (s, 3H, 2-Me), 2.36 (s, 3H, 3-Me), 5.12 (s, 2H, CH 2), 6.83 (d, J = 1.3 Hz, 1H, 8-H), 6.99 (dd, J = 1.3 Hz, 1H, 6-H), 7.34-7.45 (m, 5H, Ph), 8.09 (d, J = 8.3 Hz, 1H, 5-H). 13C NMR: 9.9 (3-Me), 18.4 (2-Me), 70.4 (CH2), 100.8 (C-8), 114.3 (C-6), 116.5, 116.8 (C-3, C-4a), 127.3, 127.5, 128.3, 128.7 (C-5, C-2′,6′, C-3′,5′, C-4′), 135.9 (C-1′), 157.4 (C-8a), 161.2 (C-2), 162.5 (C-7), 177.3 (C-4). Anal. Calcd. for C18H16O3 (280.32): C, 77.12; H, 5.75. Found: C, 76.89; H, 5.94.

2,3-Dimethyl-7-tosyloxychromone (6e). For the conditions see Table 3. Mp 109-110 °C (hexane-EtOAc). IR: 1636 (C=O), 1612 (C=C), 1448, 1381(SO 2), 1356, 1194, 1179 (SO2), 1084, 830, 817, 734 cm-1. 1H NMR: 2.04 (s, 3H, 2-Me), 2.36 (s, 3H, 3-Me), 2.46 (s, 3H, 4′-Me), 6.85 (dd, J = 2.1, 8.8 Hz, 1H, 6-H), 7.22 (d, J = 2.1 Hz, 1H, 8-H), 7.33 (d, J = 8.0 Hz, 2H, 3′,5′-H), 7.73 (d, J = 8.0 Hz, 2H, 2′,6′-H), 8.08 (d, J = 8.8 Hz, 1H, 5-H). 13C NMR: 9.8 (3-Me), 18.3 (2-Me), 21.6 (4′-Me), 111.7 (C-8), 117.4 (C-3), 119.0 (C-6), 121.4 (C-4a), 127.7 (C-5), 1286 (C-2′,6′), 130.1 (C-3′,5′), 132.1 (C-1′), 146.1 (C-4′), 152.7 (C-7), 156.2 (C-8a), 162.6 (C-2), 177.3 (C-4). Anal. Calcd. for C18H16O5S (344.38): C, 62.78; H, 4.68. Found: C, 62.99; H, 4.88.

2,3-Dimethyl-6,7-ditosyloxychromone (6f). For the conditions see Table 3. Mp 166-169 °C (EtOH). IR: 1646 (C=O), 1617 (C=C), 1478, 1448, 1381(SO2), 1356, 1194, 1179 (SO2), 1084, 830, 817, 734, 706, 694 cm-1. 1H NMR: 2.02 (s, 3H, 2-Me), 2.38 (s, 3H, 3-Me), 2.45, 2.46 (2xs, 2x3H, 4′,4″-H), 7.29 (m, 4H, 3′,5′,3″,5″-H), 7.47 (s, 1H, 8-H), 7.66 (m, 4H, 2′,6′,2″,6″-H), 7.86 (s, 1H, 5-H). 13C NMR: 9.8 (3-Me), 18.3 (2-Me), 21.6 (4′, 4″-Me), 113.8 (C-8), 117.4 (C-3), 120.8 (C-6), 121.5 (C-4a), 128.7, 128.8 (C-5, C-2′,6′, C-2″,6″), 130.0 (C-3′,5′, C-3″,5″), 131.9, 132.4 (C-1, C-1′), 138.5 (C-6)*, 145.1 (C-7)*, 146.1, 146.4 (C-4′, C-4″), 153.9 (C-8a), 162.8 (C-2), 176.4 (C-4). [“interchangeable”] Anal. Calcd. for C25H22O8S2 (514.56): C, 58.36; H, 4.31. Found: C, 58.12; H, 4.37.
7-Benzyloxy-2,3,5-trimethylchromone (6g). For the conditions see Table 3. Mp 108-112 °C (hexane-EtOAc). IR: 1654 (C=O), 1612 (C=C), 1570, 1454, 1280, 1180, 1156, 756 cm⁻¹. ¹H NMR: 1.98 (s, 3H, 2-Me), 2.32 (s, 3H, 3-Me), 2.82 (s, 3H, 5-Me), 5.10 (s, 2H, CH₂), 6.69 (d, J = 1.2 Hz, 1H, 8-H), 6.74 (br s, 1H, 6-H), 7.32-7.45 (m, 5-H, Ph). ¹³C NMR: 10.0 (3-Me), 18.1 (2-Me), 23.1 (5-Me), 70.1 (CH₂), 98.9 (C-8), 115.4, 117.2 (C-3, C-4a), 116.4 (C-6), 127.5, 128.7 (C-2’,6’, C-3’,5’), 128.2 (C-1”), 142.5 (C-5), 158.9 (C-8a), 159.4 (C-2), 161.1 (C-7), 179.3 (C-4). Anal. Calcd. for C₁₉H₁₈O₃ (294.35): C, 77.53; H, 6.16. Found: C, 77.72; H, 5.98.

2,3-Dimethyl-7-hydroxychromone (6d). A mixture of 7-benzyloxy-2,3-dimethylchromone (6c) [280 mg, 0.999 mmol], 48% hydrogen bromide (3 mL) and acetic acid (6 mL) was refluxed for 15 min, then poured on crushed ice, filtered off and washed with water to give pure 6d. Mp 268-271 °C (EtOH). IR: 3208 (OH), 1632 (C=O), 1592, 1570, 1406, 1246 (C-O), 1188, 1102, 862 cm⁻¹. ¹H NMR (DMSO-d₆): 1.90 (s, 3H, 2-Me), 2.35 (s, 3H, 3-Me), 6.76 (d, J = 1.1 Hz, 1H, 8-H), 6.87 (dd, J = 1.1, 8.6 Hz, 1H, 6-H), 7.85 (d, J = 8.6 Hz, 1H, 5-H), 10.64 (s, 1H, 7-OH). ¹³C NMR (DMSO-d₆): 10.6 (3-Me), 19.0 (2-Me), 102.6 (C-8), 115.4 (C-6), 115.8, 116.1 (C-3, C-4a), 127.7 (C-5), 158.0 (C-8a), 162.2, 163.0 (C-2, C-7), 176.8 (C-4). Anal. Calcd. for C₁₁H₁₀O₃ (190.19): C, 69.46; H, 5.30. Found: C, 69.67; H, 5.25.

1,2,3,4-Tetrahydroxanthen-9-one (9a). For the conditions see Table 3. Mp 100-100.5 °C (hexane). (Lit.¹⁶ 88-89 °C). IR: 2946 (CH₂), 1640 (C=O), 1622 (C=C), 1570, 1474, 1464, 1424, 1410, 1156, 768 cm⁻¹. ¹H NMR: 1.74, 1.86 (2xm, 2x2H, 2,3-H), 2.56, 2.63 (2xt, J = 6.2 Hz and 6.4, 2x2H, 1,4-H), 7.21 (m, 2H, 5,7-H), 7.57 (m, 1H, 6-H), 8.17 (dd, J = 1.2, 7.9 Hz). ¹³C NMR: 21.0, 21.6, 21.9 (C-2,3,4), 28.1 (C-1), 117.6 (C-5), 118.4 (C-9a), 123.1 (C-8a), 124.3, 125.7 (C-7,8), 132.9 (C-6), 155.9 (C-5a), 163.9 (C-10a), 177.6 (C-9).

7,8,9,10-Tetrahydrobenzo[b]cyclohepta[e]pyran-11(6H)-one (9b). For the conditions see Table 3. Mp 79-80.5 °C (hexane). (Lit.¹⁶ 82-83 °C). IR: 2924 (CH₂), 1632 (C=O + C=C), 1608, 1574, 1466, 1402, 1322, 1158, 762 cm⁻¹. ¹H NMR: 1.61 (m, 2H, 8-H), 1.75, 1.84 (2xm, 2x2H, 7,9-H), 2.80, 2.87 (2xm, 2x2H, 6,10-H), 7.32-7.41 (overlapping dd and m, 2H, 2,4-H), 7.61 (m, 1H, 3-H), 8.22 (dd, J = 1.5, 7.9Hz, 1H, 1-H). ¹³C NMR: 21.0, 21.6, 21.9 (C-2,3,4), 28.1 (C-1), 117.6 (C-5), 118.4 (C-9a), 123.1 (C-8a), 124.3, 125.7 (C-7,8), 132.9 (C-6), 155.9 (C-5a), 163.9 (C-10a), 177.6 (C-9).

6,7,8,9,10,11-Hexahydrobenzo[b]cycloocta[e]pyran-12(6H)-one (9c). For the conditions see Table 3. Mp 87-89 °C (hexane). (Lit. ¹⁶ 90-91 °C). IR: 2930 (CH₂), 1632 (C=O + C=C), 1612, 1574, 1466, 1456, 1400, 1334, 1224, 1188, 1128, 780, 764 cm⁻¹. ¹H NMR: 1.50 (m, 4H, 8,9-H), 1.72, 1.84 (2xm, 2x2H, 7,10-H), 2.73, 2.81 (2xt, J = 6.0 Hz, 2x2H, 6,11-H), 7.33-7.41 (overlapping dd and m, 2H, 2,4-H), 7.61 (m, 1H, 3-H), 8.21 (dd, J = 0.9, 8.1 Hz, 1H, 1-H). ¹³C NMR: 22.6, 26.0, 26.1, 28.8, 29.0, 31.2 (C-6,7,8,9,10,11), 117.6 (C-4), 120.4, 122.8 (C-11a,12a), 124.2 (C-1), 125.6 (C-2), 132.6 (C-3), 155.5 (C-4a), 168.8 (C-5a), 176.8 (C-11).

2-Phenyl-4-quinolone (17). For the conditions see Table 4. Mp 245-250 °C (MeOH). (Lit. ³¹ 252-254 °C). IR: 3432 (NH), 3064, 2964, 1632 (C=O + C=C), 1580, 1546, 1504, 1472, 1450, 1432, 1256, 1140, 770 cm⁻¹. ¹H NMR (DMSO-d₆): 6.38 (s, 1H, 3-H), 7.40 (m, 1H, 6-H), 7.62 (m, 3H, 3’,4’,5’-H), 7.71 (m, 1H, 7-H), 7.81 (d, J = 8.3 Hz, 1H, 8-H), 7.88 (m, 2H, 2’,6’-H), 8.14...
3-Phenyl-4-quinolone (19). For the conditions see Table 4. Mp 250-253 °C (MeOH). (Lit.\textsuperscript{32} 255-257 °C, Lit.\textsuperscript{33} 268-269 °C). \textsuperscript{1}H NMR (DMSO-d\textsubscript{6}): 7.33 (m, 1H, 6-H), 7.39-7.45 (m, 3H, 3',4',5'-H), 7.63 (d, \(J = 8.0\) Hz, 1H, 8-H), 7.71 (m, 1H, 7-H), 7.77 (dd, \(J = 1.1, 7.3\) Hz, 1H, 2',6'-H), 8.20 (d, \(J = 6.2\) Hz, 1H, 2-H), 8.23 (d, \(J = 7.9\) Hz, 1H, 5-H), 12.11 (d, \(J = 6.2\) Hz, 1H, NH). \textsuperscript{13}C NMR (DMSO-d\textsubscript{6}): 118.7 (C-8), 120.5 (C-3), 124.2, 126.1, 127.1 (C-5,6,4'), 126.1 (C-4a), 128.5, 129.0 (C-2',6', C-3',5'), 132.4 (C-7), 136.4 (C-1'), 138.7 (C-2), 139.6 (C-8a), 175.6 (C-4).

Acknowledgements

This work was supported financially by NATO (HTECH.LG 97.4558) and the Hungarian Scientific Research Fund (OTKA T22290). We thank Mr. I. Ócsai for some preliminary experiments.

References


