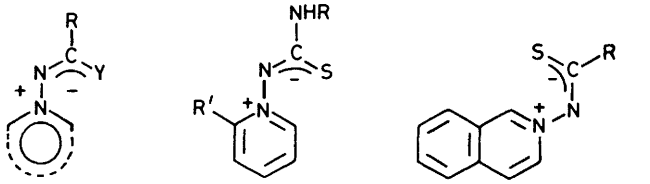
Electron Deficient Heteroaromatic Ammonioamidates. Part 26.[1] *N*-(Quinazolin-3-io)amidates. Part 13.[1] Phototransformations of an *N*-(Quinazolin-3-io)thioamidate and of a 10b*H*-1,3,4-thiadiazolo[3,2-*c*]quinazoline, the Ring Isomer of an *N*-(Quinazolin-3-io)thioamidate, and the Photochemical Formation of some 4,4'-Biquinazolinyls

Magda Lempert-Sréter *
Department of Organic Chemistry, Eötvös Loránd University, H-1088 Budapest, Múzeum krt. 4/b, Hungary
Károly Lempert
Department of Organic Chemistry, Technical University Budapest, H-1521 Budapest, Gellért tér 4, Hungary
Jørgen Møller
Department of Chemistry, Odense University, DK-5230 Odense M, Campusvej 55, Denmark

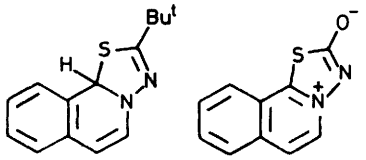
Irradiation of the *N*-(quinazolin-3-io)thioamidate (**10a**) in ethanol and butylamine solution furnished, in addition to several other compounds, the 4,4'-biquinazolinyl (**12a**), the quinazolinyl alcohol (**13a**) and the quinazolinyl ketone (**13b**), respectively, the mesoionic triazoloquinazolinylium thiolate (**18a**)and the corresponding olate (**18b**) as novel type photolysis products. In contrast, irradiation of the 10b*H*-1,3,4-thiadiazolo[3,2-*c*]quinazoline (**11b**), the ring isomer of the *N*-(quinazolin-3-io)thiomidate (**10b**) furnishes, with cleavage of either the quinazoline or the thiadiazole ring, a mixture of the thiadiazoles (**21a,b**), and the quinazoline derivatives (**14a**), (**22a,b**)in addition to 3,4-dimethoxybenzonitrile.

Irradiation of various sulphur-containing quinazoline derivatives, including the quinazolinethiones (**14a,e**), the methylthioquinazoline (**13f**) and the diquinazolinyl disulphide (**24a**), leads to the formation of 4,4'-biquinazolinyls (**12a**) and (**12b**), respectively. Irradiation of the quinazoline (**13c**), which carries no sulphur-containing substituent, does not lead to the formation of the biquinazolinyl (**12a**); irradiation of a mixture of quinazoline (**13e**) and quinazolinethione (**14a**) gives rise to the formation of a mixture of biquinazolinyls (**12a—c**) with incorporation of the ring of the sulphur-free starting quinazoline (**13e**) into the products (**12a**) and (**12b**).

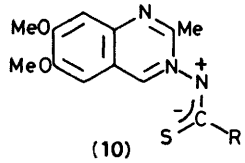
While the chemistry, including the photochemistry of electron deficient heteroaromatic ammonioamidates (**1**) has been studied extensively,[2] little is known about the corresponding thioamidates (**2**) and, in particular, about their photochemistry. In fact, only five thioamidates, *viz.* the two *N*-pyridinio(thioamidates) (**3**) and (**4**)[3] and the three *N*-isoquinolinio(thioamidates) (**5**)—(**7**)[4,†] have been subjected to irradiation so far. While simple photofragmentation of the pyridinio(thioamidates) (**3**) and (**4**) furnished the parent pyridines, an *N*-cyanoamine and sulphur,[3] the behaviour of the isoquinolinio(thioamidates) on irradiation was found to be more complicated.[4] A variety of photoproducts was obtained among which the following are of some significance in connection with the present study: the thioamides $RCSNH_2$ [from (**5**) and (**6**)], the parent isoquinoline [from (**6**)], isoquinoline-1(2*H*)-thione [from (**5**) and (**7**)], and 1,3,4-thiadiazolo[2,3-*a*]isoquinolinylium-2-olate (**9**) [from (**6**)], so far the only mesoionic compound obtained as the product of a photochemical process.



(**1**) Y = O
(**2**) Y = S
(**3**) R = Me, R' = H
(**4**) R = Ph, R' = Me
(**5**) R = 3,4-$(MeO)_2C_6H_3$
(**6**) R = OEt
(**7**) R = Bu^t



(**8**) (**9**)



(**10**)
a; R = OEt
b; R = $C_6H_3(OMe)_2$-3,4
c; R = NHBu

Here we report on our irradiation studies with *N*-(6,7-dimethoxy-2-methylquinazolin-3-io)-*N*-[ethoxy(thiocarbonyl)]-amide (**10a**)[1] in ethanol and butylamine solutions,‡ as well as of 2-(3,4-dimethoxyphenyl)-8,9-dimethoxy-5-methyl-10b*H*-1,3,4-thiadiazolo[3,2-*c*]quinazoline (**11b**), the stable tricyclic ring isomer of the *N*-(quinazolin-3-io)thioamidate (**10b**), in ethanol, and finally on the formation of some 4,4'-biquinazolinyls (**12a—c**) on irradiation of certain sulphur-containing quinazoline derivatives.

Results and Discussion

Irradiation of N-(6,7-*Dimethoxy*-2-*methylquinazolin*-3-*io*)-N-[*ethoxy*(*thiocarbonyl*)]*amide* (**10a**) *in Ethanol and Butylamine.*—Irradiation through Pyrex of the thioamidate (**10a**) in ethanol

† The thioamidate (**7**) has been shown to exist in methanol solution as an approximately 2:1 equilibrium mixture with the ring tautomer (**8**).[4]

‡ Part of our results have been described in a preliminary communication, see ref. 5.

solution under nitrogen furnished a mixture of the 4,4'-biquinazolinyl (**12a**) (36%), the quinazolinyl alcohol (**13a**) (17%), the quinazolinyl ketone (**13b**) (12%), and *O*-ethyl thiocarbamate (46%). Strikingly, the parent quinazoline (**13c**) and the quinazolinethione (**14a**),[6] whose formation was expected on the basis of the assumed analogy to the behaviour of the *N*-isoquinolinio(thioamidates) (**5**) and (**7**) on irradiation,[4] were not detected among the photoproducts. In order to explain this anomaly, it was tentatively assumed that compounds (**13c**) and (**14a**) *are* formed on irradiation of the thioamidate (**10a**) but, because of their photoinstability, are further transformed in a secondary photoprocess. Indeed, when an approximately equimolecular mixture of the quinazoline (**13c**) and the quinazolinethione (**14a**) was irradiated under the same conditions as the thioamidate (**10a**) itself, they were rapidly converted into a mixture of the biquinazolinyl (**12a**) (45%), the quinazolinyl alcohol (**13a**) (10%), and the quinazolinyl ketone (**13b**) (2%). (For related photochemical reactions, *vide infra.*)

(**11**)

a; R = OEt
b; R = $C_6H_3(OMe)_2$-3,4
c; R = NHBu

(**12**)

a; R = R' = Me
b; R = R' = Bu^t
c; R = Me, R' = Bu^t

(**13**)

	R	R'
a;	Me	MeCHOH
b;	Me	MeCO
c;	Me	H
d;	Me	BuNH
e;	Bu^t	H
f;	Me	MeS

The photochemistry of *N*-(quinazolin-3-io)amidates of type (**15**) which are closely related to the thioamidate (**10a**), has been found previously to be significantly influenced by nucleophiles present in the irradiation mixtures, *e.g.* by the nucleophilic solvent.[7] The phototransformations of the thioamidate (**10a**) have therefore been studied also in butylamine solution.

The thioamidate (**10a**) proved unstable and was completely decomposed (t.l.c.) within 2 or 3 h at room temperature in butylamine solution in the dark.* 2-Amino-4,5-dimethoxybenzaldehyde (**16a**),[9] its [ethoxy(thiocarbonyl)]hydrazone,[1] the *N*-acetyl derivative (**16b**)[9] and *O*-ethyl *N*-butylthiocarbamate[10] (**17**) were obtained, in addition to several non-identified compounds, as the products of progressive degradation. However, because of the apparently comparable rates of its photochemical and dark reactions in butylamine, some irradiation products of the thioamidate (**10a**) were also obtained.

Irradiation through Pyrex of the thioamidate (**10a**) in butylamine solution under nitrogen furnished a complex mixture of products from which, in addition to several non-identified compounds, 4-butylamino-6,7-dimethoxy-2-methylquinazoline [(**13d**); 5.5%, mostly in form of the hydrochloride], 3-butyl-6,7-dimethoxy-2-methylquinazoline-4(3*H*)-thione [(**14b**); 0.4%], 1-butyl-8,9-dimethoxy-5-methyl-1,2,4-triazolo[5,1-*a*]quinazolinylium-2-thiolate [(**18a**); 12%], the corresponding 2-olate [(**18b**); 3.5%], *O*-ethyl thiocarbamate (27%), *O*-ethyl *N*-butylthiocarbamate[10] [(**17**); 20.5%] and 2-acetylamino-4,5-dimethoxybenzaldehyde [(**16b**); 0.6%] were isolated in pure form. Except for the last two, none of these compounds was present in the mixtures resulting from the dark reaction of the thioamidate (**10a**) and butylamine.

(**14**)

a; $R^1 = R^2 = R^3 = Me$, $R^4 = H$
b; $R^1 = R^2 = R^3 = Me$, $R^4 = Bu$
c; $R^1 = R^2 = R^3 = Me$, $R^4 = NHCOC_6H_3(OMe)_2$-3,4
d; $R^1 + R^2 = CH_2$, $R^3 = Me$, $R^4 = NHBz$
e; $R^1 = R^2 = Me$, $R^3 = Bu^t$, $R^4 = H$
f; $R^1 = R^2 = R^3 = R^4 = Me$
g; $R^1 + R^2 = CH_2$, $R^3 = H, Me$, $R^4 = NHCH_2Ph$, $NHCO_2Et$

(**15**)

(**16**)

a; R = Z = H
b; R = Ac, Z = H
c; R = Bu^{t}CO, Z = H
d; R = Bu^{t}CO, Z = NH_2

BuNH—CS—OEt

(**17**)

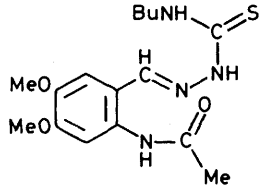
(**18**)

a; Y = S
b; Y = O

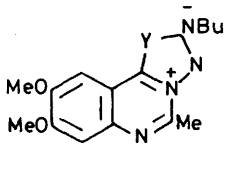
Among the photoproducts obtained on irradiation of the thioamidate (**10a**) in ethanol and butylamine, respectively, the biquinazolinyl (**12a**), the quinazolinyl ketone (**13b**), the mesoionic thiolate (**18a**) and the corresponding olate (**18b**) are novel products whose analogues have never been obtained before on irradiation of heteroaromatic ammonioamidates and thioamidates. The formation of the thiolate (**18a**) and of the olate (**18b**) is of special interest since, except for compound (**9**), they are so far the only mesoionic compounds formed as a result of a photochemical process.[11] 1-Hydroxyalkyl- and 1-alkoxyalkyl-heteroaromatics related to compound (**13a**) have been obtained before on irradiation of heteroaromatics in alcohols and ethers, respectively.[8,12] However, the quinazolinyl alcohol (**13a**) is apparently formed by a different pathway because irradiation of an ethanolic solution of the quinazoline (**13c**) [in the absence of the thione (**14a**)] did not furnish the alcohol (**13a**) [nor compounds (**12a**) and (**13b**)].[5]

* Addition of benzylamine (2.5 equiv.) or triethylamine to the $CDCl_3$ solution of the thioamidate (**10a**) also results in complete decomposition of the latter within one or two days at room temperature in the dark. On addition of benzylamine (but not of triethylamine) considerable broadening of the 4-H signal in the ^1H n.m.r. spectrum takes place immediately, which probably indicates adduct formation, *cf.* ref. 8. Strikingly, no adduct formation takes place in $CDCl_3$ solution with toluene-α-thiol.

The assignments of structures to the photoproducts on the basis of their spectral data were in most cases straightforward. Therefore, only few comments are necessary. The mesoionic thiolate (**18a**) was unexpectedly obtained from the thiosemicarbazone (**19**), instead of the expected quinazolinio(thioamidate) (**10c**) or its tricyclic tautomer (**11c**), by refluxing with ethanolic hydrogen chloride. Neither of the two modes of formation of the thiolate (**18a**) is proof of structure: the isomeric mesoionic amide (**20a**), the dehydrogenation product of compound (**11c**), could have been formed equally well. That the actual structure of the product is (**18a**) rather than (**20a**) and, similarly, that the structure of the oxygen analogue is (**18b**) rather than (**20b**) is based on the following observations: (i) treatment of the sulphur compound with 2,4,6-trimethylbenzonitrile oxide[13] in acetonitrile at room temperature furnished the oxygen analogue in excellent yield, *cf.* ref. 14; (ii)



(19)



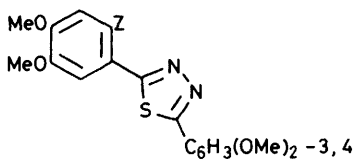
(20)

a; Y = S

b; Y = O

the chemical shifts of the *N*-butyl signals in the ^{1}H n.m.r. spectra showed relatively small changes on addition of trifluoroacetic acid, see Experimental section; (iii) the mass spectrum of the oxygen compound exhibits a significant $(M - OH)^+$ peak at *m/z* 299. [A corresponding $(M - SH)^{+\cdot}$ ion is present in the mass spectrum of the sulphur analogue, together with an $(M - S)^{+\cdot}$ ion, but the loss of ·SH in itself is of little diagnostic value.]

Irradiation of 2-(3,4-*Dimethoxyphenyl*)-8,9-*dimethoxy*-5-*methyl*-10b*H*-1,3,4-*thiadiazolo*[3,2-c]*quinazoline* (**11b**) *in Ethanol.*—Since a series of novel photoproducts were obtained on irradiation of the *N*-(quinazolin-3-io)thioamidate (**10a**) it was felt desirable to extend the irradiation studies to related thioamidates. Accordingly, the synthesis of the thioamidate (**10b**) was attempted. However, the latter was found to exist—inversely to thioamidate (**10a**)—solely in the form of the tricyclic ring isomer 2-(3,4-dimethoxyphenyl)-8,9-dimethoxy-5-methyl-10b*H*-1,3,4-thiadiazolo[3,2-*c*]quinazoline (**11b**) under



(21)

a; Z = NH_2

b; Z = NHAc

c; Z = NO_2

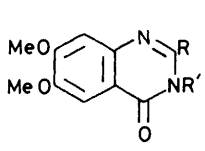
the conditions studied.[1] In order to obtain some information about the relation of the photochemistry of *N*-(quinazolin-3-io)thioamidates (**10**) and of their type (**11**) ring isomers, the photochemistry of compound (**11b**) was studied.

Compound (**11b**) was found to decompose rapidly at room temperature in several solvents (such as dichloromethane, chloroform, acetone, pyridine, butylamine, and benzene) even in the dark but proved much less unstable in ethanolic and methanolic solution which made it possible to study its photolysis in ethanol.

Irradiation through Pyrex of compound (**11b**) in ethanolic solution under nitrogen furnished (in addition to 3,4-dimethoxybenzonitrile and a product of unknown structure) with cleavage of either the quinazoline or the thiadiazole ring a complex mixture of products including 2-(2-amino-4,5-dimethoxyphenyl)-5-(3,4-dimethoxyphenyl)-1,3,4-thiadiazole (**21a**), the *N*-acetyl derivative (**21b**) of the latter, 6,7-dimethoxy-2-methylquinazoline-4(3*H*)-thione (**14a**), the corresponding quinazolinone (**22a**), and 3-[3,4-dimethoxy(thiobenzoyl)amino]-6,7-dimethoxy-2-methylquinazolin-4(3*H*)-one (**22b**). None of these products were formed (t.l.c.) when an ethanolic solution of compound (**11b**) was kept in the dark for a period twice as long as necessary for achieving its complete photolysis; and the thiadiazole (**21a**) was not formed when its *N*-acetyl derivative (**21b**) was irradiated in ethanolic solution under the conditions used in the irradiation of compound (**11b**). When the irradiation of the latter was conducted in air a significant increase in the yield of compound (**22b**) was observed.

The structure assignments of the new compounds (**21a**), (**21b**), and (**22b**) are based on their mass spectra. In addition, compounds (**21a**) and (**21b**) were obtained by an unambiguous synthesis starting with the thiadiazolines (**23a**)[1] and (**23b**),[1] respectively.

The mass spectrum (see the Experimental section) of compound (**22b**) exhibits a molecular ion of low abundance (2.3%) at *m/z* 415, corresponding to $C_{20}H_{21}N_3O_5S$ (high-resolution measurement). Loss of ·SH yields the very abundant *m/z* 382 ion to which structure (**A**) may be ascribed and from



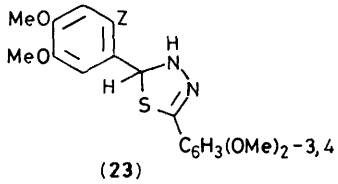
(22)

a; R = Me, R' = H

b; R = Me, R' = $NHCSC_6H_3(OMe)_2$-3,4

c; R = R' = Me

d; R = Bu^t, R = H

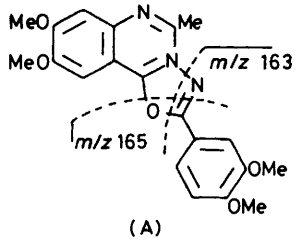


(23)

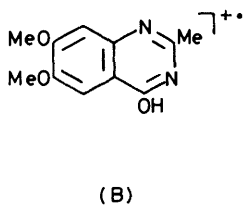
a; Z = NO_2

b; Z = NHAc

which *m/z* 165 and 163 can be formed by further fragmentation. The abundant ion at *m/z* 220 ($C_{11}H_{12}N_2O_3$) may correspond to (**B**) (or its dihydro-oxo tautomer).



(A)



(B)

The isomeric structure (**14c**) (with the carbonyl and thiocarbonyl groups interchanged), for which the above rationale might equally well account, has been ruled out on the basis of a

comparison with the mass spectrum of compound (**14d**)[15] which, in addition to the $(M - SH)^+$ ion peak (*m/z* 306), exhibits a more abundant $(M - OH)^+$ peak (*m/z* 322). Furthermore, the peak of the benzoyl cation (*m/z* 105), which corresponds to *m/z* 165 in the spectrum of compound (**22b**), is the predominant fragment ion in the spectrum of compound (**14d**).

Photochemical Conversion of some Sulphur-containing Quinazoline Derivatives into 4,4'-Biquinazolinyls.—As mentioned above, irradiation of an approximately equimolecular mixture of 6,7-dimethoxy-2-methylquinazoline (**13c**) and 6,7-dimethoxy-2-methylquinazoline-4(3*H*)-thione (**14a**) in ethanol leads to the formation of a mixture of the 4,4'-biquinazolinyl (**12a**), the alcohol (**13a**), and the ketone (**13b**). Since the total recovery of the quinazoline moieties of the starting substances in the form of these products amounted to only 57% and, in particular, the recovery in the form of the biquinazolinyl (**12a**) to only 45%, the question of the origin of the quinazolinyl rings of the biquinazolinyl (**12a**) arose. The quinazoline (**13c**) and the quinazolinethione (**14a**) were therefore separately subjected to irradiation.

While irradiation of the former caused extensive decomposition without formation of even traces of compounds (**12a**), (**13a**), and (**13b**), irradiation of the quinazolinethione (**14a**) furnished 96% of the biquinazolinyl (**12a**) but none of the alcohol (**13a**) and the ketone (**13b**). This result appeared to indicate that the biquinazolinyl (**12a**) has its origin solely in the quinazolinethione (**14a**), and that the quinazoline (**13c**) is not incorporated into the biquinazolinyl (**12a**) formed on irradiation of the mixture of compounds (**13c**) and (**14a**). In order to check this point as well as to get some insight into the nature of the reaction, the t-butylquinazoline (**13e**) and the t-butylquinazolinethione (**14e**) were prepared, and the photolysis of the thione (**14e**) as well as of a mixture of compounds (**13e**) and (**14e**) was studied; furthermore, a crossing experiment (see below) was carried out.

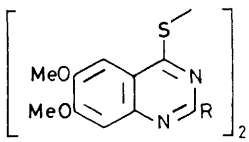
In contrast to the 2-methylquinazolinethione (**14a**), the 2-(t-butyl) analogue (**14e**) furnished less than 5% of the corresponding biquinazolinyl (**12b**) on irradiation, the main product being the 2-(t-butyl)quinazoline (**13e**) (32%). A mixture of similar composition resulted when an approximately equimolecular mixture of the t-butylquinazoline (**13e**) and the t-butylquinazolinethione (**14e**) was irradiated. Thus, the tendency of the t-butylquinazolinethione (**14e**) to furnish the corresponding biquinazolinyl (**12b**) appears to be much less distinct than that of the 2-methyl analogue (**14a**). [The t-butylquinazoline (**13e**) is not a secondary photoreduction product of the eventually formed biquinazolinyl (**12b**) since the latter does not furnish quinazoline (**13e**) when separately irradiated. Similarly, the biquinazolinyl (**12a**) was found to remain unchanged when irradiated for 7 h in ethanolic solution.]

The crossing experiment, aiming to clarify whether the quinazoline (**13c**) or the quinazolinethione (**14a**) or both provide the quinazoline rings of the biquinazolinyl (**12a**) had therefore to be carried out by irradiating a mixture of the t-butylquinazoline (**13e**) and the methylquinazolinethione (**14a**) rather than a mixture of the methylquinazoline (**13c**) and the t-butylquinazolinethione (**14e**).

An approximately equimolecular mixture of compounds (**13e**) and (**14a**) in ethanol was irradiated under the same conditions as the mixture of compounds (**13c**) and (**14a**), except that the irradiation was conducted for a period more than three times as long. In spite of the prolonged reaction time an appreciable amount of unchanged quinazoline (**13e**) and some unchanged thione (**14a**) were still present. More important, the biquinazolinyl fraction of the reaction product contained all three of the conceivable compounds: the dimethyl [(**12a**), 8%], the di(t-butyl) [(**12b**), 24%], and the mixed (t-butyl)methyl derivative [(**12c**), 9%].

These results clearly demonstrate (i) that the substituents in position 2 of the quinazoline and the quinazolinethione rings have profound effects both on the rate and direction of the photolysis and (ii) that both the quinazolines (**13c**) and (**13e**) and the quinazolinethiones (**14a**) and (**14e**) are able to provide the quinazoline rings of the biquinazolinyls (**12a—c**) *when quinazoline–quinazolinethione mixtures are irradiated.* The transformations leading ultimately to the incorporation of the quinazolines into the biquinazolinyls are rather complex as shown by the observation that *in the absence of quinazolinethiones they do not take place.* In spite of considerable efforts we were unable to isolate intermediates of the overall reactions.

Some related compounds, *viz.* the thione (**14f**), the quinazoline (**13f**) and the disulphides (**24a**)[16] and (**24b**)[16] were also subjected to irradiation. Extensive decomposition took place on irradiation of the thione (**14f**) and the only phototransformation product which could be isolated was the corresponding oxo derivative (**22c**). Some biquinazolinyl (**12a**) was obtained from the quinazoline (**13f**) but most of the starting substance was recovered unchanged. The disulphide (**24a**) furnished a mixture of the thione (**14a**) and the biquinazolinyl (**12a**) on irradiation, while no biquinazolinyl (**12b**) was obtained from the disulphide (**24b**), the thione (**14e**) being the main phototransformation product isolated.



(**24**)
a; R = Me
b; R = Bu^t

Experimental

The irradiations were carried out under nitrogen at room temperature using high-pressure mercury immersion lamps (HPK-125) with Pyrex filters. Kieselgel $PF_{254+366}$ was used as the adsorbent and, if not otherwise stated, ethyl acetate–ethanol (4:1) as the solvent for the t.l.c. separations. ^1H N.m.r. spectra were obtained at 60 and 100 MHz with Perkin-Elmer type R-12, Varian A60 and XL-100A, and JEOL FX-100 spectrometers, respectively, and, if not otherwise stated, in $CDCl_3$ solution with $SiMe_4$ (TMS) as the internal reference. Mass spectra were obtained on a Varian MAT 311A instrument (Grant from the Danish Natural Science Research Council) by electron impact (70 eV) and using the direct insertion system.

Irradiation of N-(6,7-*Dimethoxy*-2-*methylquinazolin*-3-*io*)-N-[*ethoxy*(*thiocarbonyl*)]*amide* (**10a**).—(*a*) *In ethanol.* The ethanolic (1 200 ml) solution of the title compound (**10a**)[1] (1.2 g, 3.9 mmol) was irradiated until, according to t.l.c., the starting compound was completely consumed (*ca.* 3 h). The reaction mixture was evaporated to dryness under reduced pressure and the residue was taken up in water and chloroform. The dry residue (0.24 g) of the aqueous layer turned into a crystalline compound of unknown structure when treated with ether. The chloroform solution was dried ($MgSO_4$) and evaporated to dryness. The residue was taken up in ethanol (5 ml) to give 6,7,6',7'-*tetramethoxy*-2,2'-*dimethyl*-4,4'-*biquinazolinyl* (**12a**) (70 mg) as an insoluble crystalline product. Upon addition of acetone, a further 50 mg of the biquinazolinyl (**12a**) was precipitated. The filtrate of this product was evaporated to

dryness and the residue was worked up by preparative t.l.c. to obtain the following products (in the order of decreasing R_F values): *O*-ethyl thiocarbamate (194 mg, 46%), 4-*acetyl*-6,7-*dimethoxy*-2-*methylquinazoline* (**13b**) (108 mg, 11.5%), 4-(1-*hydroxyethyl*)-6,7-*dimethoxy*-2-*methylquinazoline* (**13a**) (169 mg, 17.4%), and a further 166 mg (total yield: 286 mg, 36.4%) of the biquinazolinyl (**12a**).

O-Ethyl thiocarbamate (not further purified after elution from the t.l.c. plate since distillation even under reduced pressure causes partial decomposition); δ_H 1.23 (t) + 4.52 (q) ($J \approx 7.0$ Hz, OEt), (6.4 bs, NH_2) identical with the spectrum of an authentic sample.[17]

The biquinazolinyl (**12a**), m.p. 309—312 °C (from acetic acid and subsequently sublimed *in vacuo*) (Found: $M^{+\cdot}$, 406.1637; N, 14.05%. $C_{22}H_{22}N_4O_4$ requires $M^{+\cdot}$, 406.1640; N, 13.79%), δ_H 2.95 (s, 2- and 2′-Me), 3.8 and 4.1 (2 s, 6-, 7-, 6′-, and 7′-MeO), and 7.15 and 7.4 (2 s, 5-, 8-, 5′-, and 8′-H); *m/z* (200 °C) (rel. int.) 406 ($M^{+\cdot}$ 13), 405 (8.3), 391 (46), 376 (33), 375 (100), 360 (9), 359 (9), 348 (5.0), 333 (10), 331 (6.8), 329 (5.0), and 203 (M^{2+}, 10).

Compound (**13a**), m.p. 67—69 °C (from EtOH) (Found: $M^{+\cdot}$, 248.1142; N, 11.05%. $C_{13}H_{16}N_2O_3$ requires $M^{+\cdot}$, 248.1161; N, 11.29%), δ_H 1.55 (d, $J \approx 7$ Hz, MeCH), 2.80 (s, 2-Me), 4.00 and 4.02 (2 s, 2 × MeO), 4.5—5.1 (bs, exchangeable, OH), 5.40 (br qu, becomes sharp on addition of D_2O, $J \approx 7$ Hz, MeCHOH), and 7.12 and 7.27 (2s, 2 × ArH); *m/z* (75 °C) (rel. int.) 248 ($M^{+\cdot}$, 34), 247 (6.9), 233 (100), 231 (25), 205 (15), 204 (13), 203 (13), 189 (9.4), 163 (7.0), 147 (5.2), 104 (5.2), and 102 (5.6); $\lambda_{max.}$(EtOH) 222 (4.40)sh, 242 (4.57), 322 (3.82)sh, and 332 (3.85); the u.v. spectrum is in good agreement with the spectra of a series of 6,7-methylenedioxyquinazoline[18] model compounds.

Compound (**13b**), m.p. 181 °C (from EtOAc), Found $M^{+\cdot}$, 246.0996; N, 11.23%. $C_{13}H_{14}N_2O_3$ requires $M^{+\cdot}$, 246.1004; N, 11.38%), $\nu_{max.}$(KBr) 1 685 cm^{-1}; δ_H (60 MHz) 2.8 and 2.85 (2 s, MeCO and 2-Me), 4.0 and 4.02 (2 s, 2 × MeO), 7.25 (s, 8-H), and 8.15 (s, 5-H); *m/z* (85 °C) (rel. int.) 246 ($M^{+\cdot}$, 100), 245 (9.7), 231 (77), 218 (15), 215 (16), 204 (33), 203 (95), 189 (9.5), 187 (5.0), 163 (10), 147 (18), and 104 (15).

(*b*) *In butylamine.* A solution of the thioamidate (**10a**)[1] (1.5 g, 4.9 mmol) in butylamine (150 ml) was irradiated until the starting compound was completely consumed (t.l.c.; *ca.* 3 h). The mixture was evaporated to dryness under reduced pressure and the residue was extracted with boiling benzene (50 ml). The benzene solution was washed with water and extracted with 8% aqueous NaOH. The aqueous (**A**) and benzene layers (**B**) were separated, and the alkaline solution **A** was acidified (HCl) and extracted with CH_2Cl_2. The CH_2Cl_2 solution was dried ($MgSO_4$) and evaporated to dryness and the residue was extracted with boiling anhydrous ethanol to give 1-*butyl*-8,9-*dimethoxy*-5-*methyl*[1,2,4]*triazolo*[5,1-a]*quinazolinylium*-2-*thiolate* (**18a**) as an insoluble crystalline residue; a second crop of this thiolate [total yield 0.2 g, 12%; m.p. (crude) 224—228 °C, identical (i.r., mass spec.) with a sample obtained by double ring closure of compound (**19**), see below] was obtained from the ethanolic solution by preparative t.l.c. (benzene–chloroform–ethyl acetate, 1:1:1).

The benzene solution B was extracted with 5% HCl. The aqueous (C) and benzene layers (D) were separated, and the aqueous solution C was neutralized (Na_2CO_3) and extracted with CH_2Cl_2. The extract was worked up by successive column (neutral Al_2O_3, Brockmann; benzene–ethyl acetate, 8:1 ——→ 2:1) and t.l.c. (benzene–chloroform–ethyl acetate, 1:1:1) to obtain the following products: 4-*butylamino*-6,7-*dimethoxy*-2-*methylquinazoline* (**13d**) [7 mg, 0.5%, m.p. (crude) 155—158 °C, identical (i.r., mass spectroscopy) with an authentic sample, see below], 2-acetylamino-4,5-dimethoxybenzaldehyde (**16b**) [7 mg, 0.6%, m.p. 173—175 °C, identical (mixed m.p., i.r.) with an authentic sample[1,9]] and 1-*butyl*-8,9-*dimethoxy*-5-*methyl*[1,2,4]-*triazolo*[5,1-a])*quinazolinylium*-2-*olate* (**18b**) which crystallized when triturated with acetone [54 mg, 3.5%, m.p. 203—205 °C, identical with an authentic sample, see below].

The benzene solution D was evaporated to dryness, and the residue was triturated with methanol to give compound (**13d**)·HCl (55 mg) as the insoluble crystalline residue. The methanolic filtrate was evaporated to dryness and worked up by preparative t.l.c. to give a second crop (14 mg) of (**13d**)·HCl [total yield 5%; identical (m.p. and i.r.) with an authentic sample, see below], compound (**17**) [160 mg, 20.5%; identical (i.r., ^{1}H n.m.r.) with an authentic sample[10]],3-*butyl*-6,7-*dimethoxy*-2-*methylquinazoline*-4(3H)-*thione* (**14b**) [5 mg, 0.4%; m.p. 132—134 °C (from MeOH) (Found: $M^{+\cdot}$, 292.1245. $C_{15}H_{20}N_2O_2S$ requires *M*, 292.1263); $\lambda_{max.}$(EtOH) 227sh (4.48), 234 (4.52), 256 (4.20), 276 (4.16), 349sh (3.95), 364 (4.16), and 381 (4.16) in good agreement with the spectra of a series of model 6,7-methylenedioxyquinazoline-4(3*H*)-thiones[15]; *m/z* (110 °C) (rel. int.) 292 ($M^{+\cdot}$, 44), 291 (8.8), 277 (13), 259 (*M* − SH,* 100), 250 (7.2), 236 (*M* − C_4H_8,* 65), 235 (13), 221 (18), 203 (*M* − SH − C_4H_8,* 39), and 147 (9.2)], and *O*-ethyl thiocarbamate [138 mg, 27%; identical (i.r., ^{1}H n.m.r.) with an authentic sample[17]].

Degradation of the Thioamidate (**10a**) *by Butylamine in the Dark.*—The thioamidate (**10a**) (0.92 g, 3 mmol) was stirred with butylamine (10 ml) to obtain a clear solution with evolution of heat. The solution was allowed to stand for 3 h at ambient temperature and was then evaporated to dryness. The residue was taken up in benzene. The benzene solution was washed successively with water and 8% aqueous NaOH and extracted with 5% aqueous HCl. The acidic solution was neutralized (Na_2CO_3) and extracted with ether. The extract was worked up by preparative t.l.c. (benzene–chloroform–ethyl acetate, 8:1:1, and subsequently, for the less mobile fractions, ethyl acetate–ethanol, 4:1) to obtain the following compounds in the order of decreasing R_F values: *O*-ethyl *N*-butylthiocarbamate (**17**) (54 mg, 11%), identical (i.r., ^{1}H n.m.r.) with an authentic sample;[10] 2-*amino*-4,5-*dimethoxybenzaldehyde* [*ethoxy*(*thiocarbonyl*)]-*hydrazone* (248 mg, 29.5%), m.p. 138—139 °C, identical (m.p., i.r.) with an authentic sample obtained by reduction of the 2-nitro analogue[1] (Found: N, 14.10. $C_{12}H_{17}N_3O_3S$ requires N, 14.83%); *m/z* (145 °C) (rel. int.) 283 ($M^{+\cdot}$, 100), 250 (4.5), 237 (12), 212 (11), 195 (7.5), 180 (22), 179 (64), 178 (54), 166 (19), 165 (29, 164 (24), 163 (75), 152 (11), 150 (20), 148 (14), 135 (22), 122 (17), 120 (17), and 94 (27); 2-amino-4,5-dimethoxybenzaldehyde (**16a**) (121 mg, 22.5%), m.p. 86 °C, identical (m.p., i.r.) with an authentic sample;[9] and 2-acetylamino-4,5-dimethoxybenzaldehyde (**16b**) (8 mg, 1%), m.p. 173—175 °C, identical (mixed m.p., i.r.) with an authentic sample,[1,9] *m/z* (95 °C) (rel. int.) 223 ($M^{+\cdot}$, 76), 195 (8.3), 181 (40), 180 (13), 166 (100), 153 (22), 138 (73), 136 (10), 110 (15), and 94 (32).

Photolysis of 2-(3,4-*Dimethoxyphenyl*)-8,9-*dimethoxy*-5-*methyl*-10bH-1,3,4-*thiadiazolo*[3,2-c]*quinazoline* (**11b**).[1]—(*a*) An ethanolic (300 ml) solution of compound (**11b**) (0.5 g, 1.25 mmol) was irradiated until the starting compound was completely consumed (t.l.c.; about 2 h). The mixture was evaporated to dryness, and the residue was taken up in dichloromethane (4 ml) to give 6,7-*dimethoxy*-2-*methylquinazoline*-4(3H)-*thione* (**14a**) [identical (m.p., i.r., mass spectroscopy) with an authentic sample[6]] as an insoluble crystalline residue. The dichloromethane solution was extracted with aqueous NaOH and the organic (A) and aqueous layers (B) were separated. Acidification of the aqueous solution B, extraction with dichloromethane, and crystallization of the extract from methanol furnished an additional quantity of

* By peak matching.

compound (**14a**) (total yield: 71—150 mg, 24—51%*). Solution A was extracted with aqueous HCl, and the organic (C) and aqueous layers (D) were separated. Neutralization (Na_2CO_3) of the acidic solution D, extraction with dichloromethane, and work-up of the extract by preparative t.l.c. furnished 2-(2-amino-4,5-dimethoxyphenyl)-5-(3,4-dimethoxyphenyl)-1,3,4-thiadiazole (**21a**) [11—49 mg, 2.5—10.5%;* contaminated with a small amount of the *N*-acetyl derivative (**21b**) but otherwise identical (i.r., mass spectroscopy) with an authentic sample, see below]. Work-up of solution C by preparative t.l.c. furnished the following compounds in the order of decreasing R_F values: 3,4-dimethoxybenzonitrile [13—35 mg, 6.4—17%;* identical (m.p., i.r.) with an authentic sample[19]]; 2-(2-*acetylamino*-4,5-*dimethoxyphenyl*]-5-(3,4-*dimethoxyphenyl*)-1,3,4-*thiadiazole* (**21b**)[12.5—85 mg, 2.4—17.5%;* m.p. 185—186 °C (from EtOH), identical (m.p., i.r.) with an authentic sample, see below]; 3-[3,4-*dimethoxy*(*thiobenzoyl*)*amino*]-6,7-*dimethoxy*-2-*methylquinazolin*-4(3H)-*one* (**22b**) [8.3—62 mg, 1.6—12%;* m.p. 212—213 °C (from methanol) (Found: $M^{+\cdot}$, 415.1200. $C_{20}H_{21}N_3O_5S$ requires M, 415.1200), $\lambda_{max.}$(KBr): 3 200 and 1 675 cm^{-1}; *m/z* (180 °C) (rel. int.) 415 ($M^{+\cdot}$, 2.3), 382 (M^* − SH,† 100), 220 ($C_{11}H_{12}N_2O_3$,† 57), 205 (20), 191 (6.3), 181 (9.9), 177 (8.5), 175 (7.8), 165 (18), 163 ($C_9H_9NO_2$,† 46), 148 (15), 136 (9.0), 134 (6.0), and 120 (9.9); and 6,7-dimethoxy-2-methylquinazolin-4(3*H*)-one (**22a**) [8.8—48.5 mg, 3.5—17.6%;* identical (m.p., i.r.) with an authentic sample[6]]; a further compound of unknown structure, m.p. 269—270 °C (from AcOH), R_F = 0, was also obtained.

(*b*) When the same experiment was conducted in air the following products were obtained: 3,4-dimethoxybenzonitrile (20%), the thiadiazole (**21b**) (11%), and the quinazolinone (**22b**) (36%).

Unambiguous Syntheses of some Photoproducts.—6,7-*Dimethoxy*-2-*methyl*-4-*methylthioquinazoline* (**13f**). Sodium (23 mg, 1 mg-atom) and subsequently the quinazolinethione (**14a**)[6] (230 mg, 1 mmol) were dissolved in methanol (5 ml); methyl iodide (0.1 ml, 1.4 mmol) was added, and the solution was refluxed for 3 h and filtered to give the title compound (0.18 g, 72%), m.p. 191—192 °C (from EtOH), on cooling (Found: C, 57.75; H, 5.45; N, 10.9; S, 12.8. $C_{12}H_{14}N_2O_2S$ requires C, 57.58; H, 5.63; N, 11.19; S, 12.84%).

4-*Butylamino*-6,7-*dimethoxy*-2-*methylquinazoline* (**13d**) *and its hydrochloride.* A mixture of the above quinazoline (0.5 g, 2 mmol), butylamine (10 ml), and a small amount of butylammonium iodide was heated for 3 h at 140 °C in a sealed tube. The resulting solution was evaporated to dryness and the residue was recrystallized from methanol to give compound (**13d**) (0.26 g, 47%), m.p. 158—159 °C (from MeOH), on cooling (Found: $M^{+\cdot}$, 275.1625; N, 15.50%. $C_{15}H_{21}N_3O_2$ requires $M^{+\cdot}$, 275.1634; N, 15.26%), $\lambda_{max.}$(EtOH) 207 (4.39), 245 (4.49), 251sh (4.43), 280 (3.77), 292 (3.78), 322 (3.99), and 333 (3.95), in good agreement with the spectra of a series of model 4-amino-6,7-dimethoxyquinazolines;[8] *m/z* (110 °C) (rel. int.) 275 ($M^{+\cdot}$, 66), 274 (7.8), 260 (9.9), 259 (5.1), 246 (M − C_2H_5,† 55), 233 (27), 232 (28), 219 (M − C_4H_8,† 100), 218 (14), 204 (27), 203 (25), 147 (7.2), and 116.5 (9.3)

The hydrochloride, m.p. 264—265 °C (from EtOH) was obtained by treatment of the base with ethanolic HCl; $\lambda_{max.}$ (EtOH) 218 (4.39), 250 (4.39), 278sh (3.69), 326 (4.19), and 340 (4.17); the mass spectrum (185 °C) was identical with that of the free base.

2-*Acetylamino*-4,5-*dimethoxybenzaldehyde* 4-*butylthiosemicarbazone* (**19**). A mixture of 2-acetylamino-4,5-dimethoxybenzaldehyde (**16b**)[9] (0.55 g, 2 mmol), 4-butyl thiosemicarbazide (0.4 g, 2.7 mmol), and ethanol (10 ml) was refluxed for 0.5 h to give the title compound (0.75 g, 85%), m.p. 192—193 °C, on cooling (Found: N, 16.1; S, 9.05. Calc. for $C_{16}H_{24}N_4O_3S$: N, 15.90; S, 9.10%).

1-*Butyl*-8,9-*dimethoxy*-5-*methyl*[1,2,4]*thiazolo*[5,1-a]*quinazolinylium*-2-*thiolate* (**18a**). The thiosemicarbazone (**19**) (0.7 g, 2 mmol) was refluxed with 7% ethanolic HCl (5 ml) for 1 h. The mixture was evaporated to dryness and the residue was taken up in CH_2Cl_2 and the solution washed with aqueous $NaHCO_3$ to give, after conventional work-up, the title compound (0.6 g, 89%), m.p. 238—239 °C (from acetic acid) (Found: C, 57.95; H, 6.6; N, 16.68; S, 9.75. $C_{16}H_{20}N_4O_2S$ requires C, 57.8; H, 6.05; N, 16.85; S, 9.65%); δ_H 1.07 (t), 1.62 (m), 1.97 (m) and 4.87 (t) (*N*-Bu), 2.95 (s, 5-Me), 4.07 and 4.08 (2 s, 2 × MeO), and 7.38 and 7.40 (2 s, 2 × ArH); δ_H($CDCl_3$–TFA) 1.08 (t), 1.62 (m), 1.98 (m) and 4.57 (t) (*N*-Bu), 3.04 (s, 5-Me), 4.09 and 4.10 (2 s, 2 × MeO), 7.45 and 7.71 (2 s, 2 × ArH); *m/z* (200 °C) (rel. int.) 332 ($M^{+\cdot}$, 47), 331 (2.2), 317 (2.1), 303 (4.4), 300 (7.5), 299 (M − SH, 15), 290 (7.1), 289 (3.6), 276 (M − C_4H_8, 100), 261 (5.6), 218 (2.6), 203 (5.0), 166 (3.7), and 147 (2.7).

1-*Butyl*-8,9-*dimethoxy*-5-*methyl*[1,2,4]*triazolo*[5,1-a]*quinazolinylium*-2-*olate* (**18b**). The thiolate (**18a**) (70 mg, 0.21 mmol) was stirred with 2,4,6-trimethylbenzonitrile oxide[13] (40 mg, 0.25 mmol) in acetonitrile (2 ml) for 2 h at room temperature. The mixture was evaporated to dryness under reduced pressure and the residue was trituated with light petroleum to give the title compound (60 mg, 91%), m.p. 204—205 °C (from EtOH) (Found: C, 61.1; H, 6.95; N, 17.75. $C_{16}H_{20}N_4O_3$ requires C, 60.73; H, 6.37; N, 17.71%); δ_H 1.03 (t), 1.61 (m), 1.88 (m) and 4 34 (t) (*N*-Bu), 2.88 (s, 5-Me), 4.04 (s, 2 × MeO), 7.27 and 7.30 (2 s, 2 × ArH); δ($CDCl_3$–TFA) 1.04 (t), 1.52 (m), 1.92 (m) and 4.50 (t) (*N*-Bu), 3.07 (s, 5-Me), 4.10 and 4.11 (2 s, 2 × MeO), 7.42 and 7.70 (2 s 2 × ArH); *m/z* (175 °C) (rel. int.) 316 ($M^{+\cdot}$, 33), 315 (2.2), 301 (10), 299 (M − OH, 25), 287 (4.2), 274 (38), 273 (38), 260 (M − C_4H_8, 100), 245 (20), 243 (8.9), 228 (11), 203 (13), 163 (9.2), and 147 (7.7.)

2-(3,4-*Dimethoxyphenyl*)-5-(4,5-*dimethoxy*-2-*nitrophenyl*)-1,3,4-*thiadiazole* (**21c**). The suspension of the thiadiazoline (**23a**)[1] (0.40 g, 1 mmol) in hot ethanol (20 ml) was treated with 2M-aqueous $FeCl_3$ (2 ml). The resulting clear solution was allowed to cool when the title compound (0.39 g, 99%), m.p. 205—205.5 °C (from EtOAc), separated (Found: N, 10.25. Calc. for $C_{18}H_{17}N_3O_6S$: N, 10.42%).

2-(2-*Amino*-4,5-*dimethoxyphenyl*)-5-(3,4-*dimethoxyphenyl*)-1,3,4-*thiadiazole* (**21a**). $Na_2S_2O_4$ (0.5 g) was added to a mixture of the nitro compound (**21c**) (0.2 g, 0.5 mmol), ethanol (3 ml), and water (4 ml) with continuous stirring at room temperature. The original suspension turned into a clear greenish solution and, on dilution with water, gave the crystalline title compound (0.16 g, 86%), m.p. 167—168 °C (from butanol) (Found: C, 57.75; H, 5.45; N, 11.15. Calc. for $C_{18}H_{19}N_3O_4S$: C, 57.9; H, 5.1; N, 11.25%); $\nu_{max.}$(KBr) 3 440 and 3 320 cm^{-1}; $\lambda_{max.}$(EtOH) 214 (4.48), 320 (4.13), and 392 (4.19); *m/z* (180 °C) (rel. int.) 373 ($M^{+\cdot}$, 100), 358 (51), 342 (2.3), 330 (4.5), 314 (2.2), 210 [M − $(MeO)_2C_6H_3CN$,† 2.5], 186.5 (M^{2+}, 12), 181 (4.2), 179 ([M − 15]$^{2+}$, 8.4), and 163 (6.4).

2-(2-*Acetylamino*-4,5-*dimethoxyphenyl*)-5-(3,4-*dimethoxyphenyl*)-1,3,4-*thiadiazole* (**21b**). A suspension of the thiadiazoline (**23b**)[1] (0.42 g, 1 mmol) in hot ethanol (20 ml) was treated with 2M-aqueous $FeCl_3$ solution (2 ml) to obtain a clear solution from which the title compound (0.41 g, 98%) was deposited on cooling, m.p. 184—185 °C (from EtOH) [Found: C, 57.7; H, 4.75; N, 9.9. $C_{20}H_{21}N_3O_5S$ (415.4) requires C, 57.82; H, 5.10; N, 10.12%]; $\nu_{max.}$(KBr) 1 685 cm^{-1}; $\lambda_{max.}$(EtOH) 211 (4.33), 256 (4.15), and 364 (4.21); *m/z* (155 °C) (rel. int.) 415 ($M^{+\cdot}$, 100), 400 (14), 373 (33), 358 (36), 342 (1.8), 330 (2.0), 210 (2.2), 209 (2.2), 207.5 (M^{2+}, 2.0), 186.5 (373^{2+}, 4.6), 179 (358^{2+}, 5.4), and 163 (6.5).

* Four experiments.
† By peak matching.

Synthesis of some Quinazoline Derivatives.—6,7-*Dimethoxy*-2-*methylquinazoline* (**13c**): *Improved procedure*, cf. *ref.* 9. 2-Acetylamino-4,5-dimethoxybenzaldehyde (**16b**)[9] (1.1 g, 5 mmol) was stirred with a saturated ethanolic (50 ml) ammonia solution at room temperature until the starting aldehyde had been consumed (t.l.c.; *ca.* 24 h). The solution was evaporated to dryness, the residue was taken up in dilute aqueous HCl, and the resulting solution was made distinctly alkaline. Extraction with chloroform, drying ($MgSO_4$), evaporation of the solvent, and recrystallization of the residue from methanol furnished the title compound (0.8 g, 79%), m.p. 168—169 °C (lit.,[9] m.p. 165—166 °C) (Found: C, 64.9; H, 5.85; N, 13.85. Calc. for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.82; N, 13.72%).

2-(2,2-*Dimethylpropionylamino*)-4,5-*dimethoxybenzaldehyde* (**16c**). 2,2-Dimethylpropionyl chloride (0.15 g, 1.1 mmol) was added dropwise to a mixture of 2-amino-6,7-dimethoxybenzaldehyde (**16a**)[9] (0.18 g, 1 mmol), anhydrous benzene (3 ml), and pyridine (0.7 ml) with continuous stirring and ice cooling. The mixture was kept for 24 h at room temperature, washed successively with water and dilute hydrochloric acid, and evaporated to dryness. The residue was crystallized from a small amount of methanol to give the cream-coloured title compound (0.22 g, 82%), m.p. 122—124 °C, which turned red in the air (Found: N, 5.6. Calc. for $C_{14}H_{19}NO_4$: N, 5.28%); $\nu_{max.}$(KBr) 1 680 and 1 650 cm^{-1}; δ_H 1.38s (Bu^t), 3.96 and 4.05 (2 s, 2 × MeO), 7.11 and 8.63 (2 s, 2 × ArH), and 9.83 (s, CHO).

6,7-*Dimethoxy*-2-*t*-*butylquinazoline* (**13e**). A mixture of the above product (0.53 g, 2 mmol) and 12% ethanolic ammonia solution (40 ml) was heated in a sealed tube for 8 h at 100 °C, and then evaporated to dryness. The residue was recrystallized from benzene–light petroleum or from a small amount of methanol to obtain the title compound (0.28 g, 57%), m.p. 105—107 °C (Found: $M^{+\cdot}$, 246.1342; N, 11.60%. Calc. for $C_{14}H_{18}N_2O_2$: $M^{+\cdot}$, 246.1368; N, 11.38%); *m/z* (65 °C) 246 ($M^{+\cdot}$, 50), 245 (23), 231 (100), 215 (9.5), 204 (46), 190 (19), 189 (6.2), 187 (6.0), 123 (4.6), 115.5 (3.8), 115 (4.8), 57 (4.4)

Synthesis of some Quinazolin-4(3H)-*ones and* -*thiones.*—2-(2,2-*Dimethylpropionylamino*)-4,5-*dimethoxybenzamide* (**16d**). 4,5-Dimethoxy-2-nitrobenzaldehyde[20] (0.21 g, 1 mmol) was reduced in acetic acid (10 ml) in the presence of an 8% Pd–C catalyst at room temperature and ordinary pressure. The catalyst was filtered off and the filtrate was evaporated to dryness under reduced pressure. The crude amino derivative was dissolved in a mixture of anhydrous benzene (4 ml) and pyridine (0.8 ml) and treated with 2,2-dimethylpropionyl chloride (0.2 ml, 1.4 mmol) with ice cooling and continuous stirring. The mixture was kept overnight at room temperature. The resulting crystalline precipitate was filtered off and washed with water. A second crop of the product was obtained by evaporation to dryness of the filtrate under reduced pressure. The combined fractions of the product were taken up in CH_2Cl_2. The resulting solution was washed with 5% aqueous hydrochloric acid and water and then evaporated to dryness. The residue was crystallized from methanol to give the title compound (0.23 g, 75%), m.p. 188—189 °C (Found: C, 60.3; H, 6.95; N, 10.3. Calc. for $C_{14}H_{20}N_2O_4$: C, 59.98; H, 7.19; N, 10.00%); $\lambda_{max.}$(KBr) 3 385, 3 170, 1 645, and 1 625 cm^{-1}; δ_H 1.37s (Bu^t), 3.89 + 3.96 (2 s, 2 × MeO), 6.3 (br s, NH), and 7.10 and 8.58 (2 s, 2 × ArH).

6,7-*Dimethoxy*-2-*t*-*butylquinazolin*-4(3H)-*one* (**22d**). The benzamide (**16d**) (0.28 g, 1 mmol) was stirred with 4% aqueous NaOH (4 ml) at 60—70 °C to give a clear solution (5 min). The latter was allowed to cool, acidified with acetic acid, diluted with water, and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed successively with water and aqueous $NaHCO_3$ and evaporated to dryness. The residue was crystallized either from acetic acid or from a large volume of ethanol to give the title compound (0.24 g, 85%), m.p. 251—252 °C (Found: C, 64.2; H, 6.45; N, 10.85. Calc. for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.92; N, 10.68%); $\nu_{max.}$(KBr) 3 270 and 1 655 cm^{-1}; $\lambda_{max.}$(EtOH) 240 (4.70), 282sh (3.85), 310 (3.75), and 323 (3.69), in good agreement with the spectra of a series of model compounds;[18] δ_H 1.52 (s, Bu^t), 4.05 (s, 2 × MeO), 7.11 and 7.55 (2 s, 2 × ArH), and 11.1 (br s, NH); *m/z* (140 °C) (rel. int.) 262 ($M^{+\cdot}$, 90), 261 (37), 247 (100), 231 (15), 220 (58), 206 (9.2), 2.05 (6.1), 203 (4.1), 191 (5.9), 179 (7.4), 164 (4.2), 131 (1.5), 123.5 (8.6), and 57 (7.5).

6,7-*Dimethoxy*-2-*t*-*butylquinazoline*-4(3H)-*thione* (**14e**). A mixture of the quinazolinone (**22d**) (0.26 g, 1 mmol), P_2S_5 (0.3 g), and dry pyridine (3 ml) was refluxed for 3 h. The somewhat turbid solution was decanted from the oily precipitate and treated with M-NaOH (6 ml). The resulting clear solution was acidified with acetic acid to give the title compound (0.21 g, 74%), m.p. 172—173 °C (from AcOH) (Found: $M^{+\cdot}$, 278.1070; C, 60.15; H, 6.4; N, 10.0. Calc. for $C_{14}H_{18}N_2OS$: $M^{+\cdot}$, 278.1089; C, 60.42; H, 6.52; N, 10.06%); $\lambda_{max.}$(EtOH) 224sh (4.42), 230 (4.45), 253 (4.11), 274 (4.11), 351sh (3.92), 366 (4.15), and 380 (4.14), in good agreement with the spectra of a series of type (**14g**) model compounds;[15] *m/z* (120 °C) (rel. int.) 278 ($M^{+\cdot}$, 100), 277 (31), 263 (78), 247 (14), 236 (41), 222 (10.0), 221 (5.8), 220 (5.3), 207 (6.6), 189 (13), 139 (4.5), 110.5 (5.7), and 57 (11).

6,7-*Dimethoxy*-2,3-*dimethylquinazolin*-4(3H)-*one* (**22c**). A mixture of 6,7-dimethoxy-2-methylquinazolin-4(3*H*)-one (**22a**)[6] (0.11 g, 0.5 mmol), methanol (3 ml), 10% aqueous NaOH (0.4 ml), and methyl iodide (0.04 ml, 0.65 mmol) was gently refluxed for 3 h and then evaporated to dryness. The residue was taken up in water to give the title compound (0.11 g, 94%) as an insoluble residue, m.p. 223—224 °C (from methanol) (Found: C, 61.3; H, 6.4; N, 11.9. Calc. for $C_{12}H_{14}N_2O_3$: C, 61.54; H, 6.02; N, 11.96%); $\nu_{max.}$(KBr) 1 660 cm^{-1}; *m/z* (110 °C) (rel. int.) 234 ($M^{+\cdot}$, 100), 219 (52), 191 (18), 189 (17), 176 (2.7), 163 (2.7), 161 (3.7), 134 (13), 117 (4.5), and 56 (42).

6,7-*Dimethoxy*-2,3-*dimethylquinazoline*-4(3H)-*thione* (**14f**). A mixture of the quinazolinone (**22c**) (1.17 g, 5 mmol), dry pyridine (15 ml), and P_2S_5 (1.5 g) was heated in a sealed tube for 8 h at 150 and for 3 h at 170 °C. After being allowed to cool, the supernatant liquid was poured into water, NaOH was added, and the resulting clear solution was acidified with acetic acid to obtain the title compound (0.7 g, 56%), m.p. 229—231 °C (from MeOH) (Found: $M^{+\cdot}$, 250.0756; N, 10.9%. Calc. for $C_{12}H_{14}N_2O_2S$: $M^{+\cdot}$, 250.0776; N, 11.20%); $\lambda_{max.}$(EtOH) 226sh (4.47), 233 (4.53), 254 (4.20), 275 (4.19), 343sh (3.92), 361 (4.18), and 375 (4.19), in good agreement with the spectra of a series of type (**14g**) model compounds; [15] δ_H 2.70 (s, 2-Me), 3.98 (s, 3-Me), 4.02 and 4.10 (2 s, 2 × MeO), 6.91 (s, 8-H), and 8.03 (s, 5-H); *m/z* (130 °C) (rel. int.) 250 ($M^{+\cdot}$, 100), 235 (26), 221 (5.7), 219 (6.8), 217 (6.7), 209 (11), 207 (9.2), 205 (7.4), 204 (7.0), 203 (7.6), 194 (9.7), 166 (7.4), 134 (11), and 56 (24).

Irradiation of Mixtures of some 2-*Alkyl*-6,7-*dimethoxyquinazolines* (**13c**), (**13e**) *and* 2-*Alkyl*-6,7-*dimethoxyquinazoline*-4(3H)-*thiones* (**14a**), (**14e**).—(*a*) A mixture of compounds (**13c**) (60 mg, 0.29 mmol) and (**14a**)[6] (60 mg, 0.25 mmol) and ethanol (150 ml) was irradiated with continuous stirring under nitrogen for *ca.* 6 h and then evaporated to dryness. The residue was worked up by preparative t.l.c. to give the biquinazolinyl (**12a**) (50 mg, 45%), the quinazolinyl alcohol (**13a**) (14 mg, 10%), and the quinazolinyl ketone (**13b**) (3 mg, 2%),* identical (m.p., i.r.) with the products obtained by irradiation of the thioamidate (**10a**).

(*b*) A mixture of the quinazoline (**13e**) (200 mg, 0.8 mmol) and the quinazolinethione (**14e**) (200 mg, 0.7 mmol) was irradiated in ethanol (400 ml) for 4 h and the resulting mixture was then worked up as described below for work-up of the mixture

* Yields based on the total amount of quinazoline derivatives introduced.

obtained by photolysis of compound (**14e**); in this way the quinazoline (**13e**) (140 mg, 37%), the quinazolinone (**22d**) (12 mg, 3%), and the biquinazolinyl (**12b**) (32 mg, 3%) were obtained; all except the latter were identified by comparison with authentic samples. Two further unidentified products were formed in small amounts.

The biquinazolinyl (**12b**) crystallized when refluxed with methanol, m.p. 262—267 °C (Found: $M^{+\cdot}$, 490.2588; N, 11.17%. Calc. for $C_{28}H_{34}N_4O_4$: $M^{+\cdot}$, 490.2580; N, 11.42%); δ_H 1.57s (2 × Bu^t), 3.86 and 4.10 (2 s, 2 × MeO), and 7.41 and 7.52 (2 s, 2 × ArH); *m/z* (180 °C) (rel. int.) 490 ($M^{+\cdot}$, $C_{28}H_{34}N_4O_4$, 63), 489 (14), 475 (96), 459 ($C_{27}H_{31}N_4O_3$, 100), 448 (3.0), 445 (3.5), 443 (2.8), 245 (M^{2+}, 21), 230 ([M − 2Me]$^{2+}$, 17), and 57 (5.9).

(*c*) A mixture of the quinazoline (**13e**) (300 mg, 1.2 mmol) and the quinazolinethione (**14a**) (300 mg, 1.25 mmol) was irradiated in ethanol (300 ml) for 20 h. The resulting mixture was evaporated to dryness and the residue taken up in chloroform. The chloroform solution was extracted with 5% aqueous NaOH, and the aqueous phase was acidified to give a crystalline precipitate (A). The chloroform phase was evaporated to dryness (B). The fractions A and B were separately worked up by preparative t.l.c. (benzene–chloroform–ethyl acetate, 1:1:1) to give unchanged thione (**14a**) (13 mg, 4.3%) and the quinazolinone (**22a**) (72 mg, 26%)[6] from A, and the unchanged quinazoline (**13e**) (173 mg, 58%), the biquinazolinyl (**12b**) (70 mg, 23.8%), the biquinazolinyl (**12c**) (49 mg) [9%, based on the quinazoline (**13e**) introduced] a semisolid product which crystallized when triturated with methanol, m.p. 218—221 °C, and the biquinazolinyl (**12a**) (20 mg, 7.8%) from B, in decreasing order of their R_F values.

The biquinazolinyl (**12c**) (Found: $M^{+\cdot}$, 448.2103; N, 12.68%. Calc. for $C_{25}H_{28}N_4O_4$: $M^{+\cdot}$, 448.2110; N, 12.49%); δ_H 1.54 (s, Bu^t), 2.94 (s, Me), 3.84 and 3.86 (2 s, 2 × MeO), 4.09 (s, 2 × MeO), and 7.37, 7.48, 7.41, and 7.42 (4 s, 4 × ArH); *m/z* (180 °C) (rel. int.) 448 ($M^{+\cdot}$, $C_{25}H_{28}N_4O_4$, 43), 447 (11), 433 (87), 417 ($C_{24}H_{25}N_4O_3$, 100), 406 (2.8), 403 (2.3), 402 (2.0), 401 (3.6), 375 (5.3), 224 (M^{2+}, 17), 201 (8.2), and 57 (3.4).

Irradiation of some Quinazolines.—(*a*) An ethanolic (400 ml) solution of the quinazoline (**13c**) (0.4 g) was irradiated for 28 h. A very complex mixture of unchanged starting material (0.1 g, 25%) and of several unidentified products was obtained.

(*b*) An ethanolic (150 ml) solution of the quinazoline (**13f**) (0.25 g, 1 mmmol) was irradiated for 15 h and evaporated to dryness; the residue was taken up in CH_2Cl_2 (1 ml) to give the biquinazolinyl (**12a**) (29 mg, 15%), identical (i.r., m.p.) with an authentic sample (see above) as the insoluble residue. The CH_2Cl_2 solution was evaporated to dryness and the residue was recrystallized from ethanol to give unchanged starting material (0.16 g, 64%).

Photolysis of 2-Alkyl-6,7-dimethoxyquinazoline-4(3H)-thiones.—(*a*) A suspension of 6,7-dimethoxy-2-methylquinazoline-4(3*H*)-thione (**14a**)[6] (0.1 g, 0.4 mmol) in ethanol (150 ml) was irradiated for 7 h with continuous stirring and then evaporated to dryness. The residue was worked up by preparative t.l.c. to give the biquinazolinyl (**12a**) (78 mg, 96%), m.p. 309—312 °C (from acetic acid), identical (m.p., i.r., t.l.c.) with an authentic sample (see above).

(*b*) An ethanolic solution (150 ml) of the quinazolinethione (**14e**) (0.3 g, 1.1 mmol) was irradiated until the starting compound disappeared completely (t.l.c.; *ca.* 20 h). The solution was evaporated to dryness and worked up by preparative t.l.c. (benzene–chloroform–ethyl acetate, 1:1:1) to give the quinazoline (**13e**) (86 mg, 31.6%), the quinazolinone (**22d**) (30 mg, 10.3%), and the biquinazolinyl (**12b**) (25 mg, 4.5%), all identified by comparison with authentic samples obtained as described above.

(*c*) An ethanolic (150 ml) solution of the quinazolinethione (**14f**) (0.3 g, 1.2 mmol) was irradiated for 20 h; the starting compound did not disappear completely (t.l.c.). The dry residue of the solution was taken up in CH_2Cl_2 to give unchanged starting compound (34 mg) as an insoluble residue. The filtrate was again evaporated to dryness and the residue was taken up in hot ethanol (4 ml) to give the quinazolinone (**22c**) (27 mg) as an insoluble residue. The filtrate was worked up by preparative t.l.c. to give further (10 mg; total recovery 15%) unchanged starting substance and further (40 mg; total yield 24%) of the quinazolinone (**22c**) in addition to a non-migrating decomposition product of unknown structure.

Irradiation of the Biquinazolinyl (**12b**).—An ethanolic (150 ml) solution of the title compound (14 mg) was irradiated for 8 h and evaporated to dryness. The dry residue was worked up by t.l.c. (benzene–chloroform–ethyl acetate, 1:1:1) to give unchanged starting material (8 mg) (i.r., R_F) and trace amounts of three non-identified photolysis products, none of which was identical (R_F) with the quinazoline (**13e**).

Photolysis of Diquinazolin-4-yl Disulphides.—(*a*) Di-(6,7-dimethoxy-2-methylquinazolin-4-yl) disulphide (**24a**)[16] (0.12 g, 0.25 mmol) was irradiated in ethanol (150 ml) with ice cooling until the starting compound was completely transformed (t.l.c.; 2 h). The mixture was evaporated to dryness and the dry residue triturated with aqueous NaOH to give the biquinazolinyl (**12a**) (35 mg, 34%), m.p. 302—305 °C (from acetic acid), identical (i.r., t.l.c.) with an authentic sample. The alkaline solution was acidified with acetic acid to precipitate the quinazolinethione (**14a**) (66 mg, 54%), identical (i.r., t.l.c.) with an authentic sample.[6]

(*b*) Di-[2-t-butyl-6,7-dimethoxyquinazolin-4-yl] disulphide (**24b**)[16] (0.32 g, 0.58 mmol) was irradiated for 5 h in ethanol (150 ml) with ice cooling. The mixture was evaporated to dryness and the residue was taken up in methanol (2 ml) to give the thione (**14e**) (0.15 g, 46%) identical (i.r., t.l.c.) with an authentic sample obtained as described above, as the insoluble residue. Not even traces of the biquinazolinyl (**12b**) could be detected by t.l.c. in the methanolic solution.

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References

1 Part 25 of Electron Deficient Heteroaromatic Ammonioamidates, and Part 12 of *N*-(Quinazolin-3-io)amidates, see M. Lempert-Sréter, K. Lempert, and J. Møller, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2011.
2 For a review on the chemistry of electron deficient heteroaromatic ammonioamidates, in particular of *N*-(quinazolin-3-io)amidates, see K. Lempert, *Lect. Heterocycl. Chem.*, 1982, **6**, S-25.
3 K. T. Potts and R. Dugas, *Chem. Commun.*, 1970, 732.
4 M. Lempert-Sréter, K. Lempert, J. Tamás, and K. Vékey, *Acta Chim. Acad. Sci. Hung.*, 1980, **103**, 259 (*Chem. Abstr.*, 1981, **94**, 47070d).
5 M. Lempert-Sréter, K. Lempert, and J. Møller, *Chem. Scr.*, 1978—1979, **13**, 195.
6 M. Lempert-Sréter, K. Lempert, P. Bruck, and G. Tóth, *Acta Chim. Acad. Sci. Hung.*, 1977, **94**, 391 (*Chem. Abstr.*, 1978, **88**, 170106y).
7 Ref. 2, p. S-34.
8 G. Barta-Szalai, J. Fetter, K. Lempert, and J. Møller, *Acta Chim. Acad. Sci. Hung.*, 1980, **104**, 253 (*Chem. Abstr.*, 1981, **95**, 23822w).
9 A Rilliet, *Helv. Chim. Acta*, 1922, **5**, 549.
10 H. Gross and J. Gloede, *Chem. Ber.*, 1963, **96**, 1387.
11 W. D. Ollis and C. A. Ramsden, in *Adv. Heterocycl. Chem.*, 1976, **19**, 88 and references cited therein.

12 *E.g.*, F. R. Stermitz, C. C. Wei, and C. M. O'Donnel, *J. Am. Chem. Soc.*, 1970, **92**, 2745; G. Allen, A. Castellano, J. P. Catteau, and A. Lablache-Combier, *Tetrahedron*, 1971, **27**, 4687; A. Castellano, J. P. Catteau, A. Lablache-Combier, and B. Planchaert, *Tetrahedron Lett.*, 1973, 4185.
13 Ch. Grundman and J. M. Dean, *J. Org. Chem.*, 1965, **30**, 2809.
14 R. Grashey, M. Weidner, and G. Schroll, *Chem.-Ztg.*, 1976, **100**, 497 (*Chem. Abstr.*, 1977, **86**, 139949k).
15 G. Barta-Szalai, J. Fekete, J. Fetter, K. Lempert, and J. Møller, *Acta Chem. Scand.*, 1979, **B33**, 79.
16 M. Lempert-Sréter, K. Lempert, and J. Møller, *Acta Chim. Acad. Sci. Hung.*, 1983, **112**, 83 (*Chem. Abstr.*, 1983, **99**, 88153e).
17 H. Debus, *Liebigs Ann. Chem.*, 1850, **75**, 128.
18 J. Fetter, K. Lempert, G. Barta-Szalai, J. Møller, and L. Párkányi, *Acta Chim. Acad. Sci. Hung.*, 1977, **93**, 233 (*Chem. Abstr.*, 1978, **88**, 151718h).
19 F. Garelli, *Gazz. Chim. Ital.*, 1890, **20**, 700.
20 C. A. Fetscher and M. T. Bogert, *J. Org. Chem.*, 1939, **4**, 82.

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