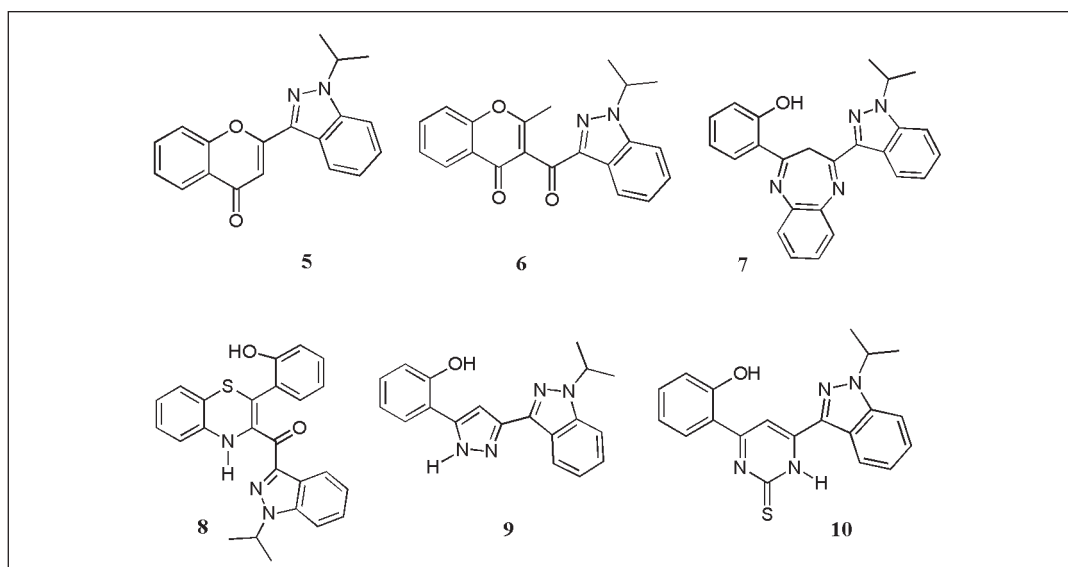


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A series of some important indazolyl derivatives of pyrazoles, diazepines, thiopyrimidines, thiazines and chromones were synthesized and characterized with the help of spectral data. Some of the synthesized compounds are tested for antimicrobial and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

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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 deriv-

atives 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**.

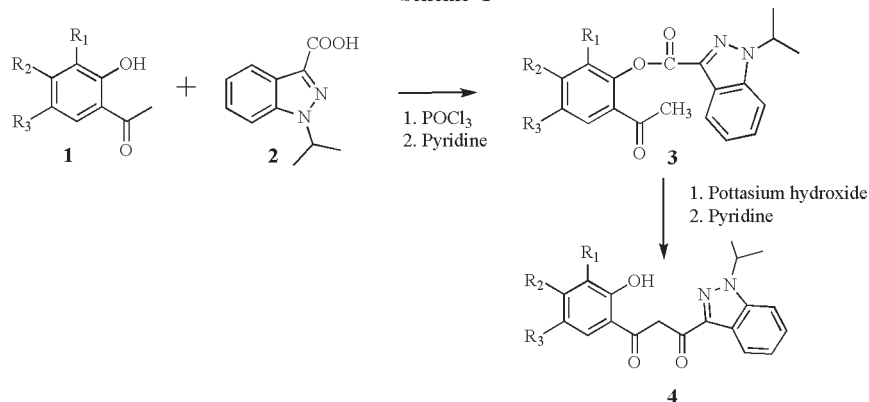
The structures of compounds **3**, **4** and **5** are confirmed by spectral techniques (ms, ir, ^1H nmr). The ir absorption spectra (cm^{-1}) of compounds **3** show a strong absorption

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 ^1H nmr). The ^1H 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 $\text{C}=\text{O}$ group and bands at 1595 and 1540 cm^{-1} appears due to $\text{C}=\text{N}$ bond. ^1H 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 O-H functionality and at 1644 cm^{-1} due to $\text{C}=\text{O}$ group. Structures of compounds **8** are also confirmed by ^1H nmr and mass spectra.

Compounds **5** on treatment with hydrazine hydrate undergoes γ -pyrone ring opening followed by cyclization

Scheme 1



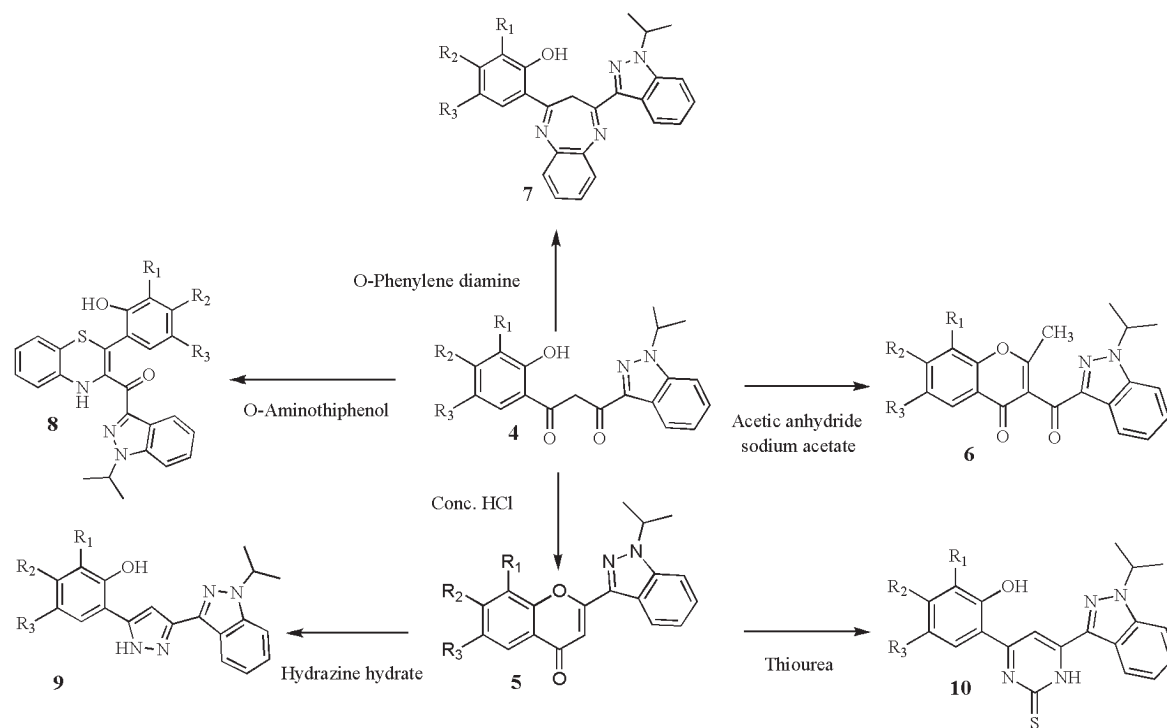
band at 1728 for $\text{O}=\text{C}=\text{O}$ group and ^1H nmr spectra show a sharp singlet at around 2.5 δ for $\text{CO}-\text{CH}_3$. The ir spectra of compounds **4** show a strong and characteristic band for 1,3 diketone linkage at 1620-1599 cm^{-1} . The ^1H nmr of compound **4** shows disappearance 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 ^1H 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**.

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 ^1H nmr). In their ir spectra, the band at 1643 cm^{-1} due to $\text{C}=\text{O}$ group are not observed and a new bands at 3160 cm^{-1} due to the OH group are observed. The ^1H 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 2



In addition to this, the ir spectra of **10** shows a band due to $\text{C}=\text{S}$ group in the region $1210\text{--}1270\text{ cm}^{-1}$. The ^1H nmr spectra show singlets at $13.4\ \delta$ and $8.06\ \delta$ 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. No.	Yield (%)	M.P. ($^{\circ}\text{C}$)	Compd. No.	Yield (%)	M.P. ($^{\circ}\text{C}$)	Compd. No.	Yield (%)	M.P. ($^{\circ}\text{C}$)
R_1	R_2	R_3									
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 ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis		
				Calcd % C	(Found %) 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 followed by water. The product was crys-

Table 3
Compounds **4a-i**

Compd. No.	IR (cm ⁻¹)	Spectral Data ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis		
				Calcd % C	(Found %) H	(Found %) 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 ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis		
				Calcd % C	(Found %) H	(Found %) 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 ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis		
				Calcd % C	(Found %) H	N
5b	1648	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)
	1619					
	1563					
	1484					
	749					
5c	1633	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)
	1603					
	1545					
	1474					
5d	1635	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)
	1607					
	1551					
	1475					
5e	1640	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)
	1610					
	1554					
	1477					
5f	1643	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)
	1613					
	1557					
	1480					
5g	1646	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)
	1617					
	1561					
	1481					
5h	1647	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)
	1619					
	1560					
	1479					
5i	1648	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)
	1617					
	1561					
	1483					

Table 5
Compounds **6a-i**

Compd. No.	IR (cm ⁻¹)	Spectral Data ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis		
				Calcd % C	(Found %) H	N
6a	1642	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)
	1618					
	1590					
	1497					
	753					
6b	1640	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)
	1615					
	1588					
	1496					
	750					
6c	1636	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)
	1611					
	1582					
	1486					
6d	1639	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)
	1612					
	1586					
	1492					

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-1H-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 ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis Calcd % (Found %)		
				C	H	N
6e	1636	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)
	1611					
	1582					
	1486					
6f	1635	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)
	1613					
	1586					
	1487					
6g	1639	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)
	1615					
	1585					
	1484					
6h	1638	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)
	1617					
	1586					
	1489					
6i	1635	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)
	1609					
	1581					
	1485					

Table 6
Compounds **7a-i**

Compd. No.	IR (cm ⁻¹)	Spectral Data ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis Calcd % (Found %)		
				C	H	N
7a	3424	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)
	1599					
	1553					
	1487					
7b	3422	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)
	1597					
	1550					
	1486					
7e	3415	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)
	1592					
	1552					
	1479					
7g	3418	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)
	1594					
	1555					
	1484					
7h	3416	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)
	1595					
	1551					
	1480					
	1035					

2-(1-Isopropyl-1H-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-1H-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-1H-indazol-3-yl)-3H-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)-4H-benzo[1,4]thiazin-3-yl]-(1-isopropyl-1H-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-1H-indazol-3-yl)-2H-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-1H-indazol-3-yl)-1H-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 % C	(Found %) 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 (60.52)	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 ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis		
				Calcd % C	(Found %) 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 ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis		
				Calcd % C	(Found %) 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 ¹ H NMR δ (ppm)	Mass M ⁺	Elemental Analysis Calcd % (Found %)		
				C	H	N
10f	3255	13.38 (s, 1H), 8.04 (s, 1H), 8.30 to 6.79 (m, 7H), 4.97 (m, 1H), 2.58 (s, 3H), 1.63(d, 6H)	410	61.38	4.66	13.63
	1573			(61.41)	(4.67)	(13.59)
	1241					
	745					
10g	3250	1340 (s, 1H), 8.07 (s, 1H), 8.31 to 6.77 (m, 8H), 4.98 (m, 1H), 1.68 (d, 6H)	440	54.43	3.88	12.69
	1573			(54.39)	(3.93)	(12.71)
	1239					
	684					
10h	3251	13.39 (s, 1H), 8.06 (s, 1H), 8.32 to 6.79 (m, 8H), 5.03 (m, 1H), 1.71 (d, 6H)	380	63.14	4.50	14.73
	1571			(63.11)	(4.47)	(14.77)
	1240					
	1021					
10i	3247	13.36 (s, 1H), 8.05 (s, 1H), 8.27 to 6.76 (m, 9H), 4.93 (m, 1H), 1.61 (d, 6H)	362	66.28	5.01	15.46
	1577			(66.31)	(5.03)	(15.41)
	1235					

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 μ l 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.

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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

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