Reactions of Heterocycles with Thiophosgene. Part VI.[1] Reactions of Tetrahydropyrazolo[1,5-*c*]quinazolines

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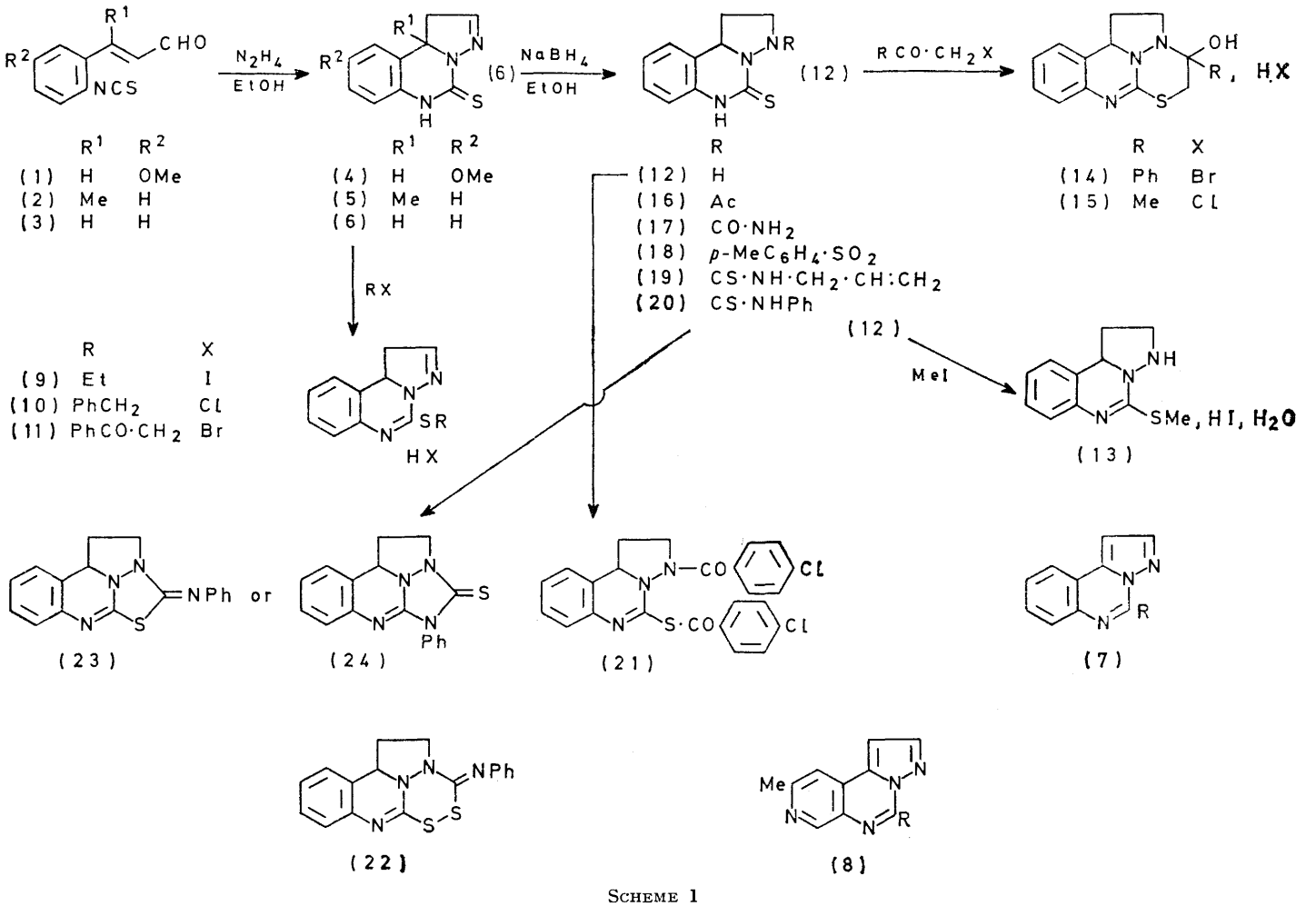
o-Isothiocyanato-*trans*-cinnamaldehyde (3), derived from quinoline, thiophosgene, and base, reacts with hydrazine to give 6,10b-dihydropyrazolo[1,5-*c*]quinazoline-5(1*H*)-thione (6), which is reduced by sodium borohydride to the 2,3,6,10b-tetrahydro-derivative (12) and undergoes ring fission with alkali to give 1,2,3,4-tetrahydro-2-thioxoquinazolin-4-ylacetic acid (25). Alkylation, acylation, sulphur replacement, esterification, ring formation, and rearrangement reactions of compounds (6), (12), and (25) are described. Some analogous reactions have been carried out with 4-methyl- and 6-methoxy-quinolines.

PREVIOUSLY we have reported the novel synthesis of *o*-isothiocyanato-*trans*-cinnamaldehydes by fission of quinolines with thiophosgene in the presence of base.[1-3] As an extension of this work we have now prepared the aldehydes (1) and (2) from 6-methoxy- and 4-methylquinoline, respectively.

The isothiocyanato-aldehydes (1)—(3) are converted into the dihydropyrazoloquinazolinethiones (4)—(6), respectively, on treatment with hydrazine. Presumably the reaction proceeds *via* hydrazone formation and conjugate addition to the pyrazoline followed by cyclisation of the isothiocyanate. We have not isolated any intermediates in this assumed stepwise scheme. Pyrazolo-[1,5-*c*]quinazolines (7) and the related aza-derivatives (8)



SCHEME 1

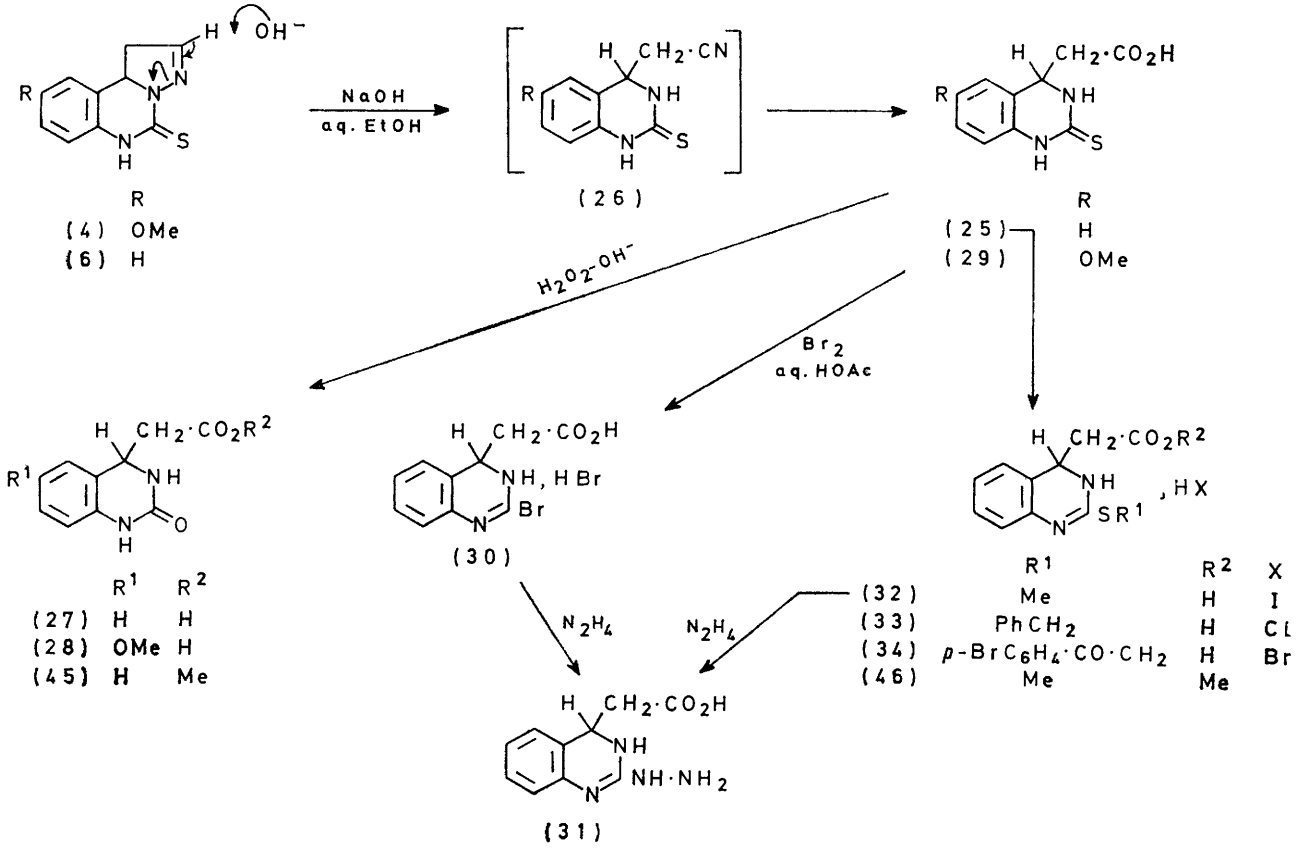
[1] Part V, R. Hull, P. J. van den Broek, and M. L. Swain, *J.C.S. Perkin I*, 1975, 2271.

[2] R. Hull, *J. Chem. Soc.* (*C*), 1968, 1777.

[3] R. Hull, P. J. van den Broek, and M. L. Swain, *J.C.S. Perkin I*, 1975, 922.

have previously been described, respectively, by de Stevens [4] and Bowie [5] and their co-workers.

Alkylation of the thione (6) (essentially a cyclic thiosemicarbazone) with ethyl iodide, benzyl chloride, and phenacyl bromide gave the alkylthio-derivatives (9)—(11) as their salts. Reduction of the thione (6) with sodium borohydride gave the tetrahydropyrazoloquinazolinethione (12). This substance formed the methylthioquinazoline (13) on treatment with methyl iodide, the presence of sodium hydroxide or ethoxide were unsatisfactory. Further examination of the reaction showed that (6) was unstable to alkali; treatment with aqueous or ethanolic 2N-sodium hydroxide gave the reduced quinazolinylacetic acid (25) (Scheme 2) in high yield. The mechanism of the ring opening is uncertain: although ammonia is evolved no trace of the postulated intermediate nitrile (26) was detected by i.r. Analogous ring-opening reactions with retention of the nitrile group



SCHEME 2

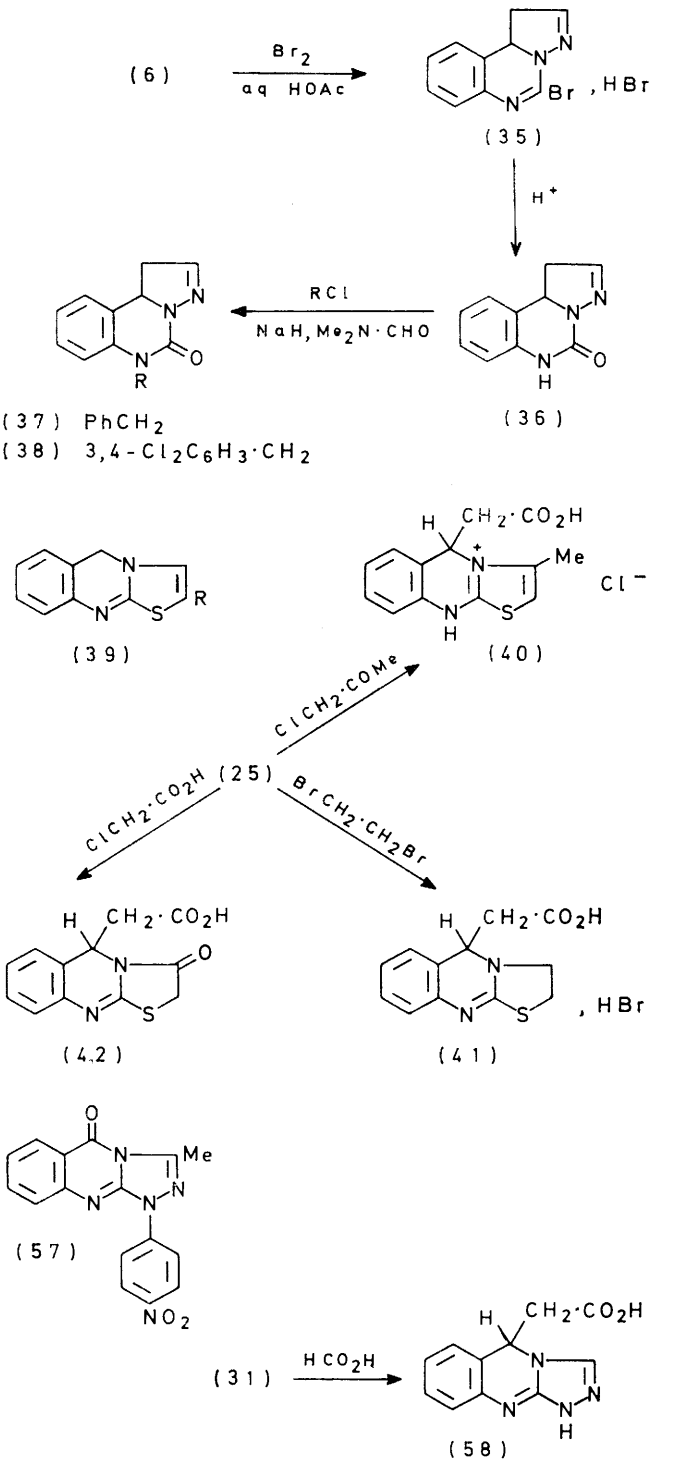
and treatment with phenacyl bromide and chloroacetone gave the tetracyclic thiadiazines (14) and (15), respectively. The pyrazoloquinazoline (12) behaved as a substituted thiosemicarbazide and on acylation gave the acetyl (16) and carbamoyl (17) derivatives; reactions with toluene-*p*-sulphonyl chloride and isothiocyanates gave the sulphonyl (18) and thiocarbonyl [(19) and (20)] derivatives; *p*-chlorobenzoyl chloride in pyridine was anomalous in that it gave the *NS*-diaroyl derivative (21). Attempts to form the novel dithiadiazine system (22) by the reaction of iodine and alkali with the thioamide (20) were unsuccessful; instead we obtained an oxidation product thought to be either (23) or (24).

Attempts to alkylate the pyrazoloquinazoline (6) in have been noted in the isoxazole [6] and isothiazoloquinoline [7] series. We have found that the thioxo-acid (25) is converted into the corresponding oxo-derivative (27) when treated with alkaline hydrogen peroxide at laboratory temperature.[8] In like manner we obtained the corresponding methoxy-acid (28) from the pyrazoloquinazoline (4); in this case no attempt was made to isolate the intermediary thioxo-acetic acid (29). Earlier investigations [9] had shown that quinazolinethiones could be converted into their bromo-hydrobromide salts by reaction with bromine in aqueous acetic acid. Applic-

[4] G. de Stevens, A. Halamandaris, M. Bernier, and H. M. Blatter, *J. Org. Chem.*, 1963, **28**, 1336.
[5] R. A. Bowie, M. J. C. Mullan, and J. F. Unsworth, *J.C.S. Perkin I*, 1972, 1106.
[6] L. Claisen, *Ber.*, 1892, **25**, 1787; 1909, **42**, 66; M. H. Palmer, 'The Structure and Reactions of Heterocyclic Compounds,' Arnold, London, 1967, p. 385.
[7] R. Hull, *J.C.S. Perkin I*, 1973, 2911.
[8] R. T. C. Loh and W. M. Dehn, *J. Amer. Chem. Soc.*, 1926, **48**, 2956.
[9] S. Gabriel and R. Stelzner, *Ber.*, 1896, **29**, 1300; A. Drawert, *ibid.*, 1899, **32**, 1259.

ation of this method to the thioxo-acetic acid (25) gave the bromo-hydrobromide (30) in good yield. The bromo-derivative (30) reacted with hydrazine hydrate to give the hydrazino-acid (31) in superior yield (64%) to an alternative preparation from the methylthio-hydriodide (32) (yield 55%). Curiously the hydrazone (31) is obtained in the free ' aminoguanidine ' form from both reactions and not as the hydrohalide salt. The bromo-compound (30) may prove to be more reactive and convenient than the methylthio-hydriodide (32) for other nucleophilic displacements. Reaction of the thione (25) with benzyl chloride or *p*-bromophenacyl bromide gave the corresponding alkylthio-derivatives (33) and (34) as their salts. The thione (6), when treated with bromine in aqueous acid, gave the bromo-hydrobromide (35), which underwent hydrolysis by acid to the oxo-derivative (36) (Scheme 3). Alkylations with benzyl and 3,4-dichlorobenzyl chlorides gave the *N*-alkylated derivatives (37) and (38), respectively.

Thiazolo[2,3-*b*]quinazolines (39) have been reported previously [10] but few synthetic approaches have been made by cyclisation reactions of quinazoline-2-thiones. Sykes [11] synthesised the methyl derivative (39; R = Me) from 3,4-dihydroquinazoline-2(1*H*)-thione and chloroacetone. We found that the thioxo-acetic acid (25) reacted with chloroacetone, ethylene dibromide, and chloroacetic acid to give respectively the linear tricyclic compounds (40)—(42). Esterification of the acids (40) and (41) with thionyl chloride in methanol gave the esters (43) and (44) in good yield. Similar esterifications were carried out on the acids (27) and (32) to give the esters (45) and (46) (Scheme 2). Two examples suffice to illustrate the usefulness of the ester function. The action of hydrazine on the ester (43) gave the hydrazide (47) and that of phenylmagnesium bromide in tetrahydrofuran on the ester (44) gave the alcohol (48) (Scheme 4). An attempt was made to form other amides by heating the ester (43) with piperidine and with *N*-methylpiperazine. The same product, $C_{13}H_{10}N_2OS$, m.p. 128—129°, was isolated from each reaction. The n.m.r. spectrum (solvent $CDCl_3$) showed that the molecule had undergone a major rearrangement to the thiazolylquinolone (49) (Scheme 5). The methyl group [τ 7.46 (d, $J < 2$ Hz)] showed a characteristic coupling to the thiazole proton [τ 2.81 (q, $J < 2$ Hz)]. The remaining aromatic proton signals [τ 2.20 (1 H, d, J 9.5 Hz, 4-H), 2.3—3.3 (4 H, m), and 3.30 (1 H, d, J 9.5 Hz, 3-H)] were similar to those of other *N*-substituted 2-quinolones. Fragmentation of the molecular ion (*m/e* 242) gave mass spectral peaks at 214 (M — CO) and 201 (M — CH_3CN). There was an i.r. band at 1 670 cm^{-1} (CO). The secondary amines evidently act as bases rather than as nucleophiles, causing the ester (43) to undergo ring opening to give the cinnamic ester (50). If the initial product is the (*E*)-cinnamic ester, isomerisation to the *Z*-form is required

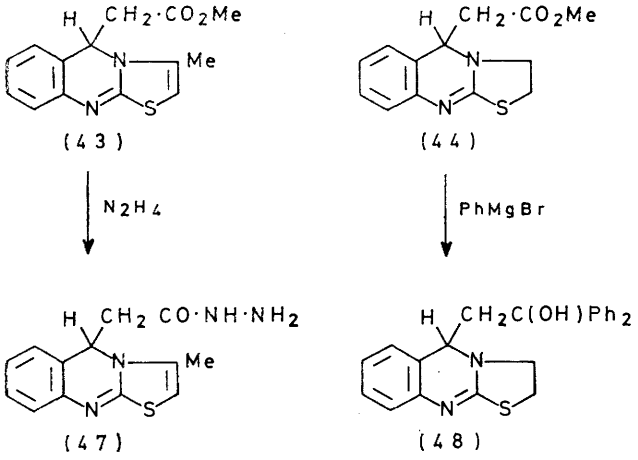


SCHEME 3

before the final ring closure to the quinolone (49). This might take place *via* an internal electron-transfer mechanism involving the quinonoid intermediate (51)

[10] W. L. F. Armarego in ' Fused Pyrimidines, Part I, Quinazolines,' Interscience, New York, 1967, p. 288; J. D. Kendall and G. F. Duffin, B.P. 634,951 (*Chem. Abs.*, 1950, **44**, 9287d); O. P. Vig, I. S. Gupta, and K. S. Narang, *Science and Culture*, 1952, **18**, 43 (*Chem. Abs.*, 1953, **47**, 10541d); M. C. Khosla, O. P. Vig, I. S. Gupta, and K. S. Narang, *J. Sci. Ind. Res., India*, 1953, **12***B*, 466 (*Chem. Abs.*, 1955, **49**, 1060a).

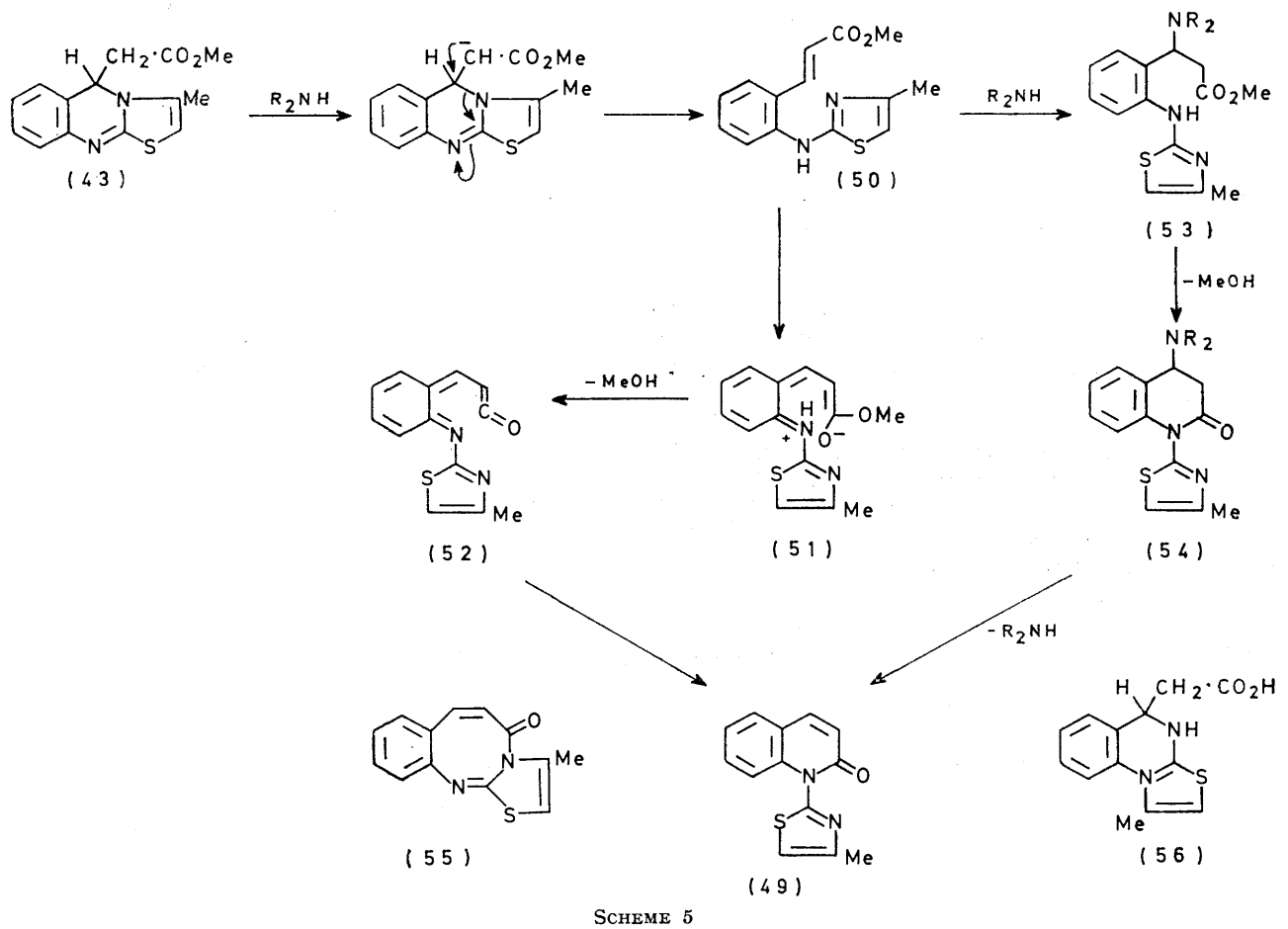
[11] P. Sykes, *J. Chem. Soc.*, 1955, 2390.



SCHEME 4

and the transient keten (52). Alternatively, addition of the secondary amine to the αβ-unsaturated system in (50) would give an intermediate (53) capable of cyclisation to (54) and subsequent elimination of the amine to give the quinolone (49). This latter mechanism is of interest since a preliminary experiment appeared to indicate that the reaction did not take place with the tertiary base triethylamine. An alternative ring closure of the ester (50) to give the diazocine (55) appears unlikely in preference to the ring closure to the quinolone (49). The conversion of (43) into (49) provides evidence for the linear nature of the acid (40). The angular isomer (56) would not lead to the quinolone (49). Some *N*-aryl-2-pyridones and -2-quinolones have been described [12] from reactions of pyridine *N*-oxide and 2-bromopyridine or 2-bromoquinoline. Our approach to the thiazolylquinolone (49) appears to be novel.

The *s*-triazolo[3,4-*b*]quinazoline system was first described by Ghosh and Betrabet, who obtained compound (57) from an *s*-triazole and anthranilic acid [13] (Scheme 3). We found that the reaction of the hydrazino-acid (31) with formic acid gave the triazoloquinazoline (58). The exploitation of this reaction to obtain other tricyclic skeletons will be the substance of future research.



SCHEME 5

EXPERIMENTAL

For general methods used see ref. 3.

3-(2-*Isothiocyanatophenyl*)*but*-2-*enal* (2).—Thiophosgene

[12] E. Ochiai, 'Aromatic Amine Oxides,' Elsevier, Amsterdam, 1967, p. 325.

[13] T. N. Ghosh and M. V. Betrabet, *J. Indian Chem. Soc.*, 1930, **7**, 900 (*Chem. Abs.*, 1931, **25**, 3651).

(15.2 ml) in methylene chloride (60 ml) was added dropwise to a 'vibromixed' suspension of 4-methylquinoline (26.2 ml) and calcium carbonate (20 g) in methylene chloride (100 ml) and water (100 ml) in an ice-bath. After 'vibromixing' for 4 h the mixture was filtered through Hyflo Supercel. The methylene chloride layer was separated from the filtrate, dried, and evaporated below 25 °C to give the crude aldehyde as an unstable dark oil (which was used immediately in the reaction with hydrazine). A portion of the oil was dissolved in methylene chloride; the solution was washed with 2N-hydrochloric acid, dried, and evaporated. The residual oil was extracted with hot light petroleum (b.p. 60—80°) and the extract was evaporated to give the aldehyde (mixed isomers) as a yellow oil, which darkened rapidly, $\nu_{max.}$ 2 100 (NCS) and 1 680 cm^{-1} (CHO), τ ($CDCl_3$) 0.46 (1 H, d, J 8 Hz, CHO), 2.1 (4 H. m. aromatic). 3.8 (1 H, dq, J 8 and 1.5 Hz, olefinic), and 7.44 and 7.69 (3 H, d, J 1.5 Hz, CH_3). Similarly prepared from quinoline (625 ml) was *o*-isothiocyanato-*trans*-cinnamaldehyde (3) [2] (688 g, 76%), m.p. 78—80° (from cyclohexane); and from 6-methoxyquinoline (48 g), 2-isothiocyanato-5-methoxy-*trans*-cinnamaldehyde (1) (41 g, 62%), m.p. 101—102° (from cyclohexane).

6,10b-*Dihydropyrazolo*[1,5-c]*quinazoline*-5(1H)-*thione* (6).—*o*-Isothiocyanato-*trans*-cinnamaldehyde (120 g) was suspended in ethanol (1 l). Hydrazine hydrate (100%; 40 ml) was added in one portion with swirling. After the initial strongly exothermic reaction had subsided the solution was refluxed for ½ h, during which time the product crystallised. The mixture was cooled and the product was collected, washed with ethanol, and dried to give the *dihydropyrazoloquinazolinethione* (yields from 114 to 121 g) as buff microneedles, m.p. 248—252°. A sample recrystallised from aqueous ethanol formed colourless needles, m.p. 250—252° (Found: C, 59.1; H, 4.6; N, 20.5. $C_{10}H_9N_3S$ requires C, 59.1; H, 4.4; N, 20.7%), $\nu_{max.}$ (Nujol) 3 200 cm^{-1} (NH), τ [$(CD_3)_2SO$] −0.83 (1 H, s, NH), 2.57 (1 H, t, J *ca.* 1.5 Hz, CH=N), 2.7—3.1 (4 H, m, aromatic), 5.10 (1 H, dd, J 10 and 12 Hz, angular CH), and 6.1—7.3 (2 H, m, CH_2), *m/e* 203 (M^+). Similarly were prepared: from 2-isothiocyanato-5-methoxy-*trans*-cinnamaldehyde and hydrazine hydrate, 6,10b-*dihydro*-9-*methoxypyrazolo*[1,5-c]*quinazoline*-5(1H)-*thione* (4) (70%) as needles, m.p. 256—258° (from aqueous ethanol) (Found: C, 57.1; H, 4.8; N, 18.2. $C_{11}H_{11}N_3OS$ requires C, 56.7; H, 4.7; N, 18.1%), τ ($CF_3{\cdot}CO_2H$) 2.25 (1 H, s, CH=N), 2.7—3.1 (3 H, m, aromatic), 4.60 (1 H, dd, J 10 and 12 Hz, angular CH), 6.00 (3 H, s, MeO), and 5.8—6.6 (2 H, m, CH_2); and from 3-(2-isothiocyanatophenyl)-but-2-enal and hydrazine hydrate, 6,10b-*dihydro*-10b-*methylpyrazolo*[1,5-c]*quinazoline*-5(1H)-*thione* (5) (3% from 4-methylquinoline) as needles, m.p. 222—224° (from aqueous ethanol) (Found: C, 60.1; H, 5.2; N, 19.4. $C_{11}H_{11}N_3S,0.25H_2O$ requires C, 59.6; H, 5.2; N, 19.0%), τ [$(CD_3)_2SO$] −0.9 (1 H, s, NH), 2.45 (1 H, t, J 1.5 Hz, CH=N), 2.6—2.9 (4 H, m, aromatic), 6.60 (2 H, m, 1-H_2 + water peak), and 8.84 (3 H, s, Me).

2,3,6,10b-*Tetrahydropyrazolo*[1,5-c]*quinazoline*-5(1H)-*thione* (12).—The dihydro-thione (6) (20 g) was dissolved in hot ethanol (2 l) and treated as rapidly as possible with sodium borohydride (8 g). After the initial exothermic reaction had subsided the solution was refluxed for 2 h. The hot solution was filtered, then cooled in ice for several hours. The product which crystallised was collected, washed with ethanol, and dried to give the *tetrahydro-thione* (15 g) as cream micro-prisms, m.p. 190—193°. A sample recrystallised from ethanol formed colourless needles, m.p. 192—194° (Found: C, 58.9; H, 5.6; N, 20.2. $C_{10}H_{11}N_3S$ requires C, 58.5; H, 5.4; N, 20.5%), $\nu_{max.}$ (Nujol) 3 200 cm^{-1} (NH), τ [$(CD_3)_2SO$] −0.25 (1 H, s, NHCS, exchanges with D_2O), 2.5—3.2 (4 H, m, aromatic), 3.88 (1 H, t, J 7 Hz, pyrazolidine NH, exchanges with D_2O), 5.23 (1 H, dd, J 6 and 9 Hz, 10b-H), and 6.5—8.1 (4 H, m, $CH_2{\cdot}CH_2$).

1,2,3,10b-*Tetrahydro*-5-*methylthiopyrazolo*[1,5-c]*quinazoline Hydriodide Monohydrate* (13).—The tetrahydrothione (12) (10 g) was stirred with methyl iodide (4 ml) in Cellosolve (150 ml) at room temperature for 1 h. The mixture was warmed on a steam-bath for 1 h and the solution formed was left at room temperature overnight, then diluted with light petroleum (b.p. 60—80°), precipitating a yellow oil, which solidified. The solution was decanted and the residue was crystallised from water (carbon) and dried *in vacuo* (40° and 10 mmHg) to give the *methylthio-derivative* (11.1 g) as needles, m.p. 154—155° (Found: C, 36.4; H, 4.4; N, 11.2. $C_{11}H_{16}IN_3OS$ requires C, 36.2; H, 4.4; N, 11.5%), τ [$(CD_3)_2SO$] 2.5—2.8 (4 H, m, aromatic), 4.90 (1 H, dd, J 8 and 10 Hz, angular CH), 6.5—8.0 (4 H, m, $CH_2{\cdot}CH_2$), and 7.22 (3 H, s, MeS).

3,4-*Dihydro*-3-*phenyl*-10bH-5-*thia*-2a,6,10c-*triaza-aceanthren*-3-*ol Hydrobromide* (14).—The tetrahydro-thione (0.5 g) was dissolved in hot acetone (50 ml) and the filtered solution was refluxed with phenacyl bromide (0.5 g) for ½ h. The crystalline product was collected, washed with acetone, and dried to give the *thiatriaza-anthrenol hydrobromide* (0.8 g) as rectangular microprisms of indefinite m.p., decomp. *ca.* 150° (Found: C, 53.1; H, 4.3; N, 10.0. $C_{18}H_{18}BrN_3OS$ requires C, 53.5; H, 4.5; N, 10.4%), $\nu_{max.}$ (Nujol) 3 200 cm^{-1} (OH). Similarly prepared from chloroacetone was 3,4-*dihydro*-3-*methyl*-10bH-5-*thia*-2a,6,10c-*triaza-aceanthren*-3-*ol hydrochloride* (15) (40%) as cream prisms of indefinite m.p., decomp. *ca.* 145° (Found: C, 52.0; H, 5.3; N, 13.8. $C_{13}H_{16}ClN_3OS$ requires C, 52.4; H, 5.4; N, 14.1%), $\nu_{max.}$ (Nujol) 3 300 cm^{-1} (OH).

3-*Acetyl*-2,3,6,10b-*tetrahydropyrazolo*[1,5-c]*quinazoline*-5(1H)-*thione* (16).—The tetrahydro-thione (12) (3.0 g) was heated with acetic anhydride (3 ml) and acetic acid (7 ml) at 90 °C overnight. The solution was diluted with water (20 ml), heated for ½ h on the steam-bath, and cooled. The product which crystallised was collected and recrystallised from aqueous acetic acid to give the N-*acetyl derivative* (3.0 g) as blades, m.p. 207—208° (Found: C, 58.2; H, 5.5; N, 17.1. $C_{12}H_{13}N_3OS$ requires C, 58.3; H, 5.3; N, 17.0%), $\nu_{max.}$ (Nujol) 3 200, 3 150 (NH), and 1 780 cm^{-1} (CO).

1,2,3,5,6,10b-*Hexahydro*-5-*thioxopyrazolo*[1,5-c]*quinazoline*-3-*carboxamide* (17).—The tetrahydro-thione (3 g) in acetic acid (30 ml), water (20 ml), and sulphuric acid (98%; 1.5 g) was stirred at room temperature during the addition of potassium cyanate (1.3 g). Water (50 ml) was added after 10 min and the solution was left overnight. The product which crystallised was collected, washed with water, and dried to give the *carboxamide* (2.6 g) as prisms, m.p. 221—223° (decomp). A sample recrystallised from dimethylformamide–ethanol had m.p. 223—225° (Found: C, 53.5; H, 4.9; N, 22.5. $C_{11}H_{12}N_4OS$ requires C, 53.1; H, 4.8; N, 22.6%), $\nu_{max.}$ (Nujol) 3 350—3 100 (NH) and 1 680 cm^{-1} (N·CO·NH_2 carbonyl).

3-(4-*Chlorobenzoyl*)-5-(4-*chlorobenzoylthio*)-1,2,3,10b-*tetrahydropyrazolo*[1,5-c]*quinazoline* (21).—The tetrahydro-thione (12) (2 g) in pyridine (15 ml) was heated with 4-chlorobenzoyl chloride (4 g) on a steam-bath for ½ h. The solution was poured into dilute sulphuric acid and extracted

with chloroform. The extract was washed with aqueous sodium hydrogen carbonate, dried, and evaporated. The yellow residue was crystallised from toluene to give the NS-*bis*-(4-*chlorobenzoyl*) *derivative* (0.9 g) as micro-needles, m.p. 232—233° (Found: C, 59.7; H, 3.7; N, 8.3. $C_{24}H_{17}Cl_2N_3O_2S$ requires C, 59.8; H, 3.5; N, 8.7%), $\nu_{max.}$ (Nujol) 1 730 (ArCO·S carbonyl) and 1 665 cm^{-1} (ArCO·N carbonyl). Similarly prepared with toluene-4-sulphonyl chloride was 2,3,6,10b-*tetrahydro*-3-(4-*tolylsulphonyl*)*pyrazolo*[1,5-c]*quinazoline*-5(1H)-*thione* (18) (55%) as prisms, m.p. 211—212° (from aqueous dimethylformamide) (Found: C, 56.8; H, 4.9; N, 11.2. $C_{17}H_{17}N_3O_2S$ requires C, 56.8; H, 4.7; N, 11.7%).

5-*Thioxo*-1,2,3,5,6,10b-*hexahydropyrazolo*[1,5-c]*quinazoline*-3-*thiocarboxanilide* (20).—The tetrahydro-thione (12) (3 g) was heated with phenyl isothiocyanate (2 ml) in dimethylformamide (10 ml) on a steam-bath for ½ h and left at room temperature overnight. The solution was diluted with hot ethanol (100 ml) and cooled. The product which crystallised was collected, washed with ethanol, and dried to give the *thioanilide* (5.2 g) as needles, m.p. 187—188°. A sample recrystallised from dimethylformamide–ethanol had m.p. 187—188° (Found: C, 60.0; H, 4.7; N, 16.3. $C_{17}H_{16}N_4S_2$ requires C, 60.0; H, 4.7; N, 16.5%), $\nu_{max.}$ (Nujol) 3 200 and 3 100 cm^{-1} (NH). Similarly prepared from allyl isothiocyanate was N-*allyl*-5-*thioxo*-1,2,3,5,6,10b-*hexahydropyrazolo*[1,5-c]*quinazoline*-3-*thiocarboxamide* (19) (73%) as needles (Found: C, 55.3; H, 5.3; N, 18.4. $C_{14}H_{16}N_4S_2$ requires C, 55.3; H, 5.3; N, 18.4%).

Reaction of the Thioanilide (20) *with Iodine*.—The thioanilide (1.0 g) was dissolved in dimethylformamide (10 ml) and heated with sodium hydroxide (0.25 g), water (2 ml), and iodine (0.75 g) at 90 °C overnight. The solution was diluted with water and extracted with chloroform. The extract was dried and evaporated to a yellow solid. Crystallisation of the solid from ethanol gave yellow needles, decomp. *ca.* 230°. The product was dissolved in chloroform and chromatographed on silica. Elution with 1 : 1 ether–chloroform and evaporation gave a solid which was dissolved in the minimum volume of chloroform. Dilution with ether precipitated compound (23) or (24) as micro-needles (decomp. *ca.* 230°) (Found: C, 66.6; H, 4.7; N, 18.0. Calc. for $C_{17}H_{14}N_4S$: C, 66.7; H, 4.6; N, 13.3%), τ ($CDCl_3$) 2.4—3.0 (9 H, m, aromatic), 4.93 (1 H, 4-line pattern, 10b-H), 5.77 and 6.28 (2 H, 2 × 8-line pattern, 2-H_2), and 7.7 (2 H, m, 1-H_2), *m/e* 306 (M^+), 305 (M − H), 278 (M − C_2H_4), 277 (278 − H).

5-*Ethylthio*-1,10b-*dihydropyrazolo*[1,5-c]*quinazoline* (9).—The dihydro-thione (6) (10 g) was refluxed with ethyl iodide (9 ml) and sodium hydrogen carbonate (6 g) in acetone (120 ml) and water (60 ml) for 2 h. The acetone was evaporated off and the residue was extracted with ether. The extract was dried and evaporated to a yellow oil. Crystallisation from light petroleum (b.p. 60—80°) (carbon) gave the *ethylthio-derivative* (7.6 g) as square prisms, m.p. 67—68° (Found: C, 62.5; H, 5.8; N, 17.8. $C_{12}H_{13}N_3S$ requires C, 62.3; H, 5.6; N, 18.2%), τ ($CDCl_3$) 2.7—3.3 (5 H, m, aromatic + CH=N), 5.19 (1 H, dd, *J* 11 and 14 Hz, angular CH), 6.4—7.4 (4 H, m, 2-H_2 + S·CH_2), and 8.64 (3 H, t, *J* 7 Hz, CH_3). Addition of ethereal hydrogen chloride to a solution of the product in acetone gave a hydrochloride, m.p. 175°.

5-*Benzylthio*-1,10b-*dihydropyrazolo*[1,5-c]*quinazoline Hydrochloride* (10).—The dihydro-thione (6) (10 g) was refluxed with benzyl chloride (7 ml) in ethanol (500 ml) for 2 h. The filtered solution was evaporated to a yellow oil, which was treated with acetone (250 ml). The product (12.8 g; m.p. 168—170°) which crystallised was collected, washed with acetone, and dried. A sample was crystallised from acetonitrile to give the *benzylthio-derivative* as prisms, m.p. 168—170° (Found: C, 61.8; H, 4.9; N, 12.6. $C_{17}H_{16}ClN_3S$ requires C, 61.9; H, 4.9; N, 12.7%).

5-*Phenacylthio*-1,10b-*dihydropyrazolo*[1,5-c]*quinazoline Hydrobromide* (11).—The dihydro-thione (6) (4.0 g) was dissolved in hot acetone and the filtered solution was refluxed with phenacyl bromide (4.1 g) for 2 h. The product which crystallised overnight (at room temperature) was collected, washed with acetone, and dried to give the *phenacylthio-derivative* (5.7 g) as rectangular micro-prisms, m.p. 147—149° (Found: C, 53.9; H, 4.1; N, 10.3. $C_{18}H_{16}BrN_3OS$ requires C, 53.7; H, 4.0; N, 10.4%), $\nu_{max.}$ (Nujol) 1 690 cm^{-1} (phenacyl CO).

1,2,3,4-*Tetrahydro*-2-*thioxoquinazolin*-4-*ylacetic Acid* (25).—The dihydro-thione (6) (80 g) was heated on a steam-bath with aqueous sodium hydroxide [60 ml; 100° Twd (≡*d* 1.5)], water (340 ml), and ethanol (120 ml) for 4 h. The bulk of the ethanol was evaporated off and the solution was brought to pH 8—9 with solid carbon dioxide, filtered (carbon), and acidified to pH 1 with hydrochloric acid. A pale yellow gum precipitated which solidified. The solid was collected, ground in a mortar, washed with water, and crystallised from aqueous dimethylformamide to give the *quinazolinylacetic acid* (62—68 g) as almost colourless blades, m.p. 222—233° (decomp., variable). A sample reprecipitated from aqueous sodium hydrogen carbonate with hydrochloric acid and crystallised from water formed blades, m.p. 222—233° (decomp., variable) (Found: C, 53.7; H, 4.6; N, 12.9. $C_{10}H_{10}N_2O_2S$ requires C, 54.1; H, 4.5; N, 12.6%), $\nu_{max.}$ (Nujol) 3 250, 3 150—2 600br (NH and OH), and 1 730 cm^{-1} (acid CO), τ [$(CD_3)_2SO$] −0.45 (1 H, s, OH, exchanges with D_2O), 1.60br (1 H, d, 3-H, exchanges with D_2O), 2.9—3.4 (4 H, m, aromatic), 5.25 (1 H, dt, *J* 3 and 6 Hz, 4-H, collapses to t, *J* 6 Hz, when 3-H exchanged with D_2O), 7.41 (2 H, d, *J* 6 Hz, CH_2).

2-*Benzylthio*-3,4-*dihydroquinazolin*-4-*ylacetic Acid Hydrochloride* (33).—The thioxo-acid (25) (7 g) was refluxed with benzyl chloride (4 ml) in ethanol (100 ml) for 2 h. If the product crystallised during the reaction it was collected and recrystallised from 2N-hydrochloric acid; otherwise the ethanol was evaporated off, and the oily residue was warmed with concentrated hydrochloric acid (10 ml) until it solidified, and was crystallised from 2N-hydrochloric acid, washed with acetone, and dried to give the *benzylthio-derivative* (8 g) as micro-prisms, m.p. 217—219° (Found: C, 58.1; H, 5.1; N, 8.0. $C_{17}H_{17}ClN_2O_2S$ requires C, 58.5; H, 4.9; N, 8.0%), $\nu_{max.}$ (Nujol) 3 270, 2 500br (NH and OH), and 1 710 cm^{-1} (acid CO), τ [$(CD_3)_2SO$] 2.4—2.9 (9 H, m, 5-, 6-, 7-, and 8-H + Ph), 4.80 (1 H, t, *J* 6 Hz, 4-H), 5.00, 5.31 (2 H, 2d, *J* 13 Hz, S·CH_2), and 7.26 (2 H, d, *J* 6 Hz, CH_2·CO). Similarly prepared by using methyl iodide in methanol was 2-*methylthio*-3,4-*dihydroquinazolin*-4-*ylacetic acid hydroiodide* (32) (67%) as needles, m.p. 243—244° (from water) (Found: C, 36.1; H, 3.6; N, 7.7. $C_{11}H_{13}IN_2O_2S$ requires C, 36.3; H, 3.6; N, 7.7%).

1,2,3,4-*Tetrahydro*-2-*oxoquinazolin*-4-*ylacetic Acid* (27).—(i) The thioxo-acid (25) (28 g) was dissolved in sodium hydroxide solution (50 ml; 100° Twd) and water (1 l). Aqueous hydrogen peroxide (30%; 35 ml) diluted with water (100 ml) was added slowly. The solution was left at room temperature overnight, then acidified with hydrochloric acid. The precipitate was collected, washed with water,

and dried to give the crude *oxoquinazoline* (20 g). A sample crystallised from water formed needles, m.p. 254—255° (Found: C, 58.7; H, 4.9; N, 13.5. $C_{10}H_{10}N_2O_3$ requires C, 58.3; H, 4.9; N, 13.6%), $\nu_{max.}$ (Nujol) 3 300, 3 200, 2 550br (NH and OH), 1 720 (acid CO), and 1 660 cm^{-1} (N·CO·N), τ [$(CD_3)_2SO$] 0.75 (1 H, s, NH), 2.6—3.3 (5 H, m, aromatic + NH), 5.20 (1 H, dt, *J* 3 and 6 Hz, angular CH), and 7.47 (2 H, d, *J* 6 Hz, CH_2·CO_2).

(ii) 3,4-Dihydro-2-methylthioquinazolin-4-ylacetic acid hydroiodide (2.2 g) was heated with sodium hydroxide solution (10 ml; 100° Twd) and water (50 ml) at 90 °C for 2 h. The solution was acidified with hydrochloric acid, and the precipitate was collected and crystallised from water to give the oxoquinazoline (1.3 g), identical with that described above.

1,2,3,4-*Tetrahydro*-6-*methoxy*-2-*oxoquinazolin*-4-*ylacetic Acid* (28).—6,10b-Dihydro-9-methoxypyrazolo[1,5-*c*]quinazoline-5(1*H*)-thione (4 g) was heated with sodium hydroxide (3 ml; 100° Twd), water (14 ml), and ethanol (6 ml) at 90 °C for 4 h. Hydrogen peroxide (30%; 5 ml) and sodium hydroxide (7 ml; 100° Twd) in water (70 ml) were added to the cooled solution, which was then left at room temperature overnight. The solution was adjusted to pH 8—9 with solid carbon dioxide and filtered. The filtrate was acidified with hydrochloric acid and the precipitate was collected, reprecipitated from aqueous sodium hydrogen carbonate, and crystallised from aqueous dimethylformamide to give the *quinazolinylacetic* acid (2.5 g) as needles, m.p. 261—262° (Found: C, 55.8; H, 5.1; N, 11.9. $C_{11}H_{12}N_2O_4$ requires C, 55.9; H, 5.1; N, 11.9%), $\nu_{max.}$ (Nujol) 3 250, 2 500 (NH and OH), 1 710 (acid CO), and 1 655 cm^{-1} (N·CO·N).

2-*Bromo*-3,4-*dihydroquinazolin*-4-*ylacetic Acid Hydrobromide* (30).—1,2,3,4-Tetrahydro-2-thioxoquinazolin-4-ylacetic acid (10 g) was dissolved in hot acetic acid (250 ml) and water (50 ml). The solution was cooled below 40 °C and stirred during dropwise addition of bromine (11 ml) in acetic acid (50 ml). The mixture was stirred on an ice-bath for 15 min and the precipitate was collected, washed with acetic acid, and dried to give the *bromo-quinazoline* (12.5 g) as micro-needles, m.p. 240—241° (Found: C, 34.1; H, 2.9; N, 8.3. $C_{10}H_{10}Br_2N_2O_2$ requires C, 34.3; H, 2.9; N, 8.0%).

2-*Hydrazino*-3,4-*dihydroquinazolin*-4-*ylacetic Acid* (31).—2-Bromo-3,4-dihydroquinazolin-4-ylacetic acid hydrobromide (5 g) was heated at 90 °C with hydrazine hydrate (100%; 5 ml) in water (50 ml) for ½ h and cooled. The product which separated was collected, washed with water, and dried to give the *hydrazinoquinazoline* (2 g, 64%) as rectangular prisms, m.p. 288—289°. A sample recrystallised from water had m.p. 288—289° (Found: C, 54.8; H, 5.6; N, 25.5. $C_{10}H_{12}N_4O_2$ requires C, 54.5; H, 5.5; N, 25.5%). The compound was prepared similarly from 3,4-dihydro-2-methylthioquinazolin-4-ylacetic acid hydroiodide and hydrazine hydrate in 55% yield.

5-*Bromo*-1,10b-*dihydropyrazolo*[1,5-c]*quinazoline Hydrobromide* (35).—The dihydro-thione (6) (4.0 g) was dissolved in hot acetic acid (90 ml) and water (10 ml). The solution was treated with carbon, filtered, and cooled rapidly to 15 °C, giving a fine crystalline precipitate. Bromine (4 ml) in acetic acid (20 ml) was added to the stirred mixture over 1 min. The starting material dissolved and cooling was applied to limit the temperature to <30 °C. The product which crystallised after several minutes was collected and washed with acetic acid and with acetone to give the *bromoquinazoline hydrobromide* (6.0 g) as cream rectangular micro-prisms, m.p. 234—235° (decomp.) (Found: C, 36.2; H, 2.6; N, 12.6. $C_{10}H_9Br_2N_3$ requires C, 36.3; H, 2.7; N, 12.7%).

6,10b-*Dihydropyrazolo*[1,5-c]*quinazolin*-5(1H)-*one* (36).—5-Bromo-1,10b-dihydropyrazolo[1,5-*c*]quinazoline hydrobromide (10 g) was heated with 2N-hydrochloric acid (60 ml) at 90 °C for 1½ h. The solution was filtered and neutralised with sodium carbonate. The product which separated slowly was collected, washed with water, and dried to give the *pyrazoloquinazolinone* (4.7 g; m.p. 190—194°). A sample recrystallised from water formed prisms, m.p. 191—193° (Found: C, 63.9; H, 4.8; N, 22.6. $C_{10}H_9N_3O$ requires C, 64.2; H, 4.8; N, 22.5%), $\nu_{max.}$ (Nujol) 3 250—3 100 (NH) and 1 690br cm^{-1} (CO), τ [$(CD_3)_2SO$] 0.37 (1 H, s, NH), 2.5—3.2 (5 H, m, aromatic + CH=N), 4.92 (1 H, dd, *J* 10 and 13 Hz, angular CH), and 6.1—7.3 (2 H, m, CH_2), *m/e* 187 (M^+), 186 (M − H), 168 (186 − H_2O), 160 (M − HCN), and 159 (186 − HCN).

6-(3,4-*Dichlorobenzyl*)-6,10b-*dihydropyrazolo*[1,5-c]*quinazolin*-5(1H)-*one* (38).—6,10b-Dihydropyrazolo[1,5-c]quinazolin-5(1H)-one (7 g) in dry dimethylformamide (50 ml) was stirred with sodium hydride (2.4 g; 50% dispersion) added in portions at room temperature. After 10 min, 3,4-dichlorobenzyl chloride (9.0 g) was added dropwise below 50 °C, then the mixture was heated at 90 °C for ½ h. The mixture was cooled and diluted with water (400 ml), and the gummy precipitate was collected after several hours. The precipitate was dissolved in chloroform and washed with aqueous sodium hydrogen carbonate. The organic phase was dried and evaporated to a brown oil. Crystallisation of the oil from toluene (× 2) gave the 3,4-*dichlorobenzyl derivative* (9.5 g; m.p. 168—172°). Crystallisation of a sample from ethanol gave needles, m.p. 170—172° (Found: C, 58.7; H, 3.8; N, 12.1. $C_{17}H_{13}Cl_2N_3O$ requires C, 59.0; H, 3.8; N, 12.1%), $\nu_{max.}$ (Nujol) 1 680 cm^{-1} (CO), τ ($CDCl_3$) 2.4—3.4 (8 H, m, aromatic and CH=N), 4.83 (2 H, 2d, *J* 17 Hz, benzylic CH_2), 4.88 (1 H, dd, *J* 10 and 13 Hz, angular CH), and 6.1—7.2 (2 H, 16 line pattern, 1-H_2). Similarly prepared from benzyl chloride was 6-*benzyl*-6,10b-*dihydropyrazolo*[1,5-c]*quinazolin*-5(1H)-*one* (37) as needles, m.p. 151—153° (from ethanol) (Found: C, 73.5; H, 5.4; N, 15.1. $C_{17}H_{15}N_3O$ requires C, 73.6; H, 5.4; N, 15.2%), $\nu_{max.}$ (Nujol) 1 680 cm^{-1} (CO), τ ($CDCl_3$) 2.6—3.3 (10 H, m, aromatic and CH=N), 4.75 (2 H, s, benzylic CH_2), 4.9 (1 H, dd, *J* 10 and 13 Hz, angular CH), and 6.1—7.2 (2 H, 16 lines, 1-H_2).

5-*Carboxymethyl*-5,10-*dihydro*-3-*methylthiazolo*[2,3-b]-*quinazolin*-4-*ylium Chloride* (40).—1,2,3,4-Tetrahydro-2-thioxoquinazolin-4-ylacetic acid (28 g) was dissolved in hot acetone (2 l) and the filtered solution was refluxed with chloroacetone (22.4 ml) for 6 h. Next day the product was collected, washed with acetone, and dried to give the *thiazoloquinazolinylium chloride* (30—34 g), m.p. 268—270° (Buchi; bulk crystals) or 252—255° (Kofler; powdered crystals) (decomp.). A sample crystallised from dilute hydrochloric acid formed blades, m.p. 270—272° (Buchi) (Found: C, 52.6; H, 4.5; N, 9.1. $C_{13}H_{13}ClN_2O_2S$ requires C, 52.6; H, 4.4; N, 9.4%), $\nu_{max.}$ 2 800br (OH) and 1 720 cm^{-1} (acid CO), τ [$(CD_3)_2SO$] 2.4—2.9 (4 H, m, 6-, 7-, 8-, and 9-H), 2.93 (1 H, q, *J* 1 Hz, 2-H), 3.83 (1 H, t, *J* 4.5 Hz, 5-H), 7.07 (2 H, d, *J* 4.5 Hz, CH_2·CO), and 7.52 (3 H, d, *J* 1 Hz, Me). Similarly prepared from 4-bromophenacyl bromide (1 equiv.) was 2-(4-*bromophenacylthio*)-3,4-*dihydroquinazolin*-4-*ylacetic acid hydrobromide* (34) (95%) as square prisms, m.p. 225—226° (decomp.) (Found: C, 43.7; H, 3.3; N, 5.4. $C_{18}H_{16}Br_2N_2O_3S$ requires C, 43.2; H, 3.2; N, 5.6%),

$\nu_{max.}$ (Nujol) 3 300, 2 500 (NH and OH), 1 710 (acid CO), and 1 680 cm^{-1} (phenacyl CO).

5-Carboxymethyl-2,3-dihydro-5H-thiazolo[2,3-b]*quinazoline Hydrobromide* (41).—1,2,3,4-Tetrahydro-2-thioxoquinazolin-4-ylacetic acid (19.8 g) was refluxed with anhydrous sodium carbonate (4.8 g) and 1,2-dibromoethane (20 ml) in ethanol (150 ml) for 3 days. The ethanol was evaporated off and the residual yellow oil was washed with ether and dissolved in concentrated hydrobromic acid (20 ml). The product, which crystallised slowly from the solution, was collected and recrystallised from the minimum volume of water to give the *thiazoloquinazoline* (8.5 g) as prisms, m.p. 266—268° (Found: C, 43.8; H, 4.0; N, 8.3. $C_{12}H_{13}BrN_2O_2S$ requires C, 43.8; H, 4.0; N, 8.5%), $\nu_{max.}$ (Nujol) 3 200—2 500br (OH) and 1 725 cm^{-1} (acid CO), τ [$(CD_3)_2SO$] 2.4—2.9 (4 H, m, aromatic), 4.63 (1 H, dd ≈ t, J 6 and 7 Hz, 5-H), 5.51 and 6.25 (4 H, 2m ≈ 2t, J *ca.* 8 Hz, $S{\cdot}CH_2{\cdot}CH_2{\cdot}N$), and 7.05 (2 H, 2d, J 6 and 7 Hz, $CH_2{\cdot}CO_2$).

2,3-Dihydro-3-oxo-5H-thiazolo[2,3-b]*quinazolin-5-ylacetic Acid* (42).—1,2,3,4-Tetrahydro-2-thioxoquinazolin-4-ylacetic acid (11 g) was heated with chloroacetic acid (4.75 g) and sodium hydrogen carbonate (4.5 g) in water (250 ml) at 90 °C overnight. The mixture was refluxed with sufficient dimethylformamide (100 ml) to form a solution, filtered (carbon), and cooled. The product (7.3 g) which crystallised was collected and a sample was recrystallised from water to give the *carboxylic acid* as rectangular needles, m.p. 203—204° (Found: C, 54.6; H, 3.8; N, 10.7. $C_{12}H_{10}N_2O_3S$ requires C, 55.0; H, 3.8; N, 10.7%), $\nu_{max.}$ (Nujol) 3 200w,br (OH) and 1 680br cm^{-1} (CO), τ [$(CD_3)_2SO$] −0.2 (1 H, s, CO_2H), 2.6—3.3 (4 H, m, aromatic), 4.37 (1 H, t, J 7 Hz, angular CH), 5.81 (2 H, s, $CO{\cdot}CH_2{\cdot}S$), and 7.10 (2 H, d, J 7 Hz, $CH_2{\cdot}CO_2$).

1,5-Dihydro-1,2,4-triazolo[5,4-b]*quinazolin-5-ylacetic Acid* (58).—2-Hydrazino-3,4-dihydroquinazolin-4-ylacetic acid (1.0 g) was refluxed in formic acid (98—100%; 10 ml) overnight. The excess of formic acid was distilled off and the residual gum was triturated with aqueous acetone. The solid obtained was crystallised from water to give the *acid* (0.6 g) as needles, m.p. 242—243° (Found: C, 57.5; H, 4.4; N, 24.3. $C_{11}H_{10}N_4O_2$ requires C, 57.4; H, 4.3; N, 24.3%), $\nu_{max.}$ (Nujol) 3 200—2 400br (OH and NH) and 1 700 cm^{-1} (CO), τ [$(CD_3)_2SO$] 0.2br (1 H, s, NH), 1.71 (1 H, s, 3-H), 2.5—3.3 (4 H, m, 6-, 7-, 8-, and 9-H), 4.09 (1 H, t, J 6 Hz 5-H), and 7.05 (2 H, d, J 6 Hz, $CH_2{\cdot}CO_2$).

Methyl 3-Methyl-5H-thiazolo[2,3-b]*quinazolin-5-ylacetate* (43).— 5-Carboxymethyl-5,10-dihydro-3-methylthiazolo-[2,3-*b*]quinazolin-4-ylium chloride (14 g) was suspended in methanol (140 ml) and stirred on an ice-bath during cautious dropwise addition of thionyl chloride (10 ml). The mixture was stirred at room temperature overnight and the bulk of the methanol was evaporated off. The residue was treated with an excess of aqueous sodium hydrogen carbonate and extracted with chloroform. The extract was dried and evaporated to a pale yellow oil (15 g) which crystallised. Recrystallisation from cyclohexane gave the *methyl ester* as flakes, m.p. 79—80° (Found: C, 61.1; H, 4.9; N, 10.4. $C_{14}H_{14}N_2O_2S$ requires C, 61.3; H, 5.1; N, 10.2%), $\nu_{max.}$ (Nujol) 1 735 cm^{-1} (ester CO), τ [$(CD_3)_2SO$] 2.6—3.2 (4 H, m, aromatic), 4.26 (1 H, q, J < 2 Hz, 2-H), 4.44 (1 H, 4 lines, H_X of ABX system, $J_{AX,BX}$ 4 and 8 Hz, 5-H), 6.42 (3 H, s, CO_2Me), 7.21 and 7.51 (2 H, 8 lines, H_AH_B of ABX system, $J_{AX,BX}$ 4 and 8, J_{AB} 15 Hz, $CH_2{\cdot}CO_2$). Similarly were prepared: *methyl 2,3-dihydro-5H-thiazolo*[2,3-b]*quinazolin-5-ylacetate* (44) (90% crude yield) as needles, m.p. 74—75° (from cyclohexane) (Found: C, 59.6; H, 5.5; N, 10.5. $C_{13}H_{14}N_2O_2S$ requires C, 59.5; H, 5.3; N, 10.7%), $\nu_{max.}$ (Nujol) 1 735 cm^{-1} (ester CO), τ ($CDCl_3$) 2.6—3.4 (4 H, m, aromatic), 4.82 (1 H, t, J 7 Hz, 5-H), 5.7—6.8 (4 H, m, 2- and 3-H_2), 6.28 (3 H, s, CO_2Me), and 7.26 (2 H, 2d, J 7 Hz, $CH_2{\cdot}CO_2$); *methyl 1,2,3,4-tetrahydro-2-oxoquinazolin-4-ylacetate* (45) (90%) as needles, m.p. 154—156° (from toluene) (Found: C, 59.9; H, 5.4; N, 12.5. $C_{11}H_{12}N_2O_3$ requires C, 60.0; H, 5.5; N, 12.7%), $\nu_{max.}$ (Nujol) 3 250, 3 150 (NH), 1 730 (ester CO), and 1 680 cm^{-1} (N·CO·N); *methyl 3,4-dihydro-2-methylthioquinazolin-4-ylacetate* (46) (60%) as needles, m.p. 122—123° (from toluene–cyclohexane) (Found: C, 58.1; H, 5.9; N, 11.1. $C_{12}H_{14}N_2O_2S$ requires C, 57.6; H, 5.6; N, 11.2%), $\nu_{max.}$ (Nujol) 3 300 (NH) and 1 725 cm^{-1} (CO_2Me).

2,3-Dihydro-5-(2-hydroxy-2,2-diphenylethyl)-5H-thiazolo-[2,3-b]*quinazoline* (48).—The thiazoloquinazolinylacetate (44) (3 g) in dry tetrahydrofuran (30 ml) was added dropwise to a stirred solution of phenylmagnesium bromide [from bromobenzene (5.2 ml) and magnesium (1.2 g) in tetrahydrofuran (30 ml)] under nitrogen on a water-bath at 35 °C. The solution was stirred overnight and then treated with an excess of aqueous ammonium chloride and extracted with ether. The extract was dried and evaporated to a yellow oil which had solidified after several weeks. Crystallisation from ethanol gave the *alcohol* (2.3 g) as almost colourless blades, m.p. 161—163° (Found: C, 74.7; H, 5.8; N, 7.2. $C_{24}H_{22}N_2OS$ requires C, 74.6; H, 5.7; N, 7.3%), $\nu_{max.}$ (Nujol) 3 300 cm^{-1} (OH), τ ($CDCl_3$) 2.2—3.6 (14 H, m, aromatic), 5.37 (1 H, dd, J 10 and 3 Hz, 5-H), 6.0—6.5 and 6.6—7.0 (4 H, 2 m, 2- and 3-H_2), 7.1—7.6 (2 H, 8 lines, H_AH_B of ABX system, J_{AB} 14, J_{AX} 10, J_{BX} 3 Hz, $CH_2{\cdot}CPh_2{\cdot}OH$).

3-Methyl-5H-thiazolo[2,3-b]*quinazolin-5-ylacetohydrazide* (47).—The ester (43) (5 g) was refluxed with hydrazine hydrate (3 ml) in methanol (20 ml) for 2 h. The solvent was evaporated off and the residue was washed with ether and a small volume of water and crystallised from water to give the *hydrazide* (4.3 g) as prisms, m.p. 201—203° (Found: C, 56.9; H, 5.0; N, 20.6. $C_{13}H_{14}N_{14}OS$ requires C, 56.9; H, 5.1; N, 20.4%), $\nu_{max.}$ 3 200 (NH) and 1 680 cm^{-1} (CO), τ [$(CD_3)_2SO$] 1.0 (1 H, s, CO·NH), 2.7—3.2 (4 H, m, aromatic), 3.90 (1 H, q, J < 2 Hz, 2-H), 4.40 (1 H, dd, J 6 and 8 Hz, 5-H), 5.7—6.8br (2 H, s, NH_2), 7.65 (2 H, 4 lines, $H_{A,B}$ of ABX system, J_{AX} 6, J_{BX} 8 Hz, $CH_2{\cdot}CO$), and 7.84 (3 H, d, J < 2 Hz, Me).

1-(4-Methylthiazol-2-yl)quinolin-2(1H)-one (49).—The ester (43) (7 g) was heated with *N*-methylpiperazine (7 ml) at 90 °C for 3 days. The *N*-methylpiperazine was evaporated off and the residue was chromatographed on silica (MFC; 250 ml) deactivated with water (25 ml). Elution with diethyl ether, evaporation, and crystallisation of the residue from cyclohexane gave the *N-thiazolylquinolone* (1.6 g) as needles, m.p. 128—129° (Found: C, 64.6; H, 4.2; N, 11.2. $C_{13}H_{10}N_2OS$ requires C, 64.5; H, 4.2; N, 11.6%), $\nu_{max.}$ (Nujol) 1 670 cm^{-1} (quinolone CO), τ ($CDCl_3$) 2.20 (1 H, d, J 9.5 Hz, quinolone 4-H), 2.3—3.3 (4 H, m, quinolone 5-, 6-, 7-, and 8-H), 2.81 (1 H, q, J < 2 Hz, thiazole 5-H), 3.30 (1 H, d, J 9.5 Hz, quinolone 3-H), and 7.46 (3 H, d, J < 2 Hz, Me), *m/e* 242 (M^+), 214w (M − CO), and 201 (M − CH_3CN). The compound (49) was similarly obtained with piperidine as the base.

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