Behavior of 5,6-Dihydrobenzo[*h*]cinnolinones Towards Hydrazine. Synthesis of Benzo[*h*]cinnolinones and of 4-Aminobenzo[*h*]cinnolinones

Stefania Villa, Giacomo Luca Evoli and Giorgio Cignarella*

Istituto di Chimica Farmaceutica e Tossicologica, Viale Abruzzi 42, 20131 Milano, Italy

Michela M. Curzu and Gérard A. Pinna

Dipartimento Farmaco Chimico Tossicologico, Via Muroni 23, 07100 Sassari, Italy

Received June 16, 1998

Dehydrogenation and amination of 4,4a,5,6-tetrahydro and 5,6-dihydrobenzocinnolinones in refluxing hydrazine hydrate to give new benzo[*h*]cinnolinones and 4-aminobenzo[*h*]cinnolinones are reported, and reaction mechanisms proposed. Experiments were also extended to 4,4a-dihydro-5*H*-indenopyridazinone which underwent hydrazine induced dehydrogenation to 5*H*-indenopyridazin-3-one but not subsequent amination.

J. Heterocyclic Chem., **36**, 485 (1999).

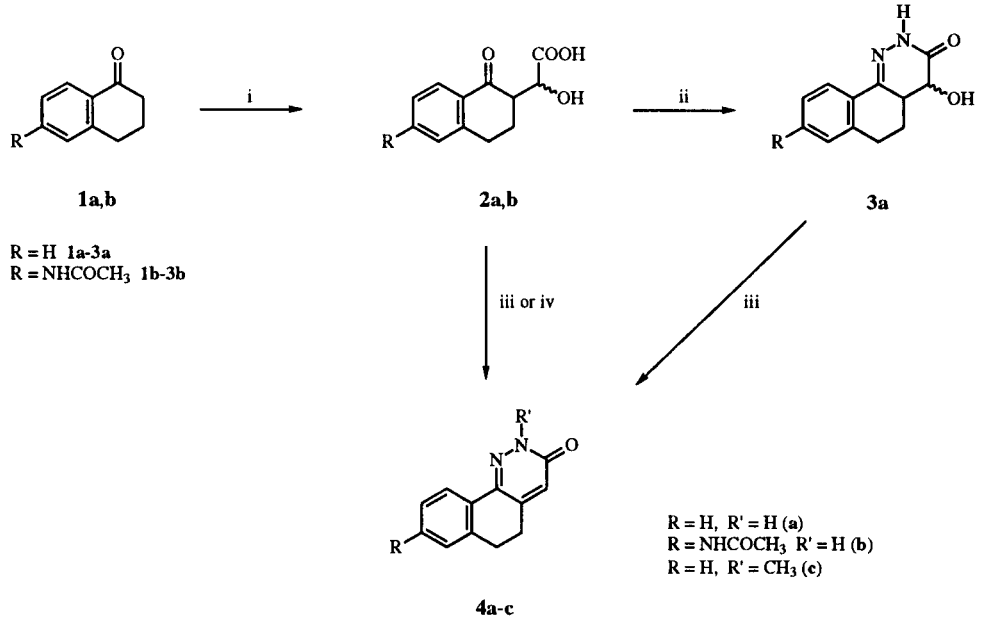
Introduction.

Continuing our interest in the chemistry and pharmacology of tricyclic pyridazinones, a versatile synthesis of 5,6-dihydrobenzo[*h*]cinnolin-3(2*H*)-one (**4a**) was devised, as an alternative to those previously reported, which were of limited applicability [1] or occurred with low overall yields [2].

Accordingly, we have found a simple approach to the known parent **4a** which was also suitable for the synthesis of other aryl substitued **4**.

Thus, the reaction of α-tetralone **1a** with glyoxylic acid in 5% aqueous sodium hydroxide at room temperature, gave 78% of α-hydroxy-2-tetralonacetic acid (**2a**) [3], which by a short heating (30 minutes) in excess refluxing hydrazine hydrate was converted into 72% of **4a**. The formation of **4a** was found to occur through the previously unreported 4-hydroxy-4,4a,5,6-tetrahydrobenzo[*h*]cinnolin-3(2*H*)-one (**3a**) which could be isolated in 46% yield under milder reaction conditions (equimolar hydrazine hydrate in refluxing ethanol for 1 hour). Following the procedure above reported for **4a**, the previously described antihypertensive agent 8-acetylamino-4,5-dihydrobenzocinnolinone **4b** [2] was synthesized from 6-acetylaminotetralone **1b** in 45% overall yields by direct cyclization of the related α-hydroxytetralonacetic acid **2b** in refluxing hydrazine hydrate. (Scheme 1).

Scheme 1



i) CHO-COOH, NaOH, H_2O, rt; ii) NH_2NH_2 H_2O, EtOH, Δ, 1 hour; iii) NH_2NH_2 H_2O excess, Δ, 0.5 hour (for **4a,b**); iv) CH_3NHNH_2 H_2O, EtOH, Δ, 24 hours (for **4c**).

The direct conversion of **2** to **4** seemed of general applicability, the condensation of **2a** with methyl hydrazine in refluxing ethanol for 24 hours leading to 69% of 2-methyl-5,6-dihydrobenzo[*h*]cinnolin-3(2*H*)-one (**4c**).

We have however observed that if the mixture of **2a** and hydrazine hydrate was allowed to reflux for many hours the initially formed **4a** underwent somewhat unexpected transformations we wish to report in this paper.

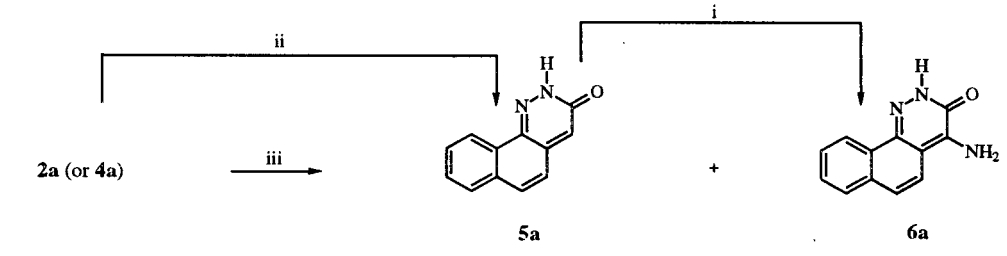
Results and Discussion.

By refluxing **2a** in excess hydrazine hydrate for 48 hours 76% of the previously unreported benzo[*h*]cinnolin-3(2*H*)-one (**5a**) was obtained besides **4a** (10%). However, by prolonging heating for 72 hours reaction time, a mixture of 26% of **5a** and 62% of 4-aminobenzo[*h*]cinnolin-3(2*H*)-one (**6a**) was isolated (Scheme 2).

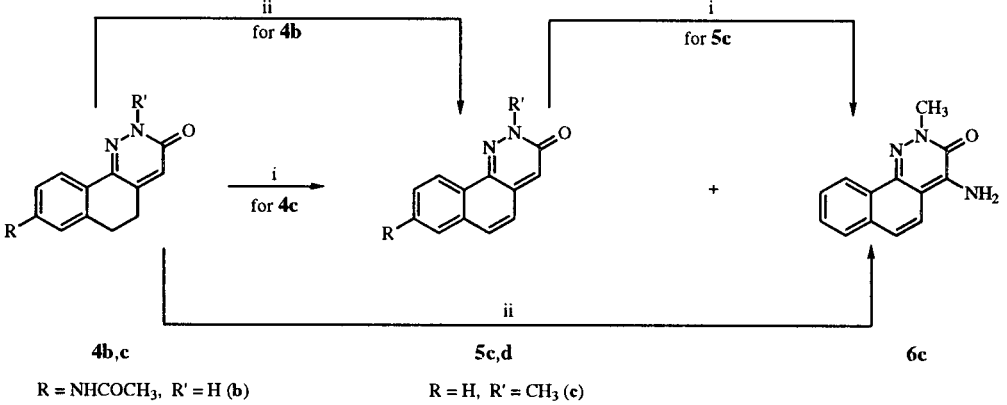
As expected **4a** in refluxing hydrazine hydrate was converted into a mixture of **5a** and **6a** in a ratio inversely proportional to the reaction time thus suggesting a mechanism involving a hydrazine induced dehydrogenation **4a** → **5a** followed by amination **5a** → **6a**. To support this reaction sequence a suspension of **5a** in hydrazine hydrate at reflux for 24 hours led to 80% of **6a**.

Similary to **4a** the N-2 methyl derivative **4c** when refluxed in hydrazine hydrate for 24 hours led to a mixture of 2-methylbenzo[*h*]cinnolin-3(2*H*)-one (**5c**) (19%) and 2-methyl-4-aminobenzo[*h*]cinnolin-3(2*H*)-one (**6c**) (36%) which was the only product isolated (70% yield) after 48 hours (Scheme 2). Conversely, the 8-acetylamino derivative **2b** when allowed to react for 48 hours in refluxing hydrazine hydrate underwent hydrolysis of the

Scheme 2



Reagents: NH_2NH_2 H_2O excess Δ 24 hours (i), 4h hours (ii), 72 hours (iii).



R = $NHCOCH_3$, R' = H (**b**)
R = H, R' = CH_3 (**c**)

R = H, R' = CH_3 (**c**)
R = NH_2, R' = H (**d**)

Reagents: NH_2NH_2 H_2O excess Δ 24 hours (i), 48 hours (ii).

The structures of **5a** and **6a** were assigned by elemental and spectroscopic analyses. The nmr spectrum of **5a** was in fact characterized by an AB system centered at δ 7.45 attributed to H-5 and H-6 and by a singlet at δ 7.22 attributed to H-4, while the nmr spectrum of **6a** exhibited the H-5, H-6 AB system at δ 7.5 and a deuterium oxide-exchangeable signal at δ 7.28 (NH_2).

In addition, the structure of **6a** was supported by single crystal X-ray analysis. (Figure 1).

8-acetylamino group followed by 5,6-dehydrogenation to give 8-aminobenzo[*h*]cinnolin-3(2*H*)-one (**5d**) which was isolated in 88% yield by filtration from the still hot mixture. The insolubility of **5d** in refluxing hydrazine hydrate did not allow further amination, the starting compound being recovered unchanged after 72 hours.

We have also found that a hydrazine induced dehydrogenation also took place in the lower homologue 4,4a-dihydro-5*H*-indeno[1.2.c]pyridazin-3-one (**8**) [4]. In this

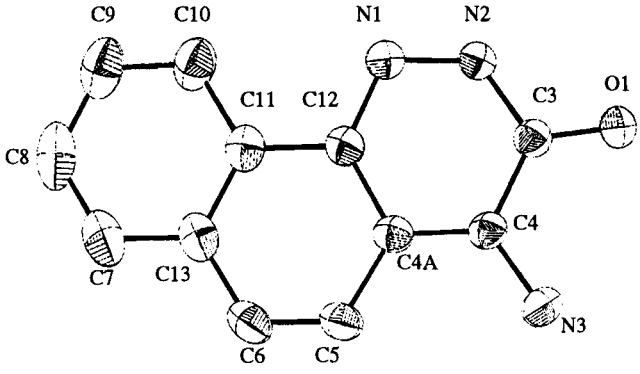
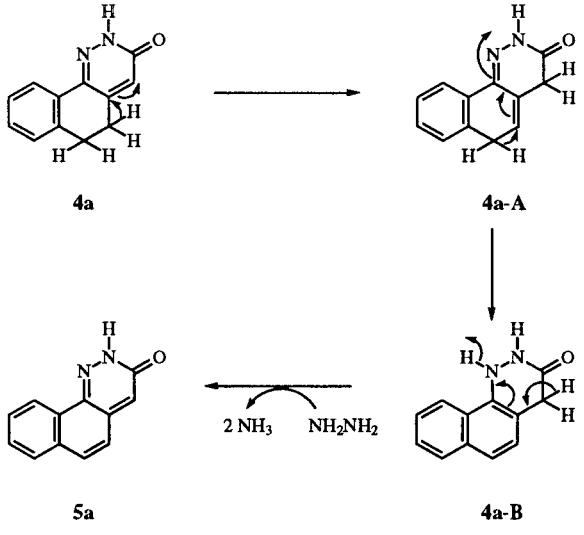


Figure 1. Ortep plot of **6a**.

case the pyridazinone ring is involved with the formation of 5*H*-indeno[1.2.c]pyridazin-3-one (**9**) [5] which could be isolated in 65% yield after 24 hours in refluxing hydrazine hydrate. However, 4-amination of **9** did not occur, this compound being recovered unchanged still by prolonging the reaction time to 72 hours.

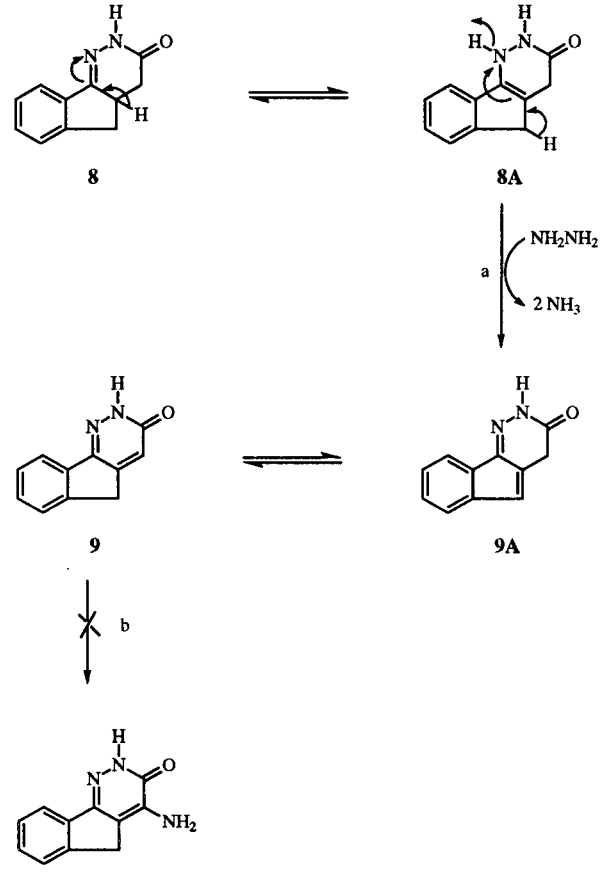
The above reported behavior of substrates like **4**, **5** and **8** deserves some comments focused on the reaction **4a** → **5a**; this possibly occurs through an initial tautomerization **4a** → **4a-A** → **4a-B**, followed by dehydrogenation to **5a** in an oxidative step mediated by hydrazine whose N-N bond is cleaved to give two ammonia molecules (Scheme 3).

Scheme 3



The conversion of **4a** to **5a** also took place under an argon atmosphere thus making unlikely the intervention of oxygen in the reaction. In the case of the lower homologue **8**, dehydrogenation would occur on the tautomer **8A** with formation of **9A** which provided **9** by C-4 → C-5 proton shift (Scheme 4).

Scheme 4



a) NH_2NH_2 H_2O excess, Δ, 24 hours; b) NH_2NH_2 H_2O excess, Δ, 72 hours.

Interestingly, **4a** was recovered almost unchanged in the presence of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in refluxing butanol for 48 hours. Under the same reaction conditions **8** was converted into 20% of **9**; and this widely employed dehydrogenating agent is known to convert 6,11-dihydro-5*H*-benzo[*a*]carbazoles into benzo[*a*]carbazoles in 90-95% yield in refluxing dichloromethane for 30 minutes [6].

As far as the amination of a pyridazinone ring is concerned, examples are known of the conversion of 6-aryl-3(2*H*)-pyridazinones [7,8] and of a 4,5-dihydro-6-aryl-3(2*H*)-pyridazinone [9] into 4-amino-6-aryl-3(2*H*)-pyridazinones in refluxing hydrazine hydrate. However, while 6-phenylpyridazinone led to 66% of the 4-amino derivative after 7 hours, the presence of an additional methyl group at position 5 was reported [7] to disfavor amination, only 11% of the 4-amino derivative being isolated after 96 hours.

We have confirmed the detrimental effect of a 5-alkyl substituent on the pyridazinone ring by recovering indenopyridazinone **9** almost unchanged after 72 hours in refluxing hydrazine hydrate.

The amination of benzo[*h*]cinnolinones **5** strongly suggests a different mechanism involving hydrazine addition to the 4,4a-5,6 conjugated system with formation of the intermediate **A** which then tautomerizes to **B**. The subsequent N-N bond cleavage would occur intramolecularly in the thus formed six membered complex to give ammonia and the imino derivative (**C**) which eventually gives **6** by proton shift [10] (Scheme 5).

The alternative mechanism involving an initial 1-4 addition of hydrazine to the pyridazinone moiety of **4** as hypothesized by Singh [8] for the 4-amination of 6-aryl-pyridazinones would not explain the failure of indenopyridazinone **9** to undergo hydrazine induced amination.

In conclusion, the synthesis is described for the previously unknown benzo[*h*]cinnolin-3(2*H*)-one system exemplified by **5** and the 4-amino derivatives **6**, which is based on an unusual hydrazine induced dehydrogenation followed by amination of 4,5-dihydro-3(2*H*)-benzo[*h*]cinnolinones **4**, in turn obtained by a new versatile procedure.

Table I

Elemental Analyses

	MW	C	H	N	%
4a	198.22	72.70	5.08	14.13	Calcd.
		72.35	5.01	14.30	Found
4b	255.27	65.86	5.13	16.46	
		65.61	5.12	16.08	
4c	212.25	73.55	5.69	13.19	
		73.27	5.59	13.05	
5a	196.20	73.45	4.11	14.27	
		73.05	4.09	14.12	
5c	210.25	74.34	4.80	13.34	
		74.73	4.64	13.17	
5d	213.23	67.59	5.20	19.70	
		67.90	5.12	19.45	
6a	211.21	68.23	4.29	19.90	
		68.53	4.08	19.50	
6c	225.24	69.39	4.92	18.67	
		69.08	4.76	18.45	

Scheme 5

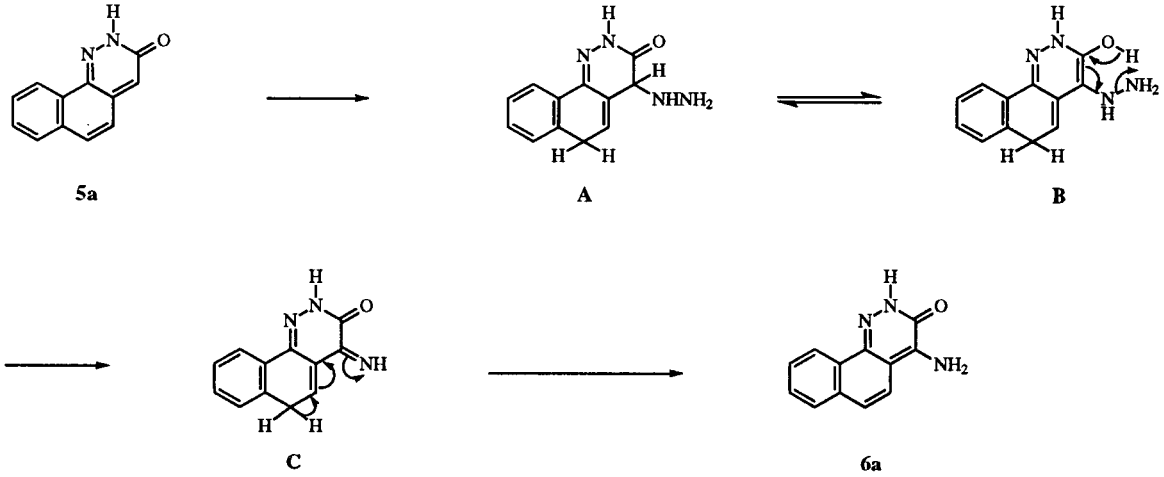


Table II

Experimental Data for the X-ray Diffraction Study of **6a**

formula	$C_{12}H_9N_3O_1$
mol wt	211.23
crystal dimensions, mm	0.2 x 0.4 x 0.3
date coll. T. C°	23
crystal system	Monoclinic
space group	$P2_1/c$
a, Å	7.957 (3)
b, Å	13.032 (8)
c, Å	9.523 (7)
β, °	81.65
V, Å^3	977.0 (3)
Z	4
ρ (calcd), g cm^{-3}	1.436
μ, cm^{-1}	0.40
radiation MoKα	(graphite monochromated λ = 0.710694)
measured reflections	± h, + k, + l
θ range, deg	2.5 < θ < 25
scan type	ω/2θ
scan width, deg	1.20 + 0.35 tanθ
max counting time, sec	100
bkgd time, sec	0.5 * scan-time
max scan speed, deg min^{-1}	16.8
prescan rejection limit	0.50 (2.0 σ)
prescan acceptance limit	0.030 (33 σ)
horiz receiving slit, mm	1.9 + tanθ
vert receiving slit, mm	4.0
no. indep. data coll.	1716
no. obs. refctl. (n_o) ($\|F_o\| > 3.0\sigma(\|F\|)$)	1174
extinction corrct.	n.a.
no. of param. refined (n_v)	146
n_o/n_v	
max. Δ(p)/σ(p)(at conv.)	< 0.2
R	0.036
R_w	0.053
GOF	2.719

$R = \Sigma(|F_o| - (1/k)|F_c|)/\Sigma|F_o|$

$R_w = [\Sigma_w (F_o - (1/k) F_c)^2 / \Sigma_w |Fo|^2]^{1/2}$

where: $w = [\sigma^2 (F_o)]^{-1}$; $\sigma(F_o) = [\sigma^2 (F_o^2) + f^4 (F_o^2)]^{1/2}/2F_o$;
With f = 0.02.

Table III

Final Positional and Isotropic Equivalent Displacement Parameters for **6a** (E.s.d.'s are given in parentheses)

Atom	x	y	z	B(A^2)
O1	0.5457(2)	0.87487(9)	0.0703(1)	3.38(2)
N1	0.2999(2)	1.0576(1)	0.2884(1)	2.79(3)
N2	0.3899(2)	1.0061(1)	0.1796(1)	2.73(3)
N3	0.5282(2)	0.7718(1)	0.3223(1)	3.29(3)
C3	0.4659(2)	0.9133(1)	0.1821(2)	2.57(3)
C4A	0.3599(2)	0.9130(1)	0.4337(2)	2.40(3)
C4	0.4519(2)	0.8640(1)	0.3183(2)	2.41(3)
C5	0.3393(2)	0.8709(1)	0.5746(2)	2.93(3)
C6	0.2498(2)	0.9201(1)	0.6837(2)	3.30(3)
C7	0.0690(3)	1.0673(2)	0.7801(2)	4.08(4)
C8	-0.0077(3)	1.1595(2)	0.7619(2)	4.55(4)
C9	0.0140(3)	1.2050(2)	0.6294(2)	4.53(4)
C10	0.1090(2)	1.1579(1)	0.5161(2)	3.77(4)
C11	0.1861(2)	1.0631(1)	0.5318(2)	2.74(3)
C12	0.2849(2)	1.0105(1)	0.4121(2)	2.41(3)
C13	0.1680(2)	1.0168(1)	0.6667(2)	3.05(3)

Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: (4/3) * [a^2*❑(1,1) + b^2 * ❑(2,2) + c^2 * ❑(3,3) + ab(cos ❑) * ❑(1,2) + ac(cos ❑) * B(1,3) + bc(cos ❑) * ❑(2,3)].

Table IV

Calculated Positional Parameters for the Hydrogen Atoms in **6a**

Atom	x	y	z	B(A^2)
H2	0.4098	1.0369	0.0886	6*
H4	0.5983	0.7544	0.2484	6*
H4'	0.5285	0.7482	0.4124	6*
H5	0.4057	0.8084	0.5847	6*
H6	0.2549	0.8947	0.7888	6*
H7	0.0731	1.0341	0.8619	6*
H8	-0.0961	1.1885	0.8557	6*
H9	-0.0368	1.2736	0.6107	6*
H10	0.1204	1.1829	0.4221	6*

Starred atoms were not refined.

EXPERIMENTAL

Chemistry.

Hydrazine hydrate was employed as pure hydrazine monohydrate. Melting points were determinated with a Büchi 510 capillary apparatus and are uncorrected. The ^{1}H-nmr spectra were recorded on a Bruker AC200 spectrometer; chemical shifts are reported as δ (ppm) relative to tetramethylsilane as internal standard; dimethyl-d_6 sulfoxide was used as the solvent, unless otherwise noted. The tlc on silica gel plates was used to check product purity. Silica gel 60 (Merck 230-400 mesh) was used for column flash cromatography.

Compounds **2a**,**b**, **3a**,**b** were isolated as diastereomeric mixtures (^{1}H-nmr).

α-Hydroxy-α-[1-oxo-1,2,3,4-tetrahydronaphth-2-yl]acetic Acid (**2a**).

To an ice-cooled mixture of 3 g (0.02 mole) of 1-tetralone and 2.07 g (0.022 mole) of glyoxylic acid monohydrate vigorously stirred, a solution of 2.46 g (0.06 mole) of sodium hydroxide in 50 ml of water was added. After stirring for 30 minutes at room temperature, the alkaline solution was washed with ether (25 ml) and then was acidified with concentrated hydrochloric acid on cooling. After stirring at room temperature overnight the product that separated was filtered, washed with water and dried to give **2a** (3.55 g, 78%), mp 187-189° (methanol); ^{1}H-nmr: 1.8-2.3 (m,

Table V

Table of General Displacement Parameter Expressions - B's for **6a**

Name	B(1,1)	B(2,2)	B(3,3)	B(1,2)	B(1,3)	B(2,3)	Beqv
O1	5.07(6)	2.64(4)	2.33(4)	0.36(4)	-0.15(4)	-0.17(4)	3.38(2)
N1	3.45(6)	2.36(5)	2.54(5)	0.15(5)	-0.37(5)	0.17(4)	2.79(3)
N2	3.65(6)	2.33(5)	2.19(5)	0.11(5)	-0.33(4)	0.16(4)	2.73(3)
N3	4.65(7)	2.28(5)	2.99(5)	0.54(5)	-0.71(5)	0.00(5)	3.29(3)
C3	3.27(6)	2.12(6)	2.38(5)	-0.28(6)	-0.60(5)	0.02(5)	2.57(3)
C4A	2.58(6)	2.21(6)	2.52(6)	-0.52(5)	-0.70(5)	0.19(5)	2.40(3)
C4	2.84(6)	1.94(6)	2.56(6)	-0.39(5)	-0.70(5)	-0.02(5)	2.41(3)
C5	3.54(7)	2.71(6)	2.57(6)	-0.53(6)	-0.52(5)	0.52(5)	2.93(3)
C6	3.94(7)	3.49(7)	2.42(6)	-0.98(6)	-0.31(6)	0.44(6)	3.30(3)
C7	3.94(7)	5.08(9)	3.06(7)	-0.95(7)	0.02(6)	-0.64(7)	4.08(4)
C8	3.54(7)	5.48(9)	4.47(8)	0.07(7)	-0.01(7)	-2.06(7)	4.55(4)
C9	4.06(8)	4.56(9)	4.95(9)	1.15(7)	-0.64(7)	-1.31(8)	4.53(4)
C10	3.71(8)	3.71(8)	3.90(7)	0.75(7)	-0.64(6)	-0.56(7)	3.77(4)
C11	2.38(6)	2.87(7)	3.00(6)	-0.30(6)	-0.47(5)	-0.36(6)	2.74(3)
C12	2.44(6)	2.42(6)	2.41(6)	-0.34(5)	-0.53(5)	0.08(5)	2.41(3)
C13	2.79(6)	3.55(7)	2.77(6)	-0.79(6)	-0.23(5)	-0.43(6)	3.05(3)

The form of the anisotropic displacement parameter is: exp[-0.25{h2a2B(1,1) + k2b2B(2,2) + 12c2B(3,3) + 2hkabB(1,2) + 2hlacB(1,3) + 2klbcB(2,3)}] where a, b, and c are reciprocal lattice constants.

Table VI

Bonds and Angles Table for **6a**

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
O1	C3	1.261(2)	C5	C6	1.336(2)
N1	N2	1.350(2)	C6	C13	1.438(3)
N1	C12	1.318(2)	C7	C8	1.370(3)
N2	C3	1.354(2)	C7	C13	1.405(3)
N3	C4	1.350(2)	C8	C9	1.382(2)
C3	C4	1.438(2)	C9	C10	1.369(3)
C4A	C4	1.385(2)	C10	C11	1.397(3)
C4A	C5	1.437(2)	C11	C12	1.459(3)
C4A	C12	1.431(3)	C11	C13	1.407(3)

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
N2	N1	C12	115.1(1)	C8	C7	C13	121.6(2)
N1	N2	C3	128.3(1)	C7	C8	C9	119.5(2)
O1	C3	N2	120.7(1)	C8	C9	C10	120.6(2)
O1	C3	C4	123.3(1)	C9	C10	C11	120.9(2)
N2	C3	C4	116.0(1)	C10	C11	C12	121.8(2)
C4	C4A	C5	122.7(2)	C10	C11	C13	119.2(2)
C4	C4A	C12	118.6(2)	C12	C11	C13	119.0(2)
C5	C4A	C12	118.7(2)	N1	C12	C4A	123.8(2)
N3	C4	C3	116.5(1)	N1	C12	C11	116.6(2)
N3	C4	C4A	125.2(1)	C4A	C12	C11	119.5(2)
C3	C4	C4A	118.3(2)	C6	C13	C7	122.5(2)
C4A	C5	C6	121.2(2)	C6	C13	C11	119.3(2)
C5	C6	C13	122.2(2)	C7	C13	C11	118.2(2)

Numbers in parentheses are estimated standard deviations in the least significant digits.

2H, H-3), 2.8-3.2 (m, 3H, H-2, H-4), 4.3 and 4.8 (2d, 1H, C_α-H), 5.0-5.8 (br s , 1H, OH exchangeable), 7.3-7.5 (m, 2H, ArH), 7.5-7.7 (m, 1H, ArH), 7.8-8.0 (m, 1H, H-5), 12.2-13.0 (br s, 1H, COOH deuterium oxide-exchangeable).

α-Hydroxy-α-[1-oxo-6-acetylamino-1,2,3,4-tetrahydronaphth-2-yl]acetic Acid (**2b**).

Compound **2b** was prepared as reported for **2a**, starting from the required **1b**, yield 60%, mp 195-197° (methanol); ^{1}H-nmr: 1.9-2.0 (m, 2H, H-3), 2.1 (s, 3H, CH_3), 2.8-3.2 (m, 3H, H-2 and H-4), 4.3 and 4.8 (2d, 1H, C_α-H), 5.3 (br s, 1H, OH deuterium oxide-exchangeable), 7.5 (dd, 1H, H-7), 7.6 (d, 1H, H-5), 7.8 (d, 1H, H-8), 10.2 (br s, 1H, deuterium oxide-exchangeable), 12.6 (br s, 1H, deuterium oxide-exchangeable).

4-Hydroxy-4,4a,5,6-tetrahydrobenzo[*h*]cinnolin-3(2*H*)-one (**3a**).

A solution of α-hydroxy-2-tetralonacetic acid (**2a**) (5 g, 0.02 mole) and hydrazine hydrate (1.1 g, 0.022 mole) in 20 ml of ethanol was refluxed for 1 hour. After cooling the product was filtered, washed with ethanol and dried to give **3a** (2.0 g, 46%), mp 225-226° (ethanol); ^{1}H-nmr: 1.58 and 1.8-2.0 (qq and m, 1H, H-4_a), 2.2-3.0 (m, 4H, H-5, H-6), 3.8-4.0 (m, 1H, H-4), 5.6 and 6.0 (2d, 1H, OH deuterium oxide-exchangeable), 7.2-7.4 (m, 3H, ArH), 7.9 (d, 1H, H-7), 11.0 (s, 1H, NH deuterium oxide-exchangeable).

4-Hydroxy-8-acetylamino-4,4a,5,6-tetrahydrobenzo[*h*]cinnolin-3(2*H*)-one (**3b**).

Compound **3b** was prepared as reported above for **3a** starting from the required **2b** and refluxing for 1 hour, yield 35%, mp 310° dec; ^{1}H-nmr 1.52 and 1.82-1.89 (qq and m, 1H, H-4_a), 2.1 (s, 3H, CH_3), 2.2-3.0 (m, 4H, H-5, H-6), 3.8-4.0 (m, 1H, H-4), 5.56 and 5.99 (2d, 1H, OH deuterium oxide-exchangeable), 7.39-7.95 (m, 3H, H-7, H-9, H-10), 10.9 (s, 1H, NH deuterium oxide-exchangeable).

5,6-Dihydrobenzo[*h*]cinnolin-3(2*H*)-one (**4a**).

A solution of **2a** (1 g, 4.5 mmoles) and hydrazine hydrate (5 ml) was refluxed for 30 minutes. After cooling the product was filtered, washed with ethanol and dried to give **4a** (0.65 g, 72%) mp 272-273° dec (Lit [2] mp 257-261°). Compound **4a** was also obtained in 80% yield from **3a** under the same reaction conditions; ^{1}H-nmr: 2.8-3.0 (m, 4H, H-5, H-6), 6.8 (s, 1H, H-4), 7.2-7.4 (m, 3H, H-7, H-8, H-9), 7.8-8.0 (m, 1H, H-10), 13.0 (s, 1H, NH deuterium oxide-exchangeable).

8-Acetylamino-5,6-dihydrobenzo[*h*]cinnolin-3(2*H*)-one (**4b**).

Compound **4b** was prepared as reported above for **4a** starting from the required **2b**, yield 75%, mp 297° dec (Lit [2] mp 297°); ^{1}H-nmr: 2.1 (s, 3H, CH_3), 2.8-3.0 (m, 4H, H-5, H-6), 6.75 (s, 1H, H-4), 7.2-8.0 (m, 3H, H-7, H-9, H-10), 12.9 (s, 1H, NH deuterium oxide-exchangeable).

2-Methyl-5,6-dihydrobenzo[*h*]cinnolin-3(2*H*)-one (**4c**).

A solution of α-hydroxy-2-tetralonacetic acid (**2a**) (1.5 g, 7 mmoles) and methylhydrazine (0.6 g, 0.013 mole) in 10 ml of ethanol was refluxed for 24 hours. After cooling the mixture was evaporated, and the residue was dissolved in methylene chloride and washed with water. After drying (sodium sulfate) the solvent was evaporated and the residue was triturated with diethyl ether to give **4c** (1.0 g, yield 69%), mp 121-123°; ^{1}H-nmr (deuteriochloroform): 2.8-3.0 (m, 4H, H-5,6), 3.85 (s, 3H, CH_3), 6.8 (s, 1H, H-4), 7.2-7.4 (m, 3H, ArH), 8.0-8.1 (m, 1H, ArH).

Benzo[*h*]cinnolin-3(2*H*)-one (**5a**).

A solution of α-hydroxy-2-tetralonacetic acid (**2a**) (1 g, 4.5 mmoles) and hydrazine hydrate (5 ml) was refluxed for 48 hours. After cooling the solid was filtered, washed with ethanol and dried to give **4a** (0.1 g). The solution was evaporated and the residue resuspended in acetone. After stirring, the insoluble was filtered, washed with acetone and dried to give **5a** (0.6 g, 76%), mp 228°; ^{1}H-nmr: 7.2 (s, 1H, H-4), 7.45 (AB system, 2H, H-5, H-6), 7.5-7.7 (m, 2H, H-8, H-9), 7.8 (m, 1H H-10), 8.5 (m, 1H, H-7), 13.8 (s, 1H, NH deuterium oxide-exchangeable). Compound **5a** was also obtained in 75% yield from **4a** under the same reaction conditions. The treatment of **4a** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (molar ratio 1:3) in 1-butanol left the starting compound unchanged after 48 hours at reflux.

4-Aminobenzo[*h*]cinnolin-3(2*H*)-one (**6a**).

a) From **2a**.

A solution of **2a** (1 g, 4.5 mmoles) and hydrazine hydrate (5 ml) was refluxed for 72 hours. After cooling the excess hydrazine was evaporated. The residue was triturated with acetone, the solid filtered and fractionated by silica gel flash chromatography eluting with dichloromethane/methanol (95:5) to give 660 mg of **6a** (62%) and 250 mg of **5a** (26%); **6a** had mp 338-340° (*N,N*-dimethylformamide).

b) From **5a**.

A mixture of **5a** (0.5 g 2.5 mmoles) and hydrazine hydrate (2.5 ml) was refluxed for 24 hours. After cooling the excess hydrazine hydrate was evaporated. The residue was triturated with acetone, the solid was filtered and purified by silica gel flash chromatography eluting with dichloromethane/methanol (95:5) to give **6a** (0.4 g, yield 80%); ^{1}H-nmr: 7.3 (s, 2H, NH_2 deuterium oxide-exchangeable), 7.5 (AB system, 2H, H-5, H-6), 7.5-7.6 (m, 2H, H-8, H-9), 7.6-7.7 (m, 1H, H-10), 8.5-8.6 (m, 1H, H-7), 13.2 (s, 1H, NH deuterium oxide-exchangeable).

8-Aminobenzo[*h*]cinnolin-3(2*H*)-one (**5d**).

A solution of **4b** (1 g, 4 mmoles) and hydrazine hydrate (10 ml) was refluxed for 48 hours. After cooling the solid was filtered, washed with water and dried to give **5d** (0.65 g, 88%) mp 350° dec. Monitoring the reaction by ^{1}H-nmr indicated that the deacetylation of **4b** was complete after 2 hours; ^{1}H-nmr: 5.75 (s, 2H, NH_2 deuterium oxide-exchangeable), 6.8 (s, 1H, H-4), 6.9 (d, 1H, H-9), 7.13 (s, 1H, H-7), 7.25 (q, AB, 2H, H-5, H-6), 8.21 (d, 1H, H-10); 13.0 (s, 1H, NH deuterium oxide-exchangeable).

2-Methylbenzo[*h*]cinnolin-3(2*H*)-one (**5c**) and 2-Methyl-4-aminobenzo[*h*]cinnolin-3(2*H*)-one (**6c**).

A solution of **4c** (2.4 mmoles) and hydrazine hydrate (5 ml) was refluxed for 24 hours. After cooling the solid was filtered, washed with ethanol and dried to give **6c** (80 mg). The filtrate was evaporated, the residue was triturated with acetone, the solid was filtered and fractionated by silica gel flash chromatography eluting with dichloromethane/methanol (98:2) to give additional **6c** (100 mg, yield 36%) and **5c** (90 mg, yield 19%). If the mixture was refluxed for 48 hours only compound **6c** was isolated (70%). Compound **6c** was also obtained in 50% yield by refluxing a suspension of **5c** (4 mmoles) in hydrazine hydrate (5 ml) for 24 hours; **5c** had mp 146-148°; ^{1}H-nmr: 4.0 (s, 3H,

CH_3), 7.3 (s, 1H, H-4), 7.35 (d, 1H), 7.6-7.8 (m, 3H), 7.8-7.9 (m, 1H), 8.5-8.7 (m, 1H). Compound **6c** had mp 226-228°; ^{1}H-nmr: 4.0 (s, 3H, CH_3), 7.3-7.5 (m, 2H, NH_2 deuterium oxide-exchangeable), 7.6-7.8 (m, 4H), 8.5-8.7 (m, 1H).

5*H*-Indeno[1,2-*c*]pyridazin-3-one (**9**).

A solution of 4,4a-dihydro-5*H*-indeno[1,2-*c*]pyridazin-3-one (**8**) [4] (0.2 g, 1.08 mmoles) and hydrazine hydrate (2 ml) was refluxed for 24 hours. After cooling the solid was filtered, washed with water and dried to give **9** (0.13 g, yield 65%), mp 293-294° (Lit [5] mp 275-280°); ^{1}H-nmr: 3.97 (s, 2H, H-5), 6.98 (s, 1H, H-4), 7.4-7.65 (m, 3H, ArH), 7.77-7.85 (m, 1H, ArH), 12.92 (br s, 1H, NH deuterium oxide-exchangeable). A mixture of **9** (130 mg, 7.06 x 10^{-1} mmole) and hydrazine hydrate (2 ml) was refluxed, monitoring the reaction progress by tlc (dichloromethane/methanol, 9:1); after 72 hours the starting material was recovered unchanged. Compound **9** was also obtained in 20% yields treating compound **8** with equimolecular amount of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in *tert*-butyl alcohol for 6 hours at reflux.

X-Ray Crystal Structure Analysis of **6a**.

Colorless, prismatic crystals of **6a** were grown by slow evaporation from an acetic acid solution.

The most important geometric parameters of compound **6a** are listed in Tables II-VI. All bond distances, angles as well as thermal parameters are in good agreement with those reported for mean crystallographic features of the organic structures. An ORTEP view of compound **6a** is shown in Figure 1.

Data were collected at room temperature using an Enraf-Nonius CAD4 diffractometer; unit cell dimensions were obtained by least-squares fit of the 2θ values of 25 high order reflections ($9.60 \leq \theta \leq 18.30°$).

The 1716 collected intensities were corrected for Lorentz and polarization to give a set of 1173 observed reflections ($F^2_0 \geq 3\sigma(F^2)$). The structure was solved by direct methods and refined by full matrix least-squares minimizing the quantity $\Sigma[w(F_o\text{-}1/k\ F_c)^2]$.

Anisotropic displacement parameters were used for non-hydrogen while the contribution of the H atoms and their calculated positions (C-H = 0.95 Å, $B_H = 1.3 * B$ (bonded atom)) was taken into account but not refined. No extinction correction was deemed necessary.

The scattering factors used, corrected for the real and imaginary parts of the anomalous dispersion, were taken from the literature [11]. The refinement was stopped when $\Delta p/\sigma(p) < 0.2$. A final Difference Fourier map showed no significant features. The final conventional R factor is 0.036.

All calculations were carried out using the MOLEN crystallographic package [12].

Acknowledgements.

We thank Professor Lucio Toma (Pavia) and Professor Riccardo Stradi (Milan) for helpful discussions.

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[*] To whom correspondence should be addressed; (e-mail: cifra@imiucca.csi.unimi.it).

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