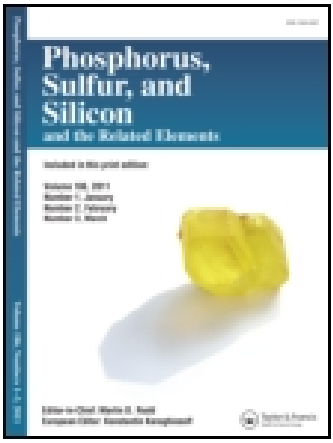


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

SYNTHESIS, SPECTRAL STUDIES, AND ANTIMICROBIAL ACTIVITIES OF [N-(UN)ALKYLATED-2-ARYLINDOL-3-YL]THIOCARBOXAMIDES

Vijai N. Pathak [a] , Rahul Joshi & Neetu Gupta
[a] Department of Chemistry, University of Rajasthan , Jaipur, India
Published online: 16 Aug 2010.

To cite this article: Vijai N. Pathak , Rahul Joshi & Neetu Gupta (2004) SYNTHESIS, SPECTRAL STUDIES, AND ANTIMICROBIAL ACTIVITIES OF [N-(UN)ALKYLATED-2-ARYLINDOL-3-YL]THIOCARBOXAMIDES, Phosphorus, Sulfur, and Silicon and the Related Elements, 179:11, 2365-2378, DOI: 10.1080/10426500490485110

To link to this article: http://dx.doi.org/10.1080/10426500490485110

Phosphorus, Sulfur, and Silicon, 179:2365–2378, 2004

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500490485110

Taylor & Francis
Taylor & Francis Group

SYNTHESIS, SPECTRAL STUDIES, AND ANTIMICROBIAL ACTIVITIES OF [N-(UN)ALKYLATED-2-ARYLINDOL-3-YL]-THIOCARBOXAMIDES

Vijai N. Pathak, Rahul Joshi, and Neetu Gupta
Department of Chemistry, University of Rajasthan, Jaipur, India

(Received July 3, 2003; accepted April 28, 2004)

*A series of [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (**6**) have been synthesized by the condensation of alkyl [N-(un)alkylated-2-arylindol-3-yl]dithiocarboxylates (**5**) with appropriate secondary amines in absolute alcohol. Compound **5** was prepared by the reaction of N-(un)alkylated-2-arylindoles with carbon disulphide in the presence of potassium-*t*-butoxide followed by alkyl iodide under nitrogen atmosphere. All of the compounds have been characterized on the basis of their elemental and spectral data and have been screened for their antibacterial and antifungal activities. Some of the synthesized compounds have shown promising activity.*

Keywords: 2-Arylindoles; antimicrobial activity; PTC; thiocarboxylate; thiocarboxamide

INTRODUCTION

The use of carbon disulphide as a solvent in Friedel-Crafts and other reactions and as a solvent in spectroscopy is well known. Carbon disulphide is also used as a starting material for the synthesis of various heterocyclic compounds. Condensation reactions of carbon disulphide with various types of nucleophiles has been reported.[1–6] Various sulphur-containing indole derivatives have been reported to possess

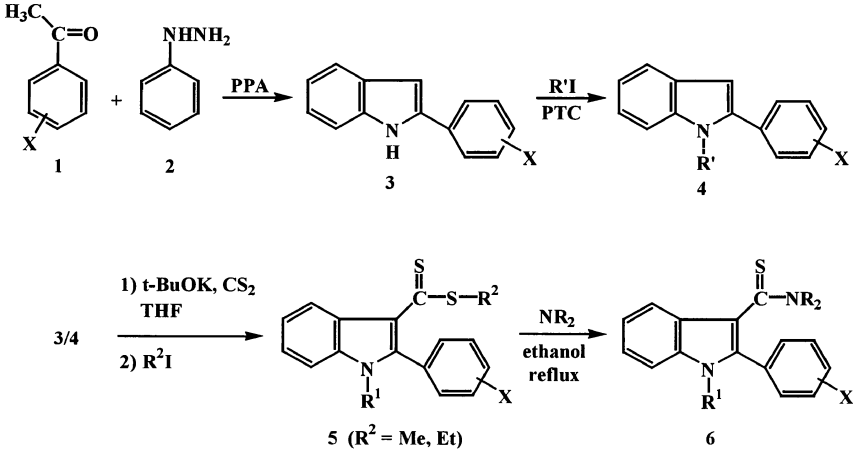
The authors would like to thank the head of the Department of Chemistry, University of Rajasthan, Jaipur for providing necessary facilities, Dr. V. J. Ram, Dy. Director (retd.) and Emeritus Scientist CDRI, Lucknow for valuable suggestions and for the help offered in obtaining the various spectra, and CSIR (New Delhi) for the award of Senior Research Fellowship to N. Gupta.

Address correspondence to Vijai N. Pathak, Department of Chemistry, University of Rajasthan, Jaipur, 302 004, India. E-mail: pathakvijain@yahoo.com

antibacterial,[7,8] antimigraine,[9] antiinflammatory,[10,11] antiasthmatic,[12] anticoagulant,[13] antidiabetic,[14] and antineoplastic[15] activities. Encouraged by these observations, a number of [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides have been synthesized and characterized.

DISCUSSION

2-Arylindoles (**3**) were prepared by the method of Joshi et al.[16] utilizing Fischer Indole synthesis. 2-Arylindoles were than N-alkylated by phase transfer catalysis method.[17] N-(un)alkylated-2-arylindoles were treated with CS_2 in the presence of potassium-*t*-butoxide followed by alkyl iodide under nitrogen atmosphere, which was in turn further treated with appropriate secondary amines to afford [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (**6a–h**). The structure of the synthesized compounds was established on the basis of their IR, ^{1}H NMR, and FAB mass spectral studies Physical and analytical data of compounds **5** and **6** are given in Tables I and II, respectively. The spectral data of



	X	R^1	NR_2		X	R^1	NR_2
6a	4-Br	H	piperidino	6e	4-Cl	H	piperidino
6b	4-Br	Et	morpholino	6f	4-Cl	H	diisopropylamino
6c	4-Br	H	morpholino	6g	4-Cl	Me	diethylamino
6d	4-Br	H	diethylamino	6h	4-Br	H	diisopropylamino

SCHEME 1

TABLE I Physical and Analytical Data of Alkyl [N-(un)-alkylated-2-arylindol-3-yl]dithiocarboxylates (**5**)

Compd. no.	X	R^1	R^2	Color	m.p. (°C)	Yield (%)	Molecular formula	Elemental analyses (%), found (calc.) C	H	N	S
5a	4-Br	H	Et	Orange	190	43	$C_{17}H_{14}BrNS_2$	54.01 (54.25)	3.73 (3.72)	3.71 (3.72)	17.09 (17.02)
5b	4-Br	H	Me	Orange	194	47	$C_{16}H_{12}BrNS_2$	52.80 (53.03)	3.32 (3.31)	3.86 (3.87)	17.76 (17.68)
5c	4-Br	Et	Me	Red	83	42	$C_{18}H_{16}BrNS_2$	55.12 (55.38)	4.12 (4.10)	3.58 (3.59)	16.48 (16.41)
5d	4-Cl	H	Et	Orange	179	52	$C_{17}H_{14}ClNS_2$	61.28 (61.54)	4.24 (4.22)	4.21 (4.22)	19.39 (19.31)
5e	4-Cl	H	Me	Red	190	50	$C_{16}H_{12}ClNS_2$	60.29 (60.47)	3.79 (3.78)	4.40 (4.41)	20.24 (20.16)
5f	4-Cl	Me	Me	Orange	94	49	$C_{17}H_{14}ClNS_2$	61.29 (61.54)	4.24 (4.22)	4.23 (4.22)	19.38 (19.31)

synthesized compounds (**5** and **6**) are given in Table III. Major mass fragments along with their relative intensities and m/z values of compounds **6** are given in Table IV. The synthesized compounds have been screened for their antibacterial activity against gram-positive bacteria *Staphylococcus aureus* and gram-negative bacteria *Escherichia coli*. Antifungal activity was done against *Candida albicans* and *Aspergillus niger*. Results of antibacterial and antifungal activities are tabulated in Tables V and VI, respectively.

IR Spectra

The IR spectra of 2-arylindoles showed absorption bands at 3350–3450 cm^{-1}, which is attributed to >N—H stretching vibration. In the IR spectra of N-alkyl-2-arylindoles (**4**), >N—H absorption band at 3350–3450 cm^{-1} disappeared and an absorption band appeared at 2850 cm^{-1} due to aliphatic C—H stretching vibration. IR spectra of alkyl [N-(un)alkylated-2-arylindol-3-yl] dithiocarboxylates (**5**) exhibited >C=S and >C—S absorptions in the region of 1161–1239 cm^{-1} and 1070–1071 cm^{-1}, respectively. The IR spectra of [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (**6**) exhibited >C=S absorption in the region of 1238–1298 cm^{-1}, whereas >N—H absorption was observed in the range of 3423–3435 cm^{-1}. Disappearance of C—S absorption in the range of 1070–1071 cm^{-1} and appearance of C—N absorption in the range of 1340–1350 cm^{-1} confirms the formation of compounds 6; however, in some cases this $C—NR_2$ absorption coalesced with indolyl C—N absorption.

TABLE II Physical and Analytical Data of [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (**6**)

Compound no.	X	R^1	NR_2	Color	UV-vis λ_{max} (dichloromethane) (nm)	m.p. (°C)	Yield (%)	Molecular formula	Elemental analyses (%), found (calc.)			
									C	H	N	S
6a	4-Br	H	Piperidino	Yellow green	369.1	110	44	$C_{20}H_{19}BrN_2S$	59.94 (60.15)	4.78 (4.76)	7.00 (7.02)	8.04 (8.02)
6b	4-Br	Et	Morpholino	Green	347.9	70	47	$C_{21}H_{21}BrN_2OS$	58.59 (58.74)	4.90 (4.89)	6.51 (6.53)	7.49 (7.46)
6c	4-Br	H	Morpholino	Yellow	349	175	48	$C_{19}H_{17}BrN_2OS$	56.67 (56.86)	4.25 (4.24)	6.96 (6.98)	8.00 (7.98)
6d	4-Br	H	Diethylamino	Yellow	352	191	50	$C_{19}H_{19}BrN_2S$	58.69 (58.91)	4.93 (4.91)	7.21 (7.23)	8.29 (8.27)
6e	4-Cl	H	Piperidino	Yellow green	350	188	43	$C_{20}H_{19}ClN_2S$	67.45 (67.70)	5.37 (5.36)	7.89 (7.90)	9.00 (9.03)
6f	4-Cl	H	Diisopropylamino	Green	349	180	51	$C_{21}H_{23}ClN_2S$	68.27 (68.02)	6.23 (6.21)	7.54 (7.56)	8.62 (8.64)
6g	4-Cl	Me	Diethylamino	Green	351	80	49	$C_{20}H_{21}ClN_2S$	67.11 (67.32)	5.91 (5.89)	7.83 (7.85)	8.99 (8.98)
6h	4-Br	H	Diisopropylamino	Green	348	190	55	$C_{21}H_{23}BrN_2S$	60.47 (60.72)	5.56 (5.54)	6.74 (6.75)	7.73 (7.71)

TABLE III Spectral Data of Alkyl [N-(un)alkylated-2-arylindol-3-yl]dithiocarboxylates (**5**) and [N-(un)-alkylated-2-arylindol-3-yl]thiocarboxamides (**6**)

Compound no.	IR (KBr) ν_{max} cm^{-1}	^1H NMR ($CDCl_3$) δ ppm	FAB mass m/z
5a	1594 (aromatic C═C str.), 2900 (aliphatic C—H str.), 3055 (aromatic C—H Str.), 1239 (>C═S str.), 1071 (C═S str.), 504 (C—Br str.), 3425 (>N—H str.)	1.56 (t, CH_3, 3H, $J = 7.13$ Hz), 3.42 (q, CH_2, 2H, $J = 7.13$ Hz), 7.11–7.64 (m, ArH, 8H), 8.26 (s, NH, 1H)	$M^+ + 1$; 376/378 M^+; 375/377 (isotopic cluster) (b.p.) 271/273
5c	1597 (aromatic C═C str.), 3071 (aromatic C—H str.), 2975 (aliphatic C—H str.), 1161 (C═S Str.), 1070 (C—S str.), 540 (C—Br str.)	1.25 (t, CH_2—CH_3,3H, $J = 7.14$ Hz), 4.18 (q, CH_2—CH_3, 2H, $J = 7.14$ Hz), 1.54 (s, S—CH_3, 3H), 7.10–7.65 (m, ArH, 8H)	$M^+ + 1$; 390/392 M^+; 389/391 (isotopic cluster) (b.p.) 285/287
6a	1620 (aromatic C═C str.), 3070 (aromatic C—H str.), 2930 (aliphatic C—H str.), 1238 (C═S str.), 503 (C—Br str.), 3435 (>N—H str.), 1340 (C—N str.)	1.44(m, –$CH_2CH_2CH_2$–, 2H), 1.66 [m, –$CH_2CH_2CH_2$– (*trans* to >C═S), 2H], 1.69 [m, –$CH_2CH_2CH_2$– (*cis* to >C═S), 2H], 2.97 [t, –NCH_2– (*trans* to >C═S), 2H], 3.14 [t, –NCH_2– (*cis* to >C═S), 2H], 7.02–7.54 (m, ArH, 8H), 8.53 (s, NH, 1H)	$M^+ + 1$; 399/401 M^+; 398/400 (isotopic cluster) (b.p.) 273
6b	1635 (aromatic C═C str.), 3065 (aromatic C—H str.), 2930 (aliphatic C—H str.), 1239 (C═S str.), 504 (C—Br str.), 1343 (C—N str.)	1.31 (t, –CH_3CH_2–, 3H, $J = 7.16$ Hz), 2.76 [t, –CH_2N– (*trans* to >C═S), 2H], 2.81 [t, –CH_2N– (*cis* to >C═S), 2H], 3.31 [t, –OCH_2– (*trans* to >C═S), 2H], 3.43 [t, –OCH_2– (*cis* to > C═S), 2H], 4.09 (q, CH_3CH_2, 2H, $J = 7.16$ Hz), 7.12–7.61 (m, ArH, 8H)	$M^+ + 1$; 429/431 M^+; 428/430 (isotopic cluster) (b.p.) 122
6c	1652 (C═C str.), 3060 (aromatic C—H str.), 2964 (aliphatic C—H str.) 1262 (C═S str.), 501 (C—Br str.), 3423 (>N—H str.), 1350 (C—N str.)	3.31 [t, –CH_2N– (*trans* to >C═S), 2H], 3.41 [t, –CH_2N– (*cis* to >C═S), 2H], 3.52 [t, –OCH_2– (*trans* to >C═S), 2H], 3.59 [t, –OCH_2– (*cis* to > C═S), 2H], 7.01–7.56 (m, ArH, 8H), 8.54 (s, NH, 1H)	$M^+ + 1$; 401/403 M^+; 400/402 (isotopic cluster) (b.p.) 147

(Continued on next page)

TABLE III Spectral Data of Alkyl [N-(un)alkylated-2-arylindol-3-yl]dithiocarboxylates (**5**) and [N-(un)-alkylated-2-arylindol-3-yl]thiocarboxamides (**6**) (Continued)

Compound no.	IR (KBr) ν_{max} cm^{-1}	^1H NMR ($CDCl_3$) δ ppm	FAB mass m/z
6d	1620 (C═C str.), 3069 (aromatic C—H str.) 2929 (aliphatic C—H str.), 1263 (C═S str.), 505 (C—Br str.), 3425 (>N—H str.), 1338 (C—N str.)	1.28 [t, $-CH_3CH_2N-$ (*trans* to >C═S), 3H], 1.34 [t, $-CH_3CH_2N-$ (*cis* to >C═S), 3H], 2.94 [q, $-NCH_2CH_3-$ (*trans* to >C═S), 2H], 3.16 [q, $-NCH_2CH_3-$ (*cis* to > C═S), 2H], 7.12–7.61 (m, ArH, 8H), 8.53 (s, NH, 1H)	$M^+ + 1$; 387/389 M^+; 386/388 (isotopic cluster) (b.p.) 88
6e	1625 (C═C str.), 3070 (aromatic C—H str.) 2930 (aliphatic C—H str.), 1280 (C═S str.), 748 (C—Clstr.), 3435 (>N—H str.), 1340 (C—N str.)	1.43 (m, $-CH_2CH_2CH_2-$, 2H), 1.63 [m, $-CH_2CH_2CH_2-$ (*trans* to >C═S), 2H], 1.70 [m, $-CH_2CH_2CH_2-$ (*cis* to >C═S), 2H], 2.99 [t, $-NCH_2-$ (*trans* to > C═S), 2H], 3.18 [t, $-NCH_2-$ (*cis* to > C═S), 2H], 7.19–7.59 (m, ArH, 8H), 8.55 (s, NH, 1H)	$M^+ + 1$; 355/357 M^+; 354/356 (isotopic cluster) (b.p.) 199
6f	1636 (C═C str.), 3068 (aromatic C—H str.) 2930 (aliphatic C—H str.), 1290 (C═S str.), 746 (C—Clstr.), 3425 (>N—H str.), 1350 (C—N str.)	1.12 [d,$NCH(CH_3)_2$ (*trans* to >C═S), 6H], 1.20 [d,$NCH(CH_3)_2$ (*cis* to >C═S), 6H], 3.97 [sept, $-NCH(CH_3)_2$ (*trans* to >C═S), 1H], 4.47 [sept, $NCH(CH_3)_2$ (*cis* to > C═S, 1H], 7.21–7.61 (m, ArH, 8H), 8.51 (s, NH, 1H)	$M^+ + 1$; 371/373 M^+; 370/372 (isotopic cluster) (b.p.) 259
6g	1652 (C═C str.), 3070 (aromatic C—H str.) 2964 (aliphatic C—H str.), 1267 (C═S str.), 748 (C—Clstr.), 1340 (C—N str.)	1.41 [s, NCH_3, 3H], 1.26 [t, $-CH_3CH_2N-$ (*trans* to >C═S), 3H], 1.31 [t, $-CH_3CH_2N-$ (*cis* to >C═S), 3H], 2.95 [q, $-NCH_2CH_3-$ (*trans* to >C═S), 2H], 3.14 [q, $-NCH_2CH_3-$ (*cis* to > C═S), 2H], 7.09–7.63 (m, ArH, 8H)	$M^+ + 1$; 357/359 M^+; 356/358 (isotopic cluster) (b.p.) 241
6h	1636 (C═C str.), 3055 (aromatic C—H str.), 2970 (aliphatic C—H str.), 1298 (C═S str.), 505 (C—Br str.), 3425 (>N—H str.), 1342 (C—N str.)	1.11 [d,$NCH(CH_3)_2$ (*trans* to >C═S), 6H], 1.21 [d,$NCH(CH_3)_2$ (*cis* to >C═S), 6H], 3.94 [sept, $-NCH(CH_3)_2$ (*trans* to >C═S), 1H], 4.29 [sept, $NCH(CH_3)_2$ (*cis* to > C═S), 1H], 7.08–7.64 (m, ArH, 8H), 8.52 (s, NH, 1H)	$M^+ + 1$; 415/417 M^+; 414/416 (isotopic cluster) (b.p.) 273

TABLE IV Major Mass Fragments of Alkyl [N-(un)alkylated-2-arylindol-3-yl]dithioarboxylates (**5**) and [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (**6**)

	5a		**5c**		**6a**		**6b**		**6c**	
Compound no. fragment no.	m/z	Relative intensity (%)	m/z	Relative intensity (%)	m/z	Relative intensity (%)	m/z	Relative intensity (%)	m/z	Relative intensity (%)
I	376/378 ($M^+ + 1$)	15.0/15.0	390/392 ($M^+ + 1$)	15.0/15.0	399/401 ($M^+ + 1$)	3.2/3.2	429/431 ($M^+ + 1$)	16.0/16.0	401/403 ($M^+ + 1$)	6.1/6.1
II	375/377 (M^+) isotopic	10.0/10.0	389/391 (M^+) isotopic	12.0/12.0	398/400 (M^+) isotopic	2.1/2.1	428/430 (M^+) isotopic	14.0/14.0	400/402 (M^+) isotopic	4.2/4.2
III	374/376	2.1/2.1	329	30.1	397/399	4.2/4.2	340	12.5	399/401	10.6/10.8
IV	327	29.7	307	50.2	391	36.1	327	50.4	383/385	12.7/12.9
V	314/316	11.2	294	41.1	327	12.7	305	66.4	356/358	2.1/2.1
VI	304	19.1	285/287 (b.p.)	100	314/316	17.0/17.2	283	68.2	325/327	38.2/38.6
VII	289	23.2	203	45.2	307	29.7	193	90.4	311/313	14.8/14.6
VIII	271/273 (b.p.)	100	193	23.1	300	21.2	147	82.3	281	29.7
IX	203	51.0	190	10.1	298/300	23.3/23.0	146	85.4	271/273	46.7/46.8
X	191	19.1	147	11.2	289	27.6	140	14.1	265/267	25.5/25.5
XI	165	87.2	142	15.2	279/281	12.7/12.9	135	15.2	237	12.7
XII	149	95.2	136	17.4	273(b.p.)	100.0	132	2.1	235	6.3
XIII	151	41.4	107	67.5	204	19.1	122 (b.p.)	100	221	19.1
XIV	—	—	—	—	193	23.3	110	15.2	207	68.0
XV	—	—	—	—	165/167	21.2/21.2	—	—	193	72.3
XVI	—	—	—	—	154	98.0	—	—	191	53.1
XVII	—	—	—	—	149	87.2	—	—	147 (b.p.)	100.0
XVIII	—	—	—	—	136	95.7	—	—	136	76.5
XIX	—	—	—	—	107	42.5	—	—	115	34.0

(continued on next page)

TABLE IV Major Mass Fragments of Alkyl[N-(un)alkylated-2-arylindol-3-yl]dithioarboxylates (**5**) and [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (**6**) (Continued)

	6d		**6e**		**6f**		**6g**		**6h**	
Compound no. fragment no.	m/z	Relative intensity (%)	m/z	Relative intensity (%)	m/z	Relative intensity (%)	m/z	Relative intensity (%)	m/z	Relative intensity (%)
I	387/389 ($M^+ + 1$)	5.2/5.2	355/357 ($M^+ + 1$)	4.3/1.4	371/373 ($M^+ + 1$)	4.8/1.6	357/359 ($M^+ + 1$)	4.3/1.4	415/417 ($M^+ + 1$)	3.2/3.2
II	386/388 (M^+) isotopic	2.1/2.1	354/356 (M^+) isotopic	3.3/1.1	370/372 (M^+) isotopic	3.2/1.1	356/358 (M^+) isotopic	3.3/1.1	414/416 (M^+) isotopic	2.1/2.1
III	328	29.2	325	51.1	355/357	2.3/0.8	343	1.1	407	6.0
IV	305	11.5	289	64.3	329	15.1	328	1.4	392/394	6.0/5.9
V	293	50.3	270	65.4	307	14.2	256	6.3	307	2.1
VI	281/283	44.0/44.0	203	14.5	259 (b.p.)	100	254	12.7	273 (b.p.)	100.0
VII	194	93.0	199 (b.p.)	100	247	51.2	243	35.0	254	2.1
VIII	148	85.0	166	12.3	244	11.2	242	68.0	242	2.1
IX	140	83.1	150	15.4	238	12.3	241 (b.p.)	100.0	204	6.3
X	137	85.5	153	2.3	229	2.1	227	4.2	193	25.5
XI	107	47.0	138	3.5	207	3.4	218	4.2	165	14.8
XII	88 (b.p.)	100.0	—	—	199	65.5	207	12.7	154	29.7
XIII	76	14.1	—	—	185	44.3	191	2.1	136	23.3
XIV	—	—	—	—	147	21.3	165	2.1	115	8.5
XV	—	—	—	—	107	12.1	152	4.2	107	10.6
XVI	—	—	—	—	89	14.2	—	—	—	—
XVII	—	—	—	—	—	—	—	—	—	—
XVIII	—	—	—	—	—	—	—	—	—	—
XIX	—	—	—	—	—	—	—	—	—	—

TABLE V Antibacterial Activity Data of [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (**6**)

	Mean value of area of inhibition in m.m. (800 ppm) IZ (AI)		Mean value of area of inhibition in m.m. (400 ppm) IZ (AI)		Mean value of area of inhibition in m.m. (200 ppm) IZ (AI)	
Compound no.	*S. aureus*	*E. coli*	*S. aureus*	*E. coli*	*S. aureus*	*E. coli*
Streptomycin	10	09	8.9	8.0	7.0	6.0
6a	05 (0.50)	08 (0.89)	—	07 (0.87)	—	4.9 (0.82)
6b	06 (0.60)	06 (0.67)	4.8 (0.54)	—	3.0 (0.42)	—
6c	07 (0.70)	10 (1.11)	5.8 (0.65)	8.9 (1.11)	4.0 (0.57)	6.8 (1.13)
6d	09 (0.90)	09 (1.0)	7.9 (0.89)	8.0 (1.0)	5.9 (0.84)	6.0 (1.0)
6e	08 (0.80)	11 (1.22)	7.0 (0.79)	9.8 (1.22)	6.1 (0.87)	7.3 (1.21)
6f	05 (0.50)	12 (1.33)	—	11.0 (1.37)	—	8.3 (1.38)

IZ, inhibition area (zone) excluding diameter of disc; AI (Activity Index), inhibition area of sample/inhibition area of standard.

TABLE VI Antifungal Activity Data of [N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (**6**)

	Mean value of area of inhibition in m.m. (800 ppm) IZ (AI)		Mean value of area of inhibition in m.m. (400 ppm) IZ (AI)		Mean value of area of inhibition in m.m. (200 ppm) IZ (AI)	
Compound no.	*C. albicans*	*A. niger*	*C. albicans*	*A. niger*	*C. albicans*	*A. niger*
Ketoconazole	15	12	12	10	9.5	8.0
6a	12 (0.80)	10 (0.83)	8.9 (0.74)	08 (0.80)	6.5 (0.68)	06 (0.75)
6b	08 (0.53)	07 (0.58)	6.1 (0.51)	4.9 (0.49)	4.0 (0.42)	4.0 (0.50)
6c	09 (0.60)	08 (0.67)	7.0 (0.58)	7.0 (0.70)	4.5 (0.47)	5.9 (0.74)
6d	13 (0.87)	14 (1.16)	10 (0.83)	11.7 (1.17)	7.4 (0.78)	9.3 (1.16)
6e	10 (0.67)	09 (0.75)	09 (0.75)	7.3 (0.73)	6.1 (0.64)	5.4 (0.67)
6f	14 (0.93)	13 (1.08)	10.9 (0.91)	11.0 (1.10)	8.2 (0.86)	9.0 (1.12)

IZ, inhibition area (zone) excluding diameter of disc; AI (Activity Index), inhibition area of sample/inhibition area of standard.

^{1}H NMR Spectra

The ^{1}H NMR spectra of ethyl [2-(4-bromophenyl)indole-3-yl]dithiocarboxylate (**5a**), exhibited triplet at δ 1.56 (t, 3H, $J = 7.13$ Hz) and quartet at δ 3.42 (q, 2H, $J = 7.13$ Hz), which is attributed to $-CH_3$ and $-CH_2$ protons of $S-CH_2-CH_3$ group. ^{1}H NMR spectra of compound **5a** showed multiplet at δ 7.38 due to aromatic protons and singlet at δ 8.26 ppm due to >NH proton. Compound **5c** exhibited triplet at δ 1.25 (t, 3H, $J = 7.14$ Hz) and quartet at δ 4.18 (q, 2H, $J = 7.14$ Hz) due to CH_3 and CH_2 protons of NCH_2CH_3 group, respectively, and a singlet at δ 1.54 ppm and multiplet at δ 7.37 due to protons of $S-CH_3$ group and aromatic protons, respectively.

^{1}H NMR spectra of compounds **6a–h** revealed the anisochronous nature of a pair of alkyl groups on a thioamide nitrogen. One set of signals is obtained due to alkyl groups *cis* to the sulphur atom, and another set is due to the alkyl groups *trans* to the sulphur atom. For example, ^{1}H NMR spectra of compound **6c** exhibited four sets of signals due to morpholino protons, a triplet centered at δ 3.31 due to *trans* NCH_2 protons, and another triplet centered at δ 3.41 due to *cis* NCH_2 protons with respect to sulphur. Similarly, one triplet centered at δ 3.52 is ascribed to *trans* OCH_2 protons, while another triplet centered at δ 3.59 is ascribed to *cis* OCH_2 protons with respect to sulphur. ^{1}H NMR spectra of compound **6** exhibited complex multiplet due to aromatic protons in the range of δ 7.04–7.64. All other NMR spectral data are given in Table III.

^{13}C NMR Spectra

Results of ^{13}C NMR spectra of compound **6** are also in harmony with results of ^{1}H NMR spectra. ^{13}C NMR spectra of compound **6c** exhibited four signals due to four carbon of morpholino group. One signal is obtained at δ 40.86 due to *trans* NCH_2 carbon, and a second signal is obtained at δ 46.05 due to *cis* NCH_2 carbon with respect to sulphur. A third signal is obtained at δ 66.15 ascribed to *trans* OCH_2 carbon, and a fourth signal is obtained at δ 66.33 ascribed to *cis* OCH_2 carbon with respect to sulphur. This is also in accordance with the anisochronous behavior of alkyl groups on thioamide nitrogen.

Fast Atom Bombardment (FAB) Mass Spectra

All FAB mass spectra of synthesized compounds exhibited $M^+ + 1$ peak due to transfer of proton from matrix. Compound **5a** exhibited ($M^+ + 1$) peak at m/z 376/378 of relative intensity of 15.0% and moleculor ion peak (M^+) at m/z 375/377 of relative intensity of 10.0%. Compound **5a**

exhibited a base peak at m/z 271 (100.0%)/273 (100.0%) corresponding to the molecular formula $C_{14}H_{10}$ ^{79}BrN/$C_{14}H_{10}$ ^{81}BrN. Compound **5c** exhibited ($M^+ + 1$) peak at m/z at 390 (15.0%)/392 (5.0%) and molecular ion peak (M^+) at m/z 389 (12.0%)/391 (12.0%). FAB mass spectra of compounds **6** exhibited ($M^+ + 1$) peak and (M^+) peak. Details are given in Tables II and III.

EXPERIMENTAL

Melting points were determined in open glass capillaries and are uncorrected (Tempo melting point apparatus). The purity of the synthesized compounds was checked by thin layer chromatography (TLC) on silica gel in various nonaqueous solvent systems. IR spectra were recorded in KBr on a Perkin Elmer 557 spectrometer, PMR spectra were recorded in $CDCl_3$ on a Brucker spectrometer (200 MHz) using tetramethylsilane (TMS) as an internal reference, and FAB mass spectra were recorded on Jeol SX-102 (FAB) spectrometer.

1. Various 2-arylindoles were prepared by the literature method.[16]
2. 2-Arylindoles were N-alkylated by phase transfer catalysis procedure.[17]

Alkyl [N-(un)alkylated-2-arylindol-3-yl]dithiocarboxylates (5a–f): Ethyl[2-(4-bromophenylindol-3-yl] Dithiocarboxylate (5a)

A mixture of 2-(4-bromophenyl)indole (10 mmol, 2.72 g) and potassium-*t*-butoxide (10 mmol, 1.12 g) was taken in 100 ml round-bottomed flask connected with vacuum manipole and nitrogen atmosphere. Then dry tetrahydrofuran (THF) (20 ml) was added to it, and the resultant dark brown solution was stirred at 5–10°C. After 30 min, carbon disulphide (10 mmol, 0.76 g) was added and the reaction mixture was stirred for an additional hour to afford orange solution of the reaction mixture followed by addition of ethyl iodide (10 mmol, 1.56 g), and the stirring was continued for 2 h. The resulting reaction mixture thus obtained was poured into a beaker containing crushed ice (50 g). The solid separated was filtered and was then recrystallized from ethanol to give orange crystals of ethyl[2-(4-bromophenyl)indol-3-yl] dithiocarboxylate. Yield 1.6 g (43%) **5a**, m.p. 190°C. All other compounds (**5b–f**) are prepared using the same procedure and are given in Table I along with their characteristics and analytical data.

[N-(un)alkylated-2-arylindol-3-yl]thiocarboxamides (6a–h): [2-(4-Bromophenyl)indol-3-yl]-piperidinothiocarboxamide (6a)

A mixture of ethyl [2-(4-bromophenyl)indol-3-yl] dithiocarboxylate (5 mmol, 1.88 g) and piperidine (5 mmol, 0.425 g) in ethanol (20 ml) was refluxed for about 7–8 h. The resultant reaction mixture was poured into a beaker containing crushed ice (50 g). The product separated was extracted with chloroform. The chloroform layer was separated and the combined chloroform extract was dried over Na_2SO_4 (anhydrous) and filtered. The filtrate was evaporated to drynes to afford yellow-green residue, which was recrystallized from chloroform to give yellow-green crystals of [2-(4-bromophenyl) indol-3-yl] piperidinothiocarboxamide. Yield: 0.87 g (44%) **6a**, m.p. 110°C. All other compounds (**6b–h**) are prepared using same procedure and are given in Table II along with their characteristics and analytical data.

Antibacterial and Antifungal Activities

Representative compounds were screened for their antibacterial activity against gram-negative bacteria *E. coli* and gram-positive bacteria *S. aureus* at 200, 400, and 800 ppm concentration. Antifungal activity was done against *C. albicans* and *A. niger* at 200, 400, and 800 ppm concentration. Streptomycin and ketoconazole were used as standard drugs for antibacterial and antifungal evaluations, respectively. The compounds were screened for their biological activity using inhibition zone technique.[18] The results obtained for antibacterial and antifungal activities are given in Tables V and VI respectively.

REFERENCES

[1] T. Takeshima, N. Fukada, M. Muraoka, and T. Miyauchi, *Yuki Gousei Kagaku Kyokaishi (J. Synth. Org. Chem. Japan)*, **31,** 808 (1973).
[2] T. Takeshima, W. Muraoka, and N. Fukada, *Yuki Gousei Kagaku Kyokaishi (J. Synth. Org. Chem. Japan)*, **40,** 123 (1982).
[3] W. O. Foye, *J. Chem. Education*, **46,** 841 (1969).
[4] M. Yokoyama and T. Imamoto, *Synthesis*, 797 (1984).
[5] Y. Tominaga, *J. Heterocyclic Chem.*, **26,** 1167 (1989).
[6] Y. Tominaga, Y. Matsuda, and G. Kobayashi, *Yakugaku Zasshi*, **95,** 1073 (1975).
[7] G. D. Cuny, J. R. Hauske, D. L. Heefner, M. Z. Hoemann, G. Kumaravel, A. Melikian-Badalian, R. F. Rossi, and R. L. Xie, *PCT Int. Appl.* WO 0034, 265 (2000); *C.A.* **133,** 43453g (2000).
[8] M. Yamada, S. Hamamoto, K. Hayashi, K. Takaoka, H. Matsukura, M. Yotsuji, K. Yonezawa, K. Ojima, T. Takamatsu, K. Taya, H. Yamamoto, T. Kiyoto, and H. Kotsubo, *PCT Int. Appl.* WO 99 21, 849 (1999); *C.A.*, **130,** 311706u (1999).
[9] R. J. Ogilvie, *PCT Int. Appl.* WO 02 50, 063 (2002); *C.A.* **137,** 47115d (2002).

[10] S. Barbey, C. Boyer-Joubert, M. Finet, R. Hanf, G. G. Le Filliatre, N. Prual, S. Yannic-Arnoult, and J. L. Torregrosa, *Fr. Demande FR* 2, 814, 166 (2002); *C.A.*, **137,** 33209a (2002).
[11] A. W. Faull and J. Kettle, *PCT Int. Appl.* WO 00 46, 198 (2000); *C.A.*, **133,** 150462f (2000).
[12] A. Gutman, G. Nisnevich, I. Zaltzman, V. Ponomarev, and M. Sotrihin, *PCT Int. Appl.* WO 02 46, 153 (2002); *C.A.*, **137,** 33210u (2002).
[13] E. Defossa, U. Heinelt, O. Klingler, G. Zoller, F. Al-Obeidi, A. Walser, P. Wildgoose, and H. Matter, *PCT Int. Appl.* WO 99 33, 800, (1999); *C.A.*, **131,** 87814p (1999).
[14] M. L. Jones, D. Gunn, J. H. Jones, and M. C. Van Zandt, *PCT Int. Appl.* WO 99 50, 268 (1999); *C.A.*, **131,** 257442k (1999).
[15] R. Pamukku and G. A. Piazza, *U.S. Patent* 6, 410, 584 (2002); *C.A.*, **137,** 47109e (2002).
[16] K. C. Joshi, V. N. Pathak, and P. Chand, *J. Prakt. Chemie.*, **320(4),** 701 (1978).
[17] K. C. Joshi, V. N. Pathak, and R. Gupta, *Ind. J. Heterocycl. Chem.*, **2,** 15 (1992).
[18] M. C. Bryant, *Antibiotics and Their Laboratory Control* (Butterworth, London, 1968).