Synthesis Anti-fungal and Anti-bacterial Screening of 3-Phenyl-1,4,5-trihydro-pyrazol and 2, 4-Dihydro[1,2,4]-triazol-3-one Derivatives of 4-Hydroxy-2-oxo-2*H*-1-benzopyran

V. V. Mulwad and Jyoti M. Shirodkar

Department of Organic Chemistry, Institute of Science,
15, Madam Cama Road, Mumbai 400032, India.

Received November 26, 2001
Received Revised November 25, 2002

4-Hydroxy-2-oxo-2*H*-1-benzopyran-3-carboxaldehydes **2a-d** are prepared from 4-hydroxy-2-oxo-2*H*-1-benzopyrans **1a-d** *via* the Vielsmeyer Haack reaction. The 4-hydroxy-2-oxo-3-(3'oxo-3'-phenylprop-1'-enyl)-2*H*-1-benzopyrans **3a-d** are obtained from **2a-d** *via* the Claisen reaction. Refluxing compounds **3a-d** with hydrazine hydrate gave the 3-phenyl-5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-1,4,5-trihydropyrazols **4a-d**. Stirring compounds **2a-d** with semicarbazide hydrochloride in acidic medium gave the 4-hydroxy-2-oxo-2*H*-1-benzopyran-3-aldehyde-semicarbazone **5a-d**, which on cyclisation with ferric chloride hexahydrate gave the 5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-2,4-dihydro[1,2,4]triazol-3-ones **6a-d**. All these compounds show significant antibacterial activities.

J. Heterocyclic Chem., **40**, 377 (2003).

Introduction.

Benzopyrans show activities such as antifungal [1], anticoagulant [2], antibacterial [3] and insecticide [4]. The biological importance and considerable therapeutic potential of 3-substituted-4-hydroxybenzopyrans generate considerable interest to us in designing the synthesis of number of 3-substituted-4-hydroxybenzopyrans which act as possible HIV protease inhibitors with a high therapeutic index [5].

Various workers have reported the synthesis of 4-hydroxy-2-oxo-2*H*-1-benzopyran-3-carboxaldehyde. However the yield obtained was poor [6,7]. Here we report the synthesis of 4-hydroxy-2-oxo-2*H*-1-benzopyran-3-carboxaldehyde **2a-d** *via* the Veilsmeyer Haack reaction by refluxing 4-hydroxy-2-oxo-2*H*-1-benzopyran [8] **1** with dimethyl formamide and phosphorous oxychloride. The yield obtained by our method is much higher than reported earlier. Compounds **2a–d** do not show positive Beilstein and Lassignes sodium fusion tests, indicating the absence of halogen. Compounds **2a-d** forms its 2,4–dinitrophenylhydrazine derivative verifying the presence of the carbonyl group, and the structure of 4-hydroxy-2-oxo-2*H*-1-benzopyran-3-carboxaldehyde has been confirmed by spectral and analytical data.

Chalcones are known to possess acute anti-inflammatory [9a,9b], antibacterial [10,11a,11b,11c,12] and antifungal [10,12,13a,13b,13c,13d] effects. Thus, the 4-hydroxy-2-oxo-2*H*-1-benzopyran-3-carboxaldehydes are converted into corresponding 4-hydroxy-2-oxo-3-(3'oxo-3'-phenylprop-1'-enyl)-2*H*-1-benzopyrans **3a-d** *via* the Claisen reaction by refluxing with the appropriate aromatic ketones, using 10% NaOH. These chalcones give coloration with ferric chloride. The formation of these chalcones has also confirmed by spectral and analytical data and also through its dibromo derivatives.

Pyrazoline derivatives are known to possess biological activities [14-17] such as analgesic, antipyretics, antiinflammatories, antirheumatic *etc*. The 4-hydroxy-2-oxo-3-(3'oxo-3'-phenylprop-1'-enyl)-2*H*-1-benzopyran (Chalcone) **3a–d** are cyclised to the 3-phenyl-5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-1,4,5-trihydropyrazols **4a-d** by refluxing with methanol and hydrazine hydrate. The structure of these compounds has been confirmed by spectral and analytical data.

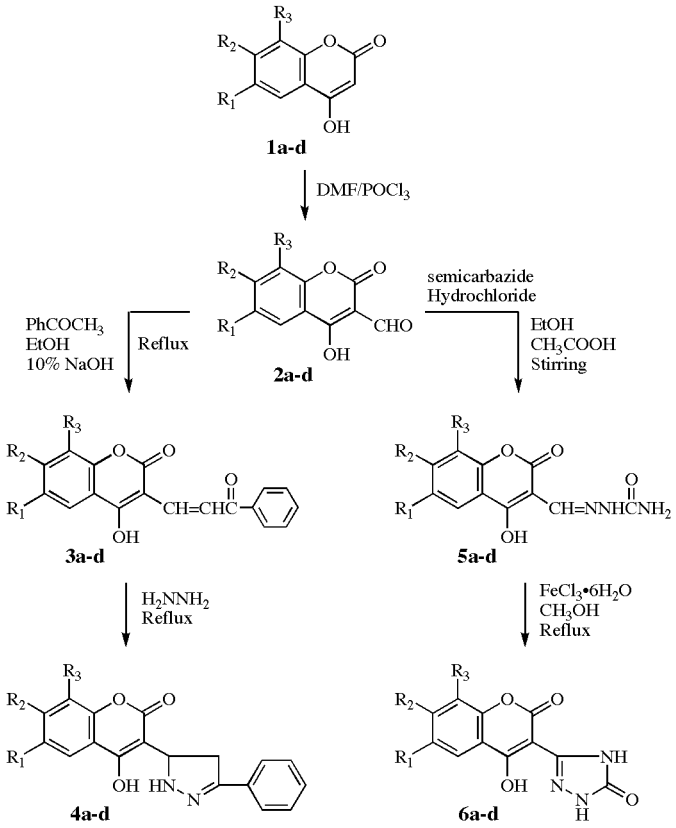
Various semicarbazones [18] are known to possess anti-inflammatory, analgesic and antibacterial activity. 4-Hydroxy-2-oxo-2*H*-1-benzopyran-3-aldehyde-semicarbazone **5a-d** have been prepared by using 4-hydroxy-2-oxo-2*H*-1-benzopyran-3-carboxaidehyde **2a-d** and semicarbazide hydrochloride in ethanol. These compounds give smell of ammonia on boiling with NaOH. The structure of compounds **5a-5d** has been confirmed by spectral and analytical data.

1,2,4-Triazoles display a wide range of pharmacological activity [19-22]. Hence, semicarbazones **5a-d** were refluxed with an ethanolic solution of ferric chloride hexahydrate to give 5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-2,4-dihydro[1,2,4]triazol-3-ones **6a-d**. These compounds do not smell of ammonia on boiling with NaOH and structure of compounds **6a-d** have been confirmed by spectral and analytical data.

Biological Screening.

Compounds **3c**, **4a**, **4b**, **4c**, **4d**, **5b**, **6a**, **6b**, **6c** and **6d** were screened for their antibacterial activity against both gram-positive and gram-negative bacteria as shown in Table I. Minimum inhibitory concentration (MIC) of these compounds was determined by tube dilution method [23] using sodium penicillin (3.3 μgm/ml), trimethoprim (2.7 μgm/ml) as standards in DMF solvent. Compounds **3b**, **4d**, **5b**, **6b** were screened for antifungal activity against *C. albicans*, *T. mentagrophytes* and *T. rubrum* however they did not show any significant antifungal activity up to 200 μgm/ml.

Scheme 1



1a, **2a**, **3a**, **4a**, **5a**, **6a**:$R_1=R_2=R_3=H$
1b, **2b**, **3b**, **4b**, **5b**, **6b**: $R_1=CH_3$, $R_2=R_3=HP$
1c, **2c**, **3c**, **4c**, **5c**, **6c**: $R_2=CH_3$, $R_1=R_3=H$
1c, **2c**, **3c**, **4c**, **5c**, **6c**: $R_3=CH_3$, $R_1=R_2=H$

Table I shows that compound **4a** R_1, R_2, R_3=H is more active than compounds **4b**, **4c** and **4d** and that **4a** show antibacterial activity at 50 μgm/ml against *S.* typhi and *S.* aureus respectively. Compounds **4b** R_1= CH_3 and **4c** R_2= CH_3 showed antibacterial activity at 100 μgm/ml against *S. typhi* and at 50 μgm/ml against *S. aureus*. Compound **4d** R_3= CH_3 showed antibacterial activity at 100 μgm/ml against *S. typhi* and *S. aureus* respectively. Compounds **6a** R_1, R_2, R_3=H and **6b** R_1= CH_3 showed antibacterial activity at 100 μgm/ml against *S. typhi* and *S. aureus* respectively. While compounds **6c** R_2= CH_3 and **6d** R_3= CH_3 showed antibacterial activity at 100 μgm/ml against *S. typhi* and 50 μgm/ml against *S. aureus* respectively.

Table I

Minimum Inhibitory Concentration

Sr. NO.	R_1, R_2, R_3	*S.* typhi	*S.* aureus
3c	$R_2=CH_3$	+++	+
4a	R_1, R_2, R_3=H	++	++
4b	$R_1=CH_3$	+	++
4c	$R_2=CH_3$	+	++
4d	$R_3=CH_3$	+	+
5b	$R_1=CH_3$	+	+
6a	R_1, R_2, R_3=H	+	+
6b	$R_1=CH_3$	+	+
6c	$R_2=CH_3$	+	++
6d	$R_3=CH_3$	+	++

Note: + =100mgm/ML, ++ =50mgm/ML, +++ =10mgm/ML

EXPERIMENTAL

General.

Melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded on Perkin –Elmer 257 spectrophotometer using KBr disks. ^{1}H NMR spectra were recorded on VXR-300 spectrometer, the chemical shifts are given in δ (ppm) downfield from internal standard tetramethylsilane (TMS) and coupling constants are given in Hz. The homogeneity of compounds were measured by TLC on silica gel plates where the spots were developed in an iodine chamber.

4-Hydroxy-2-oxo-2*H*-1-benzopyran-3-carboxaldehydes (**2a-d**).

Phosphorous oxychloride (2 ml) was added to **1** (0.01 mol) in dimethyl formamide (20 ml). The mixture was refluxed for 9 hrs; then it was poured into a saturated solution of sodium acetate. The resulting solid was collected by filtration and recrystallized form ethanol.

4-Hydroxy-2-oxo-2*H*-1-benzopyran-3-carboxaldehyde (**2a**).

Compound **2a** was obtained in 72% yield; mp: 135-136 °C; IR (KBr): 3421(-OH), 1720 (>C=O), 1670(>C=O), 1600, 1375cm^{-1}; ^{1}H NMR: δ 7.20-7.80 (m, 4H, aromatic-H), δ 8.00 (s, 1H, -CHO) and δ 10.00 (s, 1H, -OH, D_2O exchangeable). Its 2,4-DNP derivative: mp: 278 °C. IR (KBr): 3435 (-OH, -NH), 1730(>C=O), 1659, 1622, 1445, 1385 cm^{-1}.

Anal. Calcd. For $C_{10}H_6O_4$: C, 63.16; H, 3.15. Found:C, 63.12; H, 3.17.

4-Hydroxy-6-methyl-2-oxo-2*H*-1-benzopyran-3-carboxaldehyde (**2b**).

Compound **2b** was obtained in 74% yield; mp: 173-174 °C. IR (KBr): 3429(-OH), 2922 (-CH stretching), 1720 (>C=O), 1685 (>C=O), 1623, 1575, 1499, 1374cm^{-1}; ^{1}H NMR: δ 2.40 (s, 3H, CH_3), δ 7.20-7.80 (m, 3H, aromatic-H), δ 7.95 (s, 1H, -CHO) and δ 9.60 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{11}H_8O_4$: C, 64.70; H, 3.92. Found:C, 64.65; H, 3.95.

4-Hydroxy-7-methyl-2-oxo-2*H*-1-benzopyran-3-carboxaldehyde (**2c**).

Compound **2c** was obtained in 73% yield; mp: 192-193 °C; IR (KBr): 3426 (-OH), 2925 (-CH stretching), 1716 (>C=O), 1689(>C=O), 1609, 1523, 1376 cm^{-1}; ^{1}H NMR: δ 2.3 (s, 3H, CH_3), δ 7.2-8 (m, 3H, aromatic-H), δ 7.89 (s, 1H, -CHO) and δ 9.9 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{11}H_8O_4$: C, 64.70; H, 3.92. Found:C, 64.64; H, 3.95.

4-Hydroxy-8-methyl-2-oxo-2*H*-1-benzopyran-3-carboxaldehyde (**2d**).

Compound **2d** was obtained in 74% yield; mp: 232-233 °C; IR (KBr): 3420 (-OH), 2927 (-CH stretching), 1720(>C=O),

1700(>C=O), 1600, 1383 cm^{-1}; ^1H NMR: δ 2.2 (s, 3H, CH_3), δ 7.3-8 (m, 3H, aromatic-H), δ 8.3 (s, 1H, -CHO) and δ 9.8 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{11}H_8O_4$: C, 64.70; H, 3.92. Found: C, 64.69; H, 3.91.

4-Hydroxy-2-oxo-3-(3'oxo-3'-phenylprop-1'-enyl)-2*H*-1-benzopyrans (**3a-d**).

To solution of **2** (0.01 mol) in ethanol (20 ml), acetophenone (0.01 mol) and 10% NaOH were added and the mixture was stirred for 2 hrs. Then the reaction mixture was refluxed for an additional 6 hrs and neutralized with dilute HCl resulting in a sticky mass that on treatment with acetic acid gave a solid, which was recrystallized from dilute acetic acid.

4-Hydroxy-2-oxo-3-(3'oxo-3'-phenylprop-1'-enyl)-2*H*-1-benzopyran (**3a**).

Compound **3a** was obtained in 78% yield; mp: 239-240 °C;IR (KBr): 3421 (-OH), 1722 (>C=O), 1672, 1578, 1156 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.90 (d, 1H,J=9Hz, C_2'), δ 7.20-8.00 (m, 9H, aromatic-H), δ 7.80 (d, 1H,J=9Hz, C_1') and δ 9.80 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{18}H_{12}O_4$: C, 73.97; H, 4.11. Found: C, 73.93; H, 4.16.

4-Hydroxy-6-methyl-2-oxo-3-(3'oxo-3'-phenylprop-1'-enyl)-2*H*-1-benzopyran (**3b**).

Compound **3b** was obtained in 77% yield; mp: 142-143 °C; IR (KBr): 3422 (-OH), 2924(-CH stretching), 1722 (>C=O), 1680, 1621, 1432 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.40 (s, 3H, CH_3), δ 6.80 (d, 1H,J=9Hz, C_2'), δ 7.20-7.80 (m, 8H, aromatic-H), δ 8.00-8.20 (d, 1H,J=9Hz, C_1') and δ 9.80 (s, 1H, -OH, D_2O exchangeable). The dibromo derivative of **3b**: mp: 184 °C .IR (KBr): 3424(-OH), 2925(-CH stretching), 1723(>C=O), 1618, 1447, 1240 cm^{-1}.

Anal. Calcd. For $C_{19}H_{14}O_4$: C, 74.51; H, 4.58. Found: C, 74.48; H, 4.60.

4-Hydroxy-7-methyl-2-oxo-3-(3'oxo-3'-phenylprop-1'-enyl)-2*H*-1-benzopyran (**3c**).

Compound **3c** was obtained in 79% yield; mp: 129-130 °C; IR (KBr): 3371 (-OH), 2925 (-CH stretching), 1714 (>C=O), 1619, 1455, 1241 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.40 (s, 3H, CH_3), δ 6.70 (d, 1H, J=9Hz, C_2'), δ 7.20-7.70 (m, 8H, aromatic-H), δ 7.90 (d, 1H,J=9Hz, C_1') and δ 9.90 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{19}H_{14}O_4$: C, 74.51; H, 4.58. Found: C, 74.47; H, 4.62.

4-Hydroxy-8-methyl-2-oxo-3-(3'oxo-3'-phenylprop-1'-enyl)-2*H*-1-benzopyran (**3d**).

Compound **3d** was obtained in 76% yield; mp: 159-160 °C; IR (KBr): 3417 (-OH), 2925 (-CH stretching), 1717(>C=O), 1610, 1430, 1219 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), δ 6.80 (d, 1H,J=9Hz, C_2'), δ 7.10-7.70 (m, 8H, aromatic-H), δ 8.00 (d, 1H,J=9Hz, C_1') and δ 9.80 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{19}H_{14}O_4$: C, 74.51; H, 4.58. Found: C, 74.52; H, 4.56.

3-Phenyl-5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-1,4,5-trihydro-pyrazols (**4a-d**).

To a solution of **3** (0.03 mol) in methanol (20 ml) and an excess of hydrazine hydrate (8 ml) was added 0.5 ml acetic acid. The reaction mixture was refluxed for 5 hrs. On cooling solid obtained was collected by filtration, washed with water and recrystallized from ethanol.

3-Phenyl-5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-1,4,5-trihydro-pyrazol (**4a**).

Compound **4a**: was obtained in 55% yield; mp:>260 °C; IR (KBr): 3424 (-OH, -NH), 1720 (>C=O), 1615, 1340 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.70 (d, 2H, C_4-H), δ 4.80 (t, 1H, C_5-H), δ 7.00-7.70 (m, 9H, aromatic-H), δ 7.90 (broad, 1H, NH, D_2O exchangeable) and δ 9.80 (s, 1H, OH, D_2O exchangeable).

Anal. Calcd. For $C_{18}H_{14}N_2O_3$: C, 70.59; H, 4.57; N, 9.15. Found: C, 70.56; H, 4.58; N, 9.18.

3-Phenyl-5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-6-methyl-1,4,5-trihydro-pyrazol (**4b**).

Compound **4b** was obtained in 54% yield; mp: 219-220 °C; IR (KBr): 3432 (-OH, -NH), 2924 (-CH stretching), 1725 (>C=O), 1614, 1332 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.40 (s, 3H, CH_3), δ 2.65 (d, 2H, C_4-H), δ 4.60 (t, 1H, C_5-H), δ 7.00-7.60 (m, 8H, aromatic-H), δ 7.80 (broad, 1H, NH, D_2O exchangeable) and δ 9.80 (s, 1H, OH, D_2O exchangeable).

Anal. Calcd. For $C_{19}H_{16}N_2O_3$: C, 71.25; H, 5; N, 8.75. Found: C, 71.22; H, 4.49; N, 8.77.

3-Phenyl-5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-7-methyl-1,4,5-trihydro-pyrazol (**4c**).

Compound **4c** was obtained in 53% yield; mp: >266 °C; IR (KBr): 3416(-OH, -NH), 2925 (-CH stretching), 1715(>C=O), 1615, 1455 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.40 (s, 3H, CH_3), δ 2.56 (d, 2H, C_4-H), δ 4.40 (t, 1H, C_5-H), δ 7.10-7.90 (m, 8H, aromatic-H), δ 8.00 (broad, 1H, NH, D_2O exchangeable) and δ 9.90 (s, 1H, OH, D_2O exchangeable).

Anal. Calcd. For $C_{19}H_{16}N_2O_3$: C, 71.25; H, 5; N, 8.75. Found: C, 71.26; H, 4.48; N, 8.76.

3-Phenyl-5-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-8-methyl-1,4,5-trihydro-pyrazol (**4d**).

Compound **4d** was obtained in 55% yield; mp: 209-210 °C; IR (KBr): 3393 (-OH, -NH), 2921(-CH stretching), 1710(>C=O), 1599, 1426 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.30 (s, 3H, CH_3), δ 2.80 (d, 2H, C_4-H), δ 4.20 (t, 1H, C_5-H), δ 7.20-7.80 (m, 8H, aromatic-H), δ 7.90 (broad, 1H, NH, D_2O exchangeable) and δ 9.80 (s, 1H, OH, D_2O exchangeable).

Anal. Calcd. For $C_{19}H_{16}N_2O_3$: C, 71.25; H, 5; N, 8.75. Found: C, 71.24; H, 5.1; N, 8.77.

4-Hydroxy-2-oxo-2*H*-1-benzopyran-3-aldehyde-semicarbazones (**5a-d**).

An ethanolic solution of **2** (0.01 mol) was dissolved in ethanol (20 ml) to this a dilute ethanolic solution (1:1) of semicarbazide hydrochloride (0.01 mol) was added. It was then acidified with acetic acid (0.5 ml) and stirred for 6 hours at room temperature. On cooling a solid was obtained that was collected by filtration washed with water and recrystallized from ethanol.

4-Hydroxy-2-oxo-2*H*-1-benzopyran-3-aldehyde-semicarbazone (**5a**).

Compound **5a** was obtained in 73%; mp: >270 °C; IR (KBr): 3449 (-OH, -NH_2, -NH), 1722 (>C=O), 1661, 1613, 1568, 1388 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.30 (s, 1H, CH=N), δ 7.00-7.60 (m,

4H, aromatic-H), δ7.7 (s, 2H, NH_2, D_2O exchangeable), δ 7.85 (s, 1H, -NH, D_2O exchangeable) and δ 9.70 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{11}H_9N_3O_4$: C, 53.44; H, 3.67; N, 17. Found: C, 53.42; H, 3.69; N, 17.12.

4-Hydroxy-6-methyl-2-oxo-2*H*-1-benzopyran-3-aldehyde-semicarbazone (**5b**).

Compound **5b** was obtained in 75% yield; mp: >275 °C; IR (KBr): 3432(-OH, -NH_2, -NH), 2925 (-CH stretching), 1723 (>C=O), 1668, 1610, 1373 cm^{-1}.

^1H NMR ($CDCl_3$): δ 2.40 (s, 3H, CH_3), δ 5.20 (s, 1H, CH=N), δ 7.15-7.60 (m, 3H, aromatic-H), δ 7.80 (s, 2H, NH_2, D_2O exchangeable), δ 8.00 (s, 1H, -NH, D_2O exchangeable) and δ 9.80 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.21; N, 16.09. Found: C, 55.15; H, 4.25; N, 16.

4-Hydroxy-7-methyl-2-oxo-2*H*-1-benzopyran-3-aldehyde-semicarbazone (**5c**).

Compound **5c** was obtained in 72% yield; mp: 192-193 °C. IR (KBr): 3424(-OH, -NH_2, -NH), 2928 (CH, stretching), 1723 (>C=O), 1669, 1611, 1376 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.20 (s, 3H, CH_3), δ 5.10 (s, 1H, CH=N), δ 7.20-7.60 (m, 3H, aromatic-H), δ 7.75 (s, 2H, NH_2, D_2O exchangeable), δ 7.95 (s, 1H, -NH, D_2O exchangeable) and δ 9.80 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.21; N, 16.09. Found: C, 55.16; H, 4.26; N, 16.11.

4-Hydroxy-8-methyl-2-oxo-2*H*-1-benzopyran-3-aldehyde-semicarbazone (**5d**).

Compound **5d** was obtained in 74% yield; mp: 214-215 °C; IR (KBr): 3434(-OH, -NH_2, -NH), 2925 (CH, stretching), 1716 (>C=O), 1668, 1609,1355 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.30 (s, 3H, CH_3), δ 4.80 (s, 1H, CH=N), δ 7.10-7.60 (m, 3H, aromatic-H), δ 7.75 (s, 2H, NH_2, D_2O exchangeable), δ 7.95 (s, 1H, -NH, D_2O exchangeable) and δ 9.80 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.21; N, 16.09. Found: C, 55.19; H, 4.22; N, 16.10.

5-(4-Hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-2,4-dihydro[1,2,4]-triazol-3-ones (**6a-d**).

An ethanolic solution of ferric chloride hexahydrate (0.02 mol) (10 ml) was added to a solution of semicarbazone **5** (0.01 mol) in ethanol (30 ml). The mixture was refluxed for 30 min; it was then kept at room temperature for 24 hrs. The solid obtained was washed with water and recrystallized from dilute acetic acid.

5-(4-Hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-2,4-dihydro[1,2,4]-triazol-3-one (**6a**).

Compound **6a** was obtained in 62% yield; mp: 264-265 °C; IR (KBr): 3416 (-OH, -NH), 1725 (>C=O), 1680, 1610,1457, 1388 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.15-7.80 (m, 3H, aromatic-H), δ 7.60 (s, 1H, -NH, D_2O exchangeable), δ 7.80 (s, 1H, -NH, D_2O exchangeable) and δ 9.70 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{11}H_7N_3O_4$: C, 53.88; H, 2.86; N, 17.14. Found: C, 53.85; H, 2.89; N, 17.16.

5-(4-Hydroxy-2-oxo-6-methyl-2*H*-1-benzopyran-3-yl)-2,4-dihydro[1,2,4]triazol-3-one (**6b**).

Compound **6b** was obtained in 65% yield; mp: 239-240 °C; IR (KBr): 3391 (-OH, -NH), 2925(-CH Stretching), 1724 (>C=O), 1686, 1623, 1577, 1375cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.40 (s, 3H, CH_3), δ 7.10-7.60 (m, 3H, aromatic-H), δ 7.30 (s, 1H, -NH, D_2O exchangeable), δ 7.90 (s, 1H, -NH, D_2O exchangeable) and δ 9.80 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{12}H_9N_3O_4$: C, 55.60; H, 3.47; N, 16.22. Found: C, 55.58; H, 3.49; N, 16.20.

5-(4-Hydroxy-2-oxo-7-methyl-2*H*-1-benzopyran-3-yl)-2,4-dihydro[1,2,4]triazol-3-one (**6c**).

Compound **6c** was obtained in 63% yield is 63%; mp: >269 °C; IR (KBr): 3391 (-OH, -NH), 2923 (CH, Stretching), 1723(>C=O), 1682, 1621, 1567, 1350 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.30 (s, 3H, CH_3), δ 7.10-7.80 (m, 3H, aromatic-H), δ 7.40 (s, 1H, -NH, D_2O exchangeable), δ 8.20 (s, 1H, -NH, D_2O exchangeable) and δ 9.90 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{12}H_9N_3O_4$: C, 55.60; H, 3.47; N, 16.22. Found: C, 55.57; H, 3.50; N, 16.21.

5-(4-Hydroxy-2-oxo-8-methyl-2*H*-1-benzopyran-3-yl)-2,4-dihydro[1,2,4]triazol-3-one (**6d**).

Compound **6d** was obtained in 65% yield; mp: 280 °C; IR (KBr): 3382 (-OH, -NH), 2925(-CH stretching), 1721(>C=O), 1685, 1611, 1440 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.30 (s, 3H, CH_3), δ 7.20-7.80 (m, 3H, aromatic-H), δ 7.40 (s, 1H, -NH, D_2O exchangeable), δ 8.20 (s, 1H, -NH, D_2O exchangeable) and δ 9.80 (s, 1H, -OH, D_2O exchangeable).

Anal. Calcd. For $C_{12}H_9N_3O_4$: C, 55.60; H, 3.47; N, 16.22. Found: C, 55.57; H, 3.50; N, 16.20.

Acknowledgment.

We are thankful to Mr. S. V. Chiplunkar, U.D.C.T. for elemental analysis, Director R. S. I. C., I. I. T. and T. I. F. R. Mumbai for ^1H NMR spectral analysis, Haffkine Institute for studies in microbial activities and to government of Maharashtra and LADY TATA MEMORIABLE TRUST for granting scholarship

REFERENCES AND NOTES

[1] N. K. Sangwan, B. S.Verma, O. P. Malik and K. S. Dhindsa, *Indian J Chem.*, **29B**, 294 (1990).

[2] M. A. Stahman, C. F. Huebner, and K. P. Link, *J. Biol. Chem.*, **138**, 517 (1941).

[3] S. S. Honmantgad, M. V. Kulkarni and V. D. Patil, *Indian J Chem.*, **24B**, 459 (1985).

[4] J. D. Hapworth, Comprehensive, Heterocyclic Chemistry, *3* edited by J. A. Boulton and A. Mikillap, (Pergaman press oxford) 737 (1984).

[5] J. Mitra and A. K. Mitra, *Indian J. Chem.*, **Sect. B. 31**, 693 (1992); **35**, 588 (1996).

[6] E. Ziegler and H. Maier, *Monatsh*, **89**, 787 (1958); *Chem. Abstr,* **53**, 12283f (1959).

[7] R. B. Arora, N. R. Krishnaswamy, T.R. Seshadri, S. D. Seth and B. R. Sharma, *J. Med. Chem.*, **10**, 121 (1967).

[8] V. R. Shah, J. L. Bose, and R. C. Shah, *J. Org. Chem.*, **25**, 677 (1960).

[9a] E. T. Organesyan, V. I. Yakavenko, M. M. Khatryan, S. R. Preshkov, and V. S. Cherevatyi, *Khim Farm zh.*, **20**, 696 (1986); *Chem. Abstr.*, **105**, 126832 (1986);

[b] V. Dauksas, P. Gaidelis, E. Vdrenaite, O. Petraukas, A. Brukstus, *Khim Farm Zh.*, **19**, 1069 (1985); *Chem. Abstr.*, **104**, 129843 (1986).

[10] V. K. Ahkywakui, N. Kaila and S. Bala, *Indian J. Chem.*, **25B**, 663 (1986).

[11a] N. B.Poppano, O. P. De Centrorbi, N. B. Debattist, C. C. de Milan, E. J. Browkowski and F. H. Feretti, *Rev Argent microbial.*, **17**, 27 (1985); *Chem. Abstr.*, **104**, 183206 (1986); [b] J. Mathew, A. V. Subba Rao and S. Rambhav, *Curr Sci.*, **53**, 576 (1984).

[12] V. K. Ahluwalia, R. R. Manu and S. Bala, *Indian J. Chem.*, **28B**, 608 (1989).

[13a] S. Mizabuchi and Y. Sato, *Agric. Biol. Chem.*, **48**, 2771 (1984); [b] D. S. Bhakuni and R. J. Chaturvedi, *Nat Prod.*, **47**, 585 (1984); [c] A. Chaudhury, N. Mukherjee and N. Adityachaudhary, *Experientia*, **30**, 1022(1974); [d] A. K. Bhat, R. P. Bhamaria, M. R. Patel, R. A. Bellare, and C.V. Deliwala, *Indian J. Chem.*, **10**, 694 (1972).

[14] K. Tsurumi, A. Abe, H. Fujumura, H. Asai, M. Nagasaka and H. Mikaya, Folia *Pharmacol, Jpn.*, **72**, 41, (1976).

[15] Burger's Medicinal Chemistry, Wiley, New York, 4th edition, 291 (1980).

[16] L. S. Goodman and A. Gilman, The Pharmacological Basis of Therapeutics, Macmilan, New York, 295 (1980).

[17] M. N. Aboul-Enein, Y. M. Abou-Zeid and S. M. El-Difraway, *Pharma. Acta Helv.*, **44**, 570 (1969).

[18] M. M. F. Ismail, N. A. M. M. Shmeiss, HI EI-Diwani and M. S. Arbid, *Indian J. Chem.*, **36B**, 288 (1997).

[19] W. D. Jackson and J. B. Polya, *Aust. J. Sci.*, **13**, 149 (1951).

[20] A. Gasco, V. Mortarini and E. Reynaud, *Farmaco Ed. Sci.*, **28**, 624 (1973).

[21] L. Gsell, P. Ackermann and R. Wehrli, *Eur. Pat.*, 11604 (1980); *Chem. Abstr.*, **94**, 65691 (1981).

[22] M. Tandan, J. R. Bathwal, T. N. Bhatia and K. P. Bhargava, *Indian J. Chem.*, **20B**, 1017, (1981).

[23] S. Frankel, S. Reitman and A. C. Sonnenwirth, Gradwol's Clinical Laboratory Methods & Diagnosis, A textbook on laboratory procedure & their interpritation. 7th edition, Vol. **II**, (C. V. Mosby company), P. 1406-1407 (1970).