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

Saeed Emami and Abbas Shafiee*

Department of Chemistry, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Abstract- A synthesis of (*E*)- and (*Z*)-2,3-dihydro-3-(1*H*-1,2,4-triazol-1-yl)-4*H*-1-benzopyran-4-one oxime ethers [(*E*)- and (*Z*)-**13**] and (*Z*)-2,3-dihydro-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-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 $HONH_2$.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-4*H*-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)-4*H*-1-benzopyran-4-ones (**2** or **14**) with *O*-(arylmethyl)hydroxylamine hydrochloride (**19**).

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

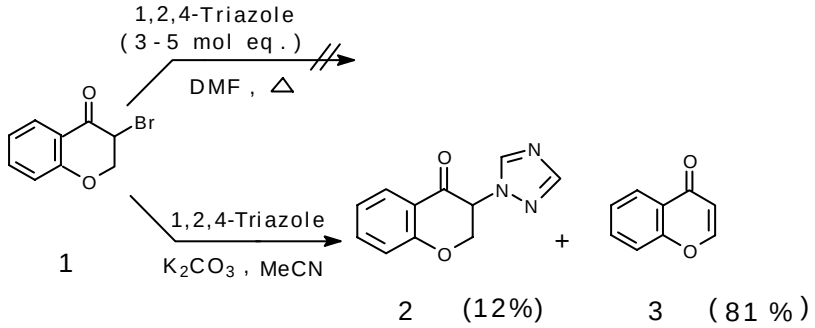
1,2,4-Triazoles constitute an important class of nitrogen heterocycles and many 1-substituted 1,2,4-triazoles have found use as antimycotic agent, agricultural fungicides, plant growth regulators or aromatase inhibitors.[2] As fungicides and antimycotics the primary mode of action is by supression of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

In the search for new antimycotic 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-(1*H*-1,2,4-triazol-1-yl)-4*H*-1-benzopyran-4-ones and some related compounds.

The synthesis of 2,3-dihydro-3-(1*H*-1,2,4-triazol-1-yl)-4*H*-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 K_2CO_3 in MeCN similar

to those reported by Lai *et al*.,[5] dehydrohalogenation of **1** took place and the corresponding chromone (**3**) was the major product and compound (**2)** was obtained in 12% yield.



Scheme 1

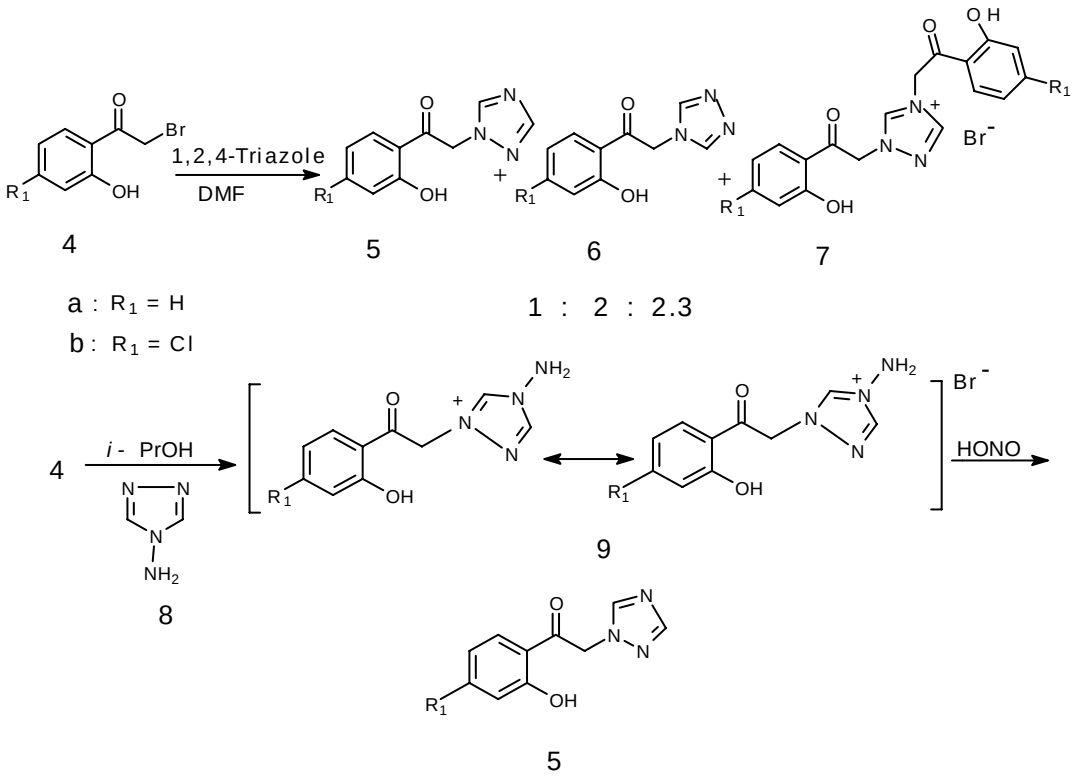
A more convenient method for the preparation of **2** was the ring closure of 2-(1*H*-1,2,4-triazol-1-yl)-2′-hydroxyacetophenones (**5**). The apparent straight-forward preparation of **5** was displacement of 2-bromo-2′-hydroxyacetophenones (**4**) by 1,2,4-triazole as reported by Baji *et al*.[6] (Scheme 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 quternary 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.[7] In our case, 1-isomer was minor product and quternary triazolium salt by-product was the major one, probably because when compound (**5**) was formed subsequently reacted with another 2-bromoacetophenone and give compound (**7**). However, the problem of preparing 2-(1*H*-1,2,4-triazol-1-yl)acetophenones (**5**) in high yield could be solved.[7] 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[8] (Scheme 3). The yield of compound (**2a,** R_1=H) was very low (11%). However, compound (**2a)** could be synthesized in good yield as shown in Scheme 3. Rection 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 $HONH_2$.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.[9] Mixich *et al*. have recently reported preparation of (*E*)-2-(imidazol-1-yl)acetophenone oximes by reaction of (*Z*)-2-haloacetophenone oximes with imidazole

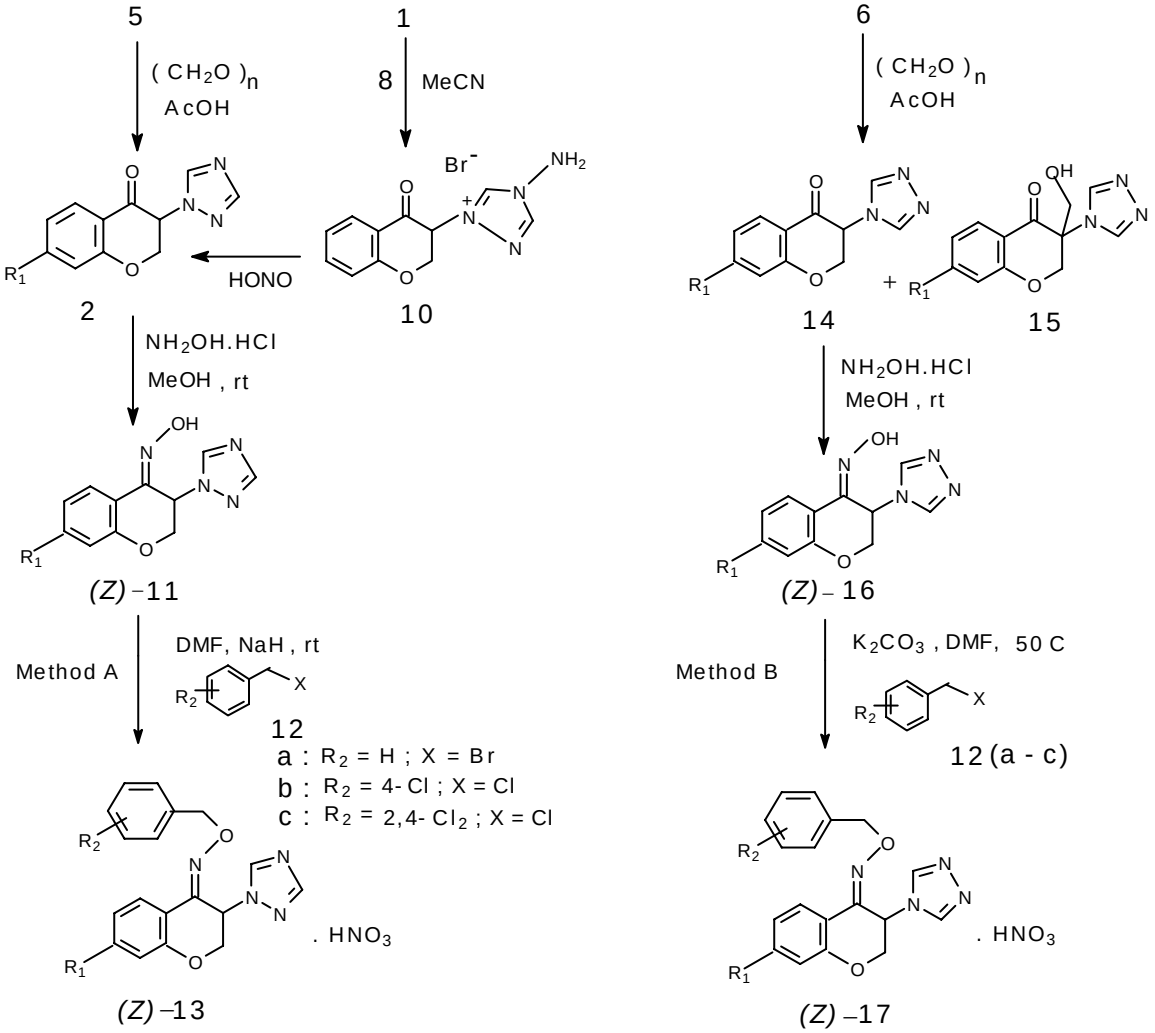


Scheme 2

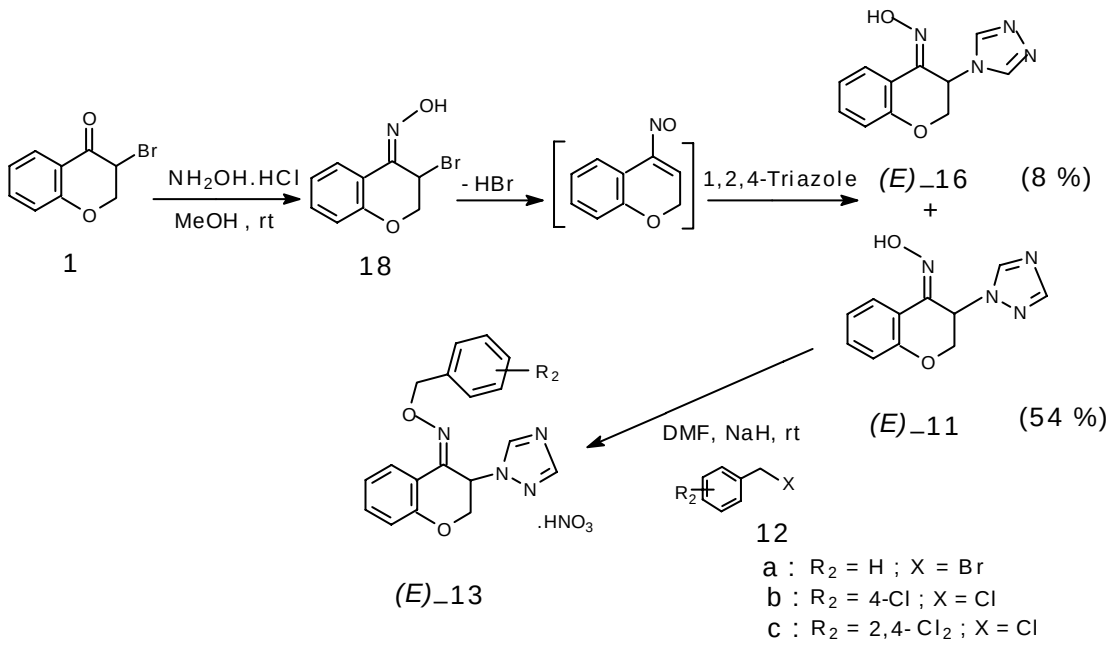
which involves the inversion of oxime.[10] In our case, stirring a mixture of compound (**1)** and three equivalent of $HONH_2.HCl$ in methanol at room temperature gave (*Z*)-3-bromo-2,3-dihydro-4*H*-1-benzopyran-4-one oxime (**18**).[11] Reaction of **18** with 1,2,4-triazole in the presence of K_2CO_3 in MeCN at room temperature yielded (*E*)-2,3-dihydro-3-(1*H*-1,2,4-triazol-1-yl)-4*H*-1-benzopyran-4-one oxime [(*E*)-**11a**] in 54% yield. (*E*)-2,3-Dihydro-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-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-nitrososty rene intermediate, which reacts more rapidly in the s-*trans* conformation than in the s-*cis*, giving (*E*)-isomer.[11,12] 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[10] (method A) or K_2CO_3 at 50°C[6] (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,

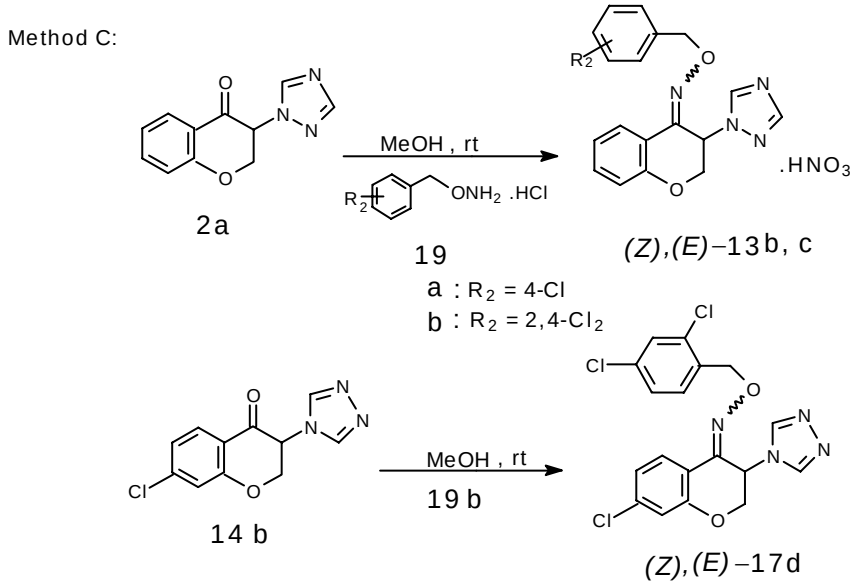


Scheme 3



Scheme 4

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), predominatly 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.



Scheme 5

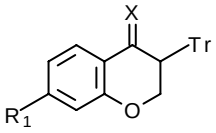
NMR spectra are generally used to assign the stereochemistry of the isomers (*E* or *Z* form) of oximes derived from ketones.[6,9,13] Table 1 shows selected chemical shifts (H-5 and H-3 of the chroman ring) of the ketones (**2** and **14**), (*Z*)- and (E)-oximes (**11** and **16**). Examination of the 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 downfiled 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

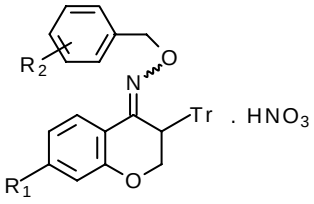
All melting points were determined using a Kofler hot stage apparatus and are uncorrected. IR spectra were recorded using a Perkin-Elmer Model 781 or Nicolet FT-IR Magna 550 spectrophotometer. NMR

Table 1. Selected ^{1}H NMR chemical shifts of substituted 4-chromanones



Compound No.	R_1	X	Tr	Chroman ring	
				H-3	H-5
2a	H	O	1,2,4-Triazol-1-yl	5.40	7.97
2b	Cl	O	1,2,4-Triazol-1-yl	5.37	7.89
14a	H	O	1,2,4-Triazol-4-yl	5.29	7.62
14b	Cl	O	1,2,4-Triazol-4-yl	5.50	7.85
(*Z*)-**11a**	H	N-OH	1,2,4-Triazol-1-yl	6.04	7.88
(*Z*)-**11b**	Cl	N-OH	1,2,4-Triazol-1-yl	6.08	7.87
(*Z*)-**16a**	H	N-OH	1,2,4-Triazol-4-yl	5.97	7.86
(*Z*)-**16b**	Cl	N-OH	1,2,4-Triazol-4-yl	5.98	7.85
(*E*)-**11a**	H	N-OH	1,2,4-Triazol-1-yl	5.44	8.69
(*E*)-**16a**	H	N-OH	1,2,4-Triazol-4-yl	5.44	8.70

Table 2. Selected ^{1}H NMR chemical shifts of substituted chromanone oxime ethers



Compound No.	R_1	R_2	Tr	Method	Chroman ring	
					H-3	H-5
(*Z*)-**13a**	H	H	1,2,4-Triazol-1-yl	A	6.63	8.37
(*Z*)-**13b**	H	4-Cl	1,2,4-Triazol-1-yl	A,C	6.11	7.83
(*Z*)-**13c**	H	2,4-Cl_2	1,2,4-Triazol-1-yl	A,C	6.14	7.86
(*Z*)-**13d**	Cl	4-Cl	1,2,4-Triazol-1-yl	A	6.16	7.81
(*Z*)-**13e**	Cl	2,4-Cl_2	1,2,4-Triazol-1-yl	A	6.17	7.81
(*Z*)-**17a**	H	H	1,2,4-Triazol-4-yl	B	6.16	7.85
(*Z*)-**17b**	H	2,4-Cl_2	1,2,4-Triazol-4-yl	B	6.16	7.83
(*Z*)-**17c**	Cl	H	1,2,4-Triazol-4-yl	B	6.17	7.83
(*Z*)-**17d**	Cl	2,4-Cl_2	1,2,4-Triazol-4-yl	B,C	6.12	7.81
(*E*)-**13a**	H	H	1,2,4-Triazol-1-yl	A	5.85	9.07
(*E*)-**13b**	H	4-Cl	1,2,4-Triazol-1-yl	A,C	5.49	8.50
(*E*)-**13c**	H	2,4-Cl_2	1,2,4-Triazol-1-yl	A,C	5.47	8.51
(*E*)-**13d**[a]	Cl	2,4-Cl_2	1,2,4-Triazol-4-yl	C	5.07	8.48

[a] Free base

spectra were measured using a Bruker FT-80 or Varian 400 Unity plus spectrometer, and chemical shifts are expressed in ppm (δ) with TMS as an internal standard. MS spectra were measured with a Finnigan TSQ 70 Mass spectrophotometer at 70 eV. All evaporations 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_2CO_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_2O, 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, $CDCl_3$) δ 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-(1*H*-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, $CDCl_3$) δ 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 $C_{11}H_9N_3O_2$: 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-(1*H*-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) δ 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),

121 (100), 93 (31), 65 (76), 56 (15). Anal. Calcd for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.43; N, 20.69. Found: C, 59.10; H, 4.09; N, 20.61.

1-(4-Chloro-2-hydroxyphenyl)-2-(1*H*-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-d_6) 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 $C_{10}H_8N_3O_2Cl$: C, 50.53; H, 3.37; N, 17.68. Found: C, 50.41; H, 3.41; N, 17.69.

1-(2-Hydroxyphenyl)-2-(4*H*-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-d_6) 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 $C_{10}H_9N_3O_2$: 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-(4*H*-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-d_6) 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 $C_{10}H_8N_3O_2Cl$: C, 50.53; H, 3.37; N, 17.68. Found: C, 50.81; H, 3.30; N, 17.78.

1,4-Bis(2-hydroxyphenacyl)-1*H*-1,2,4-triazolium Bromide (7a): yield 45%; mp 215-217°C; IR (KBr) 3061, 1669, 1607 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) 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 $C_{18}H_{16}N_3O_4Br$: 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)-1*H*-1,2,4-triazolium Bromide (7b): yield 50%; mp 214-216°C; IR (KBr) 3079, 1683, 1593 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) 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 $C_{18}H_{14}N_3O_4BrCl_2$: C, 44.35; 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-4*H*-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

cooling the colorless salt was filtered, washed with cold 2-propanol to give **9**.

1-(2-Hydroxyphenyl)-2-(4-amino-4*H*-1,2,4-triazoliumyl)ethanone Bromide (9a): yield 75%; mp 169-170°C (2-propanol); IR (KBr) 3216, 3098, 2914, 1655 cm^{-1}; ^1H NMR (80 MHz, DMSO-d_6) δ 6.05 (s, 2H), 6.80-7.70 (m, 5H), 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 $C_{10}H_{11}N_4O_2Br$: 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-4*H*-1,2,4-triazoliumyl)ethanone Bromide (9b): yield 64%; mp 177-178°C (2-propanol); IR (KBr) 3189, 3080, 1655, 1617 cm^{-1}; ^1H NMR (80 MHz, DMSO-d_6) δ 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 $C_{10}H_{10}N_4O_2BrCl$: 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-4*H*-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_2SO_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-(1*H*-1,2,4-triazol-1-yl)-4*H*-1-benzopyran-4-one (2b): yield 40%; mp 132-134°C; IR (KBr) 3129, 1697, 1597 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 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 $C_{11}H_8N_3O_2Cl$: C, 52.91; H, 3.21; N, 16.83. Found: C, 52.99; H, 3.39; N, 16.70.

2,3-Dihydro-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-1-benzopyran-4-one (14a): yield 70%; mp 143-144°C; IR (KBr) 3106, 1690, 1615 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 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=8.31, 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 $C_{11}H_9N_3O_2$: 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-(4*H*-1,2,4-triazol-4-yl)-4*H*-1-benzopyran-4-one (14b): yield 51%; mp 160-162°C; IR (KBr) 3104, 1698, 1598 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) 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 $C_{11}H_8N_3O_2Cl$: C, 52.91; H, 3.21; N, 16.83. Found: C, 52.94; H, 3.09; N, 16.70.

3-Hydroxymethyl-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-1-benzopyran-4-one (15a): yield 12%. mp 183-185°C; IR (KBr) 3155, 3117, 1702, 1612 cm^{-1}; ^1H NMR (80 MHz, DMSO-d_6) 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 $C_{12}H_{11}N_3O_3$: C, 58.77; H, 4.49; N, 17.14. Found: C, 58.39; H, 4.52; N, 16.91.

7-Chloro-3-hydroxymethyl-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-1-benzopyran-4-one (15b): yield 15%; mp 145-147°C; IR (KBr) 3023, 2947, 1703, 1608, 1488 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$+CF_3COOH) 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), 156 (31), 154 (100), 126 (22), 91 (12). Anal. Calcd for $C_{12}H_{10}N_3O_3Cl$: 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-4*H*-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-4*H*-1,2,4-triazoliumyl)-4*H*-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-d_6) 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 $C_{11}H_{11}N_4O_2Br$: 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 $HONH_2$. HCl.

A solution of ketones (**2** or **14**) (5.0 mmol) and $HONH_2$.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 $NaHCO_3$. The precipitate was filtered by filtration, washed with water, and dried to give (*Z*)-**11** or (*Z*)-**16**.

(*Z*)-2,3-Dihydro-3-(1*H*-1,2,4-triazol-1-yl)-4*H*-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-d_6) 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 $C_{11}H_{10}N_4O_2$: 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-(1*H*-1,2,3-triazol-1-yl)-4*H*-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-d_6) 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), 57 (26), 44 (100). Anal. Calcd for $C_{11}H_9N_4O_2Cl$: C, 49.91; H, 3.40; N, 21.17. Found: C, 49.76; H, 3.18; N, 21.24.

(*Z*)-2,3-Dihydro-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-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-d_6) 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), 102 (53), 92 (33), 91 (52), 90 (44), 77 (45), 70 (20), 64 (20), 63 (23), 51 (21). Anal. Calcd for $C_{11}H_{10}N_4O_2$: 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-(4*H*-1,2,4-triazol-4-yl)-4*H*-1-benzopyran-4-one oxime [(Z)-16b]: yield 92%; mp 230-231°C (methanol); IR (KBr) 3139, 1606 cm^{-1}; ^1H NMR (80 MHz, DMSO-d_6) 4.42 (dd, 1H, J=12.0, 2.9 Hz), 4.70 (dd, 1H, J=12.0, 1.8 Hz), 5.98 (m, 1H), 7.05-7.40 (m, 2H), 7. 85 (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), 57 (20), 44 (100). Anal. Calcd for $C_{11}H_9N_4O_2Cl$: 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 $HONH_2$.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 $HONH_2$.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-4*H*-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, $CDCl_3$) 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 $C_9H_8NO_2Br$: 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-4*H*-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 K_2CO_3 (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 (Na_2SO_4) 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-(1*H*-1,2,4-triazol-1-yl)-4*H*-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-d_6) 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 (38), 102 (15), 77 (20), 70 (18). Anal. Calcd for $C_{11}H_{10}N_4O_2$: C, 57.39; H, 4.35; N, 24.35. Found: C, 57.41; H, 4.21; N, 24.01.

(*E*)-2,3-Dihydro-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-1-benzopyran-4-one oxime [(*E*)-16a]: yield 8%; mp 204-206°C; IR (KBr) 3148, 1614 cm^{-1}; ^1H NMR (80 MHz, DMSO-d_6) 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 $C_{11}H_{10}N_4O_2$: 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 $CHCl_3$. The organic layer was washed (H_2O), dried (Na_2SO_4) and evaporated. The viscous oily residue was dissolved in 2-propanol and treated with 70% HNO_3 to give (*E*)- or (*Z*)-**13.**

Method B: A stirring suspension of oximes [(*Z*)-**16**] (1.0 mmol) and K_2CO_3 (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 $CHCl_3$. The organic phase was washed (H_2O), dried (Na_2SO_4) and evaporated. The viscous oily residue was dissolved in 2-propanol and treated with 70% HNO_3 to give (*Z*)-**17**.

Method C: A mixture of ketones (**2** or **14**) (1.0 mmol) and *O*-(arylmethyl)hydroxylamine 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 $CHCl_3$. The organic layer was washed (H_2O), dried (Na_2SO_4) and evaporated. The (*E*)- and (*Z*)-isomoers were separated by TLC (silica gel) eluting with $CHCl_3$-MeOH. The desired compound was dissolved in 2-propanol and treated with 70% HNO_3 to afford the corresponding oxime ethers (**13** or **17**).

(*Z*)-2,3-Dihydro-3-(1*H*-1,2,4-triazol-1-yl)-4*H*-1-benzopyran-4-one *O*-(phenylmethyl)oxime nitrate [(*Z*)-13a]: yield 52%; mp 112-115°C (2-propanol); ^1H NMR (80 MHz, $CDCl_3$) δ 4.89 (dd,1H, J=12.8, 2.4

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 $C_{18}H_{17}N_5O_5$: C, 56.34; H, 4.43; N, 18.26. Found: C, 56.37; H, 4.19; N, 18.01.

(*Z*)-2,3-Dihydro-3-(1*H*-1,2,4-triazol-1-yl)-4*H*-1-benzopyran-4-one *O*-(4-chlorophenylmethyl)oxime nitrate [(*Z*)-13b]: yield 71% (method A), 66% (method C); mp 143-145°C (2-propanol); ^{1}H 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 $C_{18}H_{16}N_5O_5Cl$: C, 51.70; H, 3.83; N, 16.75. Found: C, 51.52; H, 3.97; N, 16.88.

(*Z*)-2,3-Dihydro-3-(1*H*-1,2,4-triazol-1-yl)-4*H*-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); ^{1}H 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 $C_{18}H_{15}N_5O_5Cl_2$: C, 47.76; H, 3.32; N, 15.48. Found: 47.96; H, 3.43; N, 15.80.

(*Z*)-7-Chloro-2,3-dihydro-3-(1*H*-1,2,4-triazol-1-yl)-4*H*-1-benzopyran-4-one *O*-(4-chlorophenyl-methyl oxime nitrate [(*Z*)-13d]: yield 53%; mp 150-152°C (2-propanol); ^{1}H 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), 126 (30), 125 (100), 89 (26), 63 (16), 51 (16), 50 (12), 46 (78). Anal. Calcd for $C_{18}H_{15}N_5O_5Cl_2$: 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-(1*H*-1,2,4-triazol-1-yl)-4*H*-1-benzopyran-4-one *O*-(2,4-dichlorophenyl-methyl)oxime nitrate [(*Z*)-13e]: yield 68%; mp 152-153°C (2-propanol); ^{1}H 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 $C_{18}H_{14}N_5O_5Cl_3$: C, 44.38; H, 2.88; N, 14.38. Found: C, 44.31; H, 2.63; N, 14.31.

(*Z*)-2,3-Dihydro-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-1-benzopyran-4-one *O*-(phenylmethyl)oxime nitrate [(*Z*)-17a]: yield 56%; mp 123-125°C (2-propanol); ^{1}H 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 $C_{18}H_{17}N_5O_5$: C, 56.34; H, 4.43; N, 18.26. Found: C, 56.44; H, 4.29; N, 18.29.

(*Z*)-2,3-Dihydro-3-(4*H*-1,2,4-triazol-4-yl)-4*H*-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_6) δ 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 $C_{18}H_{15}N_5O_5Cl_2$: 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_6) δ 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 $C_{18}H_{16}N_5O_5Cl$: 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-dichlorophenyl-methyl)oxime nitrate [(*Z*)-17d]: yield 51% (method B), 46% (method C); mp 146-147°C (2-propanol); ^{1}H NMR (80 MHz, DMSO-d_6) δ 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 $C_{18}H_{14}N_5O_5Cl_3$: 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_6) δ 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 $C_{18}H_{17}N_5O_5$: 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_6) δ 4.58 (dd, 1H, J=12.8, 2.6 Hz), 5.02 (dd, 1H, J=12.8, 2.6 Hz), 5.25 (s, 2H), 5.49 (t, 1H, J=2.6 Hz), 6.98 (d, 1H, J=7.2 Hz), 7.02 (t, 1H, J=7.2 Hz), 7.25-7.50 (m, 5H), 8.10 (s, 1H), 8.50 (d, 1H, J=8.0 Hz), 8.67 (s, 1H). MS (m/z, %), 354 (M^+, 80), 194 (32), 161(12), 127 (30), 125 (100), 89 (23), 77 (15). Anal. Calcd for $C_{18}H_{16}N_5O_5Cl$: C, 51.70; H, 3.83; N, 16.75. Found: C, 51.79; H, 3.95; N, 16.58.

(*E*)-13c: yield 53% (method A), 6% (method C); mp 127-129°C (2-propanol); ^{1}H NMR (80 MHz, DMSO-d_6) δ 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} $H_{15}N_5O_5Cl_2$: 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, $CDCl_3$) δ 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 $C_{18}H_{13}N_4O_2Cl_3$: C, 50.98; H, 3.07; N, 13.22. Found: C, 50.73; H, 3.02; N, 13.02.

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