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Quinazolones. Part. IX* Syntheses of Some Thiazolido (3, 2-a) quinazolones

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Syntheses of 4-allylthiazolido(3,2-a)quinazoline-1,5(4H)-dione (III) and 4-allyl-1-arylthiazolido (3,2-a)quinazolin-5(4H)-one (X) are described and the formation of anhydro compound from 3-allylquinazolin-4(3H)-one-2-thioacetic acid discussed.

CONVERSION of 2-thionoquinazolones of the type Ia, d with monochloroacetic acid or ethyl bromoacetate in alkaline aprotic solvents to those of type IIa, d and their facile reductive cyclisation with sodium borohydride to IIIa, d has recently been reported from this laboratory[1,2]. In an attempt to extend its applicability to their oxoanalogs[3] it was observed that Ib neither condensed with chloroacetic acid, nor did it undergo acetylation under any of the experimental condition.

It thus became desirable to investigate whether the failure of such a condensation is due to the effect of the substituent at $N_{(3)}$ or is due to the difference in their tautomeric behaviour. Accordingly the reaction was extended to Ic resulting to the formation of IIc and their subsequent cyclisation to IIIc which has been realised and is described in this paper.

Condensation of 3-allyl-2-thionoquinazoline-4(3H)-one (Ic) with monochloroacetic acid and with ethyl bromoacetate in alkaline aprotic solvent dimethylformamide gave the respective 3-allylquinazoline-4(3H)-one-2-thioacetic acid (IIc) (R_2=H) and its ethyl ester ($R_2 = C_2H_5$), the alkaline solution of which when subsequently treated with sodium borohydride and followed by acidification resulted in the separation of 4-allylthiazolido-(3,2-a)quinazoline-1,5(4H)-dione (IIIc). However, cyclodehydration of thioacetic acid (IIc; R_2 = H) with a mixture of acetic anhydride and pyridine afforded the anhydro compound (IV) as dark blue crystals with a bronze lusture, the mesoionic structure of which has been assigned on the basis of the work of Duffin and Kendall[4] who had prepared similar anhydro derivatives of thiazolo (2,3-a)benzthiazole and of thiazolo(3,2-a)benzimidazole. The methylene group in IIIc is not activated in the manner as expected in analogy with V[4] and VI[5] as it did not form 2-benzylidine derivative and is supported by the observation of Singh and Chaudhury[2].

The 2-thionoquinazolone (Ic) could also be converted to 3-allyl-2-*p*-bromophenacylthioquinazoline-4 (3H)-one (VII) on interaction with *p*-bromophenacylbromide in presence of alkali. Reduction of VII with sodium borohydride not only reduced the imine double bond (: C = N) but also the carbonyl group leading to the formation of 3-allyl-1,2-dihydro-2-(α-hydroxy-*p*-bromophenethyl)-thioquinazolin-4(3H)-one (VIII) which could be easily cyclodehydrated to 4-allyl-1-*p*-bromophenylthiazolido(3,2-a) quinazolin-5 (4H)-one (IX) with a trace of *p*-toluenesulphonic acid

Experimental

All the m.p.s were determined in open capillaries in H_2SO_4 bath and are uncorrected.

3-Allylquinazoline-4 (3H)-one-2-thioacetic acid (IIc; R_2 = H) : Solution of Ic (2.18 g.; 0.01 mole) in NaOH (1.3 g.; 0.033 mole) in water (10 ml.) and DMF (20 ml.) was treated with monochloroacetic acid (1.04 g.; 0.011 mole) dissolved in Na_2CO_3 solution (hydrated Na_2CO_3; 2.9 g.; 0.01 mole) in water (10 ml.) and DMF (5 ml.) and heated on steam bath for 2 hr. The reaction mixture was subsequently diluted with water (20 ml.), cooled and acidified with conc. HCl when white solid separated out. It was collected and crystallised from glacial acetic acid to give IIc (R_2=H) as coloarless ndedles (1.65g.; be % m.p. 173°—179° νmax (KBr) 3210 broad (acid OH: –CH), 1765 (acid > C = O), 1660 (> N–C = O), λmax (EtOH) 237, 278 nm. (εmax 24980, 15915) (Found : C, 56.4; H, 4.1; N, 9.8. $C_{13}H_{12}N_2O_3S$ requires : C, 56.5; H, 4.3; N, 10.1%).

Ethyl-3-allylquinazoline-4 (3H)-one-2-thioacetat (IIc; $R_2 = C_2H_5$) : A solution of the thioquinazolone (Ic; 2.18 g.; 0.01 mole) in DMF (10 ml.), ethylbromoacetate (1 ml.; 1.5 g.; 0.012 mole) and K_2CO_3 (5 g.) were heated on steam bath for 1.5 hr. with occasional shaking. The reaction mixture was then cooled, poured into crushed ice and left overnight. The precpitate that separated was collected and crystallised from methanol to afford IIc ($R_2 = C_2H_5$) as results of colourless needles (1.5 g.; 50%), m.p. 74°–75°.

* Part VIII : S. K. P. Sinha and M. P. Thakur (Preceeding paper).

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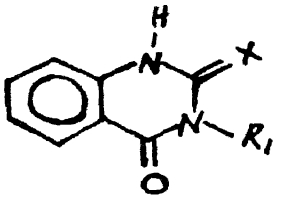

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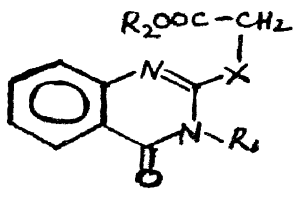

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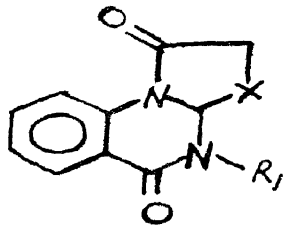
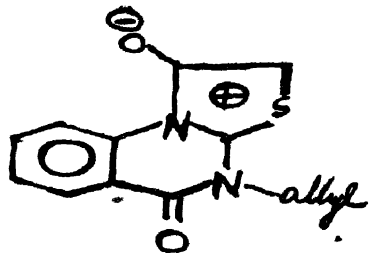


III

a : R = H, R_1 = Ph; x = S
b : R = H; R_1 = allyl; x = O
c : R = H; R_1 = allyl; x = S
d : R = alkoxy; R_1 = phenyl; x = S
e : R = H; R_1 = $CH_2CH_2NEt_2$; x = O



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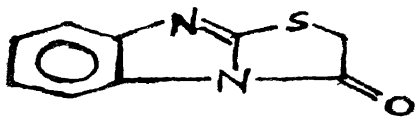

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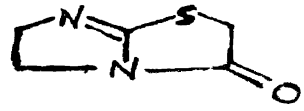

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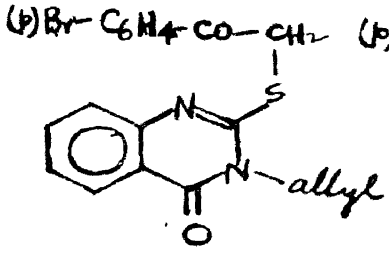

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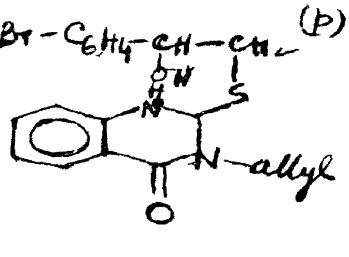
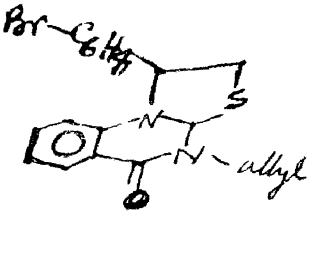


VIII



IX

νmax (KBr) 700, 775, 950, 1025, 1320 (C–O stretching), 1360 (C–S stretching), 1470, 1560, 1600 (aromatic), 1705 (quinazoline carbonyl), 1750 cm^{-1} (carbonyl, ester), λmax (EtOH) 237, 278 nm. (εmax 12589, 7367), (Found : C, 59·0; H, 5·0; N, 9·4. $C_{15}H_{16}N_2O_3S$ requires : C, 59.2; H, 5.3; N, 9.2%).

4-*Allylthiazolido* (3,2-*a*) *quinazoline*-1,5 (4*H*)-*dione* (IIIc) : (a) To a solution of IIc (R = H; 1 g.), in aq. NaOH (1%; 10 ml.) was added $NaBH_4$ (0.4 g.) in water (5 ml.), stirred (0.5 hr.) and kept overnight. The reaction mixture was filtered from traces of impurites and the clear filtrate was acidified with 6(*N*) H_2SO_4 when white precipitate separated out. It was filtered, washed successively with water, aq. $NaHCO_3$ and water. The residue on crystallisation from glacial acetic acid furnished IIIc as clusters of colourless needles (0.5 g.; 50%), m.p. 183°–184°. νmax (KBr) 750, 1275, 1330, 1440, 1460, 1485, 1640 (> C = O, tertiary amide), 1700 (quinazoline carbonyl), 1730 (cyclic γ-lactum; ring fused), 3210 cm^{-1} (-CH-). λmax (EtOH) 233, 243, 310 nm. (εmax 11746, 11846, 6024) (Found : C, 60.1; H, 4.4; N, 10.8. $C_{13}H_{12}N_2O_2S$ requires : C, 60.0; H, 4.6; N, 10.7%).

(b) A solution of IIc ($R_2 = C_2H_5$; 1 g.) in diglyme (10 ml.) was treated with $NaBH_4$ (0.4 g.) in methanol (10 ml.) and stirred till the solution became homogeneous. Next day the clear solution was cooled in ice, acidified with conc. HCl and the precipitate that separated out was collected and washed with water. It was crystallised from glacial acetic acid to afford IIIc as colourless needles (0.4 g.; 40%), m.p. and m m p 183°–184°.

Anhydro compound (IV) : Solution of quinazoline thioacetic acid (IIc; R_2 = H) (1 g.) in dry pyridine (10 ml.) when treated with acetic anhydride (5 ml.) and heated on steam bath, a blue crystalline precipitate separated out within 5 min. It was filtered, washed with a little methanol and crystallised from ethanol to yield and anhydro compound (IV) as blue needles with bronze lusture (0.35 g.), m.p. > 300°. (Found : C, 60.2; H, 3.9; N, 10.4. $C_{13}H_{10}O_2S$ requires : C, 60.4; H, 3.8; N, 10.8%).

3-*Allyl*-2-p-*bromophenacylthioquinazoline*-4 (3*H*)-*one* (VII) : *p*-Bromophenacylbromide (5.6 g.; 0.02 mole) in acetone (20 ml.) was added while shaking to a solution of Ic (4.4 g.; 0.02 mole) in 5% aq. NaOH (40 ml.) when a colourless precipitate separated out. The reaction mixture was diluted with water (20 ml.) and cooled. The solid which separated was collected, washed with a little acetone and crystallised from glacial acetic acid to give VII as colourless shining needles (4.1 g.; 50%), m.p. 147°–148°. νmax (KBr) 785, 1000, 1070, 1210, 1460, 1555, 1575, 1600, 1690 cm^{-1} (quinazoline carbonyl). λmax (EtOH) 239, 260 nm. (εmax 39021, 32517) (Found : C, 55.1; H, 3.2; N, 6.9; Br, 19.0. $C_{19}H_{15}N_2O_2BrS$ requires : C, 54.9; H, 3.6; N, 6.7; Br, 19.3%).

3-*Allyl*-1,2-*dihydro*-2(α-*hydroxy*-p-*bromophenethyl*)-*thioquinazolin*-4(3*H*)-*one* (VIII) : A solution of VII (4.15 g.; 0.01 mole) in dioxan (30 ml.) was mixed with KBH_4 (2.5 g.) in methanol (20 ml.) containing a drop of 2(*N*) aq. NaOH and left overnight. The reaction mixture was diluted with water and the precipitate that separated was filtered, washed with water. It was crystallised from glacial acetic acid to yield VIII as colourless needles (1.67 g.; 40%), m.p. 270° (decomp.) as νmax (KBr) 1410, 1490, 1630, 1700 (quinazoline carbonyl), 3410 cm^{-1} (OH; > NH). (Found : C, 54.5; H, 4.3; N, 6.4; Br, 19.2. $C_{19}H_{19}N_2O_2SBr$ requires : C, 54.4; H, 4.5; N, 6.6; Br, 19.0%).

1-p-*Bromophenyl*-4-*phenylthiazolido* (3,2-*a*) *quinazoline*-5(4*H*)-*one* (IX) : VIII (1 g.) in acetic anhydride (5 ml.) was refluxed for 15 min. and cooled when colourless crystalline material gradually deposited. It was filtered, washed with ethanol and crystallised from glacial acetic acid to afford (IX) as colourless needles (0.5 g.), m.p. 110°. νmax (KBr) 3210 (-CH-), 1750, 1660 (quinazoline carbonyl), 1480 cm^{-1}. (Found : C, 56.6; H, 4.0; N, 7.0; Br, 19.7. $C_{19}H_{17}N_2OSBr$ requires : C, 56.8, H, 4.2; N, 6.9; Br, 19.9%).

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