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PMR-Spectral Data of Some Substituted Chromones

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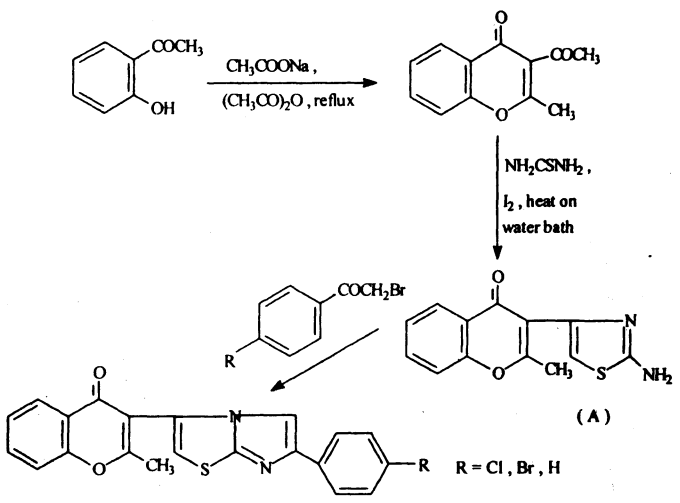
PMR-spectral data of some new substituted chromones as well as some reported substituted chromones (PMR-spectra hitherto unreported) constitutes the subject matter of the present paper. New compounds have been identified on the basis of elemental analysis, IR and PMR-data. Compounds **Ia, Ib** and **Ic** have been tested for diuretic activity, effect on blood pressure as well as central nervous system activity in gross observation. Compound **Ia** has shown diuretic activity equal to chlorothiazide standard.

Key Words: PMR-spectral data, Substituted chromones.

INTRODUCTION

In view of biological activities associated with substituted chromones[1–8], thiazoles[9–11] and imidazothiazoles[3, 12] and in continuation to synthesize biologically active chromones[1–7], new 3-(6-arylimidazo[2,1-b]thiazol-3-yl)-2-methylchromones (**Ia–c**) have been reported (**Scheme-1**) and screened for their biological activities. Synthesis and bio-assay of some 3-thiocyanatoacetyl-2-



SCHEME - I

methylchromones[1]; 3-(2-chlorothiazol-4-yl)-2-methylchromones[1]; 3-(2-N-substituted aminothiazol-4-yl)-2-methylchromones[1]; 6-(2-N-substituted amino- thiazol-4-yl)-2,3-dimethylchromones[7]; 3-[2-(3,5-disubstituted or 3,4,5-trisubstituted-1H-pyrazol-1-yl)-4-thiazolyl]-2-methylchromones[2] have been reported earlier but PMR-data being reported here are still unpublished.

EXPERIMENTAL

The melting points were taken in open capillaries in conc. sulphuric acid bath and are uncorrected. Purity of the compounds was checked by TLC on silica gel coated plates. IR-spectra were recorded in nujol mull on IR-20 spectrophotometer and PMR-spectra on Perkin-Elmer R-32 instrument using TMS as internal standard.

3-(6-Arylimidazo[2,1-b]thiazol-3-yl)-2-methylchromones (Ia–Ic)

General Procedure: To an alcoholic solution of 3-(2-aminothiazol-4-yl)-2-methylchromone (A) (10 mmol) was added alcoholic solution of appropriate phenacyl halide (10 mmol) and the reaction mixture was refluxed on a water-bath for 5–6 h. The solid that separated on cooling the reaction mixture was kept in liquid ammonia overnight. The resultant solid was filtered, washed with water and recrystallized with suitable solvent. Analytical Data is given below:

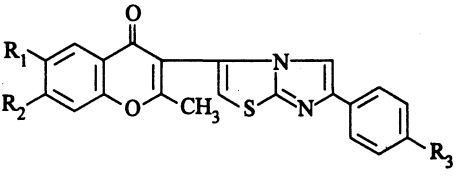
Compd. No.	R	m.p. (°C)	Yield (%)	m.f.	N %: Found (Calc.)
Ia	Cl	186	70	$C_{21}H_{13}O_2N_2SCl$	7.5 (7.1)
Ib	Br	198	80	$C_{21}H_{13}O_2N_2SBr$	6.9 (6.4)
Ic	H	148	80	$C_{21}H_{14}O_2N_2S$	8.3 (7.8)

Solvents for recrystallization: DMSO-alcohol for **Ia** and **Ib**; alcohol for **Ic.**
IR-spectra: 1630–1640 cm^{-1} (C=O str. chromone); **PMR-spectra:** (Table-1).

RESULTS AND DISCUSSION

Structures of new compounds **Ia–Ic** were elucidated by elemental analysis, IR and PMR analysis. IR-spectra of these compounds were used to identify the condensation of **A** with phenacyl halides as they were devoid of $—NH_2$ *str.* in the region 3300–3100 cm^{-1} as well as —C=O *str.* of $ArCOCH_2Br$ (around 1690 cm^{-1}). However, chromone ring was intact as —C=O *str.* of chromone ring was visible around 1630 cm^{-1}. PMR-spectra gave proton counts for all the protons (Table-1). PMR-spectrum of **Ia,** a representative compound (TFA) exhibited proton resonances in the forms of three signals. At the highest field C_2-CH_3 appeared as a sharp singlet at δ 2.80. Rest of all the signals showed up in the aromatic region below δ 7.55. An ill-resolved multiplet of nine protons appearing in the region 7.55–8.10 was assigned to C_6-H, C_7-H and C_8-H (chromone), C_2-H and C_5-H (imidazothiazole) and 4H (*p*-chlorophenyl). C_5-H of chromone appeared as a doublet of doublet centred at δ 8.42 (J = 9.0 and 2.5 Hz, *o*- and *m*-coupling) as last signal.

TABLE-1

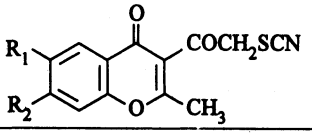


(I)

3-(6-ARYLIMIDAZO [2,1-b] THIAZOL-3-YL)-2-METHYLCHROMONES

Compd.	R_1	R_2	R_3	Solvent for PMR	Chemical shifts (δ-values)
Ia	H	H	Cl	TFA	2.80 [3H, s, C_2-CH_3(chromone)], 7.55–8.10 [9H, m, C_6-H, C_7-H, C_8-H (chromone), C_2-H and C_5-H (imidazothiazole), 4H (ClC_6H_4)], 8.42 [1H, dd, C_5-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling]
Ib	H	H	Br	TFA	2.80 [3H, s, C_2-CH_3 (chromone)], 7.50–8.20 [9H, m, C_6-H, C_7-H and C_8-H (chromone), C_2-H and C_5-H (imidazothiazole), 4H (BrC_6H_4)], 8.43 [1H, dd, C_5-H (chromone), J = 10.0 and 2.5 Hz, *o*- and *m*-coupling].
Ic	H	H	H	$CDCl_3$	2.49 [3H, s, C_2-CH_3 (chromone)], 6.80 [1H, s, C_2-H (imidazothiazole)], 7.30–7.90 [9H, m, C_5-H (imidazothiazole), 5H (C_6H_5), C_6-H, C_7-H and C_8-H (chromone)], 8.30 [1H, dd, C_5-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling, respectively].
Id	CH_3	H	Cl	TFA	2.62 [3H, s, C_6-CH_3 (chromone)], 2.75 [3H, s, C_2-CH_3 (chromone)], 7.60–7.98 [8H, m, C_2-H and C_5-H (imidazothiazole), 4H (ClC_6H_4), C_7-H and C_8-H (chromone)], 8.19 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling].
Ie	Cl	H	Cl	TFA	2.79 [3H, s, C_2-CH_3 (chromone)], 7.55–7.80 [6H, m, C_2-H and C_5-H (imidazothiazole), 4H (ClC_6H_4)], 7.86 [1H, d, C_8-H (chromone), J = 10.0 Hz, *o*-coupling], 8.00 [1H, dd, C_7-H (chromone), J = 10.0 and 3.0 Hz, *o*- and *m*-coupling], 8.35 [1H, d, C_5-H (chromone), J = 3.0 Hz, *m*-coupling]
If	Cl	H	Br	TFA	2.79 [3H, s, C_2-CH_3 (chromone)], 7.40–8.12 [8H, m, C_2-H and C_5-H (imidazothiazole), 4H (BrC_6H_4), C_7-H and C_8-H (chromone)], 8.35 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling]
Ig	Cl	CH_3	H	DMSO-d_6	2.44 [3H, s, C_2-CH_3 (chromone)], 2.50 [3H, s, C_7-CH_3 (chromone)], 7.00–7.90 [8H, m, C_2-H and C_5-H (imidazothiazole), 5H (C_6H_5), C_8-H (chromone)], 8.00 [1H, s, C_5-H (chromone)]
Ih	Cl	CH_3	Br	TFA	2.60 [3H, s, C_2-CH_3 (chromone)], 2.90 [3H, s, C_7-CH_3 (chromone)], 7.40–7.90 [7H, m, C_2-H and C_5-H (imidazothiazole), 4H (BrC_6H_4), C_8-H (chromone)], 8.32 [1H, s, C_5-H (chromone)].

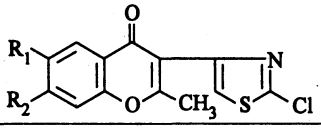
TABLE-2
3-THIOCYANATOACETYL-2-METHYLCHROMONES



(II)

Compd.	R_1	R_2	Solvent for PMR	Chemical shifts (δ-values)
IIa	Cl	CH_3	$CDCl_3$	2.57 (3H, s, C_7-CH_3), 2.73 (3H, s, C_2-CH_3), 4.60 (2H, s, C_3-$COCH_2SCN$), 7.43 (1H, s, C_8-H), 8.15 (1H, s, C_5-H).
IIb	CH_3	H	$CDCl_3$	2.52 (3H, s, C_6-CH_3), 2.75 (3H, s, C_2-CH_3), 4.64 (2H, s, C_3-$COCH_2SCN$), 7.43 (1H, d, C_8-H, J = 9.0 Hz, *o*-coupling), 7.61 (1H, dd, C_7-H, J = 9.0 and 2.5 Hz, *o*- and *m*-coupling, respectively), 8.05 (1H, d, C_5-H, J = 2.5 Hz, *m*-coupling)].

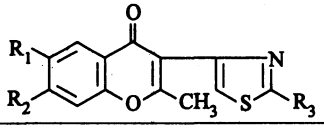
TABLE-3
3-(2-CHLOROTHIAZOL-4-YL)-2-METHYLCHROMONES



(III)

Compd.	R_1	R_2	Solvent for PMR	Chemical shifts (δ-values)
IIIa	Cl	CH_3	$CDCl_3$	2.52 [3H, s, C_7-CH_3 (chromone)], 2.63 [3H, s, C_2-CH_3 (chromone)], 7.35 [1H, s, C_8-H (chromone)], 7.81 [1H, s, C_5-H (thiazole)], 8.19 [1H, s, C_5-H (chromone)]
IIIb	CH_3	H	$CDCl_3$	2.51 [3H, s, C_6-CH_3 (chromone)], 2.66 [3H, s, C_2-CH_3 (chromone)], 7.37 [1H, d, C_8-H (chromone), J = 9.0 Hz, *o*-coupling], 7.55 [1H, dd, C_7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling, respectively], 7.81 [1H, s, C_5-H (thiazole)], 8.08 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling]

TABLE-4
3-(2-N-SUBSTITUTED AMINOTHIAZOL-4-YL)-2-METHYLCHROMONES



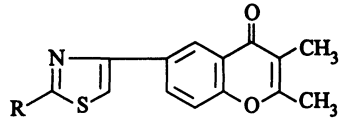
(IV)

Compd.	R_1	R_2	R_3	Solvent for PMR	Chemical shifts (δ-values)
IVa	Cl	H		$CDCl_3$	1.50–1.90 [6H, m, $(CH_2)_3$ (piperidine)], 2.61 [3H, s, C_2-CH_3 (chromone)], 3.33–3.70 [4H, m, $-N(CH_2)_2$ (piperidine)], 7.01 [1H, s, C_5-H (thiazole)], 7.35 [1H, d, C_8-H (chromone), J = 9.0 Hz, *o*-coupling], 7.56 [1H, dd, C_7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling, respectively], 8.17 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling].

Compd.	R_1	R_2	R_3	Solvent for PMR	Chemical shifts (δ-values)
IVb	Cl	CH_3		$CDCl_3$	2.50 [3H, s, C_7-CH_3 (chromone)], 2.59 [3H, s, C_2-CH_3 (chromone)], 3.33–3.65 [4H, m, $-N(CH_2)_2$ (morpholine)], 3.65–3.99 [4H, m, $-O(CH_2)_2$ (morpholine)], 7.07 [1H, s, C_5-H (thiazole)], 7.29 [1H, s, C_8-H (chromone)], 8.18 [1H, s, C_5-H (chromone)].
IVc	Cl	CH_3–NHC_6H_5		TFA	2.61 [3H, s, C_7-CH_3 (chromone)], 2.77 [3H, s, C_2-CH_3 (chromone)], 6.93 [1H, s, C_5-H (thiazole)], 7.05–7.90 [6H, m, C_8-H (chromone) and five protons of benzene ring], 8.17 [1H, s, C_5-H (chromone)].
IVd	CH_3	H		$CDCl_3$	2.45 [3H, s, C_6-CH_3 (chromone)], 2.58 [3H, s, C_2-CH_3 (chromone)], 3.32–3.64 [4H, m, $-N(CH_2)_2$ (morpholine)], 3.70–3.90 [4H, m, $-O(CH_2)_2$ (morpholine)], 7.07 [1H, s, C_5-H (thiazole)], 7.27 [1H, d, C_8-H (chromone), J = 9.0 Hz, *o*-coupling], 7.43 [1H, dd, C_7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling], 8.01 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling}].

TABLE-5

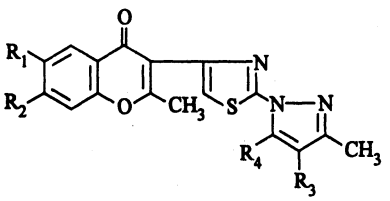
6-(2-N-SUBSTITUTED AMINOTHIAZOL-4-YL)-2,3-DIMETHYLCHROMONES



(V)

Compd.	R	Solvent for PMR	Chemical shifts (δ-values)
Va	NHC_2H_5	$CDCl_3$	1.31 [3H, t, C_2-$NHCH_2CH_3$ (thiazole), J = 8.0 Hz, vicinal coupling}], 2.10 [3H, s, C_3-CH_3 (chromone)], 2.43 [3H, s, C_2-CH_3 (chromone)], 3.37 [2H, broad hump, collapses to a 2H quartet on D_2O shake C_2-$NHCH_2Me$ (thiazole), J = 8.0 Hz, vicinal coupling], 4.50 [1H, b, disappears on D_2O shake, C_2-NHC_2H_5 (thiazole)], 6.82 [1H, s, C_5-H (thiazole)], 7.38 [1H, d, C_8-H (chromone), J = 10.0 Hz, *o*-coupling], 8.15 [1H, dd, C_7-H (chromone), J = 10.0 and 2.5 Hz, *o*- and *m*-coupling, respectively], 8.57 [1H, d, C_5- H (chromone), J = 2.5 Hz, *m*-coupling].
Vb	NHC_6H_5	$CDCl_3$/ DMSO-d_6	2.03 [3H, s, C_3-CH_3 (chromone)], 2.42 [3H, s, C_2-CH_3 (chromone)] , 6.91 [1H, s, C_5-H (thiazole)], 7.10–7.80 [6H, m, C_8-H (chromone), 5H (phenyl)], 8.22 [1H, dd, C_7-H (chromone), J = 10.0 and 2.5 Hz, *o*- and *m*-coupling, respectively], 8.55 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling], 9.81 [1H, b, disappears on D_2O shake, C_2-NH (thiazole)].

TABLE-6
3-[2-(3,5-DISUBSTITUTED- OR 3,4,5-TRISUBSTITUTED-1H-PYRAZOL-1-YL)-4-THIAZOLYL]-2-METHYLCHROMONES



(VI)

Compd.	R_1	R_2	R_3	R_4	Solvent for PRM	Chemical shift (δ-values)
VIa	Cl	H	H	2-furyl	$CDCl_3$	2.35 [3H, s, C_3-CH_3 (pyrazole)], 2.47 [3H, s, C_2-CH_3 (chromone)], 6.41 [1H, dd, C_4-H (furan), J = 3.5 Hz and 1.8 Hz, $J_{3,4}$ and $J_{4,5}$, respectively], 6.49 [1H, s, C_4-H (pyrazole)], 7.05 [1H, d, C_3-H (furan), J = 3.5 Hz, $J_{3,4}$], 7.20–7.70 [4H, m, C_5-H (furan), C_5-H (thiazole), C_7-H and C_8-H (chromone)], 8.18 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling].
VIb	Cl	H	H	CH_3	$CDCl_3$	2.28 [3H, s, C_3-CH_3 (pyrazole)], 2.67 [6H, s, C_2-CH_3 (chromone) and C_5-CH_3 (pyrazole)], 6.00 [1H, s, C_4-H (pyrazole)], 7.38 [1H, d, C_8-H (chromone), J = 9.0 Hz, *o*-coupling], 7.59 [1H, dd, C_7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling], 7.67 [1H, s, C_5-H (thiazole)], 8.22 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling].
VIc	Cl	CH_3	H	2-thienyl	$CDCl_3$	2.33 [3H, s, C_3-CH_3 (pyrazole)], 2.41 [3H, s, C_7-CH_3 (chromone)], 2.51 [3H, s, C_2-CH_3 (chromone)], 6.40 [1H, s, C_4-H (pyrazole)], 7.00–7.50 [4H, m, C_3-H, C_4-H and C_5-H (thiophene) and C_8-H (chromone)], 7.87 [1H, s, C_5-H (thiazole)], 8.18 [1H, s, C_5-H (chromone)].
VId	Cl	CH_3	H	2-furyl	$CDCl_3$	2.36 [3H, s, C_3-CH_3 (pyrazole)], 2.43 [3H, s, C_7-CH_3 (chromone)], 2.48 [3H, s, C_2-CH_3 (chromone)], 6.46 [1H, dd, C_4-H (furan), J = 3.5 and 1.8 Hz, $J_{3,4}$ and $J_{4,5}$, respectively], 6.50 [1H, s, C_4-H (pyrazole)], 7.09 [1H, d, C_3-H (furan), J = 3.5 Hz, $J_{3,4}$], 7.30 [1H, s, C_8-H (chromone)], 7.43 [1H, d, C_5-H (furan), J = 1.8 Hz, $J_{4,5}$], 7.66 [1H, s, C_5-H (thiazole)], 8.19 [1H, s, C_5-H(chromone)]. First three assignments are tentative.
VIe	Cl	$CH_3C_2H_5$		CH_3	$CDCl_3$	1.15 [3H, t, C4-CH_2CH_3 (pyrazole), J = 8.0 Hz, vicinal coupling], 2.35 [3H, s, C_3-CH_3 (pyrazole)], 2.40–2.80 [11H, m, C_7-CH_3 (chromone), C_2-CH_3 (chromone), C_5-CH_3 (pyrazole) and C_4-CH_2Me (pyrazole)], 7.41 [1H, s, C_8-H (chromone)], 7.61 [1H, s, C_5-H (thiazole)], 8.20 [1H, s, C_5-H (chromone)].

Compd.	R_1	R_2	R_3	R_4	Solvent for PRM	Chemical shift (δ-values)
VIf	Cl	CH_3	H	CH_3	$CDCl_3$	2.27 [3H, s, C_3-CH_3 (pyrazole)], 2.47 [3H, s, C_7-CH_3 (chromone)], 2.75 [6H, s, C_2-CH_3 (chromone) and C_5-CH_3 (pyrazole)], 5.98 [1H, s, C_4-H (pyrazole)], 7.30 [1H, s, C_8-H (chromone)], 7.61 [1H, s, C_5-H (thiazole)], 8.17 [1H, s, C_5-H (chromone)]. First three assignments are tentative.
VIg	CH_3	H	H	2-thienyl	$CDCl_3$	2.36 [3H, s, C_3-CH_3 (pyrazole)], 2.42 [3H, s, C_6-CH_3 (chromone)], 2.50 [3H, s, C_2-CH_3 (chromone)], 6.41 [1H, s, C_4-H (pyrazole)], 7.01–7.67 [5H, m, C_7-H and C_8-H (chromone), C_3-H, C_4-H and C_5-H (thiophene)], 7.91 [1H, s, C_5-H (thiazole)], 8.08 [1H, d, C_5-H (chromone), J = 2.5 Hz, m-coupling].
VIh	CH_3	H	H	2-furyl	$CDCl_3$	2.35 [3H, s, C_3-CH_3 (pyrazole)], 2.46 [6H, s, C_6-CH_3 and C_2-CH_3(chromone)], 6.43 [1H, dd, C_4-H (furan), J = 3.5 and 1.8 Hz, $J_{3,4}$ and $J_{4,5}$, respectively], 6.50 [1H, s, C_4-H (pyrazole)], 7.11 [1H, d, C_3-H (furan), J = 3.5 Hz, $J_{3,4}$], 7.30 [1H, d, C_8-H (chromone), J = 9.0 Hz, *o*-coupling], 7.41 [1H, d, C_5-H (furan), J = 1.8 Hz, $J_{4,5}$], 7.44 [1H, dd, C_7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling], 7.69 [1H, s, C_5-H (thiazole)], 8.01 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling].
VIi	CH_3	H	H	CH_3	$CDCl_3$	2.27 [3H, s, C_3-CH_3 (pyrazole)], 2.40 [3H, s, C_6-CH_3 (chromone)], 2.60 [6H, s, C_2-CH_3 (chromone) and C_5-CH_3 (pyrazole)], 5.97 [1H, s, C_4-H (pyrazole)], 7.27 [1H, d, C_8-H (chromone), J = 9.0 Hz, *o*-coupling], 7.42 [1H, dd, C_7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling], 7.61 [1H, s, C_5-H (thiazole)], 8.00 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling]. First three assignments are tentative.
VIj	CH_3	H	C_2H5	CH_3	$CDCl_3$	1.12 [3H, t, C_4-CH_2CH_3 (pyrazole), J = 8.0 Hz, vicinal coupling], 2.28 [3H, s, C_3-CH_3 (pyrazole)]. 2.35–2.70 [11H, m, C_4-CH_2Me (pyrazole), C_2-CH_3 (chromone), C_5-CH_3 (pyrazole), C_6-CH_3 (chromone)], 7.33 [1H, d, C_8-H (chromone), J = 9.0 Hz, *o*-coupling], 7.47 [1H, dd, C_7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling], 7.63 [1H, s, C_5-H (thiazole)], 8.05 [1H, d, C_5-H (chromone), J = 2.5 Hz, *m*-coupling].

Compounds **Ia, Ib** and **Ic** were tested for diuretic as well as central nervous system activity (in gross observation). Compound **Ia** showed excellent diuretic activity equal to 100 as compared to chlorothiazide standard. **Ib** showed diuretic activity equal to 93. Both of these compounds showed increase in spontaneous motor activity (SMA) and general body reaction. **Ia** and **Ib** showed increase in blood pressure by 16 and 20 mm/Hg respectively for 4 min in each case.

All the PMR-spectral data described in Tables-1 to 6 are in conformity to the structure assigned to them.

ACKNOWLEDGEMENT

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