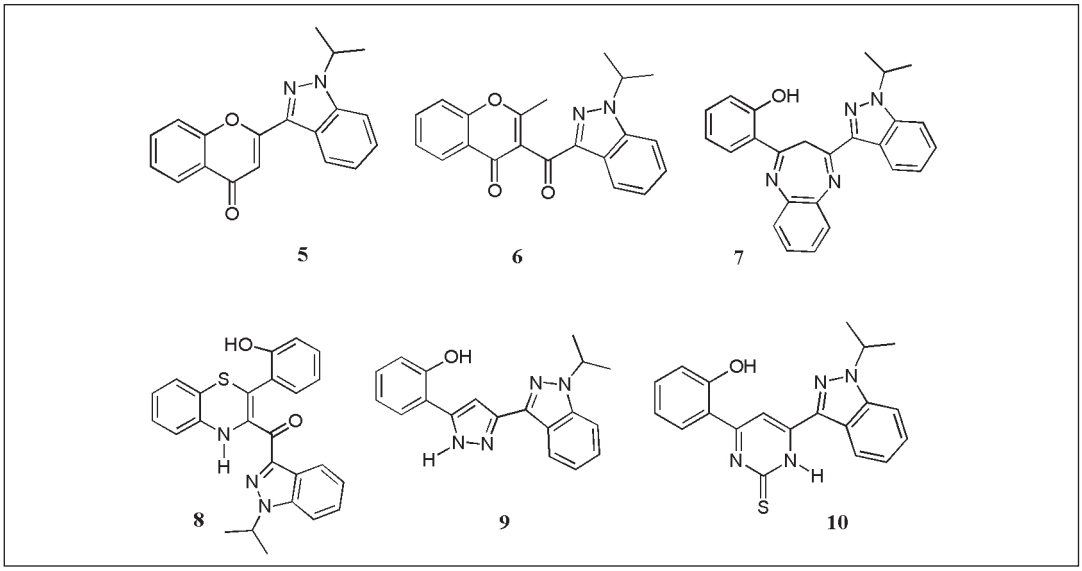
S. B. Kale and B. K. Karale*

P. G. Dept. of Chemistry, S. S. G. M. College, Kopargaon, Ahmednagar-423601.India
E-Mail:bkkarale@yahoo.com
Received February 27, 2006



A series of some important indazolyl derivatives of pyrazoles, diazepines, thiopyrimidines, thiazines and chromones were synthesized and characterized with the help of spectral data. Some of the synthesized compounds are tested for antimicrobial and antioxidant activities.

J. Heterocyclic Chem., **44**, 289 (2007).

INTRODUCTION

Nature contains widespread molecules with heteroatom rings. It is known that a number of heterocyclic compounds like chromones, pyrazoles, diazepines, thiopyrimidines and thiazines possess important biological activities.

According to the literature survey, indazole compounds are associated with various physiological and biological properties and thus, find important use in medicine. Indazole compounds are capable of mediating tyrosine kinase signal transduction and thereby inhibit unwanted cell proliferation [1-2]. Indazole derivatives are examined for analgesic and anti-inflammatory activities [3]. A ruthenium coordination complex (RuInd) is one of the most effective anticancer [4] ruthenium compounds; poisoning [5] of Topoisomerase II by indazole complex was analyzed. Indazole ring was used as the initial template to test the hypothesis in order to increase potency as Leukotriene receptor antagonists [6-8]. Indazole containing inhibitor series for SAH/MTA nucleosidase are inhibitors with broad spectrum antimicrobial activity [9]. Indazole derivatives are used as anti-inflammatory agents, anticancer [10-11] agents and also used as sunscreens [12]. Indazole derivatives are associated with anti-inflammatory, oral male contraceptive and antimicrobial activities [13-16].

Chromones having heterocyclic substituents at the 2-position have been reported to possess antitumor, antibacterial and antifungal activities and also to exhibit good phosphodiesterase IV inhibition activity and some flavones have potential HIV-integrase inhibition activity [17-20, 39].

Pyrazole and variously substituted pyrazoles exhibit a wide range of biological activities like antiviral, antipyretic, antioxidant, antivassive, antidepressant, anti-inflammatory and blood pressure lowering. Pyrazoles are also used as agrochemicals, dyestuff and sunscreen materials [21-24].

Benzodiazepines are an important class of psychotherapeutic compounds. In recent years some examples of heterocyclic rings fused to the seven member diazepine ring system have been synthesized which exhibit psychotropic activities [25-31,40].

Benzothiazines constitute an important class of heterocyclic compounds which possess a wide spectrum of pharmacological and biological activities. Thiazines also show antimalarial, antitubercular, anti-inflammatory, antibacterial and antifungal activities [32-34].

Pyrimidine and its derivatives have been studied for its pharmacological properties. Thiopyrimidines and its

derivatives have antibacterial activity and also act as anti-infective agents [20,35-38].

Owing to the biological importance of chromones, pyrazoles, indazoles, diazepines, thiopyrimidines, thiazines and in continuation of our work to synthesize biologically important heterocyclic compounds we report herein the synthesis of some chromones, diazepines, thiopyrimidines, thiazines, pyrazoles containing indazole moiety.

RESULTS AND DISCUSSION

In the present work 2-hydroxy acetophenones **1** were treated with 1-isopropyl indazole 3-carboxylic acid **2** in the presence of phosphorous oxychloride and pyridine to yield the corresponding 2-acetyl-phenyl-1-isopropyl-1*H*-indazole-3-carboxylate **3**. Compound **3** on treatment with potassium hydroxide in the presence of pyridine gave 1-(2-hydroxyphenyl)-3-(1-isopropyl-1*H*-indazol-3-yl)-propane-1,3-dione **4**. Compound **4** on treatment with Conc. HCl undergoes cyclization and afforded 2-(1-isopropyl-1*H*-indazol-3-yl)-chromon-4-one **5**.

The structures of compounds **3**, **4** and **5** are confirmed by spectral techniques (ms, ir, ^{1}H nmr). The ir absorption spectra (cm^{-1}) of compounds **3** show a strong absorption band at 1728 for O-C=O group and ^{1}H nmr spectra show a sharp singlet at around 2.5 δ for -CO-CH$_3$. The ir spectra of compounds **4** show a strong and characteristic band for 1,3 diketone linkage at 1620-1599 cm^{-1}. The ^{1}H nmr of compound **4** shows disappearance of singlet at around 2.5 δ and also shows a singlet at 10.76 δ and 11.26 δ due to phenolic and enolic protons of 1,3 diketone. The formations of compounds **5** are confirmed by ^{1}H nmr as it shows the disappearance of the signal at 10.76 δ and 11.2 δ due to –OH protons as they are used in cyclization. The structures of **3**, **4** and **5** are confirmed by mass spectra.

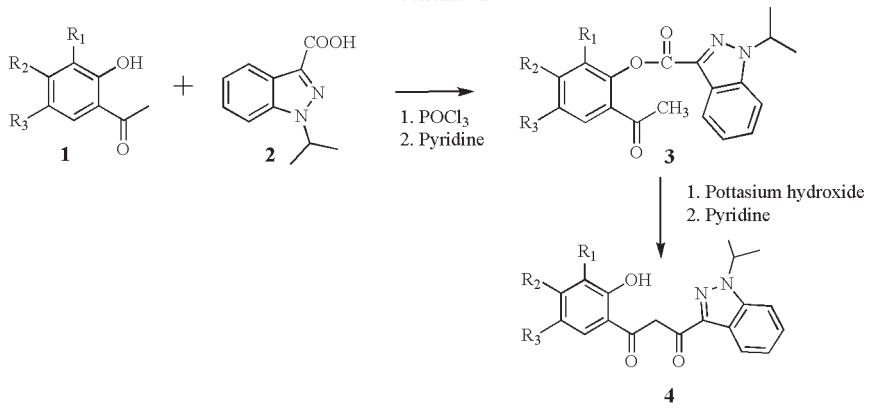
Compounds **4** on reaction with acetic anhydride in presence of sodium acetate affords 3-(1-isopropyl-1*H*-indazole-3-carbonyl)-2-methyl-chromon-4-ones **6**. Compounds **4** on treatment with *o*-phenylene diamine in presence of acetic acid yielded 2-[4-(1-isopropyl-1*H*-indazol-3-yl)-3*H*-benzo[*b*][1,4]diazepin-2-yl]-phenols **7**. Compound **4** on reaction with *ortho*-aminothiophenol in DMSO gave [2-(2-hydroxy-phenyl)-4*H*-benzo[1,4]thiazin-3-yl]-(1-isopropyl-1*H*-indazol-3-yl)-methanones **8**.

The structures of compounds **6**, **7** and **8** are confirmed by spectral techniques (ms, ir and ^{1}H nmr). The ^{1}H nmr spectra of compounds **6** shows disappearance of the signal at 10.71 δ and 11.2 δ as they are used in cyclization, a new signal at 2.5 δ appears due to C-2 methyl group and also confirmed by their ir and mass spectra. The ir spectra of compounds **7** shows disappearance of the band at 1620 cm^{-1} due to –C=O group and bands at 1595 and 1540 cm^{-1} appears due to C=N bond. ^{1}H nmr shows the disappearance of enolic proton signals and the structures are also confirmed by mass spectra. Structures of compounds **8** were confirmed by ir spectra which shows a broad band at 3316 cm^{-1} due to –N-H and –OH functionality and at 1644 cm^{-1} due to –C=O group. Structures of compounds **8** are also confirmed by ^{1}H nmr and mass spectra.

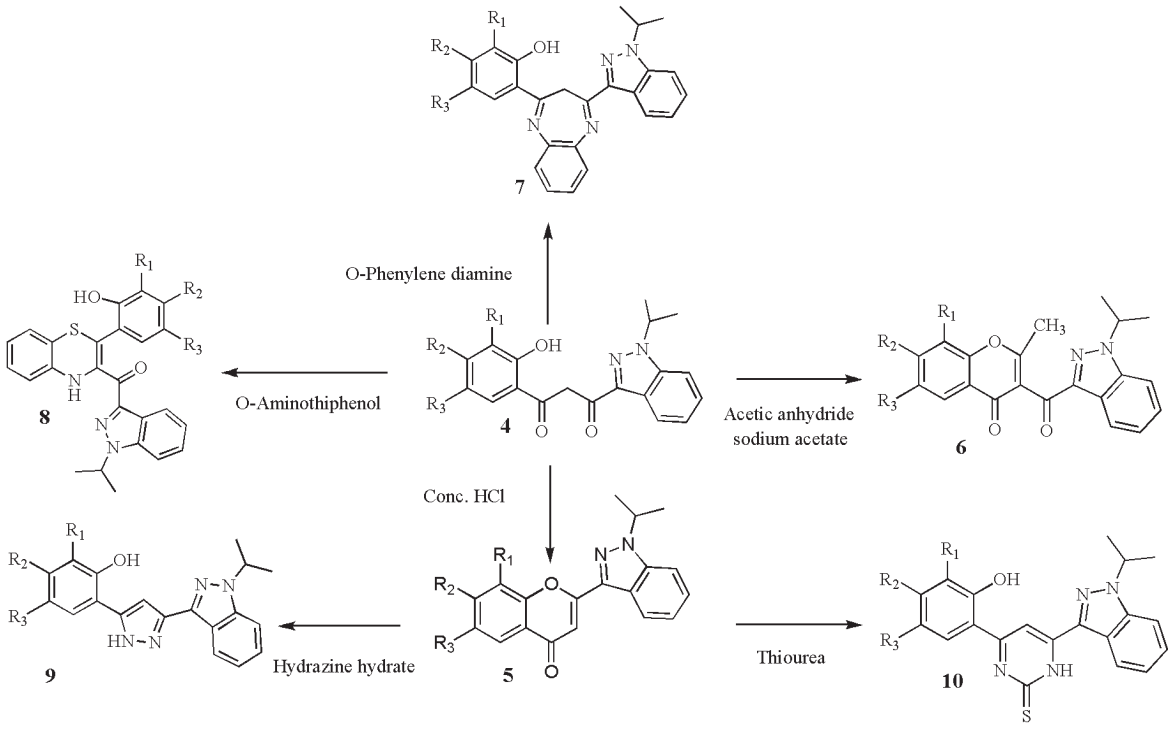
Compounds **5** on treatment with hydrazine hydrate undergoes γ-pyrone ring opening followed by cyclization to yield 2-[5-(1-isopropyl-1*H*-indazol-3-yl)-2*H*-pyrazol-3-yl]-phenol **9**. Compounds **5** on reaction with thiourea undergo 1,4 addition followed by γ-pyrone ring opening and subsequently undergoes cyclization to yield the compounds **10**.

The structures of compounds **9** are confirmed by spectral techniques (ms, ir and ^{1}H nmr). In their ir spectra, the band at 1643 cm^{-1} due to –C=O group are not observed and a new bands at 3160 cm^{-1} due to the –OH group are observed. The ^{1}H nmr spectra show a signal at 10.9 δ due to –OH proton. Structures are also confirmed by mass spectra. The structures of compounds **10** are also confirmed by ir spectra in which a new band due to –OH and -NH functionality are observed at 3250 and 3180 cm^{-1}.

Scheme 1



Scheme 2



In addition to this, the ir spectra of **10** shows a band due to –C=S group in the region 1210-1270 cm^{-1}. The ^1H nmr spectra show singlets at 13.4 δ and 8.06 δ due to –OH and –NH functionality.

Antimicrobial activity. The *in vitro* antimicrobial activity of the test compounds were assessed against 24 hr cultures of several selected bacteria and fungi. The bacteria used were *Escherichia coli*, *Staphylococcus aureus* and

Table 1

Substitution			Compd.	Yield	M.P.	Compd.	Yield	M.P.	Compd.	Yield	M.P
R_1	R_2	R_3	No.	(%)	(0°C)	No.	(%)	(0°C)	No.	(%)	(0°C)
Cl	H	Cl	**3a**	65	104	**4a**	80	146	**5a**	74	178
H	H	Cl	**3b**	72	80	**4b**	82	128	**5b**	71	175
H	H	Me	**3c**	60	105	**4c**	78	135	**5c**	68	168
Me	H	Me	**3d**	64	139	**4d**	83	196	**5d**	76	200
H	Me	H	**3e**	65	103	**4e**	79	133	**5e**	72	167
H	Me	Cl	**3f**	68	99	**4f**	70	163	**5f**	69	198
H	H	Br	**3g**	70	87	**4g**	75	146	**5g**	70	174
H	H	F	**3h**	69	86	**4h**	74	127	**5h**	73	201
H	H	H	**3i**	71	95	**4i**	68	133	**5i**	67	165
Cl	H	Cl	**6a**	79	212	**7a**	89	219	**8a**	68	157
H	H	Cl	**6b**	70	181	**7b**	80	236	**8b**	72	122
H	H	Me	**6c**	72	186	**7c**	-	-	**8c**	73	155
Me	H	Me	**6d**	71	215	**7d**	-	-	**8d**	70	195
H	Me	H	**6e**	69	158	**7e**	78	205	**8e**	75	112
H	Me	Cl	**6f**	68	228	**7f**	-	-	**8f**	69	144
H	H	Br	**6g**	72	184	**7g**	70	241	**8g**	74	119
H	H	F	**6h**	75	176	**7h**	72	212	**8h**	72	140
H	H	H	**6i**	69	173	**7i**	-	-	**8i**	70	118
Cl	H	Cl	**9a**	75	234	**10a**	67	251	-	-	-
H	H	Cl	**9b**	72	224	**10b**	70	292	-	-	-
H	H	Me	**9c**	74	218	**10c**	69	263	-	-	-
Me	H	Me	**9d**	69	222	**10d**	85	196	-	-	-
H	Me	H	**9e**	66	187	**10e**	75	256	-	-	-
H	Me	Cl	**9f**	67	227	**10f**	78	277	-	-	-
H	H	Br	**9g**	71	209	**10g**	83	273	-	-	-
H	H	F	**9h**	75	237	**10h**	68	265	-	-	-
H	H	H	**9i**	69	252	**10i**	66	235	-	-	-

Table 2
Compounds **3a-i**

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
3a	1733 1695 1610 1580 754	8.50 to 7.26 (m, 6H), 4.95 (m, 1H), 2.47(s, 3H), 1.45 (d, 6H)	390 (58.35)	58.33 (4.10)	4.12 (7.15)	7.16
3b	1730 1690 1603 1574 753	8.49 to 7.25 (m, 7H), 5.35 (m, 1H), 2.55(s, 3H), 1.65(d, 6H)	356	63.96 (63.95)	4.80 (5.81)	7.85 (7.84)
3c	1728 1685 1605 1577	8.11 to 7.31 (m, 7H), 5.25 (m, 1H), 2.50(s, 3H), 2.4(s, 3H), 1.5 (d, 6H)	336	71.41 (71.40)	5.99 (5.97)	8.33 (8.34)
3d	1725 1680 1601 1571	8.28 to 7.25 (m, 6H), 5.25 (m, 1H), 2.5(s, 3H), 2.30(s, 3H), 2.45(s, 3H), 1.55 (d, 6H)	350	71.98 (71.96)	6.33 (6.32)	7.99 (7.95)
3e	1724 1683 1603 1576	8.21 to 7.15 (m, 7H), 5.22 (m, 1H), 2.55(s, 3H), 2.31(s, 3H), 1.42 (d, 6H)	336	71.41 (71.39)	5.99 (5.96)	8.33 (8.35)
3f	1725 1688 1600 1578 751	8.43 to 7.25 (m, 6H), 4.82 (m, 1H), 2.35(s, 3H), 2.25(s, 3H), 1.45 (d, 6H)	370	64.78 (64.79)	5.16 (5.15)	7.55 (7.56)
3g	1729 1683 1604 1572 680	8.41 to 7.29 (m, 7H), 5.32 (m, 1H), 2.45(s, 3H), 1.60 (d, 6H)	400	56.87 (56.85)	4.27 (4.28)	6.98 (6.99)
3h	1732 1693 1615 1579 1050	8.51 to 7.26 (m, 7H), 5.35 (m, 1H), 2.57(s, 3H), 1.65 (d, 6H)	340	67.05 (67.07)	5.03 (5.04)	8.23 (8.22)
3i	1720 1678 1600 1574	7.05 to 8.19 (m, 8H), 5.20 (m, 1H), 2.30(s, 3H), 1.32 (d, 6H)	322	70.79 (70.80)	5.63 (5.60)	8.69 (8.67)

Streptococcus faecium; the fungi used were *Candida albicans*, *Candida krusei*, *Candida glabrata* and *Aspergillus fumigatus*.

The antimicrobial activity was performed by agar diffusion method at 1 mg/ml conc. in DMSO. Nutrient agar and potato dextrose agar were used to culture the bacteria and fungi respectively.

Fluconazole, Amphotericin, Vancomycin and Linezolid were prepared in DMSO and used as standards for comparison of antibacterial and antifungal activities respectively. The activity is reported by measuring the diameter of the inhibition zone in mm.

Amongst, the compounds screened for antimicrobial activity **4b** and **4c** have shown activity against almost all the test organisms. All the compounds are showing activity against some of the test organisms. Antimicrobial screening data is given in Table **10** and Table **11**.

Antioxidant activity. The antioxidant activity of the test compounds was determined by DPPH method by using Trolox as a reference standard. Amongst, the compounds screened for antioxidant activity none of the compounds showed promising activity as shown in Table **12**.

EXPERIMENTAL

All the recorded melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in KBr disc. ^1H nmr spectra were recorded on Varian 300 MHz spectrophotometer in DMSO as a solvent and TMS as an internal standard. Peak values

are shown in δ ppm. Mass spectra were obtained by Finnigan mass spectrometer.

2-Acetyl-phenyl-1-isopropyl-1*H*-indazole-3-carboxylates (3a-i). Equimolar amount (0.01 mole) of acetophenones **1** and 1-isopropyl-indazole-3-carboxylic acid **2** were dissolved in 10 ml dry pyridine. Contents were cooled to 0°C in ice bath. To this reaction mixture (0.01 mole) of phosphorous oxychloride was added dropwise maintaining the temperature below 5°C. After complete addition of phosphorous oxychloride the reaction mixture was kept overnight and then poured into crushed ice. The product obtained was separated by filtration and washed with cold 1% NaOH solution folowed by water. The product was crys-

Table 3

Compounds **4a-i**

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
4a	2975 1613 1590 1530 755	11.38(s, 1H), 10.88(s, 1H) 8.38 to 6.90 (m, 6H), 5.26 (m, 1H), 4.98 (s, 1H), 2.70 (d, 6H)	390	58.33 (58.30)	4.12 (4.11)	7.16 (7.12)
4b	2975 1615 1595 1531 751	11.35(s, 1H), 10.85(s, 1H), 8.35 to 6.89 (m, 7H), 5.24 (m, 1H), 4.95 (s, 1H), 2.75 (d, 6H)	356	63.96 (63.92)	4.80 (4.79)	7.85 (7.87)
4c	2978 1620 1599 1536	11.26(s, 1H), 10.71(s, 1H), 8.23 to 6.87 (m, 7H), 5.13 (m, 1H), 4.84 (s, 1H), 3.3 (s, 3H), 2.52 (d, 6H)	336	71.41 (71.39)	5.99 (5.98)	8.33 (8.36)
4d	2975 1618 1595 1533	11.28(s, 1H), 10.75(s, 1H), 8.25 to 6.82 (m, 6H), 5.15 (m, 1H), 4.85 (s, 1H), 3.52 (s, 3H), 2.68 (s, 3H), 2.54 (d, 6H)	350	71.98 (71.99)	6.33 (6.31)	7.99 (7.94)
4e	2975 1615 1595 1532	11.21(s, 1H), 10.70(s, 1H), 8.19 to 6.80 (m, 7H), 5.10 (m, 1H), 4.92 (s, 1H), 3.32 (s, 3H), 2.55 (d, 6H)	336	71.41 (71.36)	5.99 (5.94)	8.33 (8.36)
4f	2978 1618 1597 1535 752	11.23(s, 1H), 10.72(s, 1H), 8.25 to 6.84 (m, 6H), 5.13 (m, 1H), 4.89 (s, 1H), 3.37 (s, 3H), 2.59 (d, 6H)	370	64.78 (64.73)	5.16 (5.11)	7.55 (7.59)
4g	2987 1631 1606 1539 688	11.37(s, 1H), 10.88(s, 1H), 8.39 to 6.90 (m, 7H), 5.27 (m, 1H), 4.97 (s, 1H), 2.69 (d, 6H)	400	56.87 (56.89)	4.27 (4.26)	6.98 (6.94)
4h	2986 1629 1602 1537 1020	11.34(s, 1H), 10.84(s, 1H), 8.36 to 6.87 (m, 7H), 5.24 (m, 1H), 4.98 (s, 1H), 2.70 (d, 6H)	340	67.05 (67.09)	5.03 (5.06)	8.23 (8.20)
4i	2973 1612 1590 1531	11.19(s, 1H), 10.65(s, 1H), 8.16 to 6.77 (m, 8H), 5.06 (m, 1H), 4.89 (s, 1H), 2.47 (d, 6H)	322	70.79 (70.82)	5.63 (5.59)	8.69 (8.71)

Table 4

Compounds **5a-i**

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
5a	1650 1620 1563 1485	8.20 to 7.12 (m, 7H), 4.91 (m, 1H), 1.71 (d, 6H)	372	61.14 (61.09)	3.78 (3.67)	7.51 (7.54)

Table 4 (Continued)

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
5b	1648 1619 1563 1484 749	8.29 to 7.14 (m, 8H), 4.99 (m, 1H), 1.71 (d, 6H)	338	67.36 (67.32)	4.46 (4.49)	8.27 (8.30)
5c	1633 1603 1545 1474	8.20 to 7.11 (m, 8H), 4.91 (m, 1H), 2.13 (s, 3H), 1.59 (d, 6H)	318	75.45 (75.41)	5.70 (5.66)	8.80 (8.77)
5d	1635 1607 1551 1475	8.22 to 7.13 (m, 7H), 4.93 (m, 1H), 2.38 (s, 3H), 2.49 (s, 3H), 1.62 (d, 6H)	332	75.88 (75.84)	6.06 (6.09)	8.43 (8.39)
5e	1640 1610 1554 1477	8.28 to 7.20 (m, 8H), 4.99 (m, 1H), 2.52 (s, 3H), 1.68 (d, 6H)	318	75.45 (75.39)	5.70 (5.73)	8.80 (8.87)
5f	1643 1613 1557 1480 742	8.26 to 7.19 (m, 7H), 4.98 (m, 1H), 2.55 (s, 3H), 1.66 (d, 6H)	352	68.09 (68.12)	4.86 (4.89)	7.94 (7.88)
5g	1646 1617 1561 1481 686	8.29 to 7.16 (m, 8H), 4.96 (m, 1H), 1.70 (d, 6H)	382	59.55 (59.51)	3.95 (3.99)	7.31 (7.27)
5h	1647 1619 1560 1479 1022	8.28 to 7.18 (m, 8H), 4.97 (m, 1H), 1.69 (d, 6H)	322	70.80 (70.76)	4.69 (4.73)	8.69 (8.73)
5i	1648 1617 1561 1483	8.24 to 7.15 (m, 9H), 4.95 (m, 1H), 1.63 (d, 6H)	304	74.98 (74.93)	5.30 (5.27)	9.20 (9.23)

Table 5

Compounds **6a-i**

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
6a	1642 1618 1590 1497 753	8.39 to 7.46 (m, 6H), 5.19 (m, 1H), 2.50 (s, 3H), 1.58 (d, 6H)	414	60.74 (60.69)	3.88 (3.91)	6.75 (6.72)
6b	1640 1615 1588 1496 750	8.35 to 7.43 (m, 7H), 5.17 (m, 1H), 2.49 (s, 3H), 1.57 (d, 6H)	380	66.23 (66.19)	4.50 (4.53)	7.36 (7.39)
6c	1636 1611 1582 1486	8.27 to 7.38 (m, 7H), 5.13 (m, 1H), 2.51 (s, 3H), 2.45 (s, 3H), 1.52 (d, 6H)	360	73.32 (73.37)	5.59 (5.62)	7.77 (7.81)
6d	1639 1612 1586 1492	8.31 to 7.40 (m, 6H), 5.15 (m, 1H), 2.5 (s, 3H), 2.41 (s, 3H), 2.4 (s, 3H), 1.54 (d, 6H)	374	73.78 (73.75)	5.92 (5.96)	7.48 (7.51)

tallized from ethanol. The compounds synthesized by the above procedure are listed in Table 1 and their characterization data is given in Table 2.

1-(2-Hydroxy-phenyl)-3-(1-isopropyl-1*H*-indazol-3-yl)-propane-1,3-diones (4a-i). Compound **3** (0.01 mole) was dissolved in 15 ml of dry pyridine with 2 g of powdered KOH. The reaction mixture was stirred at room temperature for 3 hrs. Contents were poured into crushed ice and acidified with conc. HCl. The product obtained was separated by filtration and crystallized with alcohol. The compounds synthesized by above procedure are listed in Table 1 and their characterization data is given in Table 3.

Table 5 (Continued)

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
6e	1636 1611 1582 1486	8.25 to 7.36 (m, 7H), 5.14 (m, 1H), 2.46 (s, 3H), 2.43 (s, 3H), 1.51 (d, 6H)	360	73.32 (73.29)	5.59 (5.63)	7.77 (7.81)
6f	1635 1613 1586 1487 752	8.36 to 7.42 (m, 6H), 5.12 (m, 1H), 2.46 (s, 3H), 2.41 (s, 3H), 1.54 (d, 6H)	394	66.92 (66.95)	4.85 (4.83)	7.09 (7.12)
6g	1639 1615 1585 1484 681	8.34 to 7.43 (m, 7H), 5.18 (m, 1H), 2.47 (s, 3H), 1.58 (d, 6H)	424	59.31 (59.37)	4.03 (4.07)	6.59 (6.53)
6h	1638 1617 1586 1489 1060	8.37 to 7.45 (m, 7H), 5.17 (m, 1H), 2.49 (s, 3H), 1.56 (d, 6H)	364	69.22 (69.27)	4.70 (4.67)	7.69 (7.71)
6i	1635 1609 1581 1485	8.25 to 7.34 (m, 8H), 5.11 (m, 1H), 2.40 (s, 3H), 1.50 (d, 6H)	346	72.82 (72.79)	5.24 (5.27)	8.09 (8.12)

Table 6

Compounds **7a-i**

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
7a	3424 1599 1553 1487 755	8.60 (s, 1H), 8.54 to 6.99 (m, 12H), 5.25 (m, 1H), 1.75 (d, 6H)	462	64.80 (64.77)	4.35 (4.38)	12.09 (12.12)
7b	3422 1597 1550 1486 750	8.59 (s, 1H), 8.51 to 6.93 (m, 13H), 5.22 (m, 1H), 1.72 (d, 6H)	428	70.01 (70.05)	4.93 (4.97)	13.06 (13.01)
7e	3415 1592 1552 1479	8.18 (s, 1H), 8.52 to 6.89 (m, 13H), 5.21 (m, 1H), 2.54 (s, 3H), 1.70 (d, 6H)	408	76.45 (76.49)	5.92 (5.95)	13.72 (13.68)
7g	3418 1594 1555 1484 680	8.61 (s, 1H), 8.50 to 6.90 (m, 13H), 5.21 (m,1H), 1.71 (d, 6H)	472	63.43 (63.38)	4.47 (4.51)	11.84 (11.87)
7h	3416 1595 1551 1480 1035	8.63 (s, 1H), 8.53 to 6.92 (m, 13H), 5.23 (m,1H), 1.72 (d, 6H)	412	72.80 (72.84)	5.13 (5.09)	13.58 (13.61)

2-(1-Isopropyl-1*H*-indazol-3-yl)-chromon-4-ones (5a-i). Compound **4** (0.001 mole) was dissolved in 10 ml. of ethanol with 1 ml of conc. HCl. Reaction mixture was then heated under reflux for 1 hr. Contents were cooled and poured into crushed ice. The product obtained was separated by filtration and crystallized with alcohol. The compounds synthesized by above procedure are listed in Table 1 and their characterization data is given in Table 4.

3-(1-Isopropyl-1*H*-indazole-3-carbonyl)-2-methyl-chromon-4-ones (6a-i). Compound **4** (0.001 mole) was dissolved in 10 ml of acetic anhydride with excess of anhydrous sodium acetate (1 gm). Reaction mixture was then heated under reflux for 2 hrs. Reaction mixture was then cooled, poured into crushed ice, separated by filtration and crystallized with alcohol. Compounds synthesized by above procedure are listed in Table **1** and their characterization data is given in Table **5**.

2-[4-(1-Isopropyl-1*H*-indazol-3-yl)-3*H*-benzo[b]-[1,4]diazepin-2-yl]-phenols (7a-i). Compound **4** (0.001 mole) was dissolved in 15 ml of alcohol with (0.001 mole) *o*-phenylene diamine. Reaction mixture was heated under reflux for 3 hrs then AcOH (1 ml) was added and the contents were refluxed for another 7 hrs. The product crystallizes on cooling and was separated by filtration and purified by crystallization with acetic acid. Compounds synthesized by above procedure are listed in Table 1 and their characterization data is given in Table 6.

[2-(2-Hydroxy-phenyl)-4*H*-benzo[1,4]thiazin-3-yl]-(1-isopropyl-1*H*-indazol-3-yl)-methanones (8a-i). *ortho*-Aminothiophenol (0.002 mole) was dissolved in 10 ml of dimethyl sulphoxide. Reaction contents were stirred at room temperature for 2 hrs. To this reaction mixture compound **4** (0.001 mole) was added and the contents were heated under reflux for 2 hrs. Reaction mixture was cooled and poured into crushed ice. The product obtained was separated by filtration and crystallized from alcohol. Compounds synthesized by above procedure are listed in Table 1 and their characterization data is given in Table 7.

2-[5-(1-Isopropyl-1*H*-indazol-3-yl)-2*H*-pyrazol-3-yl]-phenols (9a-i). Compound **5** (0.001 mole) was taken with hydrazine hydrate (0.002 mole) and dissolved in 15 ml of alcohol. Reaction mixture was heated under reflux for 3 hrs. Contents were cooled, poured into crushed ice and acidified with conc. HCl. The product obtained was separated by filtration and crystallized from alcohol. Compounds synthesized by the above procedure are listed in Table **1** and their characterization is given in Table **8**.

6-(2-Hydroxy-phenyl)-4-(1-isopropyl-1*H*-indazol-3-yl)-1*H*-pyrimidine-2-thione (10 a-i). Compound **5** (0.001 mole) and thiourea (0.002 mole) were dissolved in 15 ml of alcohol. To this reaction mixture potassium hydroxide (0.001 mole) was added.

Table 7

Compounds **8a-i**

Compd. No.	IR (cm^{1})	Spectral Data ^{1}H NMR δ (ppm)	Mass M^{+}	Elemental Analysis Calcd % (Found %) C	H	N
8a	3316 1644 1596 754	8.59 (s, 1H), 8.57 (s, 1H), 7.52 to 6.80 (m, 10H), 4.91 (m, 1H), 1.35 (d, 6H)	495	60.49 (6052)	3.86 (3.89)	8.46 (8.40)
8b	3314 1642 1595 750	8.57 (s, 1H), 8.55 (s, 1H), 7.44 to 6.78 (m, 11H), 4.92 (m, 1H), 1.34 (d, 6H)	461	65.00 (65.06)	4.36 (4.33)	9.10 (9.14)
8c	3312 1648 1599	8.55 (s, 1H), 8.53 (s, 1H), 7.49 to 6.77 (m, 11H), 4.91 (m, 1H), 2.53 (s, 3H), 1.32 (d, 6H)	441	70.72 (70.75)	5.25 (5.22)	9.52 (9.49)
8d	3319 1650 1600	8.52 (s, 1H), 8.51 (s, 1H), 7.51 to 6.76 (m, 10H), 4.89 (m, 1H), 2.54 (s, 3H), 2.51 (s, 3H), 1.30 (d, 6H)	455	71.18 (71.15)	5.53 (5.49)	9.22 (9.27)
8e	3317 1647 1593	8.54 (s, 1H), 8.52 (s, 1H), 7.50 to 6.75 (m, 11H), 4.90 (m, 1H), 2.51 (s, 3H), 1.31 (d, 6H)	441	70.72 (70.69)	5.25 (5.19)	9.52 (9.57)
8f	3315 1644 1590 748	8.58 (s, 1H), 8.56 (s, 1H), 7.55 to 6.78 (m, 10H), 4.95 (m, 1H), 2.54 (s, 3H), 1.33 (d, 6H)	475	65.61 (65.57)	4.66 (4.69)	8.83 (8.79)
8g	3314 1645 1598 678	8.60 (s, 1H), 8.59 (s, 1H), 7.59 to 6.81 (m, 11H), 4.99 (m, 1H), 1.36 (d, 6H)	505	59.29 (59.33)	3.98 (4.01)	8.30 (8.27)
8h	3319 1648 1604 1025	8.62 (s, 1H), 8.60 (s, 1H), 7.62 to 6.83 (m, 11H), 5.12 (m, 1H), 1.39 (d, 6H)	445	67.40 (67.37)	4.52 (4.57)	9.43 (9.45)
8i	3314 1643 1592	8.57 (s, 1H), 8.54 (s, 1H), 7.59 to 6.80 (m, 12H), 4.90 (m, 1H), 1.33 (d, 6H)	427	70.24 (70.29)	4.95 (4.93)	9.83 (9.86)

Table 8

Compounds **9a-i**

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
9a	3156 1569 1235 752	10.88 (s, 1H), 8.19 to 7.19 (m, 8H), 4.91 (m, 1H), 1.65(d, 6H)	386	58.93 (58.89)	4.16 (4.19)	14.47 (14.51)
9b	3154 1571 1235 747	10.85 (s, 1H), 8.16 to 7.15 (m, 9H), 4.88 (m, 1H), 1.63(d, 6H)	352	64.48 (64.51)	4.86 (4.83)	15.88 (15.91)
9c	3157 1573 1238	10.83 (s, 1H), 8.15 to 7.12 (m, 9H), 4.85 (m, 1H), 2.58 (s,3H), 1.61 (d, 6H)	332	72.27 (72.30)	6.06 (6.03)	16.86 (16.89)
9d	3155 1570 1235	10.81 (s, 1H), 8.15 to 7.11 (m, 8H), 4.84 (m, 1H), 2.59 (s,3H), 2.54 (s, 3H), 1.60(d, 6H)	346	72.81 (72.86)	6.40 (6.37)	16.17 (16.19)
9e	3156 1574 1237	10.81 (s, 1H), 8.14 to 7.13 (m, 9H), 4.86 (m, 1H),2.55 (s,3H), 1.59(d, 6H)	332	72.27 (72.31)	6.06 (6.10)	16.86 (16.81)
9f	3157 1571 1236 745	10.84 (s, 1H), 8.17 to 7.14 (m, 8H), 4.89 (m, 1H),2.54 (s,3H), 1.61(d, 6H)	366	65.48 (65.51)	5.27 (5.23)	15.27 (15.30)
9g	3160 1573 1239 685	10.82 (s, 1H), 8.15 to 7.00 (m, 9H), 4.82(m, 1H), 1.61(d, 6H)	396	57.44 (57.39)	4.31 (4.29)	14.10 (14.17)
9h	3162 1574 1241 1055	10.84 (s, 1H), 8.19 to 7.05 (m, 9H), 4.86(m, 1H), 1.63(d, 6H)	336	67.84 (67.87)	5.09 (5.07)	16.66 (16.69)
9i	3159 1570 1239	10.80 (s, 1H), 8.11 to 6.98 (m, 10H), 4.80 (m, 1H), 1.57(d, 6H)	318	71.68 (71.71)	5.70 (5.67)	17.60 (17.63)

Table 9

Compounds **10a-i**

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
10a	3241 1569 1233 751	13.46 (s, 1H), 8.10 (s, 1H), 8.39 to to 6.81 (m, 7H), 5.07 (m, 1H), 1.66 (d, 6H)	430	55.69 (55.73)	3.74 (3.71)	12.99 (12.97)
10b	3245 1571 1234 749	13.44 (s, 1H), 8.08 (s, 1H), 8.37 to to 6.80 (m, 8H), 5.02 (m, 1H), 1.64 (d, 6H)	396	60.52 (60.55)	4.32 (4.37)	14.12 (14.07)
10c	3255 1565 1244	13.35 (s, 1H), 8.03 (s, 1H), 8.36 to to 6.78 (m, 8H), 4.98 (m, 1H), 2.58 (s, 3H), 1.61 (d, 6H)	376	67.00 (67.07)	5.35 (5.31)	14.88 (14.91)
10d	3259 1563 1247	13.33 (s, 1H), 8.01 (s, 1H), 8.34 to to 6.75 (m, 7H), 4.95 (m, 1H), 2.55 (s, 3H), 2.51(s, 3H), 1.59 (d, 6H)	390	67.67 (67.71)	5.68 (5.63)	14.35 (14.33)
10e	3256 1564 1244	13.35 (s, 1H), 8.02 (s, 1H), 8.38 to to 6.77 (m, 8H), 4.96 (m, 1H), 2.57 (s, 3H), 1.60(d, 6H)	376	67.00 (67.03)	5.35 (5.37)	14.88 (14.91)

The contents were heated under reflux for 3 hrs. Reaction mixture was cooled and poured into crushed ice, acidified with acetic acid. The product obtained was separated by filtration and crystallized from alcohol. Compounds synthesized by the above pro-

Table 9 (Continued)

Compd. No.	IR (cm^1)	Spectral Data ^1H NMR δ (ppm)	Mass M^+	Elemental Analysis Calcd % (Found %) C	H	N
10f	3255 1573 1241 745	13.38 (s, 1H), 8.04 (s, 1H), 8.30 to to 6.79 (m, 7H), 4.97 (m, 1H), 2.58 (s, 3H), 1.63(d, 6H)	410	61.38 (61.41)	4.66 (4.67)	13.63 (13.59)
10g	3250 1573 1239 684	1340 (s, 1H), 8.07 (s, 1H), 8.31 to to 6.77 (m, 8H), 4.98 (m, 1H), 1.68 (d, 6H)	440	54.43 (54.39)	3.88 (3.93)	12.69 (12.71)
10h	3251 1571 1240 1021	13.39 (s, 1H), 8.06 (s, 1H), 8.32 to to 6.79 (m, 8H), 5.03 (m, 1H), 1.71 (d, 6H)	380	63.14 (63.11)	4.50 (4.47)	14.73 (14.77)
10i	3247 1577 1235	13.36 (s, 1H), 8.05 (s, 1H), 8.27 to to 6.76 (m, 9H), 4.93 (m, 1H), 1.61 (d, 6H)	362	66.28 (66.31)	5.01 (5.03)	15.46 (15.41)

Table 10

Antibacterial activity of the compounds.

All the compounds were dissolved in DMSO and tested at 1 mg/ml concentration. In each well 50 µl sample was loaded. The zone of inhibition is expressed as diameter of zone in mm.

Comp.No	R_1	R_2	R_3	Staphylococcus Aureus 209P	Escherichia Coli ESS	Streptococcus Faecium 323
3a	Cl	H	Cl	-	-	-
3b	H	H	Cl	-	-	-
3c	H	H	Me	-	-	-
3d	Me	H	Me	-	-	-
3g	H	H	Br	-	-	-
4a	Cl	H	Cl	11	12	11
4b	H	H	Cl	11	12	12
4c	H	H	Me	sl	slh	sl
4d	Me	H	Me	-	-	-
4e	H	Me	H	sl	9	-
4f	H	Me	Cl	-	slh	-
4g	H	H	Br	9	12	12
4h	H	H	F	11	10	10
4i	H	H	H	10	9	10
5a	Cl	H	Cl	12	12	12
5b	H	H	Cl	-	-	-
5c	H	H	Me	11h	-	-
5d	Me	H	Me	-	-	-
5e	H	Me	H	-	-	-
5f	H	Me	Cl	-	-	-
5h	H	H	F	-	-	-
6a	Cl	H	Cl	-	9	-
6b	H	H	Cl	10h	-	-
6c	H	H	Me	11h	-	-
6d	Me	H	Me	12h	-	-
6e	H	Me	H	13	-	12
6f	H	Me	Cl	11h	-	-
6g	H	H	Br	10h	-	-
7a	Cl	H	Cl	12	11	12
7b	H	H	Cl	-	-	-
7g	H	H	Br	-	-	-
7i	H	H	H	-	-	-

cedure are listed in Table 1 and their characterization is given in Table 9.

Acknowledgement. Authors are thankful to Dr. G. T. Sangle, the Principal S.S.G.M. College, Kopargaon, Ahmednagar for his constant encouragement and providing necessary facilities. The authors are also thankful to Dr. Saji George, the Principal Research Scientist of Natural Products, Nicholas Piramal Research Centre, Mumbai, for valuable help in biological screening.

Table 10 (Continued)

All the compounds were dissolved in DMSO and tested at 1 mg/ml concentration. In each well 50 µl sample was loaded. The zone of inhibition is expressed as diameter of zone in mm.

Comp.No	R_1	R_2	R_3	Staphylococcus Aureus 209P	Escherichia Coli ESS	Streptococcus Faecium 323
9a	Cl	H	Cl	-	-	-
9c	H	H	Me	13h	-	-
9d	Me	H	Me	10h	-	-
9e	H	Me	H	12h	-	-
9h	H	H	F	-	-	-
Vancomycin (10 µg/ml)	-	-	-	13	15	13h
Linezolid (10 µg/ml)	-	-	-	14	14	13

h = hazy, sl = slightly, slh = slightly hazy, NT = not tested.

Table 11

Antifungal activity of the compounds.

All the compounds were dissolved in DMSO and tested at 1 mg/ml concentration. In each well 50 µl sample was loaded. The zone of inhibition is expressed as diameter of zone in mm.

Comp.No	R_1	R_2	R_3	Candida albicans	Candida albicans CO9	Candida krusei GO6 F^S	Candida krusei GO3 F^R	Candida glabrata HO4 F^S	Candida glabrata HO5 F^R	Aspergillus fumigatus
3a	Cl	H	Cl	11	10	12	11	11h	11h	-
3b	H	H	Cl	13	10	12	11	14	13	-
3c	H	H	Me	12	11	12	11	13	12	-
3d	Me	H	Me	12	10	13	12	10	11h	-
3g	H	H	Br	13	10	12	12	15	14	-
4a	Cl	H	Cl	-	-	10h	10h	-	-	-
4b	H	H	Cl	12	9h	11	10	13	12	-
4c	H	H	Me	10	-	11	10	11h	11h	-
4d	Me	H	Me	-	-	-	-	-	10h	-
4e	H	Me	H	-	-	10h	11	-	-	-
4f	H	Me	Cl	-	-	10h	10h	-	10h	-
4g	H	H	Br	13	10	13	12	15	12	10
4h	H	H	F	-	-	-	-	-	10h	-
4i	H	H	H	-	-	11	10h	-	11h	-
5a	Cl	H	Cl	-	-	11	10	-	12h	-
5b	H	H	Cl	-	9h	10h	-	-	10h	-
5c	H	H	Me	10h	11h	10h	10	-	10h	-
5d	Me	H	Me	10h	-	10h	-	10h	10h	-
5e	H	Me	H	10h	-	10h	11	10h	10h	-
5f	H	Me	Cl	10h	-	11	11	10h	10h	-
5h	H	H	F	10h	-	11	10	10h	10h	-
6a	Cl	H	Cl	10h	10h	12	10h	10h	13	-
6b	H	H	Cl	10h	10	-	-	-	-	-
6c	H	H	Me	10h	11	10h	11	-	-	-
6d	Me	H	Me	10h	10h	10h	11	-	-	-
6e	H	Me	H	10h	10	11h	12	10h	10	-
6f	H	Me	Cl	10h	-	11	12	10h	10h	-
6g	H	H	Br	10h	10h	12	10	10h	-	-
7a	Cl	H	Cl	-	10h	11	10	-	12h	-
7b	H	H	Cl	10h	10	10h	-	-	-	-
7g	H	H	Br	10h	10h	10h	10h	-	-	-
7i	H	H	H	10h	10h	10h	11	-	-	-
9a	Cl	H	Cl	10h	10h	10h	11	-	11	-
9c	H	H	Me	10h	11	11	10	10h	10h	-
9d	Me	H	Me	-	10	11	-	10h	12h	-
9e	H	Me	H	-	11	11	-	10h	12h	-
9h	H	H	F	10h	11	10h	-	-	-	-
Fluconazole (125 µg/ml)	-	-	-	28h	10h	30h	12h	15h	10h	-
Amphotericin B (1 µg/ml)	-	-	-	10	12	10	9	11	13	10h

h = hazy, sl = slightly, slh = slightly hazy, NT = not tested.

Table 12

% Antioxidant activity of the compounds at different concentrations is analyzed.

Compd. No.	R1	R2	R3	Concentration				
				1mg/ml	500µg/ml	250µg/ml	125µg/ml	62.5µg/ml
4a	Cl	H	Cl	39.79	31.34	26.30	21.88	17.20
4d	Me	H	Me	-44.25	9.58	16.76	16.74	14.43
4e	H	Me	H	49.71	40.71	31.59	24.09	16.11
4f	H	Me	Cl	49.76	49.13	40.32	30.03	24.24
4h	H	H	F	58.71	49.81	40.73	31.13	22.90
4i	H	H	H	45.46	37.02	26.81	19.78	12.20
5c	H	H	Me	-1.54	-0.12	-1.35	0.14	1.03
5d	Me	H	Me	-0.87	-0.05	-9.10	-1.23	-0.63
5e	H	Me	H	_0.17	0.72	0.24	0.00	-1.06
5f	H	Me	Cl	-0.22	-1.47	-0.63	0.12	-0.53
5h	H	H	F	-0.34	-0.07	-0.70	-0.84	-1.93
6a	Cl	H	Cl	7.99	7.56	9.07	8.78	7.99
6b	H	H	Cl	8.62	9.53	9.36	7.08	7.44
6c	H	H	Me	7.61	7.22	7.03	6.88	7.51
6d	Me	H	Me	6.93	-0.51	-1.01	-0.14	0.39
6e	H	Me	H	1.30	1.20	1.66	1.56	2.31
6f	H	Me	Cl	2.17	2.38	1.90	0.58	-2.89
6g	H	H	Br	8.13	6.40	6.40	5.80	6.69
7a	Cl	H	Cl	28.26	22.70	19.76	14.03	11.31
7g	H	H	Br	10.20	8.59	8.38	7.12	6.64
9a	Cl	H	Cl	15.48	12.76	10.47	8.93	7.73
9c	H	H	Me	67.68	56.87	44.74	34.37	23.97
9d	Me	H	Me	87.00	80.58	69.27	55.33	41.23
9e	H	Me	H	29.00	21.90	16.03	10.76	8.04
9h	H	H	F	27.65	24.12	19.28	10.52	7.65

REFERENCES AND NOTES

[1] U.S. Application Ser. No. 10/326,037 filed Feb. 15, (2003).

[2] I. J. McAlpine, J. G. Deal, M. C. Johnson, S. E. Kepha, Y. Park, W. H. Romines and J. G. Tikhe, U.S. Provisional Application No.60/491,821 filed on Jul.31, (2005).

[3] G. Picciola, F. Ravenna, G. Carenini, P. Gentili and Riva, *Farmaco*., **36**(**12**), 1037 (1981).

[4] B. K. Keppler, M. Henn, U. M. Juhl, M. R. Berger, R. Niebl and F. F. Wagner, *Prog. Clin. Biochem. Med*., **10,** 41 (1989).

[5] Y. N. Vashisht Gopal and A. K. Kondapi, *J. Biosci*., **26**(2), 271 (2001).

[6] F. J. Brown, Y. K. Yee, L. A. Cronk, K. C. Hebbel, R. D. Krell and D. W. Snyder, *J. Med. Chem*., **33** 1771 (1990).

[7] Y. K. Yee, P. R. Bernstein, E. J. Adams, F. J. Brown, L. A. Cronk, K. C. Hebbel, E. P. Vacek, R. D. Krell and D. W. Snyder, *J. Med. Chem*., **33**, 2437 (1990).

[8] P. R. Bernstein, *Am. J. Respir. Crit. Care Med*., **157**, S220 (1998).

[9] X. Li, S. Chu, V. A. Feher, M. Khalili, Z. Nie, S. Margosiak, V. Nikulin, J. Levin, K. G. Sprankle, M. E. Tedder, R. Almassy, K. Appelt and K. M. Yager, *J. Med. Chem*., **46**, 5663 (2003).

[10] P. Lennon, D. Bonafoux, D. S. Oburn and S. G. Wolfson, (Pharmacia Corporation, USA)., PCT Int. Appl. WO 2003095430 A1 Nov., 20, 2003, 312.

[11] N. Conception, M. Patrick, T. Faienne, T. Michel, B. Eric, W. Sylvie and C. Cecile, PCT Int. Appl. WO 200311833 A1 Feb., 13, 2003, 188 pp.

[12] D. Erich, J. William and L. Ronald, Ger. Offen. DE 10206562 A1, Aug., 28, 2003, 30 (German).

[13] A. Breteche, M. Duflos, A Dassonville, M. R. Nourrisson, J. Brelet, G. LeBaut, N. Grimand and J. Y. Petit, *J. Enzym. Inhib. Med. Chem*., **17**, 415 (2002).

[14] J. Grima, B. Silverstrini and C. Y. Cheng, *Biol. Reprod*., **64**, 1500 (2001).

[15] K. Ramaligam, K. D. Wong, K. D. Berlin, R. A. Brown, Fisher, J. Blunk and N. N. Durham, *J. Med. Chem*., **20**, 664 (1977).

[16] X. D. Gong, P. Linsdell, K. H. Cheung, G. P. H. Leung and P. Y. D. Wong, *Biol. Reprod*. **67(6)**, 1888 (2002).

[17] K. A. Thakar, D. D. Goswami and D. G. Pachpor, *J. Ind. Chem. Soc*., **50**, 420 (1973).

[18] P. F. Devitt, A. Timoney and M. A. Vickars, *J. Org. Chem*., **26**, 4941 (1961).

[19] B. K. Karale, V. P. Chavan, A. S. Mane, R. V. Hangarge, C. H. Gill and M. S. Shingare, *Korean J. Med. Chem*., **10**, 84 (2000).

[20] N. S. Joshi, B. K. Karale, S. B. Bhirud and C. H. Gill, *J. Heterocyclic Chem*., **41**, 541 (2004).

[21] A. Kumar, S. Malhotra, A. Vats, Himanshu, S. K. Singh, S. K. Sharma, A. K. Prasad, W. Errington, C. E. Olsen, S. C. Jain and V. S. Parmar, *Ind. J. Chem*., **41B**, 360 (2002).

[22] H. Suzuki, M. Hannue and M. Nishikubo, Jpn. Kokai Tokkyo Koho JP, **03**, 236, 368; *Chem. Abstr*., **116**, 106285 (1993).

[23] M. Londershausen, *Pestic. Sci*., **48**, 269 (1996).

[24] B. S. M. Fahmey and M. H. Elnagdi, *J. Chem. Tech. Technol*., **30,** (1980); *Chem. Abstr*. 94 48804 (1981).

[25] P. Pigeon and B. Decroix, *Tett. Lett*., **39**, 8659 (1998).

[26] M. J. Fray, D. J. Bull, K. Cooper, M. J. Parry and H. M. Stefanaik, *J. Med. Chem*., **38**, 3524 (1995).

[27] Y. Kawakami, H. Kitani, S. Yuasa, M. Abe, M. Moriwaki, M. Kagoshima, M. Tersawa and T. Tahara, *Eur. J. Med. Chem*., **31**, 683 (1996).

[28] V. P. Rajappan and R. S. Hosmane, *Nucleosides Nucleotides*., **17**, 1141 (1998).

[29] L. Bertellia, G. Biagi, L. Giorgi, O. Livi, and C. Manera, *Farmaco*., **53**, 305 (1998).

[30] K. Goerlitzer, C. Wilpert, H. Ruebsamen-Waigmann, H. Suhartono, L. Wang and A. Immelmann, *Arch. Pharm. (Weinheim Ger.)* **328**, 247 (1995).

[31] H. Zimmer, C. P. Libera, S. H. J. Bauer and A. Amer, *Molecules*., **8**, 735 (2003).

[32] R. R. Gupta (Ed), Phenothiazines and 1,4-Benzothiazines, *Chemical and Biomedical Aspects*., Elsevier Amsterdam (1988).

[33] J. L. Vennerstrom, M. T. Makler, C. K. Angerhofer and J. A. Williams, *Antimicrob Agents Chemother*., **39** (**12**), 2671 (1995).

[34] R. H. Udupi, A. R. Bhat and J. Jacob, *Ind. J. Heterocyclic Chem*., **15**, 89 (2005).

[35] A. K. Padhey, M. Bardhan and C. S. Panda, *Ind. J. Chem*., **42B**, 910 (2003).

[36] M. Kidwai, S. Saxena, S. Rastogi and R. Venkatramanan, *A Current Medicinal Chem*., **2**, 269 (2004).

[37] N. D. Argade, V. K. Bhujade, A. A. Deshpande, R. T. Bachute, B. K. Karale and C. H. Gill, *Ind. J. Heterocyclic Chem*., **12**, 53 (2002).

[38] B. K. Karale, C. H. Gill, M. Khan, V. P. Chavan, A. S. Mane and M. S. Shingare, *Ind. J. Chem*., **41B**, 1957 (2002).

[39] N. N. Mateeva, R. N. Kode and K. K. Redda, *J. Heterocyclic Chem*., **39**, 1251 (2002).

[40] E. C. Cortes, I. E. Martinez and O. G. Mellado, *J. Heterocyclic Chem*., **39**, 1189 (2002).