Reduction and Stereochemical Studies through N.M.R. and *X*-Ray Techniques of Indolo[2,1-*b*]quinazolines

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Indolo[2,1-*b*]quinazoline-6,12-dione (**1**) has been reduced by various methods and the stereochemistry of the products [e.g. 6-acetoxy-5a,6-dihydroindolo[2,1-*b*]quinazolin-12(5*H*)-one (**10b**) and 6-acetoxy-5-acetyl-5,5a,6,12-tetrahydroindolo[2,1-*b*]quinazoline (**30b**)] has been studied by n.m.r. spectroscopic methods. The detailed structure of the acetylated products, obtained from compound (**1**) by reduction with $NaBH_4$, [(**10b**)], and $LiAlH_4$, [(**30b**) and 1-(2-acetamidobenzyl)-3-acetoxyindole (**34**)], have been determined by *X*-ray crystallography.

Reduction of the dione (**1**) with hypophosphorus acid yielded the 6,6′-coupled dimeric product (**40**) which readily underwent dehydrogenation to the violet compound (**41**).

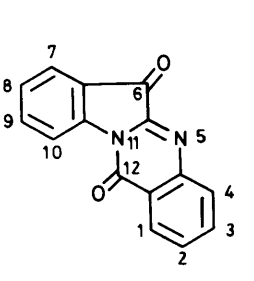
Indolo[2,1-*b*]quinazoline-6,12-dione (**1**)[1-3] is a compound with a long history and it appears to have been obtained[4] by O'Neill as early as 1892. A few years ago compound (**1**) was identified as a natural product[1,2,5-7] from *e.g. Couroupita guianensis* and the name tryptanthrin was coined.[5] Tryptanthrin has also been isolated from culture solutions of the yeast *Candida liplytica*, by Fiedler and Zähner,[5] together with a violet compound (**2**), candidine.[3]

In addition, tryptanthrin was identified as the active principle in the leaves of *Strobilanthes cusia*, a remedy traditionally used against dermatophytic infections. This antimycotic effect is similar to that of griseofulvin (**3**), a drug well-known to be effective against such dermatophytic infections,[8] and this has triggered a lot of interest[2,9] in tryptanthrin.

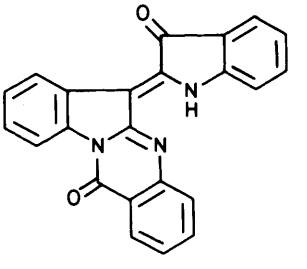
Results and Discussion

Tryptanthrin (**1**) which has a very limited solubility in water and simple alcohols, is similar to isatin in many reactions involving the 6-oxo function and compounds with for example active methylene groups which readily undergo condensation. Thus, malonodinitrile gives[3,10] the diacyanomethylene compound (**4**). More interestingly, tryptanthrin also has redox properties similar to those of isatin,[11-14] and is able to dehydrogenate and subsequently convert α-amino acids to secondary products—a possible indication of its biological activity. Both compounds also interact in a similar way with amines, giving intensely blue dyes.

In view of this we decided to study some transformations, particularly reductions, of compound (**1**), along with reactions with older, less well established compounds, notably the so-called isatoids.[15,16] Methylisatoid, a substance first noted[17] as a product formed by exposure or *O*-methylisatin (**5**) to moist air is conveniently made by dissolution of compound (**5**) in aqueous acetic acid.[18] Many formulations such as (**6**) had been advocated for methylisatoid until in 1976 Cornforth[15] finally established the ester (**7b**) as the correct structure. Mild hydrolysis of (**7b**) gave the acid (**7c**) which readily underwent decarboxylation to the orange compound (**7a**).[15] Previously[19,20] (**7a**) had been assigned the incorrect isomeric structures (**8**) and (**9**). Both structures correspond to reduced derivatives of tryptanthrin and none of them has so far been synthesized.



(**1**)



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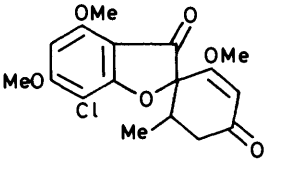
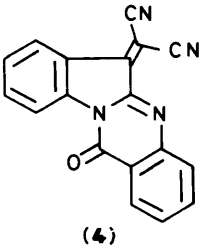
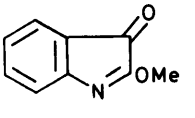


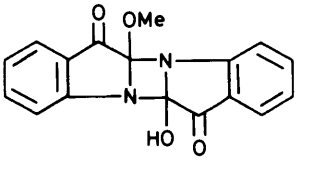
(**3**)



(**4**)



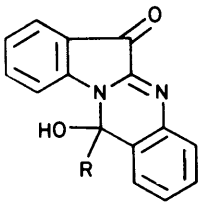
(**5**)



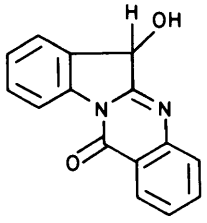
(**6**)

Reduction of the dione (**1**) with $NaBH_4$ in acetic acid readily afforded the alcohol (**10a**). Dehydration of (**10a**) with hot concentrated H_2SO_4† or hot PPA afforded the expected product as a mixture of the two tautomeric forms (**14a**) and (**12a**). In the solid state the tautomer (**14a**) appeared to be more stable than (**12a**) indicated by the absence of NH vibrations in the i.r. spectrum. Furthermore, i.r. data from the *gem*-dimethyl derivative (**14b**)[21] previously prepared by Domanig agreed

† Sulphuric acid had earlier been used to effect[21] the transformation (**10c**)→(**12c**).



(7) **a**; R = H
b; R = CO_2Me
c; R = CO_2H



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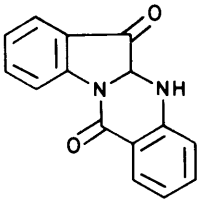

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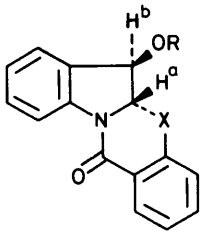
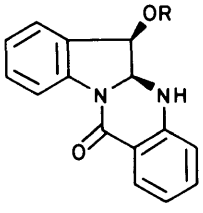
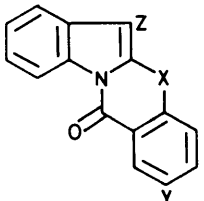


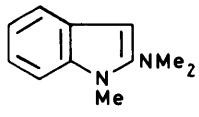
(10) **a**; R = H, X = NH
b; R = COMe, X = NH
c; R = H, X = CH_2
d; R = COMe, X = NCOMe



(11) **a**; R = H
b; R = COMe



(12) **a**; X = NH, Y = Z = H
b; X = CH_2, Y = Z = H
c; X = NMe, Y = Z = H
d; X = NCOMe, Y = Z = H
e; X = NMe, Y = Cl, Z = H
f; X = NH, Y = H, Z = Me



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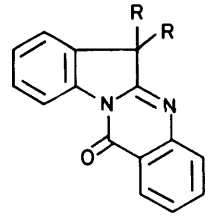
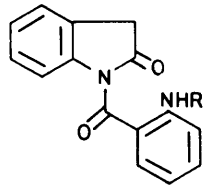
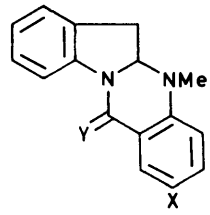


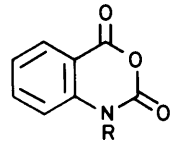
(14) **a**; R = H
b; R = Me



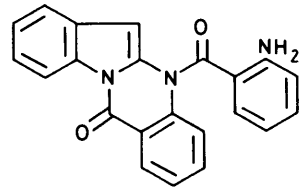
(15) **a**; R = H
b, R = Me



(16) **a**; X = H, Y = O
b; X = Cl, Y = O
c; X = Cl, Y = H_2



(17) **a**; R = H
b; R = Me



(18)

nicely with those of (**14a**) (C=O, C=N, C=C, 1 675, 1 645, 1 605, and 1 465 cm^{-1} respectively) for (**14b**); (1 675, 1 640, 1 605, and 1 465 cm^{-1}) for (**14a**).

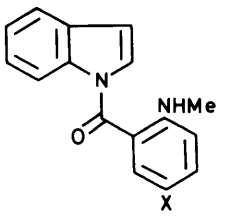
The picture is more complicated in solution and the choice of solvent has a strong influence on the tautomeric equilibrium (**14a**)⇌(**12a**). Thus the ^1H n.m.r. spectrum in $CDCl_3$ exhibits a broad singlet at 4.1 p.p.m. corresponding to the 6-H_2 group in (**14a**), whereas in $(CD_3)_2SO$ it is completely different with a sharp singlet at 6.05 p.p.m. due to the 6-H_2 group in (**12a**). In $CDCl_3$–$(CD_2)_2SO$ (4:1) the ^1H n.m.r. spectrum shows the two tautomers (**12a**) and (**14a**) to be present in equal amounts. The chemical shift in $(CD_3)_2SO$ (6.05 p.p.m.) for (**12a**) corresponds nicely with the observed shifts (6.1 p.p.m.) for compound (**12c**) and (6.27 p.p.m.) for (**12e**).[22] Pedersen[23] has reported an even lower shift for compound (**13**) (5.87 p.p.m.). The ^{13}C n.m.r. shifts in $(CD_3)_2SO$ are also in good agreement for compounds (**12a**) and (**12c**) (80.3 and 82.2 p.p.m.) respectively. The chemical shifts of C-6 in (**12a** and **c**) reflects the push-pull effects of the donating 5-substituent and the slightly accepting N-acylated indole nitrogen atom. Normally C-3 in indoles resonates between 100—110 p.p.m.[24]

Not unexpectedly, compound (**14a**) is sensitive to even mild oxidants and to dissolution, *e.g.* Me_2SO will transform (**14a**) to a complex mixture of oxidized products within a few hours. From this mixture only tryptanthrin (**1**) and the dimeric product (**41**) were identified. In acidic media (**14a**) is even more sensitive towards oxidation and the only isolable product from its reaction in BF_3–HOAc was compound (**41**).

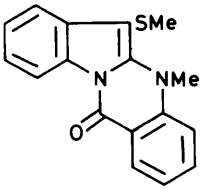
Compound (**14a**) could also be obtained in relatively poor yield by sublimation of the *N*-acylated oxindole (**15a**), which was the main product when oxindole and isatoic anhydride (**17a**) were melted together with a catalytic amount of tetramethylethylenediamine (TMEDA) at 200 °C for 10 min. A minor product (**18**) with low solubility was also collected from this condensation in yields varying from 10 to 20%. Melting isatoic anhydride (**17a**) of *N*-methylisatoic anhydride (**17b**) and oxindole derivatives together was found to be a quick and convenient method for the preparation of compounds (**12b**—**f**) and (**14b**).

A similar experiment with *N*-methylisatoic anhydride (**17b**) and oxindole yielded (**12c**) which could also be obtained by dehydrogenation (MnO_2) of compound (**16a**). This in turn was prepared by the acid-induced cyclization of the *N*-benzoyl indole (**19a**) which was readily obtained by *N*-acylation of the indole Grignard (or better sodioindole) reagent with *N*-methylisatoic anhydride (**17b**). Fryer[22] *et al.* had previously similarly prepared the 2-chloro substituted compounds (**19b**) and (**16b**).

Compound (**12c**) could likewise be obtained by the desulphurization with Raney nickel of the sulphide (**20**) which Coppola[25] had previously assigned the erroneous structure (**21**). Compound (**20**) was prepared from 3-mercaptomethyloxindole[26] and *N*-methylisatoic anhydride (**17b**) with NaH as the base. We have not reinvestigated the other compounds of similar type that Coppola reported but we suggest that all structures should be reassigned [*i.e.* (**22**) is in fact (**23**)]. This view is also supported by the reported i.r. data, which included C=O vibrations at 1 690 and 1 675 cm^{-1} for (**20**) and (**23**) respectively. The purported structures (**21**) and (**22**) would be



(19) a; X = H
b; X = Cl



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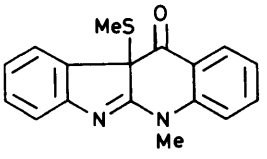

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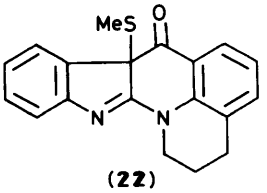

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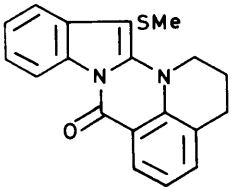

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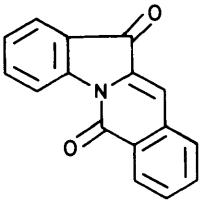


(24)

expected to exhibit C=O vibrations in the range 1 640—1 620, *i.e.* similar to anthranilamide.

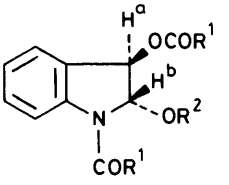
Stereochemistry.—The *trans*-stereochemistry for the $NaBH_4$-reduced compound (**10a**) and the acetylated compound (**10b**) was established by a detailed analysis of the n.m.r. data [*e.g.* (**10a**) J_{AB} 6.2 Hz, (**10b**) J_{AB} 5.5 Hz]. Dreiding models were built for (**10a** and **b**) as well as for the corresponding *cis* isomers (**11a** and **b**), and all the dihedral angles between H_A and H_B were measured and correlated with the n.m.r. data using the Karplus equation.[27–29] For compound (**10a**) the angle was estimated to be *ca.* 145° [for the corresponding *cis*-isomer (**11a**) *ca.* 15°], and for (**10b**) *ca.* 135° [the *cis*-isomer (**11b**) *ca.* 10°]. For the pair (**10a**) and (**11a**) alone it was not possible to make a direct assignment and consequently the more bulky pair was studied. The steric hindrance will decrease the dihedral angle in (**11b**), which implies an increased coupling constant. This is the opposite of what was found experimentally. In the *trans* form (**10b**) the steric hindrance should also decrease the dihedral angle, which in this case will lead to a decrease in the coupling constant. The conclusion then, based on n.m.r. spectroscopy is that the reduction of the dione (**1**) with $NaBH_4$ in acetic acid gives exclusively the *trans* form (**10a**). No indications for the formation of the *cis* isomer were obtained in spite of the fact that the reduction was studied under various conditions ($NaBH_4$ in MeOH, TFA, or dioxane).

trans-Stereochemistry for compound (**10c**) was reported in 1972 by Hooper and Pitkethly,[30] who obtained (**10c**) by reduction with $NaBH_4$ of the dione (**24**) in methanol. The assignment was based on an n.m.r. study. The estimated dihedral angle for H_A–H_B was 155°. Judging from the n.m.r. data the compounds (**10a** and **c**) seemed to be closely related and hence *trans* stereochemistry was tentatively assigned to these compounds.

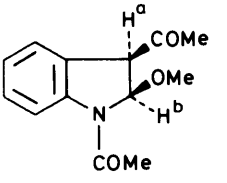
To ascertain the stereochemistry of compound (**10a**) as well as (**10b**), and to verify the correctness of the n.m.r. study based on the Karplus equations for indoline systems, compound (**10b**) was subjected to an *X*-ray investigation. This study confirmed the conclusions based on n.m.r. spectroscopy, with a dihedral angle of (−)142° (see the crystallographic section for further details).

Table 1.

Compound	J_{AB} (Hz)	Disposition	Ref.
(**25a**)	0	*trans*	31, 32
(**26**)	6	*cis*	31, 32
(**25b**)	0	*trans*	35
(**27**)	6.6	*cis*	33
(**28**)	15	*cis*	37
(**29**)	12.8	*cis*	37



(25) a; $R^1 = R^2$ = Me
b; R^1 = Ph, R^2 = COPh



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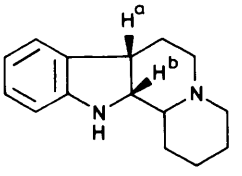

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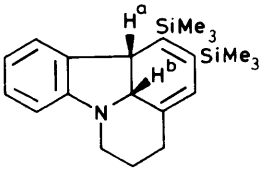

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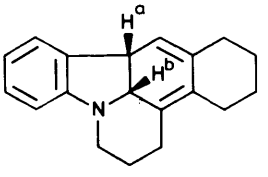

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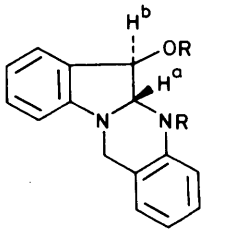


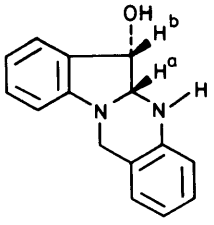
(30) a; R = H
b; R = COMe

Many other n.m.r. studies[31–37] of indoline systems have indicated that the Karplus equation can be useful (Table 1). Due care is however necessary.

Attempts to prepare compound (**10d**) by reflux of (**10a**) in acetic anhydride with a catalytic amount of 4-dimethylaminopyridine resulted in an elimination reaction yielding compound (**12d**).

Reduction of tryptanthrin (**1**) with $LiAlH_4$ in ether gave a mixture of the air sensitive *cis* and *trans* isomers (**30a**) and (**31**). Both isomers were quickly dehydrogenated by air to the red compound (**32**) which showed a u.v.–visible spectrum similar to that of the well-known 2-anil of *N*-methylisatin (**33**).[38] Acetylation with pyridine–AcCl (Ac_2O or *N*-acetylimidazole) of compound (**30a**) gave the expected diacetate (**30b**) (J_{AB} 0.7 Hz), which is in good agreement with a dihedral angle of approximately 90°. To ascertain the structure of (**30b**) an *X*-ray determination was undertaken which showed the dihedral angle in (**30b**) to be 95°.

Acetylation of the *cis* isomer (**31**) with AcCl/pyridine (Ac_2O or *N*-acetylimidazole) yielded a diacetylated product whose i.r.



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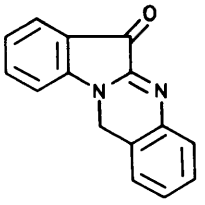

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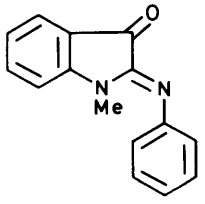
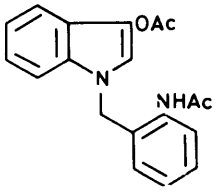
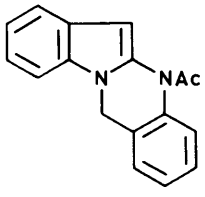


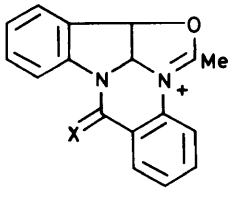
(33)



(34)



(35)

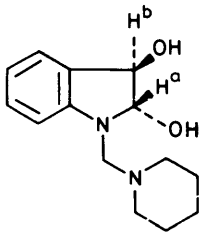


(36) a; X = H_2
b; X = O

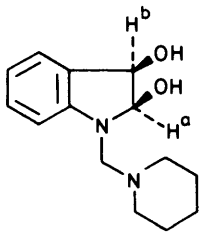
spectrum exhibited strong NH vibrations. The ^{13}C n.m.r. study indicated a ring opening, to the diacetyl compound (**34**). This assignment was crystallographically verified, although the data were not fully satisfactory and are therefore not included in the crystallographic section. The ^{13}C n.m.r. signals from the indoxyl* moiety of (**34**) agreed nicely with the corresponding signals from a model compound (3-acetoxy-*N*-methylindole).[39] The fact that $LiAlH_4$ reduction of compound (**10a**) followed by acetylation gave (**30b**) [but not (**34**)] does not correlate the *trans* stereochemistry.

Acetylation of a crude mixture of compounds (**30a**) and (**31**) (acetic anhydride and 4-dimethylaminopyridine in methylene chloride) afforded the elimination product (**35**). This is the same type of elimination as the transformation of (**10a**) into the *N*-acetyl compound (**12d**). When (**10a**) was treated with acetic anhydride–DMAP under milder conditions in refluxing methylene chloride the only isolated product was the mono-*O*-acetate (**10b**). The fact that (**10b**) could be subsequently transformed to (**12d**) in refluxing acetic anhydride containing a small amount of DMAP, indicates that (**10b**) is an intermediate in the reaction. To test whether that the diacetate is an intermediate in the reaction, *via* elimination of acetic acid, compound (**30b**) was treated with acetic anhydride and DMAP in refluxing methylene chloride. Under these conditions however, (**30b**) proved to be inert and compound (**35**) was not detected in the reaction mixture. Not even the much stronger base KOBu^t could effect the *cis*-elimination of acetic acid from (**30b**). These facts exclude the diacetate as an intermediate in the elimination reaction. To account for the results we suggest that 5a-H in an intermediate species such as (**36**) is attacked by DMAP, resulting in the formation of the *N*-acetylated product.

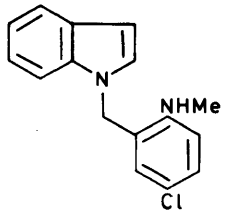
* Indol-3-ol.



(37)



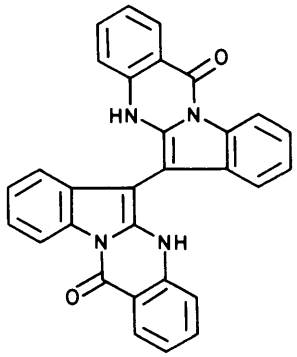
(38)



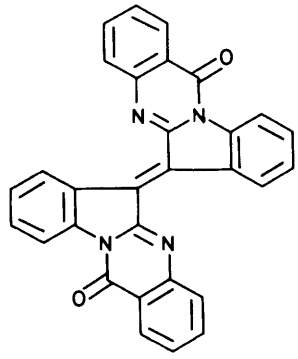
(39)

trans-Stereochemistry has also been reported for a product (**37**), obtained[40] by Roth and Lausen by the reduction of 1-(piperidinomethyl)isatin with $LiAlH_4$ in ether.[41] The suggested stereochemistry was based on u.v. studies using model compounds and the Kershaw–Taylor rule.[42] Some n.m.r. spectroscopic data were also reported but unfortunately not the coupling constant, which now has been determined as 2.2 Hz. Roth and Lausen apparently did not obtain any evidence for the formation of the *cis* isomer (**38**). We have now repeated this experiment and arrived at the same conclusion.

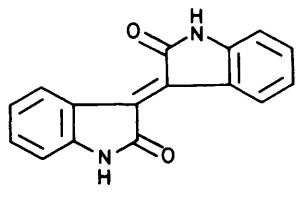
A ring opening related to the elimination [(**31**)→(**34**)] had earlier been reported by Fryer *et al.*,[22] who found that compound (**16b**), on treatment with $LiAlH_4$ in THF, gave the amine (**39**). The reaction pathway was assumed to include compound (**16c**) as an intermediate.



(40)



(41)



(42)

In 1924 Kalb and Berrer[43] reported the reduction of 5,7-diiodoisatin with hypophosphorous acid to the corresponding 3-hydroxyindol-2-one. Treatment of tryptanthrin (**1**) with hypophosphorous acid yielded the 6,6′-coupling product (**40**) rather than the expected product (**8**). Compound (**40**) is

Table 2. Least-squares planes (in terms of orthogonalized co-ordinates) with distances (Å) of the atoms from the plane with standard deviations in parentheses

Compound (**10b**)

(*a*) Plane through benzene ring C(2)—C(5), C(13), and C(14)

$$0.884x - 0.342y - 0.319z + 2.304 = 0$$

C(2)	−0.006(4)	C(5)	−0.002(4)
C(3)	−0.000(4)	C(14)	−0.004(4)
C(4)	0.005(4)	C(13)	0.008(4)

(*b*) Plane through five-membered ring C(6), C(14), C(13), N(1), and C(15)

$$0.907x - 0.351y - 0.233z + 1.480 = 0$$

C(6)	−0.103(4)	N(1)	−0.088(4)
C(14)	0.051(4)	C(15)	0.121(4)
C(13)	0.028(4)		

(*c*) Plane through right side of six-membered ring C(12), N(1), C(15), and N(7)

$$0.708x - 0.224y - 0.670z + 4.748 = 0$$

C(12)	0.122(3)	C(15)	0.206(3)
N(1)	−0.200(3)	N(7)	−0.090(3)

(*d*) Plane through benzene ring and left side of six-membered ring N(7), C(16), C(8)—C(11), C(17), and C(12)

$$0.775x - 0.505y - 0.380z + 4.042 = 0$$

N(7)	0.015(3)	C(10)	0.074(4)
C(16)	0.025(3)	C(11)	0.030(4)
C(8)	−0.028(4)	C(17)	0.033(3)
C(9)	−0.034(4)	C(12)	0.054(3)

(*e*) Dihedral angle between plane *a* − *b* 5.2(1)
Dihedral angle between plane *b* − *c* −28.8(1)
Dihedral angle between plane *c* − *d* 23.6(1)
Dihedral angle between plane *a* − *d* 11.8(1)

Compound (**30b**)

(*a*) Plane through benzene ring C(2)—C(5), C(13), and C(14)

$$-0.389x + 0.739y - 0.551z + 4.408 = 0$$

C(2)	0.001(4)	C(5)	0.001(4)
C(3)	0.001(5)	C(13)	−0.002(4)
C(4)	−0.003(5)	C(14)	0.001(4)

(*b*) Plane through five-membered ring C(6), C(14), C(13), N(1), and C(15)

$$-0.344x + 0.676y - 0.651z + 0.497 = 0$$

C(6)	−136(4)	N(1)	−0.110(4)
C(14)	0.037(4)	C(15)	0.177(4)
C(13)	0.071(4)		

(*c*) Plane through right side of six-membered ring C(12), N(1), C(15), and N(7)

$$-0.220x - 0.315y - 0.923z + 0.455 = 0$$

C(12)	−0.131(4)	C(15)	−0.231(4)
N(1)	0.158(4)	N(7)	0.072(4)

(*d*) Plane through benzene ring and left side of six-membered ring N(7), C(16), C(8)—C(11), C(17), and C(12)

$$-0.136x - 0.878y - 0.459z + 2.858 = 0$$

N(7)	−0.036(4)	C(10)	−0.030(5)
C(16)	−0.022(4)	C(11)	−0.047(4)
C(8)	0.065(4)	C(17)	−0.047(4)
C(9)	0.036(4)	C(12)	0.100(4)

Table 2 (*continued*)

Compound (**30b**)

(*e*) Dihedral angle between plane *a* − *b* 7.3(1)
Dihedral angle between plane *b* − *c* 62.4(2)
Dihedral angle between plane *c* − *d* 43.1(1)
Dihedral angle between plane *a* − *d* 110.0(1)

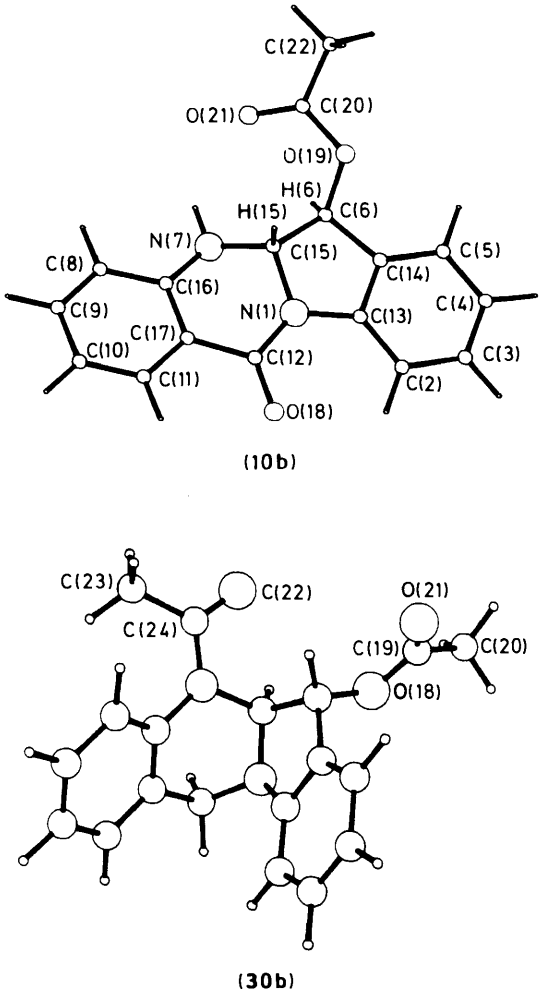


Figure. General view of compounds (**10b**) and (**30b**)[51]

sensitive towards oxidation and is readily converted to (**41**), a violet coupling product, which is related to (**1**) in the same way as isoindigo (**42**) is related to isatin.

Crystallographic Results.—6-Acetoxy-5a,6-dihydroindolo-[2,1-*b*]quinazolin-12(5H)-one (**10b**) and 6-acetoxy-5-acetyl-5,5a,6,12-tetrahydroindolo[2,1-*b*]quinazoline (**30b**) have been studied by *X*-ray crystallography. A comparison is given with the previously published[44] structure report on tryptanthrin, (1) the parent compound of this family. For clarity in the comparison [see compound (**1**)] with the work of Fedeli and Mazza[44] we have used their numbering of the atoms in the crystallographic section.

One aim with this study was to confirm the positional geometry of H(6) and H(15) in the five membered ring. A comparison with tryptranthrin shows that compound (**10b**) is somewhat less planar. The major deviation from planarity occurs between planes *b* and *c*, since the five membered ring is

Table 3. Atomic positional (fractional) co-ordinates for compounds (**10b**) and (**30b**) with estimated standard deviations in parentheses

Atom	*x*	*y*	*x*
Compound (**10b**)			
N(1)	0.290 5(2)	0.475 8(1)	0.546 8(1)
C(2)	0.413 5(3)	0.532 7(2)	0.696 2(1)
C(3)	0.447 2(3)	0.487 0(2)	0.780 7(1)
C(4)	0.405 5(3)	0.368 8(2)	0.805 6(1)
C(5)	0.327 2(3)	0.292 1(2)	0.745 7(1)
C(6)	0.207 2(2)	0.274 9(2)	0.585 2(1)
H(6)	0.082(3)	0.255(2)	0.602(2)
N(7)	0.106 3(2)	0.384 5(2)	0.448 3(1)
C(8)	0.050 7(3)	0.478 7(2)	0.303 6(1)
C(9)	0.075 9(3)	0.573 4(3)	0.243 7(2)
C(10)	0.180 5(3)	0.668 5(2)	0.264 8(2)
C(11)	0.256 1(3)	0.668 5(2)	0.346 5(2)
C(12)	0.304 3(2)	0.581 5(2)	0.497 8(1)
C(13)	0.337 3(2)	0.454 8(2)	0.636 0(1)
C(14)	0.293 3(2)	0.336 5(2)	0.660 7(1)
C(15)	0.240 5(2)	0.359 9(2)	0.504 8(1)
H(15)	0.340(2)	0.329(2)	0.468 0(1)
C(16)	0.130 2(3)	0.477 1(2)	0.386 1(1)
C(17)	0.232 1(2)	0.574 4(2)	0.407 9(1)
O(18)	0.365 3(2)	0.674 8(1)	0.528 6(1)
O(19)	0.271 5(2)	0.152 6(1)	0.572 8(1)
C(20)	0.199 4(2)	0.081 8(2)	0.511 1(1)
O(21)	0.094 2(2)	0.119 8(1)	0.464 7(1)
C(22)	0.267 7(3)	−0.044 6(2)	0.508 7(2)
Compound (**30b**)			
N(1)	0.382 5(2)	0.102 7(4)	0.512 2(3)
C(2)	0.359 4(3)	−0.147 5(5)	0.242 4(5)
C(3)	0.278 8(4)	−0.302 2(5)	0.126 5(5)
C(4)	0.161 5(4)	−0.362 2(5)	0.144 7(5)
C(5)	0.120 6(3)	−0.266 0(5)	0.281 9(5)
C(6)	0.183 5(3)	0.017 4(5)	0.552 7(4)
H(6)	0.104(3)	0.043(4)	0.529(4)
N(7)	0.278 8(2)	0.292 0(3)	0.510 5(3)
C(8)	0.265 7(3)	0.311 4(4)	0.227 2(4)
C(9)	0.317 4(4)	0.318 6(5)	0.084 0(5)
C(10)	0.425 7(4)	0.303 9(5)	0.068 5(5)
C(11)	0.482 4(3)	0.278 8(5)	0.196 8(5)
C(12)	0.481 7(3)	0.227 9(5)	0.475 3(4)
C(13)	0.317 7(3)	−0.054 9(4)	0.377 1(4)
C(14)	0.200 0(3)	−0.112 4(4)	0.397 1(4)
C(15)	0.297 4(3)	0.174 2(4)	0.589 4(4)
H(15)	0.329(3)	0.249(4)	0.724(5)
C(16)	0.325 5(3)	0.295 3(4)	0.358 2(4)
C(17)	0.433 0(3)	0.275 1(4)	0.341 3(4)
O(18)	0.189 1(2)	−0.031 9(3)	0.701 2(3)
C(19)	0.087 6(4)	−0.102 7(5)	0.747 5(5)
C(20)	0.105 3(4)	−0.140 7(6)	0.903 8(5)
O(21)	−0.004 8(3)	−0.135 6(6)	0.668 2(5)
C(22)	0.224 5(3)	0.396 2(5)	0.604 3(4)
C(23)	0.211 8(4)	0.535 4(5)	0.550 8(5)
O(24)	0.188 1(2)	0.378 2(4)	0.732 6(3)

fairly distorted (see Table 2). The pyrimidine ring adopts a chair conformation, and the molecule regains its overall planarity between planes *c* and *d*.

Compound (**30b**) shows a totally different conformation. The five membered ring has the same kind of distortion as (**10b**), but the deviation between planes *b* and *c* is over twice as big and of the opposite sign. Furthermore, the pyrimidine ring adopts a boat conformation. The molecule folds around the C(15)–N(1) bond. The main differences in bond distances and angles are found around C(12)–N(1)–C(15)–N(7). An elongation of bond length is seen between C(15) and N(1) in both compounds (**10b**) and (**30b**) compared to tryptanthrin, due to the absence of a

Table 4. Bond distances (Å) and bond angles (°) for compounds (**10b**) and (**30b**) with estimated standard deviations in parentheses

Distances

(**10b**)		(**30b**)	
N(1)–C(12)	1.370(3)	N(1)–C(12)	1.474(5)
N(1)–C(13)	1.405(3)	N(1)–C(13)	1.416(4)
N(1)–C(15)	1.470(3)	N(1)–C(15)	1.458(5)
C(2)–C(3)	1.384(3)	C(2)–C(3)	1.392(4)
C(2)–C(13)	1.391(3)	C(2)–C(13)	1.382(5)
C(3)–C(4)	1.388(3)	C(3)–C(4)	1.388(6)
C(4)–C(5)	1.388(3)	C(4)–C(5)	1.404(6)
C(5)–C(14)	1.386(3)	C(5)–C(14)	1.380(4)
C(6)–H(6)	1.12(2)	C(6)–H(6)	1.10(4)
C(6)–C(14)	1.497(3)	C(6)–C(14)	1.496(5)
C(6)–C(15)	1.546(3)	C(6)–C(15)	1.539(5)
C(6)–O(19)	1.454(2)	C(6)–O(18)	1.476(5)
N(7)–C(15)	1.437(3)	N(7)–C(15)	1.504(6)
N(7)–C(16)	1.388(3)	N(7)–C(16)	1.428(5)
C(8)–C(9)	1.385(4)	N(7)–C(22)	1.371(5)
C(8)–C(16)	1.399(3)	C(8)–C(9)	1.393(6)
C(9)–C(10)	1.400(4)	C(8)–C(16)	1.389(6)
C(10)–C(11)	1.373(4)	C(9)–C(10)	1.384(7)
C(11)–C(17)	1.393(3)	C(10)–C(11)	1.398(7)
C(12)–C(17)	1.472(3)	C(11)–C(17)	1.383(6)
C(12)–O(18)	1.228(3)	C(12)–C(17)	1.515(6)
C(13)–C(14)	1.394(3)	C(13)–C(14)	1.395(5)
C(15)–H(15)	1.07(2)	C(15)–H(15)	1.08(3)
C(16)–C(17)	1.405(3)	C(16)–C(17)	1.396(5)
O(19)–C(20)	1.344(3)	O(18)–C(19)	1.330(5)
C(20)–O(21)	1.198(3)	C(19)–C(20)	1.504(7)
C(20)–C(22)	1.497(3)	C(19)–O(21)	1.192(6)
		C(22)–C(23)	1.519(7)
		C(22)–O(24)	1.224(5)

Bond angles

(**10b**)		(**30b**)	
C(12)–N(1)–C(13)	128.2(2)	C(12)–N(1)–C(13)	118.4(3)
C(12)–N(1)–C(15)	121.4(2)	C(12)–N(1)–C(15)	112.9(3)
C(13)–N(1)–C(15)	110.0(2)	C(13)–N(1)–C(15)	106.6(3)
C(3)–C(2)–C(13)	117.4(2)	C(3)–C(2)–C(13)	117.1(4)
C(2)–C(3)–C(4)	121.8(2)	C(2)–C(3)–C(4)	121.9(4)
C(3)–C(4)–C(5)	120.6(2)	C(3)–C(4)–C(5)	120.2(4)
C(4)–C(5)–C(14)	118.3(2)	C(4)–C(5)–C(14)	118.2(4)
H(6)–C(6)–C(14)	112(1)	H(6)–C(6)–C(14)	112(2)
H(6)–C(6)–C(15)	119(1)	H(6)–C(6)–C(15)	113(2)
H(6)–C(6)–O(19)	102(1)	H(6)–C(6)–O(18)	114(2)
C(14)–C(6)–C(15)	103.0(2)	C(14)–C(6)–C(15)	102.4(3)
C(14)–C(6)–O(19)	109.0(2)	C(14)–C(6)–O(18)	110.3(3)
C(15)–C(6)–O(19)	112.2(2)	C(15)–C(6)–O(18)	104.5(3)
C(15)–N(7)–C(16)	114.0(2)	C(15)–N(7)–C(16)	118.9(3)
C(9)–C(8)–C(16)	120.2(2)	C(15)–N(7)–C(22)	114.1(3)
C(8)–C(9)–C(10)	120.6(3)	C(16)–N(7)–C(22)	126.8(3)
C(9)–C(10)–C(11)	119.4(2)	C(9)–C(8)–C(16)	119.5(4)
C(10)–C(11)–C(17)	121.0(2)	C(8)–C(9)–C(10)	120.6(4)
N(1)–C(12)–C(17)	113.9(2)	C(9)–C(10)–C(11)	119.5(4)
N(1)–C(12)–O(18)	122.3(2)	C(10)–C(11)–C(17)	120.3(4)
C(17)–C(12)–O(18)	123.7(2)	N(1)–C(12)–C(17)	107.5(3)
N(1)–C(13)–C(2)	129.7(2)	N(1)–C(13)–C(2)	127.5(4)
N(1)–C(13)–C(14)	109.2(2)	N(1)–C(13)–C(14)	110.6(4)
C(2)–C(13)–C(14)	121.2(2)	C(2)–C(13)–C(14)	121.9(4)
C(5)–C(14)–C(6)	129.0(2)	C(5)–C(14)–C(6)	130.7(4)
C(5)–C(14)–C(13)	120.8(2)	C(5)–C(14)–C(13)	120.7(4)
C(6)–C(14)–C(13)	110.2(2)	C(6)–C(14)–C(13)	108.6(3)
N(1)–C(15)–C(6)	103.8(2)	N(1)–C(15)–C(6)	104.6(3)
N(1)–C(15)–N(7)	108.3(2)	N(1)–C(15)–N(7)	111.4(3)
N(1)–C(15)–H(15)	105(1)	N(1)–C(15)–H(15)	110(2)
C(6)–C(15)–N(7)	114.7(2)	C(6)–C(15)–N(7)	110.3(3)
C(6)–C(15)–H(15)	112(1)	C(6)–C(15)–H(15)	113(2)
N(7)–C(15)–H(15)	112(1)	N(7)–C(15)–H(15)	107(2)
N(7)–C(16)–C(17)	119.2(2)	N(7)–C(16)–C(8)	122.3(4)
C(8)–C(16)–N(7)	121.7(2)	N(7)–C(16)–C(17)	117.5(3)

Table 4 (*continued*)

Bond angles			
(10b)		**(30b)**	
C(8)–C(16)–C(17)	119.0(2)	C(8)–C(16)–C(17)	120.2(3)
C(11)–C(17)–C(12)	120.0(2)	C(11)–C(17)–C(12)	123.2(4)
C(11)–C(17)–C(16)	119.9(2)	C(11)–C(17)–C(16)	119.8(3)
C(12)–C(17)–C(16)	120.0(2)	C(12)–C(17)–C(16)	116.6(3)
C(6)–O(19)–C(20)	116.4(2)	C(6)–O(18)–C(19)	117.0(3)
O(19)–C(20)–C(22)	111.7(2)	O(18)–C(19)–C(20)	111.8(4)
O(19)–C(20)–O(21)	122.0(2)	O(18)–C(19)–O(21)	122.5(4)
O(21)–C(20)–C(22)	126.3(2)	C(20)–C(19)–O(21)	125.7(5)
		N(7)–C(22)–C(23)	120.0(3)
		N(7)–C(22)–O(24)	119.6(4)
		C(23)–C(22)–O(24)	120.4(4)

double bond between N(7) and C(15). A difference between (**10b**) and (**30b**) in the angle C(12)–N(1)–C(15) occurs, due to different substitution on C(12); compound (**10b**) here agrees with tryptanthrin.

Hydrogens H(6) and H(15) have a *trans* disposition within both compounds (**10b**) and (**30b**) although in opposite orientation in the two compounds. The torsion angle formed by H(6)–C(6)–C(15)–H(15) is (−)142(2)° for compound (**10b**) and 95(3)° for compound (**30b**). The final atomic co-ordinates are given in Table 3. Bond distances and angles are listed in Table 4. Anisotropic thermal parameters for non-hydrogen atoms, and positional and thermal parameters for hydrogen atoms have been deposited at the Cambridge Crystallographic Data Centre.* All geometrical calculations have been done with PARST.[4,5] Atomic scattering factors are taken from ref. 46.

Experimental

Elemental analyses were performed by the Novo Microanalytical Laboratory, DK-2880 Bagsvaerd, Denmark. All melting points are uncorrected. I.r. spectra (KBr discs) were run on a Perkin-Elmer 257 instrument. N.m.r. spectra were recorded on a Bruker WP 200 or a Varian EM-360 instrument as solutions in $(CD_3)_2SO$ or $CDCl_3$ and using $SiMe_4$ as the internal standard. Mass spectra were obtained on an LKB 9000 (70 eV) mass spectrometer. Raney nickel (Aldrich) pore size 50 μm surface area 80—100 $m^2\ g^{-1}$ was used in the desulphurizations.

6-*Hydroxy*-5a,6-*dihydroindolo*[2,1-*b*]*quinazolin*-12(5H)-*one* (**10a**).—To a mixture of tryptanthrin (**1**) (2.48 g, 10 mmol) and acetic acid (50 ml) was added $NaBH_4$ (4.0 g) in small portions at 15 °C. The reaction mixture was quenched after 1 h by pouring into ice–water, and the solid formed was collected, dried, and recrystallized from ethanol, to give the *title compound* (2.25 g, 90%), m.p. 202—205 °C; $\nu_{max.}$(KBr) 3 250 (NH), 1 620, 1 570, 1 510, 1 470, 1 420, 1 050, and 755 cm^{-1}; δ_H [$(CD_3)_2SO$–D_2O; 200 MHz] 5.1 (1 H, d, *J* 6.2 Hz), 5.3 (1 H, d, *J* 6.2 Hz), and 6.95—8.1 (8 H, m) (Found: C, 71.3; H, 4.8; N, 11.1. $C_{15}H_{12}N_2O_2$ requires C, 71.42; H, 4.80; N, 11.10%).

6-*Acetoxy*-5a,6-*dihydroindolo*[2,1-*b*]*quinazolin*-12(5H)-*one* (**10b**).—Acetyl chloride (1.0 ml) was added dropwise to a well-stirred solution of the alcohol (**10a**) (1.26 g, 5 mmol) in dry pyridine (30 ml) at 0 °C. After the addition was complete the temperature was raised to 45 °C and was maintained for 2 h. Quenching with water gave a solid which was collected, dried, and crystallized from methylene chloride–pentane, to give *compound* (**10b**) (1.3 g, 85%), m.p. 177—178 °C, $\nu_{max.}$(KBr) 3 380 (NH), 1 730, 1 655, 1 610, 1 490, 1 230, 1 030, and 760 cm^{-1}; δ_H ($CDCl_3$; 200 MHz) 2.1 (3 H, s, Me), 5.2 (1 H, d, *J* 5.5 Hz), 5.7 (1 H, s, NH), 6.05 (1 H, d, *J* 5.5 Hz), and 6.7—8.3 (8 H, m); *m*/*z* 294 (M^+, 4%), 251 (M^+ − HOAc, 35), 234 (100), 205 (10), and 132 (6) (Found: C, 69.1; H, 4.8; N, 9.45. $C_{17}H_{14}N_2O_3$ requires C, 69.38; H, 4.79; N, 9.52%).

Indolo[2,1-*b*]*quinazolin*-12(6H)-*one* (**14a**).—*Method A.* Compound (**10a**) (2.52 g, 10 mmol) was dissolved in concentrated H_2SO_4 (10 ml) and the mixture was heated under N_2 for 1 h at 80—90 °C and then poured into ice-saturated aqueous K_2CO_3. The solid formed was collected, dried, and chromatographed on silica gel eluting with methylene chloride–methanol (95:5) to give the *title compound* (**14a**) (1.4 g, 60%), an analytical sample of which was sublimed at reduced pressure, m.p. 213—215 °C, $\nu_{max.}$(KBr) 1 680, 1 640, 1 605, 1 560, 1 465, 1 360, 1 330, 1 310, 775, and 760 cm^{-1}; δ_H [$(CD_3)_2SO$; 60 MHz] 6.05 (1 H, s) and 6.7—8.8 (9 H, m); δ_C [$(CO_3)_2SO$] 80.36 (d), 111.18 (s), 114.97 (d), 155.29 (d), 117.81 (d), 119.40 (d), 119.98 (d), 123.99 (d), 127.48 (d), 129.18 (s), 130.16 (s), 134.70 (d), 137.33 (s), 140.40 (s), and 158.82 (s); δ_H ($CDCl_3$; 60 MHz) 4.1 (2 H, s) and 6.8—8.5 (8 H, m); δ_C($CDCl_3$) 35.65 (t) (Found: C, 76.7; H, 4.4; N, 12.0. $C_{15}H_{10}N_2O$ requires C, 76.91; H, 4.30; N, 11.96%); *m*/*z* 234 (M^+, 100).

Method B. Compound (**10a**) (1.26 g) was taken up in polyphosphoric acid (20 ml). The mixture was heated under N_2 for 1 H at 100—110 °C, then poured into ice–water. The solid formed was filtered off, dried, and crystallized from acetonitrile (1.0 g, 85%), m.p. 215—217 °C.

Method C. A mixture of oxindole† (1.33 g, 10 mmol) and isatoic anhydride (**17a**) (1.80 g, 11 mmol) was heated with a catalytic amount of tetramethyl ethylenediamine (TMEDA) at 180 °C for 15 min. Methanol (10 ml) was added to the hot mixture and the solid formed was collected and dried, to give 5-(2-*aminobenzoyl*)*indolo*[2,1-*b*]*quinazolin*-12(5H)-*one* (**18**) (0.4 g), which was recrystallized from DMF–methanol, m.p. 242—245 °C (decomp.), $\nu_{max.}$(KBr) 3 454 (NH), 1 705, 1 630, 1 605, 1 540, 1 490, and 760 cm^{-1}; *m*/*z* 354 (*M* + 1, 10), 353 (M^+, 45), 260 (46), 234 (57), and 120 (100) (Found: C, 74.45; H, 4.25; N, 11.85. $C_{22}H_{15}N_3O_2$ requires C, 74.80; H, 4.24; N, 11.86%). The filtrate was concentrated to 5 ml and cooled to give a solid (**15a**) which was collected and dried. This solid sublimed at reduced pressure, to give compound (**14a**) (200 mg, 8.5%), m.p. 215—216 °C. This product was identical with material obtained using methods A and B.

5-*Methylindolo*[2,1-*b*]*quinazolin*-12(5H)-*one* (**12c**).—*Method A.* A mixture of oxindole (1.33 g, 10 mmol) and *N*-methylisatoic anhydride (**17b**) (1.96 g, 11 mmol) was heated with a catalytic amount of TMEDA at 180 °C for 2 h. Methanol (10 ml) was added to the hot mixture and the solid formed was collected to give *compound* (**12c**) (0.8 g) which was crystallized from ethanol, m.p. 212—214 °C, $\nu_{max.}$(KBr) 1 680, 1 615, 1 595, 1 500, 1 370, 1 350, 1 330, 1 250, 880, and 750 cm^{-1}; δ_H [$(CD_3)_2SO$; 60 MHz] 3.5 (3 H, s, Me), 6.1 (1 H, s), 6.9—8.6 (8 H, m); δ_C [$(CD_3)_2SO$; 200 MHz] 33.69 (q), 82.18 (d), 113.09, 115.36, 118.04, 120.05, 120.25, 124.15, 127.93, 129.68, 138.05, and 140.78 (Found: C, 77.4; H, 5.0; N, 11.30. $C_{16}H_{12}O$ requires C, 77.40; H, 4.87; N, 11.28%); *m*/*z* 248 (M^+, 100), 234 (70), 224 (42), 192 (23).

Method B. To a solution of compound (**16a**) (252 mg, 1 mmol) in dry methylene chloride (5 ml) was added active MnO_2 (150 mg) and the mixture was stirred for 24 h. The MnO_2 was then filtered off and washed with methylene chloride. The combined filtrate and washings were evaporated and the residue was chromatographed on silica gel eluting with methylene chloride–methanol (95:5) to yield compound (**12c**) (130 mg, 52%) together with unchanged (**16a**) (70 mg).

* See 'Instructions for Authors 1986,' *J. Chem. Soc., Perkin Trans. 1*, 1986, Issue 1, Section 5.6.3.

† Indolin-2-one.

N-(2-*Methylaminobenzoyl*)*indole* (**19a**).—Sodium hydride (2.65 g, 0.11 mol) was added in portions to a well-stirred solution of indole (11.7 g, 0.10 mol) in dry DMF (60 ml) at 30 °C under nitrogen. When the evolution of hydrogen had ceased (*ca.* 1 h) the stirring was continued for an additional hour whereupon a solution of *N*-methylisatoic anhydride (**17b**) (17.9 g, 0.10 mol) in dry DMF (60 ml) was added during 30 min at 25 °C. The temperature was then increased to 40 °C for 1 h and the reaction mixture was concentrated to *ca.* 25 ml and then poured into water. The solid formed was collected, washed with water, and recrystallized from propan-2-ol–di-isopropyl ether to give *compound* (**19a**) (16.5 g, 66%), m.p. 90—91 °C, $\nu_{max.}$(KBr) 3 400, 1 660, 1 610, 1 575, 1 520, 1 450, 1 350, 1 290, 1 206, and 750 cm^{-1} (Found: N, 11.30. $C_{16}H_{14}N_2O$ requires N, 11.9%).

5a,6-*Dihydro*-5-*methylindolo*[2,1-*b*]*quinazolin*-12(5H)-*one* (**16a**).—A solution of *N*-2-(2-methylaminobenzoyl)indole (**19a**) (2.50 g, 10 mmol) in ethanol (20 ml) and 6M-hydrochloric acid (20 ml) was heated under reflux for 3 h. The reaction mixture was allowed to cool overnight and the crystals formed were collected to give *compound* (**16a**) (58%), m.p. 135—136 °C. $\nu_{max.}$(KBr) 1 650, 1 600, 1 480, 1 460, 1 420, 1 330, and 755 cm^{-1}; δ_H [$(CD_3)_2SO$; 200 MHz] 2.9 (3 H, s), 3.4 (2 H, d), 5.2 (1 H, t), and 6.9—8.3 (8 H, m) (Found: C, 76.9; H, 5.6; N, 11.05. $C_{16}H_{14}N_2O$ requires C, 76.78; H, 5.64; N, 11.19%).

5-*Acetylindolo*[2,1-*b*]*quinazolin*-12(5H)-*one* (**12d**).—Compound (**10a**) (1.26 g) was dissolved in acetic anhydride (40 ml) and a catalytic amount of DMAP (4-dimethylaminopyridine) was added. The mixture was refluxed for 2 h, the acetic anhydride evaporated, and the residue crystallized from acetonitrile (0.8 g, 58%), m.p. >260 °C, $\nu_{max.}$(KBr) 1 690, 1 620, 1 595, 1 550, 1 475, 1 150, and 750 cm^{-1}; *m/z* 277 (M^+ + 1.20%) 276 (M^+, 100), 261 (86), 234 (27), 233 (27), and 205 (32) (Found: C, 73.55; H, 4.35; N, 10.15. $C_{17}H_{12}N_2O_2$ requires C, 73.90; H, 4.38; N, 10.14%).

6-*Methylindolo*[2,1-*b*]*quinazolin*-12(5H)-*one* (**12f**).—Method A as described for the preparation of compound (**12d**) was used starting with 3-methyloxindole, to give the title compound (62%), m.p. 218—220 °C, $\nu_{max.}$(KBr) 3 340, 1 680, 1 650, 1 605, 1 490, 1 180, and 750 cm^{-1}; *m/z* 249 (M^+ + 1.36%), 248 (M^+, 100), 247 (54), 147 (95), and 119 (69).

6,6-*Dimethylindolo*[2,1-*b*]*quinazolin*-12(6H)-*one* (**14b**).—Method A as described for the preparation of compound (**12d**) was used starting with 3,3-dimethyloxindole, to give compound (**14b**) (75%), m.p. 154 °C (lit.,[21] m.p. 154 °C).

Reduction of Tryptanthrin with $LiAlH_4$.—Compound (**1**) (2.48 g) and $LiAlH_4$ (1.3 g) were refluxed in ether for 6 h under N_2, whereupon water was added to quench the mixture. The organic phase was separated and the water was extracted with ether (3 × 50 ml). The combined organic phases were washed with water, dried, and evaporated to afford a reddish solid residue (2.3 g).

Further elaborations of the crude product mixture. The solid was dissolved in dry pyridine (20 ml) under N_2, the solution cooled to 0 °C and acetyl chloride (2 ml) was added dropwise. The mixture was heated (45 °C) for 2 h, poured into ice–water, filtered, and dried. Crystallization from methylene chloride/pentane yielded the diacetyl compound (**30b**) (1.0 g), m.p. 182—183 °C, $\nu_{max.}$(KBr) 1 740, 1 650, 1 610, 1 490, 1 370, 1 250, and 760 cm^{-1}; δ_H ($CDCl_3$; 200 MHz) 2.1 (3 H, s), 2.2 (3 H, s), 4.2 (1 H, d, *J* 15.6 Hz), 4.45 (1 H, d, *J* 15.6 Hz), 6.0 (1 H, s), 6.2 (1 H, s), and 6.5—7.3 (8 H, m); *m/z* 322 (M^+, 5%), 262 (M^+ − HOAc, 33), 230 (100), 229 (72), 228 (44), and 113 (50). Chromatography of the evaporated mother liquor yielded 1-(2-*acetamidobenzyl*)-3-*acetoxyindole*, m.p. 148—151 °C (**34**) (0.7 g), $\nu_{max.}$(KBr) 3 360, 1 740, 1 680, 1 510, 1 470, 1 230, 755, and 740 cm^{-1}; *m/z* 322 (M^+, 29%), 281 (45), 280 (100), and 148 (98); δ_C [$(CD_3)_2SO$; 200 MHz] 20.50, 23.07, 45.76, 110.05, 117.27, 118.30, 119.12, 120.08, 121.97, 125.56, 125.87, 126.96, 127.50, 128.62, 132.35, 133.13, 135.15, 135.28, and 168.41 (Found: N, 8.72. $C_{19}H_{18}N_2O_3$ requires N, 8.69%).

Indolo[2,1-*b*]*quinazoline*-6(12H)-*one* (**32**). The crude product (1.0 g) was dissolved in methylene chloride (30 ml) and active MnO_2 (0.5 g) was added. The mixture was stirred for 24 h, filtered, and evaporated to dryness. Crystallization of the resulting red solid from acetonitrile yielded *compound* (**32**) (0.8 g), m.p. 226—227 °C, $\nu_{max.}$(KBr) 1 715, 1 605, 1 590, 1 475, 1 455, 1 315, 1 095, and 755 cm^{-1}; *m/z* 235 (M^+ + 1, 18%), 234 (M^+, 54), 233 (100), 167 (14), 151 (6), 150 (7), and 149 (57); δ_H [$(CD_3)_2SO$; 200 MHz] 5.0 (2 H, s) and 7.1—7.8 (8 H, m) (Found: C, 76.55; H, 4.15; N, 12.0. $C_{15}H_{10}N_2O$ requires C, 76.91; H, 4.30; N, 11.96%).

5-*Acetyl*-5,12-*dihydroindolo*[2,1-*b*]*quinazoline* (**35**). The crude product mixture (1.0 g) was dissolved in methylene chloride (50 ml)–acetic anhydride (10 ml) and a catalytic amount of DMAP was added. The mixture was refluxed for 24 h, evaporated to dryness, and the residue crystallized twice from ethanol to afford the *title compound* (0.6 g), m.p. 237—238 °C; δ_H [$(CD_3)_2SO$; 60 MHz] 2.6 (3 H, s), 5.2 (2 H, s), and 6.95—7.7 (9 H, m); *m/z* 263 (M^+ + 1, 20%), 262 (M^+, 100), 261 (20), 248 (15), 247 (82), 246 (16), 219 (30), and 218 (35), $\nu_{max.}$(KBr) 1 630, 1 600, 1 530, 1 480, 1 410, 1 210, and 740 cm^{-1} (Found: N, 10.55. $C_{17}H_{14}N_2O$ requires N, 10.68%).

6-*Acetoxy*-5-*acetyl*-5,5a,6,12-*tetrahydroindolo*[2,1-*b*]-*quinazoline* (**30b**).—Compound (**10a**) (2.5 g) and $LiAlH_4$ (0.5 g) in ether was refluxed for 6 h under N_2, whereupon water was added and the mixture was extracted with ether. The combined ether phases were washed with water, dried, and evaporated. The residue was acetylated according to the earlier procedure with acetyl chloride–pyridine to yield the *title compound* (**30b**) (2.7 g, 65%), m.p. 182—183 °C, $\nu_{max.}$(KBr) 1 730, 1 640, 1 610, 1 480, 1 360, 1 230, and 760 cm^{-1}; δ_H ($CDCl_3$; 200 MHz) 2.10 (3 H, s), 2.24 (3 H, s), 4.18 (1 H, d, *J* 15.5 Hz), 4.46 (1 H, d, *J* 15.5 Hz), 6.04 (1 H, s), 6.17 (1 H, s), and 6.58—7.29 (8 H, m).

3-*Acetoxy*-1-*methylindole*.—The compound was prepared as described by Guilbault *et al.*[39] and showed δ_C [$(CD_3)_2SO$; 200 MHz] 20.48 (q), 32.30 (q), 109.79 (d), 117.08 (d), 118.68 (d), 118.85 (d), 118.82 (2), 121.72 (d), 128.09 (s), 133.52 (s), and 168.55 (s).

The Coupling Product (**40**).—A mixture of compound (**1**) (2.48 g) and hypophosphorous acid (10 ml) was refluxed for 2 h. The solid formed was collected and crystallized from DMF, to yield compound (**40**) (1.8 g, 78%), m.p. >260 °C, $\nu_{max.}$(KBr) 3 210, 1 650, 1 610, 1 580, 1 350, and 740 cm^{-1}; *m/z* 466 (M^+, 19%), 234 (80), 233 (100), and 205 (13).

The Coupling Product (**41**).—*Method A.* To a solution of compound (**12a**) (234 mg) in acetic acid (2 ml) a catalytic amount of BF_3–etherate was added. The mixture was allowed to stand for 24 h, the crystals formed were collected and washed with methanol, to yield the *product* (**41**) (200 mg, 86%), m.p. >260 °C, $\lambda_{max.}$(Me_2SO) 262 (log ε 4.28), 318 (4.02), 332 (3.94), and 582 nm (3.28), $\nu_{max.}$(KBr) 1 680, 1 640, 1 600, 1 460, 1 350, 1 320, and 760 cm^{-1}; *m/z* 464 (M^+) (Found: C, 73.35; H, 3.8; N, 11.05. $C_{30}H_{16}N_4O_2 \cdot 1.5H_2O$ requires C, 73.31; H, 3.89; N, 11.39%).

Method B. Compound (**40**) (466 mg, 1 mmol) was dissolved in Me_2SO (30 ml) and heated to 160 °C for 30 min and methanol

(30 ml) was added to the cooled solution. The crystals formed were collected and dried (340 mg, 73%).

Method C. To a mixture of compound (**40**) (466 mg, 1 mmol) and acetic acid (40 ml) a catalytic amount of BF_3–diethyl ether was added. The mixture was refluxed for 6 h and the crystals formed were collected, washed with methanol, and dried (410 mg, 88%).

Isoindigo (**42**).—$\lambda_{max.}$(Me_2SO) 270 (log ε 4.39), 368 (4.07), 388 (4.02), and 488 nm (3.66).

6-*Acetoxy*-5a,6-*dihydroindolo*[2,1-*b*]*quinazolin*-12(5H)-*one* (**10b**).—*Crystal Data.* $C_{17}H_{14}N_2O_3$, M = 294.3. Monoclinic, space group $P2_1/c$, a = 8.505(4), b = 10.898(3), c = 14.940(5) Å, β = 90.69(9)°, V = 1 385(1) Å^3 (by least-squares refinement of 22 centred reflections,[47] λ = 1.5418 Å), Z = 4, D_x = 1.41 g cm^{-3}. Brown, transparent slightly rhombic, obelisk shaped crystals. Dimensions 0.30 × 0.28 × 0.15 mm, μ-(Cu-K_α) = 7.66 cm^{-1}.

Data Collection and Processing. STOE DIF4 Diffractometer, ω/2θ mode with ω scan width = 1.225 deg, scan speed 1.4—4.2 deg min^{-1}, graphite monochromated Cu-K_α, 4 523 reflections measured ($2.96 \leqslant \theta \leqslant 64.94°$, $\pm h, \pm k, l$), 2 177 unique (merging R = 0.0550), 1 997, $I > 1.5\sigma(I)$ used in refinement.

Structure Analysis and Refinement. Solved by direct methods,[48] full matrix least squares refinement[49] with non-hydrogen atoms anisotropic, hydrogen atoms in calculated positions with isotropic group temperature factors except for H(6) and H(15) which were taken from a difference map and individually and isotropically refined. Structure refined to R = 0.048, R_w = 0.066, $w = 1/[\sigma^2(F) + 0.004\,324\,F^2]$, maximum shift/e.s.d. for non-hydrogen atoms ±0.002, final difference synthesis showed no peaks ⩾0.14 of ⩽ −0.21 e Å^{-3}.

6-*Acetoxy*-5-*acetyl*-5,5a,6,12-*tetrahydroindolo*[2,1-*b*]*quinazoline* (**30b**).—*Crystal Data.* $C_{19}H_{18}N_2O_3$, M = 322.4, Triclinic, space group $P\bar{1}$, a = 12.273(4), b = 8.970(4), c = 8.458(3), α = 110.35(2), β = 91.39(2), γ = 109.86(5)°, V = 810.3(6) Å^3 (by least-squares refinement of 14 centred reflections, λ = 1.5418 Å), Z = 2, D_x = 1.32 g cm^{-3}. Colourless, strongly rhombic crystals. Dimensions 0.38 × 0.33 × 0.20 mm, μ(Cu-K_α) = 6.97 cm^{-1}.

Data Collection and Processing. PW1100 PHILIPS Diffractometer, ω/2θ mode with ω scan width = 1.20 deg, scan speed 1.8 deg min^{-1}, graphite monochromated Cu-K_α, 2 937 reflections measured ($0.50 \leqslant \theta \leqslant 66.99°$, $h, \pm k, \pm l$), 2 676 unique (merging R = 0.0106), 2 475 $I > 1.5\sigma(I)$ used in refinement. Crystal decay less than 1% for 3 reflections monitored every 90 min.

Structure Analysis and Refinement. Solved by direct methods,[50] full matrix least squares refinement[49] with non-hydrogen atoms anisotropic, hydrogen atoms in calculated positions with isotropic group temperature factors, except for H(6) and H(15) which were taken from a difference map and individually and isotropically refined. Convergence reached at R = 0.0596 with unit weights, maximum shift/e.s.d. in positional parameters for non-hydrogen atoms ±0.007, no peaks ⩾0.21 or ⩽ −0.30 e Å^3 in least difference synthesis.

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