STEREOSELECTIVE SYNTHESES OF (E)- AND (Z)-2,3-DIHYDRO-3-(1,2,4-TRIAZOLYL)-4H-1-BENZOPYRAN-4-ONE OXIME ETHERS

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Abstract- A synthesis of (E)- and (Z)-2,3-dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one oxime ethers [(E)- and (Z)-13] and (Z)-2,3-dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one oxime ethers [(Z)-17] are described. Ring closure of 2-(1,2,4-triazolyl)-2′-hydroxyacetophenones (5 or 6) followed by reaction with HONH₂.HCl gave the corresponding (Z)-oximes [(Z)-11 or (Z)-16]. O-Alkylation of (Z)-oximes afforded (Z)-oxime ethers [(Z)-13 or (Z)-17]. Reaction of (Z)-3-bromo-2,3-dihydro-4H-1-benzopyran-4-one oxime (18) with 1,2,4-triazole afforded (E)-oxime [(E)-11]. O-Alkylation of (E)-oxime gave the desired (E)-oxime ethers [(E)-13]. In addition, (Z)-oxime ethers [(Z)-13 or (Z)-17] could also be obtained from the reaction of 2,3-dihydro-3-(1,2,4-triazolyl)-4H-1-benzopyran-4-ones (2 or 14) with O-(aryl)methylhydroxylamine hydrochloride (19).

Chroman-4-ones are important synthetic intermediates for chromans, chromenes and chromanols which themselves possess diverse pharmacological properties such as β-blockade, anticonvulsant, antiestrogen and antimicrobial.¹

1,2,4-Triazoles constitute an important class of nitrogen heterocycles and many 1-substituted 1,2,4-triazoles have found use as antifungal agents, agricultural fungicides, plant growth regulators or aromatase inhibitors.² As fungicides and antifungals the primary mode of action is by suppression of cytochrome P-450 activity which is required in the demethylation of 14α-methylsterols to ergosterol biosynthesis.³

In the search for new antifungal agents and agricultural fungicides a number of derivatives containing the 1,2,4-triazole and the chroman ring in the same molecule have been considered. This paper describes the synthesis of (E)- and (Z)-oxime ethers of 2,3-dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-ones and some related compounds.

The synthesis of 2,3-dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-ones (2) was first attempted by reaction of the corresponding 3-bromo-4-chromanone (1) with excess 1,2,4-triazole in DMF similar to the procedure described by Strehlke et al.⁴ (Scheme 1). The latter reaction did not give compound (2) and was recovered (98%). When 1,2,4-triazole was reacted with 1 in the presence of K₂CO₃ in MeCN similar
to those reported by Lai et al., dehydrohalogenation of 1 took place and the corresponding chromone (3) was the major product and compound (2) was obtained in 12% yield.

A more convenient method for the preparation of 2 was the ring closure of 2-(1H-1,2,4-triazol-1-yl)-2′-hydroxyacetophenones (5). The apparent straightforward preparation of 5 was displacement of 2-bromo-2′-hydroxyacetophenones (4) by 1,2,4-triazole as reported by Baji et al. (Scheme 2). Treatment of 4 with excess 1,2,4-triazole in DMF, gave mixture of compounds (5) and (6) in 1 to 2 ratio. In addition, the quaternary triazolium salt by-product (7) was isolated in 45-50% yield. Direct alkylation of 1,2,4-triazole usually affords a mixture of mainly 1- and some 4-substituted products. Ratios vary with the nature of the alkylating agent and the conditions employed, but range from 70:30 to 90:10. In our case, 1-isomer was minor product and quaternary triazolium salt by-product was the major one, probably because when compound (5) was formed subsequently reacted with another 2-bromoacetophenone and gave compound (7). However, the problem of preparing 2-(1H-1,2,4-triazol-1-yl)acetophenones (5) in high yield could be solved. Reaction of 4-amino-1,2,4-triazole (8) with 4 gave pure triazolium salt (9), which on subsequent deamination with nitrous acid yielded exclusively the 1-substituted product (5).

Ring closure of compound (5) by paraformaldehyde in acetic acid at 90-100°C gave the corresponding 3-triazolylchromanones (2) in low to moderate yield (Scheme 3). The yield of compound (2a, R1=H) was very low (11%). However, compound (2a) could be synthesized in good yield as shown in Scheme 3. Reaction of compound (1) with 8 in MeCN under reflux for 1 d gave the desired triazolium salt (10) in 76% yield. Chromone (3) was isolated in 8% yield as a by-product. Diazotization of 10 (with the loss of nitrous oxide) readily provided 2a in good yield (94%).

Compound (6) was cyclized through similar procedure which was employed for 5 and compound (14) was obtained in moderate yield. In the latter reaction, in addition to 14, the corresponding 3-hydroxymethyl derivatives (15) were obtained as by-products.

As illustrated in Scheme 3, the ketones (2) and (14) were converted to the pure (Z)-oxime derivatives [(Z)-11] and [(Z)-16] in good yield by stirring with 3 equivalent of HONH2.HCl in methanol at room temperature.
An attempt to synthesis the (E)-oximes by isomerisation of (Z)-oximes (11) and (16) in acidic medium failed, and the starting materials were recovered. Mixich et al. have recently reported preparation of (E)-2-(imidazol-1-yl)acetophenone oximes by reaction of (Z)-2-haloacetophenone oximes with imidazole which involves the inversion of oxime. In our case, stirring a mixture of compound (1) and three equivalent of HONH$_2$.HCl in methanol at room temperature gave (Z)-3-bromo-2,3-dihydro-4H-1-benzopyran-4-one oxime (18). Reaction of 18 with 1,2,4-triazole in the presence of K$_2$CO$_3$ in MeCN at room temperature yielded (E)-2,3-dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one oxime [(E)-11a] in 54% yield. (E)-2,3-Dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one oxime [(E)-16a] was isolated as a by-product in 8% yield (Scheme 4). Smith et al. previously described the reaction of (Z)-2-bromoacetophenone oxime with nucleophiles which involves the trapping of a reactive α-nitrosostyrene intermediate, which reacts more rapidly in the s-trans conformation than in the s-cis, giving (E)-isomer. Similar mechanism may be involved in our case (Scheme 4).

The O-substituted oximes (13 or 17) were prepared by reacting (Z)-or (E)-oximes with substituted benzyl halides (12) in DMF in the presence of NaH at room temperature (method A) or K$_2$CO$_3$ at 50°C (method B).

In all cases there was no evidence for stereochemical alteration (Schemes 3,4). In addition, the O-substituted oximes could directly be obtained from the corresponding ketones (method C). Thus,
treatment of ketones (2 or 14) with \( O \)-(arylmethyl)hydroxylamine hydrochloride (19) in methanol afforded a mixture of \((Z)\)- and \((E)\)-oxime ethers (Scheme 5), predominantly in the \(Z\) configuration, which was established by \(^1\)H NMR spectral data. The \(Z/E\) ratio was approximately 90:10 %. In most cases the work-up of the crude product led to the practically pure \(Z\)-isomers.

NMR spectra are generally used to assign the stereochemistry of the isomers \((E\) or \(Z\) form) of oximes derived from ketones.\(^6,9,13\) Table 1 shows selected chemical shifts (H-5 and H-3 of the chroman ring) of the ketones (2 and 14), \((Z)\)- and \((E)\)-oximes (11 and 16). Examination of the proton at the 5-position showed that the chemical shifts of compounds [(Z)-11] and [(Z)-16] (7.86-7.88 ppm) were virtually the same as those (7.62-7.97) of their parent ketones. On the other hand, chemical shifts of the H-3 for compounds [(Z)-11] and [(Z)-16] were at 5.97-6.08 and for ketones (2 and 14) at 5.29-5.50. The H-3 of (Z)-11 and (Z)-16 are deshielded by the presence of the nearby hydroxyl function and must therefore be the (Z)-isomers. On the other hand, the chemical shifts of the H-5 of \((E)\)-isomers [(E)-11 and (E)-16] are substantially influenced by the hydroxyl group and the signals appeared downfield at 8.67-8.70. The chemical shifts (5.44) of the H-3 in \((E)\)-isomers are the same as those (5.29-5.40) of their parent ketones (2, 14).

Similar result were observed in the \(^1\)H MNR of the oxime ethers (13, 17, see Table 2).

**EXPERIMENTAL**

All melting points were determined using a Kofler hot stage apparatus and are uncorrected. IR spectra were recorded using a Perkin-Elmer Model 781 or Nicolet FT-IR Magna 550 spectrophotometer. NMR
Table 1. Selected $^1$H NMR chemical shifts of substituted 4-chromanones

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>R$_1$</th>
<th>X</th>
<th>Tr</th>
<th>Chroman ring</th>
<th>H-3</th>
<th>H-5</th>
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<tbody>
<tr>
<td>2a</td>
<td>H</td>
<td>O</td>
<td>1,2,4-Triazol-1-yl</td>
<td>H-3</td>
<td>5.40</td>
<td>H-5</td>
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<tr>
<td>2b</td>
<td>Cl</td>
<td>O</td>
<td>1,2,4-Triazol-1-yl</td>
<td>H-3</td>
<td>5.37</td>
<td>H-5</td>
</tr>
<tr>
<td>14a</td>
<td>H</td>
<td>O</td>
<td>1,2,4-Triazol-4-yl</td>
<td>H-3</td>
<td>5.29</td>
<td>H-5</td>
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<tr>
<td>14b</td>
<td>Cl</td>
<td>O</td>
<td>1,2,4-Triazol-4-yl</td>
<td>H-3</td>
<td>5.50</td>
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<td>1,2,4-Triazol-1-yl</td>
<td>H-3</td>
<td>6.04</td>
<td>H-5</td>
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<tr>
<td>(Z)-11b</td>
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<td>N-OH</td>
<td>1,2,4-Triazol-1-yl</td>
<td>H-3</td>
<td>6.08</td>
<td>H-5</td>
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<td>(Z)-16a</td>
<td>H</td>
<td>N-OH</td>
<td>1,2,4-Triazol-4-yl</td>
<td>H-3</td>
<td>5.97</td>
<td>H-5</td>
</tr>
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<td>(Z)-16b</td>
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<td>N-OH</td>
<td>1,2,4-Triazol-4-yl</td>
<td>H-3</td>
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<td>H-5</td>
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<td>H</td>
<td>N-OH</td>
<td>1,2,4-Triazol-1-yl</td>
<td>H-3</td>
<td>5.44</td>
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<td>1,2,4-Triazol-4-yl</td>
<td>H-3</td>
<td>5.44</td>
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Table 2. Selected $^1$H NMR chemical shifts of substituted chromanone oxime ethers

<table>
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<tr>
<th>Compound No.</th>
<th>R$_1$</th>
<th>R$_2$</th>
<th>Tr</th>
<th>Method</th>
<th>Chroman ring</th>
<th>H-3</th>
<th>H-5</th>
</tr>
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<tbody>
<tr>
<td>(Z)-13a</td>
<td>H</td>
<td>H</td>
<td>1,2,4-Triazol-1-yl</td>
<td>A</td>
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<td>8.37</td>
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<tr>
<td>(Z)-13b</td>
<td>H</td>
<td>4-Cl</td>
<td>1,2,4-Triazol-1-yl</td>
<td>A,C</td>
<td>6.11</td>
<td>7.83</td>
<td></td>
</tr>
<tr>
<td>(Z)-13c</td>
<td>H</td>
<td>2,4-Cl$_2$</td>
<td>1,2,4-Triazol-1-yl</td>
<td>A,C</td>
<td>6.14</td>
<td>7.86</td>
<td></td>
</tr>
<tr>
<td>(Z)-13d</td>
<td>Cl</td>
<td>4-Cl</td>
<td>1,2,4-Triazol-1-yl</td>
<td>A</td>
<td>6.16</td>
<td>7.81</td>
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<td>Cl</td>
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<td>1,2,4-Triazol-1-yl</td>
<td>A</td>
<td>6.17</td>
<td>7.81</td>
<td></td>
</tr>
<tr>
<td>(Z)-17a</td>
<td>H</td>
<td>H</td>
<td>1,2,4-Triazol-4-yl</td>
<td>B</td>
<td>6.16</td>
<td>7.85</td>
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<td>H</td>
<td>2,4-Cl$_2$</td>
<td>1,2,4-Triazol-4-yl</td>
<td>B</td>
<td>6.16</td>
<td>7.83</td>
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<tr>
<td>(Z)-17c</td>
<td>Cl</td>
<td>H</td>
<td>1,2,4-Triazol-4-yl</td>
<td>B</td>
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<td>7.83</td>
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<tr>
<td>(Z)-17d</td>
<td>Cl</td>
<td>2,4-Cl$_2$</td>
<td>1,2,4-Triazol-4-yl</td>
<td>B,C</td>
<td>6.12</td>
<td>7.81</td>
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<tr>
<td>(E)-13a</td>
<td>H</td>
<td>H</td>
<td>1,2,4-Triazol-1-yl</td>
<td>A</td>
<td>5.85</td>
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<td>H</td>
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<td>A,C</td>
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<td>8.50</td>
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<tr>
<td>(E)-13c</td>
<td>H</td>
<td>2,4-Cl$_2$</td>
<td>1,2,4-Triazol-1-yl</td>
<td>A,C</td>
<td>5.47</td>
<td>8.51</td>
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<tr>
<td>(E)-13d$^a$</td>
<td>Cl</td>
<td>2,4-Cl$_2$</td>
<td>1,2,4-Triazol-4-yl</td>
<td>C</td>
<td>5.07</td>
<td>8.48</td>
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</table>

$^a$ Free base
spectra were measured using a Bruker FT-80 or Varian 400 Unity plus spectrometer, and chemical shifts are expressed in ppm ($\delta$) with TMS as an internal standard. MS spectra were measured with a Finnigan TSQ 70 Mass spectrophotometer at 70 eV. All evaporation were performed under reduced pressure. Column chromatography was performed on silica gel (grade 60, 230-400 mesh).

The desired 4-amino-1,2,4-triazole$^{14}$ (8), 2-bromo-2'-hydroxyacetophenones$^{15}$ (4), 3-bromo-4-chromanone$^{16}$ (1) and $O$-(arylmethyl)hydroxylamine hydrochloride (19)$^{17}$ were prepared by the Literature procedures.

**Reaction of 3-bromo-4-chromanone (1) with 1,2,4-triazole.**

A mixture of 1 (227 mg, 1.0 mmol), 1,2,4-triazole (104 mg, 1.5 mmol) and K$_2$CO$_3$ (276 mg, 2.0 mmol) in MeCN (5 mL) was stirred at 40°C for 5 h. The mixture was poured into water and then extracted with CHCl$_3$. The organic phase after washing with H$_2$O, was shaken with a solution of 10% HCl. The organic phase was evaporated to dryness yielding 118 mg of 3 (81%). The aqueous acid solution was neutralized with NaHCO$_3$ and extracted with CHCl$_3$. The solvent was evaporated to afford 2a (26 mg, 12%).

**4$H$-1-Benzopyran-4-one (3):** mp 55-57°C (hexane, lit.$^{16}$ mp 57°C); $^1$H NMR (80 MHz, CDCl$_3$) $\delta$ 6.34 (d, 1H, J=6.0 Hz), 7.30-7.78 (m, 3H), 7.80 (d, 1H, J=6.0 Hz), 8.21 (dd, 1H, J=8.0, 1.6 Hz).

**2,3-Dihydro-3-(1H-1,2,4-triazol-1-yl)-4$H$-1-benzopyran-4-one (2a):** mp 136-138°C (methanol); IR (KBr) 2919, 1700, 1603 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.90 (m, 2H), 5.40 (dd, 1H, J=9.6, 7.2 Hz), 7.08 (d, 1H, J=8.4 Hz), 7.14 (t, 1H, J=7.6 Hz), 7.59 (t, 1H, J=8.0 Hz), 7.97 (d, 1H, J=7.6 Hz), 8.04 (s, 1H), 8.35 (s, 1H); MS (m/z, %) 215 (M$^+$, 6), 146 (20), 120 (57), 92 (100), 64 (13), 63 (24). Anal. Calcd for C$_{11}$H$_7$N$_3$O$_2$: C, 61.39; H, 4.19; N, 19.53. Found: C, 61.31; H, 4.23; N, 19.42.

**General procedure for the reaction of 2-bromo-2'-hydroxyacetophenones (4) with 1,2,4-triazole.**

To a solution of 1,2,4-triazole (8280 mg, 0.12 mol) in DMF (50 mL) was added the appropriate 2-bromo-2'-hydroxyacetophenone (0.04 mol) in small portions. The temperature of the mixture must not exceed 15°C. After the addition was complete, the mixture was stirred at 0°C for 3 h. The resulting solution was poured into ice-water (200 mL) and the precipitate was filtered off. The precipitate was extracted with boiling toluene and filtered hot. The solvent was removed and the residue was crystallized from toluene and then methanol to give 5. The material insoluble in toluene was taken up with 10% HCl solution. The white to light brown insoluble solid was filtered , washed with water and dried to afford 7. The acidic solution was neutralized with NaHCO$_3$ and the precipitate was filtered off and crystallized from methanol to afford 6.

**1-(2-Hydroxyphenyl)-2-(1H-1,2,4-triazol-1-yl)ethanone (5a):** yield 12%; mp 135-137°C; IR (KBr) 2934, 1669 cm$^{-1}$; $^1$H NMR (80 MHz, DMSO-d$_6$) $\delta$ 5.84 (s, 2H), 6.97 (t, 1H, J=8.8 Hz), 7.03 (d, 1H, J=8.8 Hz), 7.54 (t, 1H, J=8.8 Hz), 7.81 (d, 1H, J=8.8 Hz), 8.00 (s, 1H), 8.50 (s, 1H); MS (m/z, %) 203 (M$^+$, 13),
1-(4-Chloro-2-hydroxyphenyl)-2-(1H-1,2,4-triazol-1-yl)ethanone (5b): yield 10%; mp 146-148°C; IR (KBr) 3139, 1675 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 5.81 (s, 2H), 7.05 (dd, 1H, J=8.6, 2.0 Hz), 7.10 (d, 1H, J=2.0 Hz), 7.81 (d, 1H, J=8.8 Hz), 8.01 (s, 1H), 8.51 (s, 1H); MS (m/z, %) 237 (M⁺, 22), 157 (32), 155 (100), 83 (10). Anal. Calcd for C₁₀H₉N₃O₂Cl: C, 50.53; H, 3.37; N, 17.69. Found: C, 50.41; H, 3.41; N, 17.69.

1-(2-Hydroxyphenyl)-2-(4H-1,2,4-triazol-4-yl)ethanone (6a): yield 25%; mp 237-239°C; IR (KBr) 3129, 1655 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 5.70 (s, 2H), 6.99 (t, 1H, J=7.6 Hz), 7.05 (d, 1H, J=8.0 Hz), 7.53 (dt, 1H, J=7.6, 1.6 Hz), 7.83 (dd, 1H, J=8.0, 1.6 Hz), 8.47 (s, 2H); MS (m/z, %) 204 (11), 203 (M⁺, 20), 176 (12), 134 (35), 121 (100), 105 (80), 93 (60), 77 (40), 76 (52), 65 (80), 55 (12). Anal. Calcd for C₁₀H₉N₃O₂: C, 59.11; H, 4.43; N, 20.69. Found: C, 59.23; H, 4.23; N, 20.83.

1-(4-Chloro-2-hydroxyphenyl)-2-(4H-1,2,4-triazol-4-yl)ethanone (6b): yield 21%; mp 241-243°C; IR (KBr) 3347, 3128, 1670 cm⁻¹; ¹H NMR (80 MHz, DMSO-d₆) δ 5.66 (s, 2H), 6.80-7.15 (m, 2H), 7.84 (d, 1H, J=8.3 Hz), 8.43 (s, 2H), 11.57 (s, 1H); MS (m/z, %) 237 (M⁺, 6), 157 (30), 155 (85), 127 (13), 99 (22), 83 (100), 63 (15). Anal. Calcd for C₁₀H₈N₃O₂Cl: C, 50.53; H, 3.37; N, 17.69. Found: C, 50.81; H, 3.30; N, 17.78.

1,4-Bis(2-hydroxyphenacyl)-1H-1,2,4-triazolium Bromide (7a): yield 45%; mp 215-217°C; IR (KBr) 3061, 1669, 1607 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 6.05 (s, 2H), 6.18 (s, 2H), 6.98 (t, 1H, J=6.8 Hz), 6.99 (t, 1H, J=6.8 Hz), 7.19 (d, 1H, J=8.4 Hz), 7.23 (d, 1H, J=8.4 Hz), 7.56 (t, 2H, J=7.6 Hz), 7.82 (d, 1H, J=8.4 Hz), 7.85 (d, 1H, J=8.4 Hz), 9.24 (s, 1H), 10.09 (s, 1H), 11.47 (s, 1H), 11.53 (s, 1H); MS (m/z, %) 337 (M⁺, 1), 204 (40), 203 (23), 176 (11), 134 (32), 121 (100), 105 (83), 104 (25), 93 (64), 83 (22), 77 (42), 76 (77), 65 (73), 63 (21), 53 (12), 51 (13), 50 (25). Anal. Calcd for C₁₈H₁₆N₃O₄Br: C, 51.67; H, 3.83; N, 10.05. Found: C, 51.90; H, 3.71; N, 90.90.

1,4-Bis(4-chloro-2-hydroxyphenacyl)-1H-1,2,4-triazolium Bromide (7b): yield 50%; mp 214-216°C; IR (KBr) 3079, 1683, 1593 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 6.00 (s, 2H), 6.14 (s, 2H), 7.06 (m, 2H), 7.29 (d, 1H, J=1.6 Hz), 7.34 (d, 1H, J=1.6 Hz), 7.82 (d, 1H, J=8.4 Hz), 7.85 (d, 1H, J=8.4 Hz), 9.20 (s, 1H), 10.04 (s, 1H), 12.04 (s, 1H), 12.13 (s, 1H); MS (m/z, %) 406 (M⁺, 2), 237 (12), 157 (35), 155 (89), 127 (11), 99 (25), 83 (100), 63 (18). Anal. Calcd for C₁₈H₁₄N₃O₄BrCl₂: C, 51.67; H, 2.87; N, 8.62. Found: C, 44.15; H, 2.54; N, 8.68.

General procedure for the reaction of 2-bromo-2′-hydroxyactophenones (4) with 4-amino-4H-1,2,4-triazole (8).

A solution of 4 (4 mmol) and 8 (0.37 g, 4.4 mmol) in 2-propanol (8 mL) was refluxed for 3 h. Upon
cooking the colorless salt was filtered, washed with cold 2-propanol to give 9.

1-(2-Hydroxyphenyl)-2-(4-amino-4H-1,2,4-triazoliumyl)ethanone Bromide (9a): yield 75%; mp 169-170°C (2-propanol); IR (KBr) 3216, 3098, 2914, 1655 cm\(^{-1}\); \(^1\)H NMR (80 MHz, DMSO-\(d_6\)) \(\delta\) 6.05 (s, 2H), 7.79 (d, 1H, J=8.0 Hz), 9.30 (s, 1H), 10.20 (s, 1H), 11.21 (s, 1H). MS (m/z, %) 219 (M\(^+\), 1), 203 (14), 121 (100), 104 (14), 92 (32), 83 (12), 82 (35), 65 (64), 64 (33). Anal. Calcd for C\(_{10}\)H\(_{11}\)N\(_4\)O\(_2\)Br: C, 40.13; H, 3.68; N, 18.73. Found: C, 40.02; H, 3.81; N, 18.71.

1-(4-Chloro-2-hydroxyphenyl)-2-(4-amino-4H-1,2,4-triazoliumyl)ethanone Bromide (9b): yield 64%; mp 177-178°C (2-propanol); IR (KBr) 3189, 3080, 1655, 1617 cm\(^{-1}\); \(^1\)H NMR (80 MHz, DMSO-\(d_6\)) \(\delta\) 6.01 (s, 2H), 6.98-7.35 (m, 4H), 7.81 (d, 1H, J=8.0 Hz), 9.28 (s, 1H), 10.12 (s, 1H), 11.71 (s, 1H). MS (m/z, %) 253 (M\(^+\), 1), 237 (16), 157 (40), 155 (100), 83 (12), 64 (17), 43 (16). Anal. Calcd for C\(_{10}\)H\(_{10}\)N\(_4\)O\(_2\)BrCl: C, 35.98; H, 3.00; N, 16.79. Found: C, 35.95; H, 2.81; N, 16.91.

General procedure for the deamination of 1-(2-hydroxyphenyl)-2-(4-amino-4H-1,2,4-triazoliumyl)ethanone Bromide (9).

To a vigorously stirred ice-cold aqueous suspension of 9 (10.0 mmol in 25 mL) was added concentrated HCl (1.98 g, 20.0 mmol). A solution of sodium nitrite (0.72 g, 10.5 mmol) in water (5 mL) was added dropwise at a rate to prevent excessive foaming (30 min). The mixture was permitted to come to rt and was stirred for another 45 min. Upon neutralization with NaHCO\(_3\), the precipitate was filtered, washed with water and crystallized from MeOH to give 5 (yield 89-95%).

General procedure for the cyclization of 5 or 6 with paraformaldehyde.

A solution of 2-(1,2,4-triazolyl)acetophenones (5 or 6) (5.0 mmol) and paraformaldehyde (0.15 g, 5.0 mmol) in glacial AcOH (20 mL) was refluxed for 3-6 h. The solvent was evaporated and the residue taken up with CHCl\(_3\). The organic layer was washed with water, dried (Na\(_2\)SO\(_4\)), and evaporated to dryness. The products (2, 14 and 15) were separated by silica gel column chromatography, eluting with CHCl\(_3\)-MeOH (20:1). The first fraction gave 2 or 14 which crystallized from MeOH.

7-Chloro-2,3-dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one (2b): yield 40%; mp 132-134°C; IR (KBr) 3129, 1697, 1597 cm\(^{-1}\); \(^1\)H NMR (80 MHz, CDCl\(_3\)) \(\delta\) 4.95 (m, 2H), 5.38 (dd, 1H, J=9.8, 7.0 Hz), 7.12 (m, 2H), 7.90 (d, 1H, J=8.8 Hz), 8.00 (s, 1H), 8.31 (s, 1H). MS (m/z, %) 249 (M\(^+\), 30), 180 (55), 156 (50), 154 (100), 126 (37), 96 (15), 57 (11), 44 (12). Anal. Calcd for C\(_{11}\)H\(_8\)N\(_3\)O\(_2\)Cl: C, 52.91; H, 3.21; N, 16.83. Found: C, 52.99; H, 3.39; N, 16.70.

2,3-Dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one (14a): yield 70%; mp 143-144°C; IR (KBr) 3106, 1690, 1615 cm\(^{-1}\); \(^1\)H NMR (80 MHz, CDCl\(_3\)) \(\delta\) 4.79 (m, 2H), 5.26 (dd, 1H, J=8.7, 5.4 Hz), 6.90-7.30 (m, 2H), 7.62 (dt, 1H, J=8.3, 1.8 Hz), 7.92 (dd, 1H, J=8.0, 1.8 Hz), 8.28 (s, 2H). MS (m/z, %) 215 (M\(^+\), 20), 120 (23), 92 (100), 64 (14). Anal. Calcd for C\(_{11}\)H\(_9\)N\(_3\)O\(_2\): C, 61.39; H, 4.19; N, 19.53. Found: C, 61.08; H, 3.97; N, 19.64.
7-Chloro-2,3-dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one (14b): yield 51%; mp 160-162°C; IR (KBr) 3104, 1698, 1598 cm⁻¹; ¹H NMR (80 MHz, CDCl₃) δ 4.60-5.15 (m, 2H), 5.50 (m, 1H), 7.00-7.30 (m, 2H), 7.85 (d, 1H, J=9.0 Hz), 8.22 (s, 2H). MS (m/z, %) 249 (M⁺, 66), 156 (43), 154 (100), 128 (12), 126 (35). Anal. Calcd for C₁₁H₈N₃O₂Cl: C, 52.91; H, 3.21; N, 16.83. Found: C, 52.94; H, 3.09; N, 16.70.

3-Hydroxymethyl-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one (15a): yield 12%. mp 183-185°C; IR (KBr) 3155, 3117, 1702, 1612 cm⁻¹; ¹H NMR (80 MHz, DMSO-d₆) δ 4.06 (d, 2H, J=6.4 Hz), 4.83 (d, 1H, J=11.4 Hz), 5.12 (d, 1H, J=11.4 Hz), 5.76 (t, 1H, J=6.4 Hz), 7.07-7.30 (m, 2H), 7.57-7.96 (m, 2H), 8.65 (s, 2H). MS (m/z, %) 245 (M⁺, 18), 215 (32), 120 (20), 92 (100), 64 (11). Anal. Calcd for C₁₂H₁₁N₃O₃: C, 58.77; H, 4.49; N, 17.14. Found: C, 58.39; H, 4.52; N, 16.91.

7-Chloro-3-hydroxymethyl-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one (15b): yield 15%; mp 145-147°C; IR (KBr) 3023, 2947, 1703, 1608, 1488 cm⁻¹; ¹H NMR (80 MHz, CDCl₃+CF₃COOH) δ 4.28 (s, 2H), 4.96 (s, 2H), 7.05-7.23 (m, 2H), 7.89 (d, 1H, J=9.0 Hz), 9.27 (s, 2H). MS (m/z, %) 279 (M⁺, 22), 251 (12), 249 (38), 249 (38), 215 (32), 120 (20), 92 (100), 64 (11). Anal. Calcd for C₁₂H₁₀N₃O₃Cl: C, 51.52; H, 3.58; N, 15.03. Found: C, 51.68; H, 3.69; N, 14.86.

Reaction of 3-bromo-4-chromanone (1) with 4-amino-4H-1,2,4-triazole (8).

A solution of 1 (2.27 g, 10.0 mmol) and 8 (0.92 g, 11.0 mmol) in MeCN (40 mL) was refluxed for 30 h. Upon cooling, the white salt 10 was collected, washed with cold MeCN, and dried.

2,3-Dihydro-3-(4-amino-4H-1,2,4-triazoliumyl)-4H-1-benzopyran-4-one Bromide (10): yield 76%; mp 151-153°C (MeCN); IR (KBr) 3289, 3199, 3004, 2956, 1717, 1612 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 4.99 (m, 2H), 6.30 (dd, 1H, J=11.2, 6.0 Hz), 7.17 (d, 1H, J=6.8 Hz), 7.21 (t, 1H, J=8.0 Hz), 7.72 (dt, 1H, J=7.2, 1.2 Hz), 7.86 (dd, 1H, J=7.6, 1.2 Hz), 9.19 (br s, 2H), 9.36 (s, 1H), 10.37 (s, 1H). MS (m/z, %) 231 (M⁺, 2), 223 (20), 214 (30), 188 (18), 186 (31), 172 (25), 121 (69), 120 (67), 105 (46), 104 (51), 96 (30), 92 (100), 83 (47), 64 (48). Anal. Calcd for C₁₁H₁₁N₄O₂Br: C, 42.44; H, 3.54; N, 18.01. Found: C, 42.27; H, 3.61; N, 18.05.

Deamination of 10.

According to the general procedure for deamination of 9, the product (2a) was obtained as a pale yellow solid (94%) and crystallized from MeOH.

General procedure for the reaction of ketones (2 or 14) with HONH₂·HCl.

A solution of ketones (2 or 14) (5.0 mmol) and HONH₂·HCl (1.04 g, 15.0 mmol) in MeOH (25 mL) was stirred at rt for 2-3 d. After concentrating the reaction mixture by evaporation under reduced pressure, MeOH was replaced with water (100 mL) and neutralized with NaHCO₃. The precipitate was filtered by filtration, washed with water, and dried to give (Z)-11 or (Z)-16.

(Z)-2,3-Dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one oxime [(Z)-11a]: yield 85%; mp
170-172°C (methanol); IR (KBr) 3119, 1608 cm⁻¹; ¹H NMR (80 MHz, DMSO-d₆) δ 4.32 (d, 1H, J=12.0 Hz), 4.63 (d, 1H, J=12.0 Hz), 6.04 (br s, 1H), 6.80-7.46 (m, 3H), 7.88 (d, 1H, J=7.4 Hz), 7.93 (s, 1H), 8.41 (s, 1H), 11.92 (s, 1H). MS (m/z, %) 230 (M⁺, 3), 171 (28), 81 (33), 76 (13), 54 (100). Anal. Calcd for C₁₁H₁₀N₄O₂: C, 57.39; H, 4.35; N, 24.35. Found: C, 57.01; H, 4.21; N, 24.47.

(Z)-7-Chloro-2,3-dihydro-3-(1H-1,2,3-triazol-1-yl)-4H-1-benzopyran-4-one oxime [(Z)-11b]: yield 98%; mp 171-173°C (methanol); IR (KBr) 3452, 3092, 3017, 1614 cm⁻¹; ¹H NMR (80 MHz, DMSO-d₆) δ 4.20-4.90 (m, 2H), 6.08 (m, 1H), 7.10 (m, 2H), 7.87 (d, 1H, J=9.1 Hz), 8.01 (s, 1H), 8.61 (s, 1H), 12.15 (s, 1H). MS (m/z, %) 264 (M⁺, 68), 249 (19), 195 (55), 165 (32), 154 (42), 97 (12), 83 (14), 75 (20), 44 (100). Anal. Calcd for C₁₁H₉N₄O₂Cl: C, 49.91; H, 3.40; N, 21.17. Found: C, 49.76; H, 3.18; N, 21.24.

(Z)-2,3-Dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one oxime [(Z)-16a]: yield 65%; mp 207-208°C (methanol); IR (KBr) 3128, 1617 cm⁻¹; ¹H NMR (80 MHz, DMSO-d₆) δ 4.37 (dd, 1H, J=12.0, 3.2 Hz), 4.68 (dd, 1H, J=12.0, 2.0 Hz), 5.97 (m, 1H), 6.95-7.20 (m, 2H), 7.37 (t, 1H, J=8.0 Hz), 7.86 (d, 1H, J=8.0 Hz), 8.39 (s, 2H), 12.09 (s, 1H). MS (m/z, %) 230 (M⁺, 100), 161 (51), 131 (20), 103 (50), 92 (33), 91 (52), 90 (44), 77 (45), 75 (20), 63 (23), 51 (21). Anal. Calcd for C₁₁H₁₀N₄O₂: C, 57.39; H, 4.35; N, 24.35. Found: C, 57.55; H, 4.38; N, 24.25.

(Z)-7-Chloro-2,3-dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one oxime [(Z)-16b]: yield 92%; mp 230-231°C (methanol); IR (KBr) 3139, 1606 cm⁻¹; ¹H NMR (80 MHz, CDCl₃) δ 4.30 (dd, 1H, J=12.8, 1.8 Hz), 4.52 (dd, 1H, J=12.8, 1.8 Hz), 5.48 (t, 1H, J=1.8), 6.80-7.10 (m, 2H), 7.83 (d, 1H, J=8.0 Hz), 8.41 (s, 2H), 12.20 (s, 1H). MS (m/z, %) 264 (M⁺, 80), 249 (18), 195 (67), 165 (30), 154 (42), 97 (12), 83 (14), 75 (20), 44 (100). Anal. Calcd for C₁₁H₁₀N₄O₂Cl: C, 49.91; H, 3.40; N, 21.17. Found: C, 49.92; H, 3.49; N, 21.05.

Reaction of 3-bromo-4-chromanone (1) with HONH₂.HCl.
To a stirring solution of 1 (0.91 g, 4.0 mmol) in MeOH (15 mL) at rt, was added an aqueous solution of HONH₂.HCl (0.83 g, 12.0 mmol, in 4 mL). After 3 d water (20 mL) was added and the white solid was filtered off, washed with water and dried to give 18.

(Z)-3-Bromo-2,3-dihydro-4H-1-benzopyran-4-one oxime (18): yield 93%; mp 168-170°C (methanol); IR (KBr) 3201, 3066, 1608, 1450 cm⁻¹; ¹H NMR (80 MHz, CDCl₃) δ 4.30 (dd, 1H, J=12.8, 1.8 Hz), 4.52 (dd, 1H, J=12.8, 1.8 Hz), 5.48 (t, 1H, J=1.8), 6.80-7.10 (m, 2H), 7.31 (dt, 1H, J=6.4, 2.4 Hz), 7.83 (dd, 1H, J=8.4, 2.4 Hz). MS (m/z, %) 241 (M⁺, 100), 227 (33), 225 (40), 201 (41), 199 (66), 195 (42), 194 (98), 164 (80), 162 (87), 146 (76), 144 (75), 131 (79), 89 (40), 63 (84). Anal. Calcd for C₇H₈NO₂Br: C, 44.63; H, 3.31; N, 5.78. Found: C, 44.82; H, 3.42; N, 5.67.

Reaction of (Z)-3-bromo-2,3-dihydro-4H-1-benzopyran-4-one oxime (18) with 1,2,4-triazole.
A mixture of 18 (1.45 g, 6.0 mmol), 1,2,4-triazole (1.04 g, 15.0 mmol) and K₂CO₃ (1.24 g, 9.0 mmol) in MeCN (40 mL), was stirred at rt for 2 d. After concentration under reduced pressure, the reaction mixture
was diluted with water and extracted with AcOEt. The organic layer was dried (Na₂SO₄) and the solvent evaporated. The isomers [(E)-11a and (E)-16a] was separated by silica gel column chromatography with AcOEt-EtOH (10:1) and crystallized from MeOH.

(E)-2,3-Dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one oxime [(E)-11a]: yield 54%; mp 185-187°C; IR (KBr) 3175, 3113, 1612 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 4.55 (dd, 1H, J=12.1, 2.4 Hz), 4.90 (dd, 1H, J=12.1, 3.2 Hz), 5.44 (dd, 1H, J=3.2, 2.4 Hz), 6.96 (d, 1H, J=8.0 Hz), 7.03 (t, 1H, J=7.4 Hz), 7.36 (t, 1H, J=7.0 Hz), 7.96 (s, 1H), 8.45 (s, 1H), 8.69 (d, 1H, J=8.0 Hz), 12.13 (s, 1H). MS (m/z, %) 230 (M⁺, 65), 161 (100), 131 (70), 130 (20), 103 (15), 77 (20), 70 (18). Anal. Calcd for C₁₁H₁₀N₄O₂: C, 57.39; H, 4.35; N, 24.35. Found: C, 57.41; H, 4.21; N, 24.01.

(E)-2,3-Dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one oxime [(E)-16a]: yield 8%; mp 204-206°C; IR (KBr) 3148, 1614 cm⁻¹; ¹H NMR (80 MHz, DMSO-d₆) δ 4.55 (dd, 1H, J=11.2, 2.4 Hz), 4.92 (dd, 1H, J=11.2, 4.0 Hz), 5.44 (dd, 1H, J=4.0, 2.4 Hz), 6.80-7.55 (m, 3H), 8.45 (s, 2H), 8.70 (d, J=8.0 Hz), 12.10 (br s, 1H). MS (m/z, %) 230 (M⁺, 59), 161 (100), 131 (73), 130 (21), 103 (30). Anal. Calcd for C₁₁H₁₀N₄O₂: C, 57.39; H, 4.35; N, 24.35. Found: C, 57.13; H, 4.46; N, 23.99.

General procedure for the preparation of oxime ethers (13, 17)

Method A: A solution of (E)- or (Z)-11 (1.0 mmol) in DMF (2 mL) was added to a suspension of NaH (24 mg, 1.0 mmol) in DMF (1 mL). The reaction mixture was stirred at rt for 30 min and then a solution of substituted benzyl halides (12) (1.0 mmol) in DMF (1 mL) was added. After stirring at room temperature for 6-12 h, the reaction mixture was poured into water and extracted with CHCl₃. The organic layer was washed (H₂O), dried (Na₂SO₄) and evaporated. The viscous oily residue was dissolved in 2-propanol and treated with 70% HNO₃ to give (E)- or (Z)-13.

Method B: A stirring suspension of oximes [(Z)-16] (1.0 mmol) and K₂CO₃ (1.0 mmol) in DMF (4 mL) was heated at 50°C and substituted benzyl halides (12) (1.0 mmol) dissolved in DMF (1 mL) was added dropwise. After 6-10 h the mixture was poured into water and extracted with CHCl₃. The organic phase was washed (H₂O), dried (Na₂SO₄) and evaporated. The viscous oily residue was dissolved in 2-propanol and treated with 70% HNO₃ to give (Z)-17.

Method C: A mixture of ketones (2 or 14) (1.0 mmol) and O-(arylmethyl)hydroxyamine hydrochloride (19) (2.5 mmol) in MeOH (5 mL) was refluxed for 4-6 h. After cooling the reaction mixture to room temperature, water (40 mL) was added and then extracted with CHCl₃. The organic layer was washed (H₂O), dried (Na₂SO₄) and evaporated. The (E)- and (Z)-isomers were separated by TLC (silica gel) eluting with CHCl₃-MeOH. The desired compound was dissolved in 2-propanol and treated with 70% HNO₃ to afford the corresponding oxime ethers (13 or 17).

(Z)-2,3-Dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one O-(phenylmethyl)oxime nitrate [(Z)-13a]: yield 52%; mp 112-115°C (2-propanol); ¹H NMR (80 MHz, CDCl₃) δ 4.89 (dd, 1H, J=12.8, 2.4 Hz), 4.90-5.00 (2H, m), 5.44-5.50 (2H, m), 6.90-7.00 (2H, m), 7.30-7.50 (5H, m), 8.45-8.50 (2H, m), 8.70-8.80 (1H, m), 12.10 (s, 1H). MS (m/z, %) 324 (M⁺, 59), 161 (100), 131 (73), 130 (21), 103 (29). Anal. Calcd for C₁₅H₁₃N₅O₂: C, 57.39; H, 4.05; N, 24.35. Found: C, 57.13; H, 4.26; N, 24.01.
Hz), 5.25 (dd, 1H, J=12.8, 2.0 Hz), 5.69 (s, 2H), 6.63 (dd, 1H, J=2.4, 2.0 Hz), 7.30-7.63 (m, 2H), 7.65-7.90 (m, 6H), 8.37 (d, 1H, J=8.0 Hz), 8.44 (s, 1H), 8.81 (s, 1H). MS (m/z, %) 320 (M+, 38), 252 (11), 160 (35), 92 (13), 91 (100), 77 (17), 66 (15), 51 (11). Anal. Calcd for C_{18}H_{17}N_{5}O_{5}: C, 56.34; H, 4.43; N, 18.26. Found: C, 56.37; H, 4.19; N, 18.01.

(Z)-2,3-Dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one O-(4-chlorophenylmethyl)oxime nitrate [(Z)-13b]: yield 71% (method A), 66% (method C); mp 143-145°C (2-propanol); ^1H NMR (80 MHz, DMSO-d$_6$) δ 4.39 (dd, 1H, J=12.8, 2.4 Hz), 4.64 (dd, 1H, J=12.8, 2.0 Hz), 5.18 (s, 2H), 6.11 (dd, 1H, J=2.4, 2.0 Hz), 6.88-7.50 (m, 7H), 7.83 (d, 1H, J=8.0 Hz), 7.97 (s, 1H), 8.54 (s, 1H). MS (m/z, %) 354 (M+, 11), 161 (11), 139 (11), 127 (28), 125 (100), 89 (20), 63 (11), 44 (12). Anal. Calcd for C$_{18}$H$_{16}$N$_{5}$O$_{5}$Cl: C, 51.70; H, 3.83; N, 16.75. Found: C, 51.52; H, 3.97; N, 16.88.

(Z)-2,3-Dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one O-(2,4-dichlorophenylmethyl)oxime nitrate [(Z)-13c]: yield 73% (method A), 61% (method C); mp 149-151°C (2-propanol); ^1H NMR (80 MHz, DMSO-d$_6$) δ 4.40 (dd, 1H, J=12.8, 2.4 Hz), 4.65 (dd, 1H, J=12.8, 2.0 Hz), 5.25 (s, 2H), 6.14 (dd, 1H, J=2.4, 2.0 Hz), 6.86-7.15 (m, 2H), 7.20-7.65 (m, 4H), 7.86 (d, 1H, J=8.0 Hz), 8.06 (s, 1H), 8.69 (s, 1H). MS (m/z, %) 388 (M+, 2), 228 (12), 163 (14), 162 (20), 161(73), 159 (100), 102 (18), 90 (21), 89 (49), 77 (35), 76 (35), 68 (28), 51 (30), 50 (23), 41 (78). Anal. Calcd for C$_{18}$H$_{15}$N$_{5}$O$_{5}$Cl$_{2}$: C, 47.76; H, 3.32; N, 15.48. Found: C, 47.96; H, 3.43; N, 15.80.

(Z)-7-Chloro-2,3-dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one O-(4-chlorophenylmethyl)oxime nitrate [(Z)-13d]: yield 53%; mp 150-152°C (2-propanol); ^1H NMR (80 MHz, DMSO-d$_6$) δ 4.30-4.80 (m, 2H), 5.18 (s, 2H), 6.16 (m, 1H), 6.95-7.50 (m, 6H), 7.81 (d, 1H, J=8.8 Hz), 8.04 (s, 1H), 8.71 (s, 1H). MS (m/z, %) 388(M+,2), 228 (12), 125 (100), 89 (26), 63 (16), 51 (16), 50 (12), 46 (18). Anal. Calcd for C$_{18}$H$_{15}$N$_{5}$O$_{5}$Cl: C, 47.76; H, 3.32; N, 15.48. Found: C, 47.74; H, 3.21; N,15.63.

(Z)-7-Chloro-2,3-dihydro-3-(1H-1,2,4-triazol-1-yl)-4H-1-benzopyran-4-one O-(2,4-dichlorophenylmethyl)oxime nitrate [(Z)-13e]: yield 68%; mp 152-153°C (2-propanol); ^1H NMR (80 MHz, DMSO-d$_6$) δ 4.30-4.82 (m, 2H), 5.24 (s, 2H), 6.17 (m, 1H), 6.95-7.67 (m, 5H), 7.81 (d, 1H, J=8.3 Hz), 8.10 (s, 1H), 8.80 (s, 1H). MS (m/z, %) 424 (M+, 8), 161 (65), 159 (100), 89 (15), 75 (11). Anal. Calcd for C$_{18}$H$_{14}$N$_{5}$O$_{5}$Cl$_{3}$: C, 44.38; H, 2.88; N, 14.38. Found: C, 44.31; H, 2.63; N, 14.31.

(Z)-2,3-Dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one O-(phenylmethyl)oxime nitrate [(Z)-17a]: yield 56%; mp 123-125°C (2-propanol); ^1H NMR (80 MHz, DMSO-d$_6$) δ 4.40 (dd, 1H, J=12.8, 2.4 Hz), 4.74 (dd, 1H, J=12.8, 2.0 Hz), 5.24 (s, 2H), 6.16 (dd, 1H, J=2.4, 2.0 Hz), 6.94-7.60 (m, 8H), 7.85 (d, 1H, J=8.8 Hz), 9.10 (s, 2H). MS (m/z, %) 322 (20), 321 (80), 320 (M+, 42), 252 (20), 161 (70), 160 (73), 131 (22), 103 (19), 92 (24), 91 (100), 77 (24). Anal. Calcd for C$_{18}$H$_{17}$N$_{5}$O$_{5}$: C, 56.34; H, 4.43; N, 18.26. Found: C, 56.44; H, 4.29; N, 18.29.

(Z)-2,3-Dihydro-3-(4H-1,2,4-triazol-4-yl)-4H-1-benzopyran-4-one O-(2,4-dichlorophenylmethyl)-
oxime nitrate \((Z)-17b\): yield 51%; mp 119-121°C (2-propanol); \(^1\)H NMR (80 MHz, DMSO-d<sub>6</sub>) \(\delta\) 4.45 (d, 1H, J=12.8, 2.4 Hz), 4.75 (d, 1H, J=12.8, 2.0 Hz), 5.31 (s, 2H), 6.16 (dd, 1H, J=2.4, 2.0 Hz), 6.90-7.22 (m, 2H), 7.25-7.65 (m, 4H), 7.83 (d, 1H, J=8.0 Hz), 9.08 (s, 2H). MS (m/z, %) 389 (M\(^+\), 100), 322 (13), 320 (20), 229 (30), 228 (50), 161 (72), 160 (64), 89 (19), 76 (11), 63 (11). Anal. Calcd for C\(_{18}\)H\(_{15}\)N\(_5\)O\(_5\)Cl\(_2\): C, 47.76; H, 3.32; N, 15.48. Found: C, 47.49; H, 3.38; N, 15.34.

(Z)-7-Chloro-2,3-dihydro-3-(4\(H\)-1,2,4-triazol-4-yl)-4\(H\)-1-benzopyran-4-one \(O\)-(phenylmethyl)oxime nitrate \((Z)-17c\): yield 43%; mp 139-140°C (2-propanol); \(^1\)H NMR (80 MHz, DMSO-d<sub>6</sub>) \(\delta\) 4.48 (dd, 1H, J=12.8, 2.4 Hz), 4.75 (dd, 1H, J=12.8, 1.9 Hz), 5.24 (s, 2H), 6.17 (dd, 1H, J=2.4, 1.9 Hz), 7.05-7.45 (m, 7H), 7.83 (d, 1H, J=8.8 Hz), 9.11 (s, 2H). MS (m/z, %) 354 (M\(^+\), 30), 249 (11), 195 (32), 160 (100), 154 (30), 91 (97), 45 (23), 44 (48). Anal. Calcd for C\(_{18}\)H\(_{16}\)N\(_5\)O\(_5\)Cl: C, 51.70; H, 3.83; N, 16.75. Found: C, 51.79; H, 3.95; N, 16.73.

(Z)-7-Chloro-2,3-dihydro-3-(4\(H\)-1,2,4-triazol-4-yl)-4\(H\)-1-benzopyran-4-one \(O\)-(2,4-dichlorophenylmethyl)oxime nitrate \((Z)-17d\): yield 51% (method B), 46% (method C); mp 146-147°C (2-propanol); \(^1\)H NMR (80 MHz, DMSO-d<sub>6</sub>) \(\delta\) 4.49 (dd, 1H, J=12.8, 2.4 Hz), 4.77 (dd, 1H, J=12.8, 2.0 Hz), 5.30 (s, 2H), 6.12 (dd, 1H, J=2.4, 2.0 Hz), 7.10-7.70 (m, 5H), 7.81 (d, 1H, J=8.0 Hz), 8.93 (s, 2H). MS (m/z, %) 422 (M\(^+\), 6), 230 (60), 228 (70), 197 (64), 195 (83), 160 (100), 123 (40), 102 (56), 89 (50), 75 (35), 63 (22). Anal. Calcd for C\(_{18}\)H\(_{14}\)N\(_5\)O\(_5\)Cl\(_3\): C, 44.38; H, 2.88; N, 14.38. Found: C, 44.36; H, 2.63; N, 14.51.

(E)-13a: yield 45%; mp 116-118°C (2-propanol); \(^1\)H NMR (80 MHz, DMSO-d<sub>6</sub>) \(\delta\) 5.20 (dd, 1H, J=12.8, 2.9 Hz), 5.50 (dd, 1H, J=12.8, 3.0 Hz), 5.70 (s, 2H), 5.85 (t, 1H, J=2.9 Hz), 7.30-7.52 (m, 2H), 7.67-7.95 (m, 6H), 8.4 (s, 1H), 8.77 (s, 1H), 9.07 (d, 1H, J=8.0 Hz). MS (m/z, %) 320 (M\(^+\), 40), 161 (11), 160 (39), 92 (12), 91 (100), 77 (20), 64 (16). Anal. Calcd for C\(_{18}\)H\(_{17}\)N\(_5\)O\(_5\): C, 56.34; H, 4.43; N, 18.26. Found: C, 55.98; H, 4.56; N, 18.14.

(E)-13b: yield 43% (method A), 7% (method B); mp 128-130°C (2-propanol); \(^1\)H NMR (80 MHz, DMSO-d<sub>6</sub>) \(\delta\) 4.58 (dd, 1H, J=12.8, 2.6 Hz), 5.02 (dd, 1H, J=12.8, 2.6 Hz), 5.85 (t, 1H, J=2.9 Hz), 7.30-7.52 (m, 2H), 7.67-7.95 (m, 6H), 8.4 (s, 1H), 8.77 (s, 1H), 9.07 (d, 1H, J=8.0 Hz). MS (m/z, %) 354 (M\(^+\), 80), 194 (32), 161(12), 127 (30), 125 (100), 89 (23), 77 (15). Anal. Calcd for C\(_{18}\)H\(_{16}\)N\(_5\)O\(_5\)Cl: C, 56.34; H, 4.43; N, 18.26. Found: C, 55.98; H, 4.56; N, 18.14.

(E)-13c: yield 53% (method A), 6% (method C); mp 127-129°C (2-propanol); \(^1\)H NMR (80 MHz, DMSO-d<sub>6</sub>) \(\delta\) 4.55 (dd, 1H, J=12.8, 2.4 Hz), 4.94 (dd, 1H, J=12.8, 3.0 Hz), 5.32 (s, 2H), 5.47 (dd, 1H, J=3.0, 2.4 Hz), 7.02 (m, 2H), 7.26-7.70 (m, 4H), 8.05 (s, 1H), 8.51 (d, 1H, J=8.8 Hz), 8.62 (s, 1H). MS (m/z, %) 388 (M\(^+\), 16), 230 (17), 228 (27), 161 (89), 159 (100), 89 (11). Anal. Calcd for C\(_{18}\)H\(_{15}\)N\(_5\)O\(_5\)Cl\(_2\): C, 47.76; H, 3.32; N, 15.48. Found: C, 47.95; H, 3.38; N, 15.45.

(E)-17d (as a free base): yield 5%; mp 72-74°C (methanol); \(^1\)H NMR (80 MHz, CDCl\(_3\)) \(\delta\) 4.55 (dd, 1H, J=12.1, 2.0 Hz), 4.85 (dd, 1H, J=12.1, 2.0 Hz), 5.07 (t, 1H, J=2.0 Hz), 5.34 (s, 2H), 7.03 (m, 2H), 7.36 (m,
3H), 8.22 (s, 2H), 8.48 (d, 1H, J=8.8 Hz). MS (m/z, %) 422 (M⁺, 4), 230 (54), 228 (67), 197 (70), 195 (90), 160 (100), 102 (45), 64 (26). Anal. Calcd for C₁₈H₁₃N₄O₂Cl₃: C, 50.98; H, 3.07; N, 13.22. Found: C, 50.73; H, 3.02; N, 13.02.

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