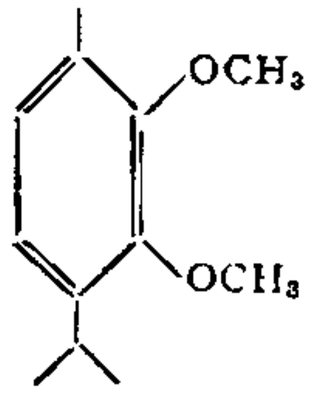
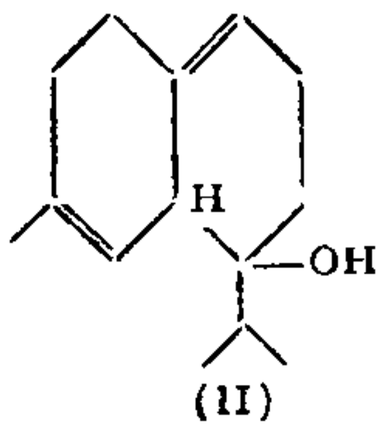
p-cymene has not yet been reported. However, it occurs in the essential oil of *Blumea membrancea* as presently reported by Joshi[11].



(I)

Compound 'E', b p. 109°/3·5 mm ; n_D^{29}, 1·586 ; $(\alpha)_D^{29}$, — 12·07° analysed for $C_{15}H_{20}O$ ($\overset{+}{M}$, m/e ; 222). ν_{max} 3430 (hydroxyl group), 1365, 1378, 1165 (isopropyl group), 890, 865 and 800 (trisubstituted double bond) and 2900 cm^{-1} (C–H). NMR (CCl_4, τ) : 9·18, 9·12, 9·08 and 9·02 (2*d*, 6 H, 2 CH_3 of isopropyl group) ; 8·38 (S, 6 H, two methyl groups on two double bonds) ; 8·09 (broad S, three methylene groups conjugated to the double bonds) ; 4·79 (S, a proton on the trisubstituted double bond) and 7·72 (broad S, disappeared on D_2O exchange, hydroxyl group). The compound, therefore, seems to be a sesquiterpenic alcohol.



(II)

On selenium dehydrogenation in the presence of nitrogen, this compound gave cadalene in considerable yield which has been identified on the basis of melting point of its picrate. The formation of cadalene showed the presence of bisabolene skeleton in this compound. Therefore, the following tentative structure (II) has been proposed for it and named as Laggerol.

Ether fraction (3·12 g) of neutral oil was chromatographed over silica-gel impregnated with silver nitrate (15%) which gave two compounds 'F' and 'G' in TLC pure form.

Compound 'F', b p. 163–165°/3 mm ; m.p. 70–71° ; n_D^{29}, 1·4942 ; $(\alpha)_D^{29}$, — 20·06° analysed for $C_{15}H_{26}O$ and was identified as α-cadinol[12] by IR, NMR and chemical evidence.

Compound 'G', b. p. 148°/8 mm ; n_D^{29}, 1·471 ; $(\alpha)_D^{29}$, 29·40° analysed for $C_{10}H_{18}O$ and was identified as m-menth-6-en-8-ol[13] by IR, NMR and chemical evidence.

ACKNOWLEDGEMENT

Our thanks are due to the Director, Royal Botanic Gardens, England, for the identification of the plant material. Two of us (S. K. Z. and B. K. B.) thank the Council of Scientific and Industrial Research, New Delhi, for the award of Junior Research Fellowships.

1. Cooke, T., *Flora of Bombay*, Vol. II, 1904, p, 80, reprinted edition, 1958.
2. Kraft, *Berichte der Chem. Gessel,*, 1882, 15, 1713.
3. Power, Tutin, Archiv, *der Pharmezie,* 1907, 245, 304.
4. Kraft, Weilandt, *Berichte der Chem. Gessel.*, 1896, 23, 1323 ; Lenene, West, Vander Scherr, *J. Biol. Chem.*, 1926, 20, 530.
5. Muhlamann, *Pharm. Acta Helv.*, 1938, 13, 282.
6. Herout, V. and Santary, F., *Collect. Czech. Chem. Comm.*, 1954, 19, 1792.
7. Peyron, L., Benezet, L. and Garnero, J., *Bull. Soc. Chem. Fr.*, 1967, 8, 3035.
8. Randle, and Whiffen, *Molecular Spectroscopy*, Institute of Petroleum, 1955, p. 111.
9. Sherk, *Chem. Zentr.*, 1921, 3, 218.
10. Sabatier, Maithe, *Compt. rend.*, 1908, 146, 458.
11. Joshi, S. K., *Ph D. Thesis,* Vik. Univ., 1975.
12. Plattner, P. A. and Markus, R., *Helv. Chem. Acta,* 1942, 25, 1674.
13. Howorth, W. N., Perkin, W. H. Jr. and Wallach, O., *J. Chem. Soc.*, 1913, 103, 1234.

STUDIES ON QUINAZOLONES DERIVATIVES

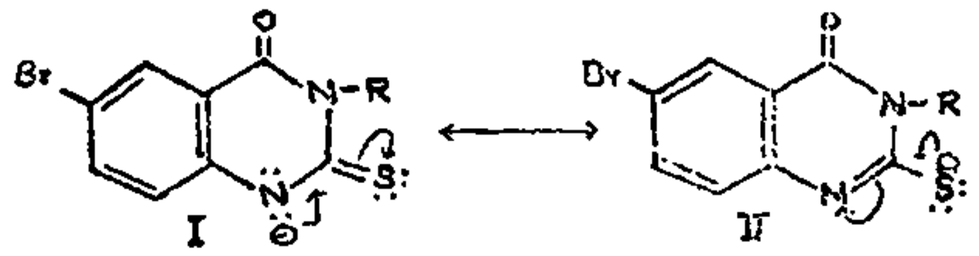
RADHEY SHYAM* AND I. C. TIWARI

Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi-221005

THE discovery of various types of quinazolones as antimalarials[1], CNS potent[2] and antibacterials[3] as well as their hydrazides as antiflammatory agents[4] have created the interest of authors to prepare some 6-bromo-2-(β-diethylaminoethylthio)-3-aryl (or alkyl)-4 (3 H) quinazolones and 6-bromo-2-carboethoxymethylthio-3-aryl-4 (3H)quinazolones as chemotherapeutical interest. The syntheses were carried out by the reaction of 6-bromo-3-aryl(or alkyl)-2-thio-4 (3 H) quinazolones with equivalent

* All communications to be sent to Dr. Radhey Shyam, Department of Chemistry, Digvijai Nath Degree College, Gorakhpur.

amount of β-diethylaminoethyl chloride and ethyl bromoacetate in 10% alcoholic NaOH solution at room temperature with occasional stirring for 2–3 hr. The reaction is simple and straightforward and completes in good yields. The two tautomeric structures of 6-bromo-2-thio-3-aryl-4 (3 H) quinazolones arising by the shift of proton and a pair of electrons may exist as resonance hybrids (I ↔ II). Therefore, in the alkylation, the entering group may become attached either to the nitrogen atom forming N-alkyl derivatives or to the sulphur atom giving thioether or a mixture of both.



The hydrolysis of alkylated product (8) with alcoholic hydrochloric acid gives the sulphur free compound 6-bromo-3-*p*-ethoxyphenyl-quinazonaline-2-4-dione (3). The alkaline solution of mercaptan on treatment with lead acetate or silver nitrate gives characteristic coloured salts. The IR spectrum of compound (8) shows two characteristic absorption bands one at 1678 cm^{-1} and another at 1650 cm^{-1} for the exocyclic and cyclic (position-4) carbonyl groups respectively. But the IR spectrum of compound (3), as expected, shows the two absorption bands one at 1668 cm^{-1} for the ring carbonyl group at position-4 and another at 1738 cm^{-1} for the ring carbonyl group at position-2 along with a broad absorption band at 3245 cm^{-1} for –NH bond. These evidences prove that the 6-bromo-2-thio-3-aryl-4(3H)quinazolones are more reactive in the thiol form (II) and are alkylated quantitatively on the sulphur atom rather than nitrogen atom. The structures of these quinazolones (Tables I and II) were also supported by their spectral as well as analytical data. The NMR spectrum of compound[1] shows along with other normal peaks, one doublet for C_5-proton due to long range coupling with C_7-proton at δ 8·45 (J = 2·0 Hz). The C_7-proton appears as a pair of doublet or a quartet at δ 7·88 ; being doublet (J = 2·0 Hz) due to long range coupling with C_5-proton and double doublet (J = 9·0 Hz) due to coupling with adjacent C_8-proton. The IR spectrum, as expected, does not show any absorption in –NH region characteristic of starting material.

Experimental

The melting points of the compounds were recorded on GALLENCAMP Melting Point apparatus and are uncorrected. The compounds were chromatographed on developing the TLC plates in suitable solvents using silica gel (BDH) as adsorbent and R_f values were recorded. *Varian A60D* model was used for recording of NMR spectra, a *Perkin-Elmer 257* for IR and a *Coleman Analyzer* for analyses.

6-Bromo-2-(β-diethylaminoethylthio)-3-p-tolyl-4(3H) quinazolone (*1*).—6-Bromo-2-thio-3-*p*-tolyl-4(3H) quinazolone[5] (2·1 g) was dissolved in the minimum quantity of 10% alcoholic NaOH solution and to this was added β-diethylaminoethyl chloride (1·0 ml). The reaction mixture was stirred and allowed to stand for about two hours at room temperature, when crystals separated out. They were filtered, washed with water and then with a little of alcohol. Recrystallisation from 80% ethanol afforded the needles, yield 78%, m.p. 106°. TLC : $R_f = 0·70$ (Benzene-Ether, 3 : 1). *Anal.* Calcd for $C_{21}H_{24}N_3OSBr$: N, 9·41 ; S, 7·17. Found : N, 9·23 ; S, 6·73%. IR ν_{max}^{nujol} cm^{-1} : 1725s, 1680s, 1605m, 1550s, 1535m. NMR($CDCl_3$) δ (J=Hz) : 8·45-(1 H, d, J = 2·0), 7·93(1 H, q, J = 2·0 and 9·0), 7·45(5H, m), 2·46(3H, s), 2·54(2H, m), 3·50(8H, m), 2·65(4H, q, J = 7·0) and 1·11(6H, m). Likewise, other quinazolones were prepared. Their structures, melting points and the purity of the compounds are listed as in Table I.

6-Bromo-2-carboethoxymethylthio-3-p-chlorophenyl-4(3H) quinazolone (*2*).—Ethyl chloroacetate (1·0 ml) was added to a solution of 6-bromo-2-thio-3-*p*-chlorophenyl-4(3H)quinazolone (2·2 g) dissolved in 5% alcoholic NaOH solution and the mixture was stirred for 6–8 hr at room temperature. It was acidified with 5% HCl solution. The crude mass thus obtained was regenerated by dissolving in 5% $NaHCO_3$ solution and precipitated with 5% –HCl solution. It was further crystallised from alcohol, yield 66%, m.p. 197°. TLC : $R_f = 0·40$ (Benzene-Ether, 12 : 1). *Anal.* Calcd. for $C_{10}H_{10}N_2O_3SClBr$: N, 6·18 ; S, 7·06. Found : N, 6·03 ; S, 7·20. IR ν_{max}^{nujol} cm^{-1} : 1730s, 1700s, 1610s, 1585s, 1550s.

Following the same procedure, other derivatives were prepared and listed as in Table II.

Hydrolysis of 6-Bromo-2-β-diethylaminoethylthio-3-p-ethoxy-4 (3 H)quinazolone (8).—A mixture of 6-bromo-2-β-diethylaminoethylthio-3-*p*-ethoxyphenyl-4-(3H)quinazolone (8) (2·40 g), 6N–HCl (25 ml) and ethanol (30 ml) was refluxed on a water-bath at 80–90° for 6–8 hr. On cooling, the crystalline product was separated out. It was washed with water and finally with a little of ethanol. Crystallisation from chlorobenzene and ethanol mixture gave the product 6-bromo-3-*p*-methoxyphenyl-quinazoline-2-4-dione (3) yield, 64%, m.p. 287°. *Anal.* Calcd. for $C_{16}H_{13}N_2O_4Br$: N, 7·75. Found : N, 7·58%. IR ν_{max}^{nujol} cm^{-1} : 3245 broad, 1738s, 1668s, 1620s, 1605s and 1500m.

TABLE I

Physical data and IR peaks of 6-bromo-2-(β-diethylaminoethylthio)-3-aryl (or alkyl)-4(3H)quinazolones

Comp. No.	Substituent R	Molecular formula	Yield (%)	M.P. (° C)	Nitrogen (%) Found	Nitrogen (%) Calcd.	Sulphur (%) Found	Sulphur (%) Calcd.	Characteristic IR peaks (cm^{-1})	R_f* values
4.	Phenyl	$C_{20}H_{22}N_3OSBr$	48	145	9·48	9·72	7·29	7·40	1695s, 1605m, 1550s, 1515m	0·68
5.	*p*-Chlorophenyl	$C_{20}H_{21}N_3OSClBr$	85	310	8·85	9·00	6·37	6·85	..	0·75
6.	*p*-Bromophenyl	$C_{20}H_{21}N_3OSBr_2$	91	149	7·67	8·21	6·02	6·26	1695s, 1645w, 1565w, 1545s	0 65
7.	Benzyl	$C_{21}H_{24}N_3OSBr$	59	250	9·06	9·41	6·58	7·17	..	0·63
8.	*p*-Ethoxyphenyl	$C_{22}H_{24}N_3O_2SBr$	73	216	8·82	8·86	6·85	6·73	1678s, 1650s, 1560s, 1550s	0·72

* R_f values were measured on developing the TLC plates (adsorbent, silica gel BDH) in benzene-ether (3 : 1) mixture.

TABLE II

Physical data and IR peaks of 6-bromo-3 aryl-2-carboethoxymethylthio-4 (3H) quinazolones

Comp. No.	Substituent R	Molecular formula	Yield (%)	M.P. (°C)	Nitrogen (%) Found	Nitrogen (%) Calcd.	Sulphur (%) Found	Sulphur (%) Calcd.	Characteristic IR peaks (cm^{-1})	R_f* values
9.	Phenyl	$C_{18}H_{15}N_2O_3SBr$	68	310	6·62	6·68	7·68	7·64	1725s, 1675s, 1590s, 1560s	0·43
10.	*o*-Tolyl	$C_{19}H_{17}N_2O_3SBr$	52	265	6·13	6·46	7·25	7·39	..	0·38
11.	*m*-Tolyl	$C_{19}H_{17}N_2O_3SBr$	59	308	6·25	6·46	7·48	7·39	..	0·25
12.	*p*-Tolyl	$C_{19}H_{17}N_2O_3SBr$	72	245	6·35	6·46	7·42	7·39	1730s, 1675s, 1600m, 1570s	0·28
13.	*p*-Bromophenyl	$C_{19}H_{16}N_2O_3SBr_2$	67	206	5·45	5·62	6·61	6·42	..	0·35
14.	*o*-Methoxyphenyl	$C_{19}H_{17}N_2O_4SBr$	54	280	6·10	6·23	7·35	7·11	..	0·20
15.	*p*-Methoxyphenyl	$C_{19}H_{17}N_2O_4SBr$	74	222	6·19	6·23	7·02	7·11	1725s, 1680s, 1610m, 1565s	0·27
16.	*p*-Ethoxyphenyl	$C_{20}H_{19}N_2O_4SBr$	65	266	5·93	6 04	7·15	6·91	1735s, 1680s, 1615m, 1565s	0·23

* R_f values were measured on developing the TLC plates (adsorbent silica gel) in benzene-ether (3:1) mixture.

The screening test of these compounds is in progress and will be reported in due course.

ACKNOWLEDGEMENT

Thanks are due to Prof. P. N. Bhargava for his kind interest, to Prof. G. B. Singh and Sri B. M. Singh for providing facilities, to CSIR, New Delhi, for financial assistance, to R. S. and PGIIM, B.H.U., for assistance to I.C.T.

1. Grout, R. J. and Patridge, M. W., *J. Chem. Soc.*, 1960, pp. 3546, 3551.
2. Gupta, C. M., Bhaduri, A. P. and Khanna, N. M., *J. Med. Chem.*, 1968, 11, 392.
3. Bhargava, P. M. and Singh, H., *Indian J. Pharm.*, 1969, 31, 111.
4. Parmar, S. S. and Arora, R. C., *Canadian J. Chem.*, 1968, 46, 2519.
5. Chaurasia, M. R., *J. Chem. UAR*, 1969, 12, 289.