minant fields for late-magmatic, metasomatic, and anatectic granitic rocks are defined in Fig. 3, a plot of $(Nb)_{biotite}$ *versus* $(Ti)_{biotite}$. Figure 4, wherein $(Ti/Nb)_{biotite}$ is plotted against $(Ti)_{biotite}$ helps to distinguish magmatic granites from metasomatic granites.

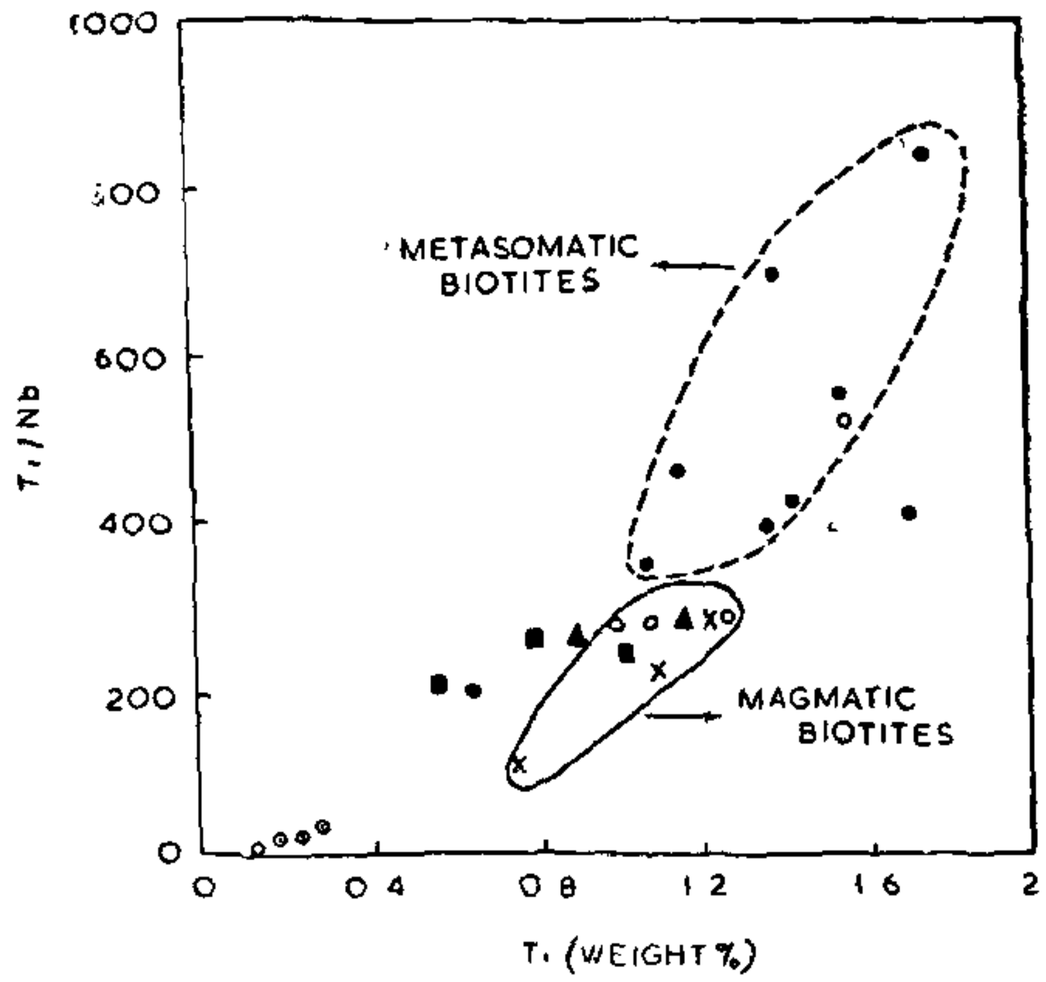

FIG. 4. Discriminant diagram for magmatic and metasomatic granites based on the Ti/Nb ratios and Ti contents of their constituent biotites. Symbols as defined in Fig. 1.

CONCLUSIONS

(1) Biotites from granitic rocks of late-magmatic origin have higher Nb contents and lower Ti/Nb ratios than biotites from the early-magmatic phases to which they are genetically related.

(2) Biotites from granitic rocks of metasomatic origin have lower Nb contents and higher Ti/Nb ratios than biotites from granitic rocks of magmatic origin.

(3) Muscovites have higher Nb contents and lower Ti/Nb ratios than biotites.

(4) In the biotites considered here, Nb^{5+} is found to substitute for Zr^{4+}, thus making the Nb-Zr geochemical association as significant as the more commonly accepted Nb-Ti coherence.

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SYNTHESES OF SOME NEW THERAPEUTIC N-*p*-BROMOPHENYL-N′-2-(SUBSTITUTED) BENZOTHIAZOLYL GUANIDINES

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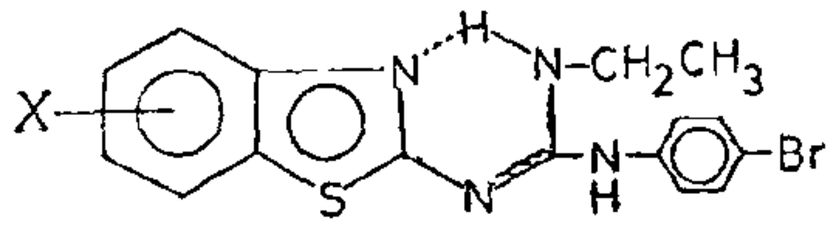
AMONG a series of mono and *bis* diguanides showing antibacterial activities prepared by Rose and Swain[1-2], one compound, chlorhexidine B.P.C. (Hibitane), has found practical use as an antibacterial agent in medicinal and veterinary practice. Encouraging antibacterial properties *in vitro* against *Mycobacterium tuberculosis* have been reported in several biguanide derivatives[3-4]. The heterocyclic diguanidine derivatives[5] have been found to be active to mice when administered. These activities have also been found in many thiazole compounds[6].

Antibacterial activity against *Esch. coli* and *Staph. aureus* of some N-aryl-N′-2-(4, 5, 6-methyl)

TABLE I



Sl. No.	Subst. X	Molecular Formulae	Yield %	M.P. °C	% Nitrogen Found	% Nitrogen Calcd.	% Sulphur Found	% Sulphur Calcd.	Characteristic I.R. peaks ν_{max}^{nujol} cm^{-1}			R_f* values
1.	H	$C_{16}H_{15}N_4SBr$	75	215	14·86	14·93	8·43	8·53	3160m, 1460s	1570s	1524s	·888
2.	4–CH_3	$C_{17}H_{17}N_4SBr$	73	132	14·29	14·39	..	..	3280m, 1550s	3225m, 1475s	1612s	·913
3.	5–CH_3	$C_{17}H_{17}N_4SBr$	67	136	14·32	14·39	8·26	8·22	3250m, 1470s	3100w	1616s	·675
4.	6–CH_3	$C_{17}H_{17}N_4SBr$	69	208	14·28	14·39	..	..	3170,. 1465s	1570s	1528s	·784
5.	4–Cl	$C_{16}H_{14}N_4SClBr$	72	134	13·54	13·67	7·84	7·78		..		·474
6.	5–Cl	$C_{16}H_{14}N_4SClBr$	48	174	..	..	7·90	7·78	3170w,	1605s	1478s	·893
7.	6–Cl	$C_{16}H_{11}SClBr$	78	131	13·62	13·67	7·89	7·78	3430s, 1565s	3200m, 1525s	1605s	·892
8.	4–OCH_3	$C_{17}H_{17}N_4OSBr$	56	154	13·72	13·83	..	..	3420m, 1552s	3180w, 1480s	1608s	·727
9.	6–OCH_3	$C_{17}H_{17}N_4OSBr$	62	139	13·62	13·83	7·82	7·89		..		·644
10.	4–OC_2H_5	$C_{18}H_{19}N_4OSBr$	68	145	13·34	13·36	7·82	7·64	3440m, 1468s	1618s	1560m	·801

w = weak, m = medium, s = sharp.

*R_f values were measured by developing the T.L.C. plates (adsorbent, silica gel) in benzene and ether (3 : 1) mixture.

benzothiazolyl guanidine hydrochlorides[7-8] were found more active against gram-positive bacteria than against gram-negative ones. Recently, Bhargava *et al.*[9-11] have reported some benzothiazolyl guanidines as various biological and pharmacological screening results.

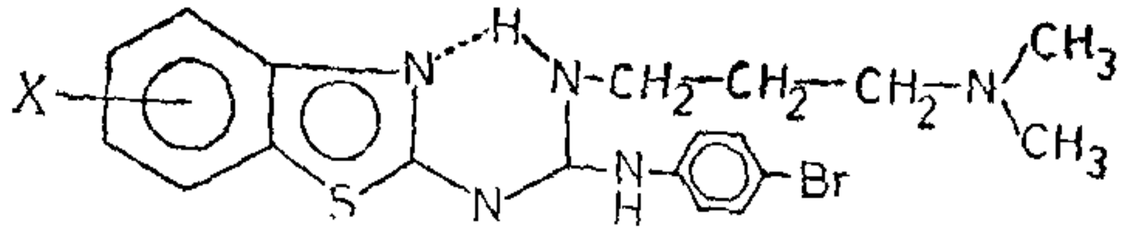
The above findings have led the authors to synthesize some new N-*p*-bromophenyl-N'-2-(substituted) benzothiazolyl-N"-(ethyl and γ-dimethylaminopropyl) guanidines as chemotherapeutical interest. The present communication is concerned with the chemistry of these substances.

N-p-Bromophenyl - N'-2 (4 - methylbenzothiazolyl) thiocarbamide.—This was obtained by interaction of equimolecular quantity of 4-methylbenzothiazolyl and *p*-bromophenylisothiocyanate in an inert solvent dry benzene on a water-bath for about 16–20 hours.

N-p-Bromophenyl - N'-2 (4 - methylbenzothiazolyl) N"-ethyl guanidine.—N - *p*- bromophenyl-N'-2-(4-methylbenzothiazolyl) thiocarbamide (3·78 g), yellow lead oxide (5·00 g), ethylamine (1·50 ml) and absolute alcohol (50 ml) were refluxed in a glass autoclave on a water-bath for about 4-6 hours. After cooling, the autoclave was opened and the black residue was filtered by further extraction of 20 ml of hot alcohol. The combined filtrate upon concentration gave the desired guanidine in shining needles. It was recrystallised from alcohol, yield 65%, m.p. 132° (Found : N, 14·29 ; S, 8·11. $C_{17}H_{17}N_4SBr$ requires N, 14·39 ; S, 8·22%).

The PMR spectra of this compound in $CDCl_3$ shows a singlet at δ 2·6 for the ring methyl protons, a multiplet between δ 7·84 and δ 7·13 for the aromatic protons, a triplet at δ 1·23 for the

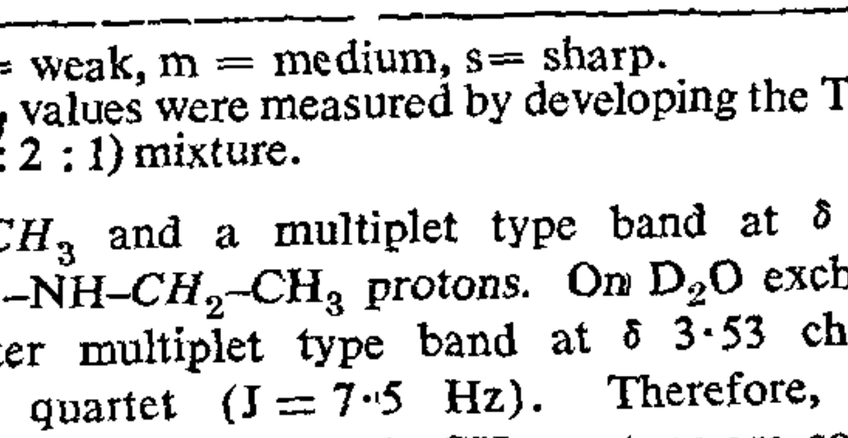
TABLE II



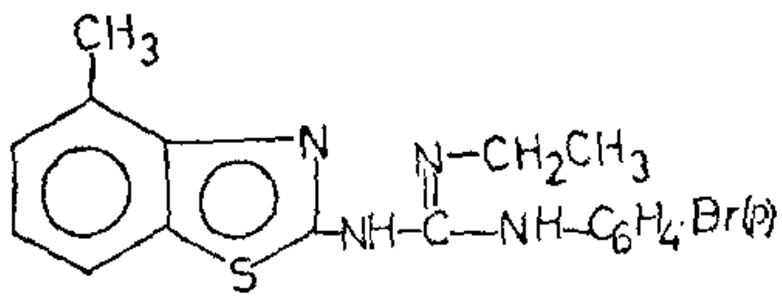
S. No.	Subst. X	Molecular Formulae	Yield %	M.P. °C	% Nitrogen Found	% Nitrogen Calcd.	% Sulphur Found	% Sulphur Calcd.	Characteristic I.R. peaks ν_{max}^{nujol} cm^{-1}			R_f* Values
1.	H	$C_{19}H_{22}N_5SBr$	92	160	16·31	16·20	7·49	7·40	3180m, 1590s	3070w, 1485s	1610s	·504
2.	4–CH_3	$C_{20}H_{24}N_5SBr$	78	152	16·65	15·69	..	..		..		·492
3.	5–CH_3	$C_{20}H_{24}N_5SBr$	80	101	15·62	15·69	7·23	7·17	3192m, 1598s	3080w, 1472s	1615s	·490
4.	6–CH_3	$C_{20}H_{24}N_5SBr$	82	151	15·52	15·69	7·28	7·17	3180m, 1592s	3070w, 1464s	1610s	·442
5.	4–Cl	$C_{19}H_{21}N_5SClBr$	72	103	..	..	6·66	6·86		..		·466
6.	5–Cl	$C_{19}H_{21}N_5SClBr$	40	130	14·82	15·00	..	..		..		·483
7.	6–Cl	$C_{19}H_{21}N_5SClBr$	58	147	14·92	15·00	6·97	6·86	3175m, 1572s	3085m, 1445s	1598s	·458
8.	6–Br	$C_{19}H_{21}N_5SBr_2$	84	143	13·63	13·69	6·15	6·26	3180m, 1564s	3090,m 1445s	1595s	·563
9.	4–OCH_3	$C_{20}H_{24}N_5OSBr$	48	142	15·35	15·15	..	..		..		·405
10.	6–OCH_3	$C_{20}H_{24}N_5OSBr$	66	141	15·19	15·15	6·83	6·92	3180m, 1468s	3070w	1605s	·414
11.	4–OC_2H_5	$C_{21}H_{26}N_5OSBr$	63	149	14·86	14·70	6·65	6·72	3172m, 1568s	3080, 1470s	1594s	·508

w = weak, m = medium, s= sharp.
* R_f values were measured by developing the T.L.C. plates (adsorbent, silica gel) in *n*-butanol, water and acetic acid (4 : 2 : 1) mixture.

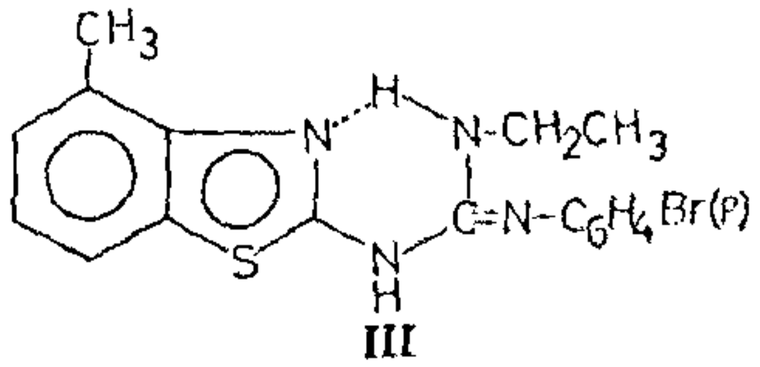
$-CH_2-CH_3$ and a multiplet type band at δ 3·53 for the $-NH-CH_2-CH_3$ protons. On D_2O exchange, the latter multiplet type band at δ 3·53 changes into a quartet ($J = 7·5$ Hz). Therefore, it is evident that the $-NH-CH_2-CH_3$ protons are coupled with an exchangeable proton ($J = 5·0$ Hz) as well as with the adjacent methyl protons. These facts suggest the structure I, but not II, for the compound. The structure III is discarded since the structure I is more stable by the more effective conjugation of the planar six membered ring formed by the hydrogen bonding.



I



II



III

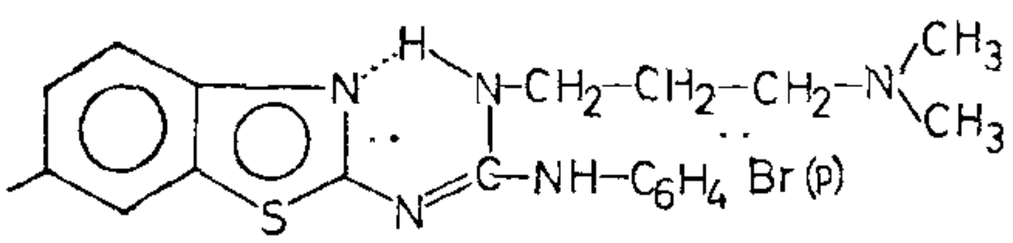
The strong I.R., peak at ν_{max}^{nujol} 1612 for the $-C=N-$ bond also support the above structure.

Similarly, other N-*p*-bromophenyl-N′-2-(substituted) benzothiazolyl N″-ethylguanidines were prepared

by condensing different N-*p*-bromophenyl-N'-2-(substituted) benzothiazolyl thiocarbamides with ethylamine. Their structure and the purity of the compounds were confirmed by the analytical and spectral data as given in Table I.

N-p-*Bromophenyl-N'-2-(6-chlorobenzothiazolyl)-N"-(γ-dimethylaminopropyl) guanidine.*—N-*p*-Bromophenyl-N'-2-(6-chlorobenzothiazolyl) thiocarbamide (3·99 g), yellow lead oxide (5·00 g), γ-dimethylaminopropylamine (1·00 ml) and absolute alcohol (50 ml) were refluxed in a sealed tube and the resulting guanidine was obtained by the same procedure as described before. Recrystallised from alcohol, yield 72%; m.p. 147° (Found: N, 14·92; S. 6·97. $C_{19}H_{21}N_5SClBr$ requires N, 15·00; S, 6·86%).

The PMR spectra of this compound also shows along with other normal signals, a multiplet type band at δ 3·56 for the –NH–CH_2–CH_2– protons which, on D_2O exhange, changes into a triplet (J = 5·5 Hz) These evidences also suggest the structure IV for this compound. The strong I.R. peak at ν_{max}^{nujol} 1598 for the –C=N– bond also support the above structure.



IV

Similarly, other substituted benzothiazolyl guanidines were prepared by condensing different substituted benzothiazolyl thiocarbamides with γ-dimethylaminopropylamine. Their structure and the purity of the compounds were confirmed by the analytical and spectral data as given in Table II.

Screening results.—The screening results of these compounds *in vitro* were carried out at Bristol Laboratories, Syracuse, New York. The compounds, which have shown activity at the maximum dose tested, are indicated in Table III.

ACKNOWLEDGEMENT

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TABLE III

S. No.	Microbiological activity	MED MIC
4.	M.607	2·5 mcg/ml
	T. mentag.	6·25–12·5 mcg/ml
	M. canis	6·25 mcg/ml
	C. neoform.	2·5–5 mcg/ml
7.	M.607	1·3–2·5 mcg/ml
	T. mentag.	3·13–6·25 mcg/ml
	M. canis	3·13 mcg/ml
	C. neoform.	1·3–2·5 mcg/ml
8.	M.607	2·5 mcg/ml
	T. mentag.	3·13–6·25 mcg/ml
	M. canis	3·13–6·25 mcg/ml
	C. neofrem.	2·5 mcg/ml
11.	M.607	1·3–2·5 mcg/ml
	T. mentag	12·5 mcg/ml
	M. canis	6·25–12·5 mcg/ml

* S. nos. correspcnd to the serial number of the compounds in Table II.
MED = Minimum Effective Dose.
MIC = Minimum Inhibitory Concentration.

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