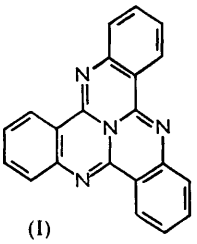
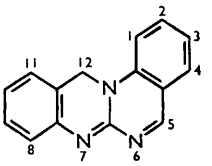
293. *Cyclic Amidines. Part VIII.* Derivatives of* 12H-6 : 7 : 12a-*Triazabenz*[a]*anthracene and* 5a*H*-5 : 6 : 11a-*Triazanaphthacene.*

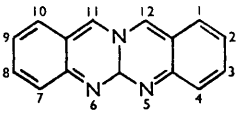
By K. Butler and M. W. Partridge.

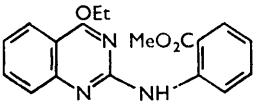
The formation of derivatives of the triazabenz[*a*]anthracene (II) and the triazanaphthacene (III) and their behaviour on alkylation are described. Interconversions of these ring systems were effected with certain derivatives.

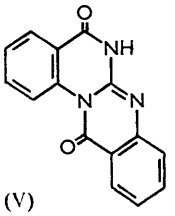
The unusual carcinogenic properties of tri*cyclo*quinazoline [1] (I) prompted an investigation of triazatetracyclic compounds, for which there are six possible structures resulting from the fusion of two quinazoline rings and having one nitrogen atom common to the two rings. The work now reported relates to derivatives of 12*H*-6 : 7 : 12a-triazabenz[*a*]anthracene (II) and 5a*H*-5 : 6 : 11a-triazanaphthacene (III).

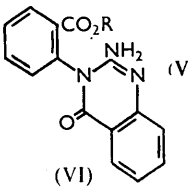

(I)

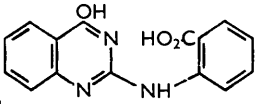

(II)

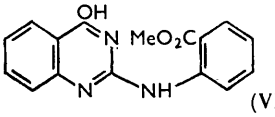

(III)

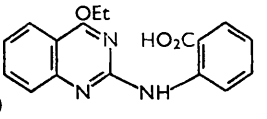

(IV)

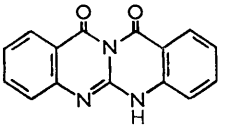

(V)


(VI)


(VII)


(VIII)


(IX)


(X)

2-Chloro-4-ethoxyquinazoline and methyl anthranilate in ethanol yielded 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV). This compound, on being boiled with aqueous hydrochloric acid or with potassium hydroxide, afforded, according to the conditions, 5 : 6-dihydro-5 : 12-dioxo-12*H*-6 : 7 : 12a-triazabenz[*a*]anthracene (V) and/or 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) and not, as might have been expected, 2-*o*-carboxyanilino-4-hydroxyquinazoline (VII). With ethanolic potassium hydroxide, the products were 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (VIII), also synthesised directly from 2-chloro-4-hydroxyquinazoline and methyl anthranilate, and 2-*o*-carboxyanilino-4-ethoxyquinazoline (IX), otherwise obtained unequivocally by the treatment of anthranilic acid with 2-chloro-4-ethoxyquinazoline.

The structure assigned to the triazabenzanthracene (V) followed from its formation, in high yield, by direct cyclisation of 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H).

Evidence for the constitution of 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) was provided by a comparison of its methyl ester (VI; R = Me) with the unequivocally synthesised isomer (VIII); they were different (Table 1). The ester (VIII) on being heated furnished the two possible cyclisation products, namely the

* Part VII, *J.*, 1958, 2086.

[1] Baldwin, Butler, Cooper, Partridge, and Cunningham, *Nature*, 1958, **181**, 838.

triazabenzanthracene (V), and its isomer, 11 : 12-dihydro-11 : 12-dioxo-5*H*-5 : 6 : 11a-triazanaphthacene (X), whereas the ester (VI; R = Me) gave, as expected, only the triazabenzanthracene (V). Furthermore, 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) formed a well-defined hydrochloride, whereas the hydrochloride of the isomer (VII), obtained from 2-chloro-4-hydroxyquinazoline and anthranilic acid, was unstable, and when heated in water cyclised to the triazabenzanthracene (V).

TABLE 1. *Ultraviolet absorption spectra in ethanol.*

Compound	Maxima (λ, mμ) and ε (in parentheses)					
(VI; R = Me)	218 (90,000)	290 (18,800)	330 (16,700)		382 (14,800)	
(VIII)	281 (17,500)	288 (18,000)	326 (14,100)			
(V)	235 (43,000)	283 (20,800)		320 (4,100)		335 (4,400)
(XV; R = Me)	236 (46,000)	283 (20,300)		325 (5,600)		
(XV; R = Et)	236 (51,000)	285 (21,800)		320 (5,960)		[335] 4,400
(XV; R = Pr^n)	236 (60,200)	284 (25,000)		320 (6,200)		
(XV; R = Bu^n)	235 (35,000)	285 (19,800)		320 (9,740)		
(XV; R = *n*-C_5H_{11})	234 (54,000)	282 (23,000)		320 (5,700)		
(XV; R = *n*-C_6H_{13})	235 (50,000)	282 (21,800)		320 (5,500)		
(XV; R = CH_2Ph)	236 (57,000)	282 (24,900)		320 (5,700)		
(XIV; R = Me)	235 (41,000)	283 (18,000)		320 (4,660)	[335] (4,350)	
(XIV; R = Et)	236 (55,000)	282 (24,000)		320 (5,300)	335 (4,800)	
(XVI; R = R′ = Me)	232 (24,300)	250 (16,600)	262 (14,400)	282 (21,600)	290 (28,000)	342 (15,500)
(XVI; R = R′ = Et)	[232] (24,000)	251 (15,800)	[263] (14,200)	282 (20,800)	291 (26,600)	342 (15,100)
(XVI; R = Me, R′ = Et)	[232] (24,000)	[251] (15,600)	[262] (14,000)	282 (21,800)	291 (26,600)	342 (15,900)

Data in [square] brackets refer to points of inflexion.

The ready cyclisation of this acid (VII) accounted for its absence from the products of treatment of 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV) with acids and alkalis. This property also implied that conversion of the ester (IV) into the triazabenzanthracene (V) in boiling aqueous acid involved the intermediate formation of a salt of the hydroxy-acid (VII). A similar cyclisation of the hydroxy-ester (VIII) to the triazabenzanthracene (V) was readily effected under the same conditions.

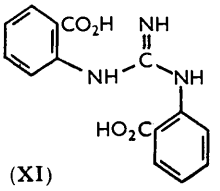
Formation of 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) from 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV) is probably an indirect process which included, in addition to the steps described above, a two-step degradation of the triazabenzanthracene (V) *via* the guanidine derivative (XI). The necessary fission of both heterocyclic rings was demonstrated by production of *NN*′-diphenylguanidine (XII) when a solution of the triazabenzanthracene (V) in two equivalents of sodium hydroxide was evaporated to dryness and heated with copper bronze in quinoline. The direct formation of the aminoquinazoline (VI; R = H) by fission of one ring of the triazabenzanthracene (V) is unlikely, since with only one equivalent of alkali, half of the tetracyclic compound remained undissolved; addition of hydrochloric acid to the alkaline filtrate afforded the hydrochloride of the aminoquinazoline (VI; R = H), formed, it is suggested, by cyclisation of the guanidine derivative (XI).

Heating of 2-chloro-4-ethoxyquinazoline and methyl anthranilate in the absence of solvent at 112° yielded ethyl chloride and a mixture of the triazabenzanthracene (V) and 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (VIII); before the onset of the exothermic phase of this reaction, the hydrochloride of the ester (IV) was isolable. This hydrochloride at 130° gave the same two products. Conversion of 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (VIII) into the mixture of the tetracyclic compounds (V) and (X), previously mentioned, occurred at 250°.

The triazabenzanthracene (V) and the triazanaphthacene (X) were interconverted when a solution of either in concentrated sulphuric acid was poured into methanol. In addition,

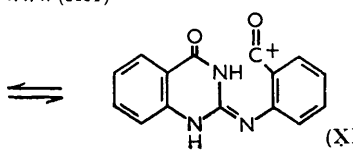
the methyl ester (VIII) was formed from both compounds. Accordingly, it is suggested that in sulphuric acid the cation (XIII) is in equilibrium with the cyclic compounds (V) and (X) or their cations.

The formation of the methyl ester (VIII) by reaction of the acylium ion (XIII) with methanol is then accounted for. Partial isomerisation to the linear system (X) was effected when a solution of the triazabenzanthracene (V) in concentrated sulphuric acid was poured into water. The linear compound (X) was slowly but almost quantitatively converted into the angular compound (V) when boiled in 2-ethoxyethanol.



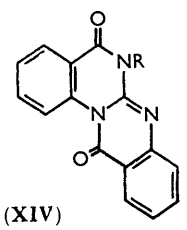
(XI)

NHPh·C(:NH)·NHPh (XII)

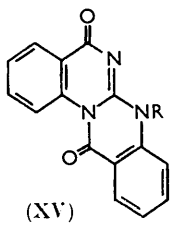


(V) (XIII) (X)

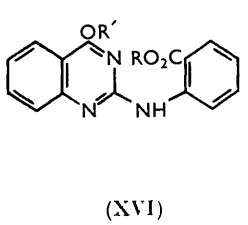
Methylation of the triazabenzanthracene (V) with methyl sulphate and sodium hydroxide afforded a 6- or 7-methyl derivative (XIV or XV; R = Me) which was stable to 48% hydrobromic acid and had an ultraviolet absorption spectrum very similar to the non-methylated compound (see Table 1). The same *N*-methyl derivative was formed when 2-*o*-methoxycarbonylanilino- (XVI; R = R′ = Me) or 2-*o*-carboxyanilino-4-methoxyquinazoline (XVI; R = H, R′ = Me) was heated. The observation that, under similar conditions, 2-*o*-methoxycarbonylanilino-4-*iso*propoxyquinazoline (XVI; R = Me, R′ = Pr^i) gave an *iso*propyl ether which was readily hydrolysed to the triazabenzanthracene (V) suggested that the *N*-methyl derivative, produced by thermal cyclisation, resulted from a rearrangement of an initially formed *O*-methyl ether. The triazabenzanthracene (V) could not be methylated with methyl iodide in acetone.



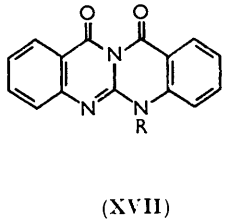
(XIV)



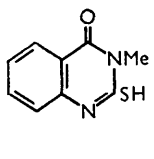
(XV)



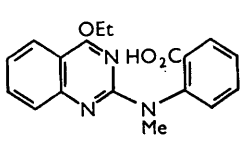
(XVI)



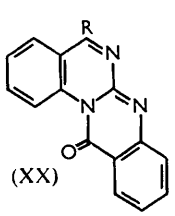
(XVII)



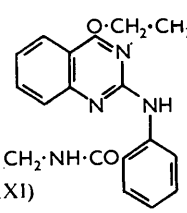
(XVIII)



(XIX)



(XX)



(XXI)

A direct synthesis of the 7-methyltriazabenzanthracene (XV; R = Me) may be ambiguous, because the possibility of its isomerisation to a methylated triazanaphthacene (XVII; R = Me) cannot be excluded. The 6-methyl isomer (XIV; R = Me) cannot undergo such transformation into a methyltriazanaphthacene without intermediate demethylation or other equally improbable fissions of C–N bonds. This compound was synthesised and shown to be different from the original methylation product of the triazabenzanthracene (V), although, as expected, the ultraviolet absorption spectra of the two compounds were very similar (Table 1). Anthranilic acid and methyl *iso*thiocyanate furnished 3 : 4-dihydro-2-mercapto-3-methyl-4-oxoquinazoline (XVIII) which with methyl

iodide yielded a waxy methyl derivative. This evolved methanethiol in moist air and did not give satisfactory analytical results, but, when heated with methyl anthranilate, it yielded the 6-methyl derivative (XIV; R = Me).

Several projected syntheses of the 6-methyltriazabenzanthracene (XIV; R = Me) were unsuccessful because of the inaccessibility of starting materials. Thus 2-chloro-3 : 4-dihydro-3-methyl-4-oxoquinazoline could not be prepared by treatment of the corresponding 2-hydroxyquinazoline with phosphorus chlorides or thionyl chloride, by thermal rearrangement of 2-chloro-4-methoxyquinazoline, or by methylation of 2-chloro-4-hydroxyquinazoline. 2-Ethoxy-3 : 4-dihydro-3-methyl-4-oxoquinazoline, on being heated with methyl anthranilate, furnished only 3 : 4-dihydro-2-hydroxy-3-methyl-4-oxoquinazoline.

The triazanaphthacene (X) with methyl iodide and potassium carbonate in acetone readily gave a methyl derivative which was not demethylated by hydrobromic acid. That alkylation occurred at position 5 (XVII; R = Me) was shown by direct synthesis of the same compound by cyclisation of the hydrochloride of 2-*o*-carboxy-*N*-methylanilino-4-ethoxyquinazoline (XIX), itself prepared by interaction of 2-chloro-4-ethoxyquinazoline and *N*-methylanthranilic acid.

On methylation with methyl sulphate and sodium hydroxide, the triazanaphthacene (X) yielded the 5-methyl derivative (XVII; R = Me), the 7-methyltriazabenzanthracene (XV; R = Me), and the triazabenzanthracene (V). These isomerisations are most simply explained by assuming the intermediate formation of the guanidine (XI). Support for this was provided by the production of the hydrochloride of 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) when the triazanaphthacene (X) was dissolved in two equivalents of sodium hydroxide and a large excess of hydrochloric acid was added. Because of the behaviour of the triazabenzanthracene (V) towards sodium hydroxide, it is probable that the guanidine (XI) was involved in the analogous methylation of the triazabenzanthracene (V) with methyl sulphate.

Ethylation of the triazanaphthacene (X) in acetone with ethyl iodide and potassium carbonate occurred very slowly. The product was identical with one of two isomers formed by thermal cyclisation of 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV), and its light-absorption characters (Table 1) were so similar to those of the 7-methyltriazabenzanthracene (XV; R = Me), that it was considered to be the corresponding 7-ethyl derivative (XV; R = Et). Moreover, isomerisation of the product of direct ethylation of the triazanaphthacene (XVII; R = Et) is likely to produce only the 7-ethyltriazabenzanthracene (XV; R = Et). The similarity of the absorption spectrum of the second ethyl derivative (Table 1) formed by thermal cyclisation indicated its structure to be (XIV; R = Et).

Alkylation of the triazanaphthacene (X) with propyl, butyl, pentyl, hexyl, or benzyl halide was also slow; this observation together with the ultraviolet absorption spectra of the products (Table 1) led to the supposition that isomerisation had occurred and that these derivatives had the structures (XV; R = Alk or CH_2Ph). Attempts to alkylate or acylate the triazanaphthacene (X) with ethylene chlorohydrin, acetyl chloride, chloroacetyl chloride, benzoyl chloride, or ethyl chloroformate merely caused rearrangement to the triazabenzanthracene (V).

5-Chloro-12-oxo-12*H*-6 : 7 : 12a-triazabenz[*a*]anthracene (XX; R = Cl) was a readily hydrolysable compound prepared from the 5-oxo-derivative (V) and thionyl chloride. With sodium methoxide it gave 2-*o*-carboxyanilino-4-methoxyquinazoline (XVI; R = H, R′ = Me), the structure of which followed from the identity of its methyl ester (XVI; R = R′ = Me) with a specimen synthesised unequivocally from 2-chloro-4-methoxyquinazoline and methyl anthranilate. With sodium ethoxide, the chloro-compound (XX; R = Cl) gave a compound which had an ultraviolet absorption spectrum closely resembling that of 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV) (see Table 1), and which furnished the triazabenzanthracene (V) when heated with hydrobromic acid. It was considered to be the ester (XVI; R = R′ = Et).

The chloro-compound (XX; R = Cl) with simple aliphatic bases yielded mixtures which were not separated, but with piperidine and with morpholine, crystalline derivatives (XX; R = $C_5H_{10}N$ and C_4H_8ON, respectively) were obtained. Ethanolamine gave a compound, $C_{19}H_{21}O_3N_5$, containing one primary aliphatic amino-group and readily hydrolysable to the triazabenzanthracene (V). Since hydrolysis occurs readily with 4-alkoxyquinazolines, but not with 4-aminoquinazolines, this compound was evidently (XXI).

Experimental

2 : 4-*Dichloroquinazoline.*—The following procedure was more satisfactory than earlier methods.[2] 2 : 4-Dihydroxyquinazoline (20 g.) was heated with phosphoryl chloride (40 ml.) in a bath at 160° for 14 hr., or until the solid had dissolved completely. The hot mixture was poured on crushed ice (500 g.), and the precipitate, after being thoroughly washed with ice-water, was stirred with ether (700 ml.) for 3 hr. The ethereal solution was washed with N-sodium hydroxide and with water, dried ($MgSO_4$), and evaporated (yield, 21 g.), m. p. 116—118°.

4-*Ethoxy*-2-o-*methoxycarbonylanilinoquinazoline* (IV).—2-Chloro-4-ethoxyquinazoline [3] (4 g.) and methyl anthranilate (2·5 g.) in ethanol (30 ml.) were refluxed for 1 hr. The *base* (5·6 g.), precipitated by aqueous sodium carbonate, crystallised as prisms, m. p. 118—119°, from ethanol (Found: N, 13·3. $C_{18}H_{17}O_3N_3$ requires N, 13·0%). Its *picrate* crystallised from benzene as needles, m. p. 198° (decomp.) (Found: C, 52·4; H 4·1; N, 15·3. $C_{24}H_{20}O_{10}N_6$ requires C, 52·2; H, 3·7; N, 15·2%). The *hydrochloride*, precipitated from a benzene solution of the base, crystallised from ethanol; it had m. p. 172—173° (Found: C, 60·1; H, 5·1; N, 11·5. $C_{18}H_{18}O_3N_3Cl$ requires C, 60·1; H, 5·0; N, 11·7%).

Reactions of 4-*Ethoxy*-2-o-*methoxycarbonylanilinoquinazoline.*—(i) The solid which separated when the quinazoline (0·5 g.) in 5N-hydrochloric acid (7·5 ml.) was refluxed for 5 hr. was recrystallised from 2N-hydrochloric acid and gave 2-*amino*-3-o-*carboxyphenyl*-3 : 4-*dihydro*-4-*oxoquinazolinium chloride* (0·5 g.), m. p. 236—238° (Found: C, 56·7; H, 3·9; N, 13·0; Cl, 11·3. $C_{15}H_{12}O_3N_3Cl$ requires C, 56·7; H, 3·8; N, 13·2; Cl, 11·2%).

(ii) With 2N-hydrochloric acid and 30 minutes' heating, the insoluble material, after recrystallisation from 2-ethoxyethanol, gave 5 : 12-*dihydro*-5 : 12-*dioxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (39%), m. p. 254—256° (Found: C, 68·5; H, 3·2; N, 16·0. $C_{15}H_9O_2N_3$ requires C, 68·4; H, 3·5; N, 16·0%).

(iii) The quinazoline (0·5 g.) was boiled with concentrated hydrochloric acid (2 ml.) for 5 min. The triazabenzanthracene (0·1 g.), m. p. and mixed m. p. 255—256°, produced was separated from the hydrochloride of the starting material (0·16 g.) by extraction with 2-ethoxyethanol.

(iv) The solution obtained when the quinazoline (0·5 g.) was boiled for 30 min. with 2N-potassium hydroxide (10 ml.) was neutralised with acetic acid. Extraction of the gelatinous precipitate with 2-ethoxyethanol gave the triazabenzanthracene (0·05 g.), m. p. and mixed m. p. 255—255·5°. The gelatinous, amphoteric material furnished 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazolinium chloride, m. p. and mixed m. p. 236—238°, with concentrated hydrochloric acid.

(v) After 5 minutes' heating, a solid separated from a solution of the quinazoline (0·5 g.) in ethanol (10 ml.) containing potassium hydroxide (0·05 g.). An aqueous extract of the solid at pH 7 furnished 2-o-*carboxyanilino*-4-*ethoxyquinazoline* (0·1 g.), m. p. 200—201°, after recrystallisation from aqueous ethanol (Found: C, 65·6; H, 4·7; N, 13·9. $C_{17}H_{15}O_3N_3$ requires C, 66·0; H, 4·9; N, 13·6%). The water-insoluble fraction yielded on crystallisation from ethanol 4-*hydroxy*-2-o-*methoxycarbonylanilinoquinazoline* (0·05 g.), m. p. 290—294°, after sintering and turning yellow at 200—210° (Found: C, 65·1; H, 4·3; N, 14·1. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%).

4-*Hydroxy*-2-o-*methoxycarbonylanilinoquinazoline* (VIII).—2-Chloro-4-hydroxyquinazoline (2 g.) was heated in ethanol for 2 hr. with methyl anthranilate (1·7 g.). The product (2·6 g.) precipitated by aqueous sodium carbonate crystallised from ethanol as needles, m. p. and mixed m. p. 290—296°, after sintering and turning yellow at 200° and crystallising at 210—215° (Found: C, 65·5; H, 4·4. Calc. for $C_{16}H_{13}O_3N_3$: C, 65·1; H, 4·4%).

[2] Curd, Landquist, and Rose, *J.*, 1947, 775.
[3] Lange, Roush, and Asbeck, *J. Amer. Chem. Soc.*, 1930, **52**, 3696.

2-o-*Carboxyanilino-4-ethoxyquinazoline* (IX).—2-Chloro-4-ethoxyquinazoline (2 g.) and anthranilic acid (1·4 g.) were boiled in ethanol (20 ml.) for 90 min. The sodium salt precipitated when the mixture was poured into aqueous sodium carbonate furnished the free carboxylic acid as yellow prisms (1·2 g.), m. p. and mixed m. p. 200—201°, on crystallisation from aqueous ethanol containing 1% of acetic acid.

2-Amino-3-o-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H).—5 : 6-Dihydro-5 : 12-dioxo-12*H*-6 : 7 : 12a-triazabenz[*a*]anthracene (1 g.) was heated with N-sodium hydroxide (7·7 ml.) for 15 min. Concentrated hydrochloric acid (30 ml.) was added to the filtered liquid at 0°; a solid separated and redissolved. The aminoquinazolinium chloride (0·8 g.) which crystallised slowly was recrystallised from 2N-hydrochloric acid; it had m. p. and mixed m. p. 236—238°.

Decomposition of this hydrochloride with ammonia gave the gelatinous, free amino-acid which with diazomethane in ether, afforded its *methyl ester* (VI; R = Me) (58%) as prisms (from ethanol) m. p. 224—225°, depressed to 195—200° on admixture with the isomeric 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (Found: C, 65·5; H, 4·6; N, 14·2. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%).

5 : 6-*Dihydro-5 : 12-dioxo-*12H-6 : 7 : 12*a-triazabenz*[a]*anthracene* (V).—(i) 2-*o*-Carboxyanilino-4-ethoxyquinazolinium chloride (1 g.), precipitated from a benzene solution of the base by hydrogen chloride, was heated at 130° for 1 hr. Ethyl chloride was evolved and the melt solidified. The triazabenzanthracene (0·58 g., 80%) was obtained as needles, m. p. and mixed m. p. 255—255·5°, by crystallisation of the melt from 2-ethoxyethanol.

(ii) 2-Chloro-4-hydroxyquinazoline (1 g.) and anthranilic acid (0·75 g.) were boiled in ethanol (10 ml.) for 1 hr. The hydrochloride (m. p. above 360°) which separated was unstable and could not be characterised; when boiled in water (10 ml.) for 10 min. it gave the triazabenzanthracene (1·12 g., 78%), m. p. and mixed m. p. 255—256°.

(iii) 2-Amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline, precipitated from a solution of its hydrochloride (4 g.) by ammonia, was dried by azeotropic distillation with benzene and heated at 200° for 4 min. Crystallisation of the product from 2-ethoxyethanol furnished the triazabenzanthracene (3·2 g., 97%), m. p. and mixed m. p. 255—256°.

(iv) The methyl ester of this 2-aminoquinazoline was heated at 255° for 2 hr. Recrystallisation of the resulting melt from 2-ethoxyethanol afforded the triazabenzanthracene in 88% yield.

Cyclisation of 4-Hydroxy-2-o-methoxycarbonylanilinoquinazoline.—(i) This ester (20 g.) on being heated at 255° for 2 hr. afforded yellow crystals which by fractional crystallisation from 2-ethoxyethanol and dimethylformamide were separated into the triazabenzanthracene (9·6 g.), m. p. and mixed m. p. 255—256°, and 11 : 12-*dihydro-*11 : 12-*dioxo-*5H-5 : 6 : 11*a-triazanaphthacene* (X) (3·8 g.), yellow prisms, m. p. 359—362° (Found: C, 68·7; H, 3·3; N, 15·8. $C_{15}H_9O_2N_3$ requires C, 68·4; H, 3·5; N, 16·0%).

(ii) The solid produced when this ester (30 g.) was boiled in 2N-hydrochloric acid (300 ml.) for 2 hr. gave the triazabenzanthracene (23 g., 85%) on crystallisation from 2-ethoxyethanol.

Degradation of the Triazabenzanthracene (V).—(i) A solution of the triazabenzanthracene (12 g.) in boiling 2N-sodium hydroxide (44 ml.) was evaporated to dryness. The residue, mixed with copper bronze (2 g.), was refluxed in quinoline (10 ml.) for 3 hr. After removal of the quinoline in steam, *NN'*-diphenylguanidine (0·77 g.) was collected in ether, recovered and crystallised from ethanol; it had m. p. 146—148° undepressed by an authentic specimen.[4]

(ii) The triazabenzanthracene (1 g.) was boiled for 30 min. with 0·1N-sodium hydroxide (37 ml., 1 equiv.). The alkali-insoluble material (0·48 g.) was unchanged triazabenzanthracene. Addition of hydrochloric acid (*d* 1·18) to the concentrated alkaline filtrate furnished 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazolinium chloride (0·51 g., 42%), m. p. and mixed m. p. 236—238°.

Reaction of 2-Chloro-4-ethoxyquinazoline with Methyl Anthranilate.—2-Chloro-4-ethoxyquinazoline (5 g.) and methyl anthranilate (3·6 g.) were heated at 112°. After the exothermic phase of the reaction and the evolution of ethyl chloride (40 min.), the solid produced gave as an ethanol-soluble fraction 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (1·9 g.), m. p. and mixed m. p. 290—296° after sintering at 210—215°, and, as an ethanol-insoluble fraction, the triazabenzanthracene (V) (2·9 g.), m. p. and mixed m. p. 255—255·5°.

[4] Partridge and Turner, *J. Pharm. Pharmacol.*, 1953, **5**, 103.

From a sample removed from the reaction mixture after 10 minutes' heating, 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazolinium chloride, m. p. and mixed m. p. 172—173°, was isolated. This hydrochloride (2 g.) was heated at 130° for 30 min. Fractionation of the cooled melt with ethanol again furnished 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (0·4 g.) and the triazabenzanthracene (1 g.).

Interconversion of the Triazabenzanthracene (V) *and the Triazanaphthacene* (X).—(i) A solution of the triazabenzanthracene (10 g.) in concentrated sulphuric acid (30 ml.) was kept at 50° for 20 min. and then poured into anhydrous methanol (150 ml.); this gave a white solid which in contact with water turned yellow and on crystallisation from dimethylformamide furnished the triazanaphthacene (3·8 g.), m. p. and mixed m. p. 358—360°. The methanolic mother-liquor was concentrated to a small volume and diluted with water. From the resulting precipitate were obtained: (*a*) an ethanol-soluble fraction, 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (4·3 g.), m. p. and mixed m. p. 290—296° after sintering at 195—200°, and (*b*) an ethanol-insoluble fraction, the triazabenzanthracene (1·6 g.), m. p. and mixed m. p. 255—256°.

(ii) The yellow solid obtained when a solution of the triazabenzanthracene (10 g.) in concentrated sulphuric acid (30 ml.) was poured on crushed ice afforded the triazabenzanthracene (5·5 g.) and, as a fraction insoluble in 2-ethoxyethanol, the triazanaphthacene (2·6 g.).

(iii) The triazanaphthacene (0·5 g.) was treated with concentrated sulphuric acid (5 ml.) as described for the triazabenzanthracene. The products isolated when the solution was poured into methanol were the triazabenzanthracene (0·1 g.), the triazanaphthacene (0·185 g.), and 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (0·2 g.).

(iv) A suspension of the triazanaphthacene (1 g.) in 2-ethoxyethanol (20 ml.) was boiled for 24 hr.; the yellow colour gradually disappeared and the colourless solution deposited the triazabenzanthracene (0·95 g.).

4-*Methoxy*-2-o-*methoxycarbonylanilinoquinazoline* (XVI; R = R′ = Me) was precipitated (1·4 g.) when the solution obtained by refluxing 2-chloro-4-methoxyquinazoline [2] (0·9 g.) and methyl anthranilate (0·6 ml.) in ethanol (10 ml.) was poured into aqueous sodium carbonate; it formed needles, m. p. 128—129°, from ethanol (Found: C, 66·2; H, 4·7; N, 13·8. $C_{17}H_{15}O_3N_3$ requires C, 66·0; H, 4·9; N, 13·6%). Its *picrate*, needles from ethanol, had m. p. 176—178° (Found: N, 15·9. $C_{23}H_{18}O_{10}N_6$ requires N, 15·6%).

5 : 6-*Dihydro*-7-*methyl*-5 : 12-*dioxo*-12H-6 : 7 : 12*a*-*triazabenzanthracene* (XV; R = Me).—(i) The triazabenzanthracene (V) (5 g.) in 5N-sodium hydroxide (20 ml.) was treated with methyl sulphate (3 ml.) during 10 hr. Neutralisation of the reaction mixture gave the 7-*methyl derivative* (1·9 g.), which crystallised from ethanol as needles, m. p. 165—166° (Found: C, 69·2; H, 3·7; N, 15·2. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·2%).

(ii) 4-Methoxy-2-*o*-methoxycarbonylanilinoquinazoline (0·5 g.) was heated at 255° for 2 hr. Crystallisation of the product from ethanol yielded the same 7-methyltriazabenzanthracene (0·72 g.), m. p. and mixed m. p. 165—166°.

(iii) 2-*o*-Carboxyanilino-4-methoxyquinazoline (1·5 g.) when heated at 250° for 6 hr. gave the 7-methyltriazabenzanthracene (0·48 g.), m. p. and mixed m. p. 165—166°, after crystallisation from ethanol.

This compound was recovered after an attempted demethylation with 48% hydrobromic acid.

2-*Chloro*-4-iso*propoxyquinazoline*.—2 : 4-Dichloroquinazoline (20 g.) was heated at 40° for 30 min. with sodium (2·3 g.) in propan-2-ol (100 ml.). The iso*propyl ether* (9·8 g.) crystallised slowly from the oil precipitated by dilution of the mixture with water; it formed lustrous plates, m. p. 47—48°, from aqueous methanol (Found: N, 12·7. $C_{11}H_{11}ON_2Cl$ requires N, 12·6%).

2-o-*Methoxycarbonylanilino*-4-iso*propoxyquinazoline* (XVI; R = Me, R′ = Pr^i).—2-Chloro-4-*iso*propoxyquinazoline (1 g.) and methyl anthranilate (0·6 ml.) were refluxed in ethanol (10 ml.) for 3 hr. The *base* (1·2 g.) precipitated by aqueous sodium carbonate crystallised from aqueous ethanol as needles, m. p. 91—92° (Found: C, 68·0; H, 5·5; N, 12·4. $C_{19}H_{19}O_3N_3$ requires C, 67·6; H, 5·7; N, 12·5%). Its *picrate* (needles from benzene) had m. p. 196—197° (decomp.) (Found: C, 53·1; H, 3·9; N, 14·9. $C_{25}H_{22}O_{10}N_6$ requires C, 53·0; H, 3·9; N, 14·8%).

iso*Propoxy*-12-*oxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene*.—2-*o*-Methoxycarbonylanilino-4-*iso*propoxyquinazoline (4 g.), after being heated at 250° for 5 hr., was extracted with benzene. The benzene-insoluble fraction after recrystallisation from 2-ethoxyethanol yielded the triazabenzanthracene (V) (0·25 g.). An ethereal solution of the benzene-soluble material, by

fractional precipitation with light petroleum and repeated filtration through charcoal and kieselguhr, gave the iso*propyl ether* (0·43 g.) as yellow needles, m. p. 85—88° (Found: C, 70·6; H, 4·9; N, 13·5. $C_{18}H_{15}O_2N_3$ requires C, 70·8; H, 5·0; N, 13·8%).

When boiled with 2N-hydrochloric acid (3 ml.) for 30 min., this ether (0·1 g.) gave the triazabenzanthracene (V) (0·065 g.), m. p. and mixed m. p. 255—256°.

3 : 4-*Dihydro*-2-*mercapto*-3-*methyl*-4-*oxoquinazoline* (XVIII).—Anthranilic acid (2 g.), methyl *iso*thiocyanate (1 g.), and acetic acid (6 ml.) were heated in a sealed tube at 150° for 90 min. The solid which crystallised gave the pure *thiol* (1·1 g.) on crystallisation from ethanol and then from acetic acid; this formed yellow prisms, m. p. 260—261° (Found: C, 56·5; H, 4·2; S, 16·4. $C_9H_8ON_2S$ requires C, 56·3; H, 4·2; S, 16·6%).

5 : 6-*Dihydro*-6-*methyl*-5 : 12-*dioxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XIV; R = Me).—The foregoing thiol (20 g.) in dry acetone (150 ml.) was refluxed with methyl iodide (10 ml.) for 10 hr. After isolation the product was distilled at 138—142°/0·5—0·7 mm. and had m. p. 57—58°. No satisfactory analytical results were obtained. The redistilled material (18 g.) and methyl anthranilate (14·5 g.) were heated at 255° for 5 hr. After removal of basic material with dilute acid, the residue, on repeated crystallisation from ethanol, gave the 6-*methyl derivative* (6 g.) as needles, m. p. 175—176°, depressed to 165—172° by the 7-methyl isomer (Found: C, 69·0; H, 3·9; N, 15·2. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·2%).

2-*o*-Carboxy-*N*-methylanilino-4-ethoxyquinazoline (XIX) was formed as its *hydrochloride* (11 g.) when *N*-methylanthranilic acid (7·5 g.) and 2-chloro-4-ethoxyquinazoline (10 g.) were boiled in ethanol (100 ml.) for 2 hr. and the solution was evaporated. It crystallised from 2N-hydrochloric acid as needles, m. p. 143—144° (Found: N, 11·6; Cl, 10·1. $C_{18}H_{18}O_3N_3Cl$ requires N, 11·7; Cl, 9·9%). The free *base*, m. p. 66—68°, could not be recrystallised; it had $\lambda_{max.}$ 235, 277 mμ (ε 36,800, 16,300, respectively) (Found: C, 66·4; H, 5·1; N, 12·7. $C_{18}H_{17}O_3N_3$ requires C, 66·9; H, 5·3; N, 13·0%).

11 : 12-*Dihydro*-5-*methyl*-11 : 12-*dioxo*-5H-5 : 6 : 11*a*-*triazanaphthacene* (XVII; R = Me).—2-*o*-Carboxy-*N*-methylanilino-4-ethoxyquinazolinium chloride (3 g.) was heated at 255° for 2 hr.; ethyl chloride was evolved. Crystallisation of the cooled melt from benzene furnished the 5-*methyltriazanaphthacene* (1·35 g.) as needles, m. p. 283—284° (Found: C, 69·0; H, 4·2; N, 14·9. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·2%).

Methylation of the Triazanaphthacene (X).—(i) The triazanaphthacene (0·5 g.) in dry acetone (20 ml.) was boiled for 4 hr. with methyl iodide (0·2 ml.) and potassium carbonate (0·1 g.). The product (0·47 g.) crystallised from benzene and had m. p. 283—284°, undepressed by the foregoing 5-methyltriazanaphthacene.

(ii) The solution resulting from the treatment of the triazanaphthacene (3 g.) in 2N-sodium hydroxide (15 ml.) with methyl sulphate (0·6 ml.) for 8 hr. was neutralised. 2-Ethoxyethanol extracted from the precipitate the triazabenzanthracene (V) (0·36 g.), m. p. and mixed m. p. 255—255·5°. Dilution of the mother-liquor with water gave a precipitate from which the 5-methyltriazanaphthacene (XVII; R = Me) (1·1 g.), m. p. and mixed m. p. 283—284°, was obtained by crystallisation from ethanol. On the addition of water to the ethanol mother-liquor, the 7-methyltriazabenzanthracene (XV; R = Me) (0·48 g.), m. p. and mixed m. p. 165—166°, crystallised. The 2-ethoxyethanol-insoluble solid was the triazanaphthacene (0·24 g.).

The 5-methyltriazanaphthacene was recovered after being boiled with 48% hydrobromic acid for 2 hr.

Degradation of the Triazanaphthacene (X).—A solution prepared by boiling the triazanaphthacene (0·5 g.) with 2N-sodium hydroxide (20 ml.) for 30 min. was concentrated to 10 ml., mixed with concentrated hydrochloric acid (10 ml.), and kept at 0° overnight. After recrystallisation from 2N-hydrochloric acid, the product (0·35 g.) had m. p. 236—238°, undepressed by 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazolinium chloride.

7-*Ethyl*-5 : 6-*dihydro*-5 : 12-*dioxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XV; R = Et).—The triazanaphthacene (X) (0·7 g.) in dry acetone (15 ml.) was boiled for 24 hr. with potassum carbonate (0·1 g.) and ethyl iodide (0·3 ml.). The *ethyl derivative* (0·29 g., 39%) crystallised from ethanol as solvated needles, m. p. 166—168° (Found, on dried material: C, 69·8; H, 4·6; N, 14·4. $C_{17}H_{13}O_2N_3$ requires C, 70·1; H, 4·5; N, 14·4%).

The following 7-substituted-5 : 6-dihydro-5 : 12-dioxo-12*H*-6 : 7 : 12a-triazabenz[*a*]anthracenes were similarly prepared from the triazanaphthacene (X): 7-*Propyl*, needles from ethanol, m. p. 155—156° (Found: N, 13·6. $C_{18}H_{15}O_2N_3$ requires N, 13·8%); yield 35%. 7-*Butyl*,

needles from ethanol, decomposed at 180—190° without melting (Found: N, 13·3. $C_{19}H_{17}O_2N_3$ requires N, 13·2%); yield 58%. 7-*Pentyl*, needles from ethanol, decomposed at 180—190° without melting (Found: N, 12·5. $C_{20}H_{19}O_2N_3$ requires N, 12·6%); yield 44%. 7-*Hexyl*, needles from ethanol, decomposed at 180—190° without melting (Found: N, 12·0. $C_{21}H_{21}O_2N_3$ requires N, 12·1%); yield 76%. 7-*Benzyl*, yellow needles from ethanol, m. p. 189—191° (Found: N, 12·3. $C_{22}H_{15}O_2N_3$ requires N, 11·9%); yield 51%.

Cyclisation of 4-*Ethoxy*-2-o-*methoxycarbonylanilinoquinazoline*.—This quinazoline (10 g.) was heated at 255° for 10 hr. The fraction of the product insoluble in hot ethanol gave on crystallisation from benzene–light petroleum the 7-ethyltriazabenzanthracene (XV; R = Et) (1 g.), m. p. and mixed m. p. 166—168° (Found: C, 69·9; H, 4·4; N, 14·5. Calc. for $C_{17}H_{13}O_2N_3$: C, 70·1; H, 4·5; N, 14·4%). The hot ethanol-soluble fraction (6 g., m. p. 135°) furnished the 6-*ethyl isomer* (XIV; R = Et), m. p. 135—136°, after recrystallisation from light petroleum (Found: C, 70·2; H, 4·9; N, 14·6. $C_{17}H_{13}O_2N_3$ requires C, 70·1; H, 4·5; N, 14·4%).

Both the foregoing compounds were stable to 48% hydrobromic acid.

5-*Chloro*-12-*oxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XX; R = Cl).—The triazabenzanthracene (V) (0·5 g.) was refluxed with thionyl chloride (10 ml.) for 3 hr. After removal of excess of reagent, the 5-*chloro-derivative* (0·35 g.) was sublimed at 150°/0·01 mm., forming bright yellow prisms, m. p. 191—192° (Found: C, 63·8; H, 3·0; N, 14·9; Cl, 12·8. $C_{15}H_8ON_3Cl$ requires C, 64·0; H, 2·8; N, 14·9; Cl, 12·6%). This compound was readily hydrolysed in moist air to the triazabenzanthracene (V).

2-o-*Carboxyanilino*-4-*methoxyquinazoline* (XVI; R = H, R′ = Me).—To the above, freshly prepared 5-chloro-derivative (1 g.) was added sodium ethoxide [from sodium (0·15 g.)] in dry methanol (20 ml.), and the mixture was shaken until the solid had dissolved, neutralised, and poured into water (200 ml.). The precipitated oil, which solidified when warmed, afforded 2-o-*carboxyanilino*-4-*methoxyquinazoline* (0·7 g.) as needles, m. p. 120—121°, on crystallisation from methanol; $\lambda_{max.}$ 248, 282, 291, 341 mμ (ε 20,300, 23,300, 25,400, 14,400, respectively) (Found: C, 65·0; H, 4·3; N, 14·1. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%).

An ethanol solution of this compound yielded with diazomethane 4-methoxy-2-*o*-methoxycarbonylanilinoquinazoline (76%), m. p. and mixed m. p. 128—128·5°. On being heated with 48% hydrobromic acid, it gave the triazabenzanthracene (V) and 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline which was characterised as its hydrochloride, m. p. and mixed m. p. 236—238°.

4-*Ethoxy*-2-o-*ethoxycarbonylanilinoquinazoline* (XVI; R = R′ = Et) was obtained by treatment of the 5-chlorotriazabenzanthracene (1·1 g.) with sodium ethoxide [from sodium (0·2 g.)] in ethanol (25 ml.) in a similar way and crystallised from methanol forming needles (0·49 g.), m. p. 104—105°; $\lambda_{max.}$ 251, 291, 342 mμ (ε 15,800, 26,600, 15,100, respectively) (Found: C, 67·4; H, 5·4; N, 12·4. $C_{19}H_{19}O_3N_3$ requires C, 67·6; H, 5·7; N, 12·5%). It yielded the same products as the foregoing compound on treatment with 48% hydrobromic acid. On being refluxed with 2·5N-sodium hydroxide (7 ml.), this compound (0·1 g.) afforded, after addition of excess of concentrated hydrochloric acid, 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazolinium chloride (0·065 g.).

12-*Oxo*-5-*piperidino*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XX; R = $C_5H_{10}N$).—The 5-chlorotriazabenzanthracene (8·5 g.) and dry piperidine (30 ml.) were shaken for 30 min., warmed to 60°, and poured into water (250 ml.). A solution of the precipitated resin in 2N-hydrochloric acid (30 ml.) was treated fractionally with aqueous ammonia and repeatedly filtered through charcoal and kieselguhr. The final fractions (3·6 g.) furnished the pure *piperidino-derivative* m. p. 205—206° (from ether); $\lambda_{max.}$ 245, 269, 311, 360, 405 mμ (ε 31,000, 22,000, 22,000, 19,000, 10,200, 3500, respectively) (Found: C, 72·4; H, 5·1; N, 16·7. $C_{20}H_{18}ON_4$ requires C, 72·7; H, 5·5; N, 17·0%). Its *picrate* crystallised from ethanol as prisms, m. p. 220—221° (decomp.) (Found: C, 55·8; H, 3·8; N, 17·8. $C_{26}H_{21}O_8N_7$ requires C, 55·8; H, 3·8; N, 17·5%).

5-*Morpholino*-12-*oxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XX; R = C_4H_8ON), prepared in a similar manner, crystallised from light petroleum (b. p. 100—120°) as yellow needles, m. p. 230—232°; $\lambda_{max.}$ 242, 265, 313, 365 mμ (ε 31,000, 22,000, 18,000, 10,000, respectively) (Found: C, 68·3; H, 4·6; N, 16·4. $C_{19}H_{16}O_2N_4$ requires C, 68·7; H, 4·9; N, 16·9%). The *picrate* (prisms from ethanol) had m. p. 246—247° (Found: C, 53·3; H, 3·4; N, 17·3. $C_{25}H_{19}O_9N_7$ requires C, 53·5; H, 3·4; N, 17·5%).

4-2′-*Aminoethoxy*-2-(o-N-2′-*hydroxyethylcarbamoylanilino*)*quinazoline* (XXI).—The 5-chlorotriazabenzanthracene (1 g.) was brought into reaction with sodium (0·09 g.) in dry ethanolamine

(10 ml.). The *amide* (0·75 g.), precipitated by water, crystallised from ethanol as yellow needles, m. p. 207—208° (Found: C, 62·4; H, 6·1; N, 18·8; NH_2, 4·5, 4·0, 4·3. $C_{19}H_{19}O_3N_4 \cdot NH_2$ requires C, 62·1; H, 5·8; N, 19·0; NH_2, 4·4%). The *picrate* crystallised as prisms, m. p. 184—185°, from ethanol (Found: C, 50·5; H, 4·2; N, 18·3. $C_{25}H_{24}O_{10}N_8$ requires C, 50·3; H, 4·0; N, 18·8%).

THE UNIVERSITY, NOTTINGHAM. [*Received, November 5th*, 1958.]