Synthesis, Crystal Structure and Spectroscopic Studies of 3-Hydrazono- and 3-Hydroxyiminoquinolin-2-ones

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3-(Hydrazonoethyl)quinolinones **6-11, 13** and 3-(hydroxyiminoethyl)quinolinones **14, 15** are prepared by a condensation reaction of 3-acetylquinolinones **4, 5** with a variety of 1,2-(bis)nucleophiles. The structures of the isolated compounds have been elucidated using ^{1}H and ^{13}C nmr spectroscopy. X-ray diffraction studies of compound **14** were also performed.

The development of new methods for the synthesis of 3-substituted quinoline-2,4-diones and of condensed derivatives with nucleophiles is a topic of continuing interest because of their potential biological activity. Our current interest on the chemistry and structure elucidation of nitrogen heterocyclic compounds containing the "enolic β,β'-tricarbonyl" system [1] led us to study the NH- and NMe-3-acetyl-4-hydroxyquinolin-2(1*H*)-ones, as possible intermediates in the condensation reactions with 1,2-(bis)nucleophiles, where one of the nucleophilic centers is a nitrogen atom. One reason for this is their use as precursors for heterocyclic nitrogen derivatives containing interesting biological properties [2,3]. Moreover these compounds can form metal complexes which increase the biological activity. In addition this condensation reaction provides an entry to characterization and structure elucidation of this series of compounds.

The reaction of 3-acetyl-4-hydroxyquinolin-2(1*H*)-ones with nitrogen bases has been recently described [2,3]. On the other hand, the reaction of five membered nitrogen heterocycles containing the "enolic β,β'-tricarbonyl system", such as 3-acyl-4-hydroxypyrrolin-2-ones (tetramic acids), with substituted hydrazines has been reported [4]. Similar reactions of tetramic acids with hydrazine, mono- and 1,1-bisubstituted hydrazines, and hydroxylamine have been recently studied by Jones and co-workers [5].

Several examples of the reactions of both NH- and NMe-3-acetyl-4-hydroxyquinolin-2-ones **4** and **5** (Scheme 1) with hydrazine, phenylhydrazine and 1,1-dimethylhydrazine are presented in this paper. In addition, the reactions of **4** with 1,1-diphenylhydrazine hydrochloride, hydroxylamine hydrochloride and methoxyamine hydrochloride are described.

A nucleophile could attack the 3-acetyl-4-hydroxyquinolin-2-one ring at any of the three reactive sites: the carbonyl of the acetyl group at the 3-position, the carbonyl at the 2-position, and the carbon atom at the 4-position (the carbon of a potential carbonyl group). The structural distinction between the different isomers prompted us to examine the spectral parameters based on the ^{1}H and ^{13}C nmr data. In order to confirm the structure and the tautomerism of the coupling products X-ray crystallographic studies were also performed.

Recently, we have described [1b] an easy synthesis to the NH-3-acetyl-4-hydroxyquinolin-2-one **4** (Scheme 1) through an acylation reaction of ethyl acetoacetate with the 2-methyl-3,1-benzoxazin-4-one **2**, using as a base potassium *tert*-butoxide in *tert*-butyl alcohol. The molecular ratio of benzoxazinone:potassium *tert*-butoxide:active methylene compound was 1:2:2 and the reaction time 1.5-2 hours. Under these reaction conditions the *C*-acylated compound **3** has been prepared in good yield. Cyclization of this compound to quinolinone **4** was performed in aqueous sodium hydroxide combined with sodium carbonate in moderate yield.

The requisite acylating agent, the 2-methyl-3,1-benzoxazin-4-one **2**, was synthesized from anthranilic acid using the procedure previously described [1], but with minor modifications. The crude product **2** was worked up with chloroform and aqueous sodium hydroxide to give a compound stable for several weeks (see Experimental).

In particular, the previously described method [1] provides the unsubstituted NH-quinolinones. Nevertheless, *N*-alkyl-3-substituted quinolinones are interesting compounds having pharmacological activities [6]. On the other hand, it was necessary to employ an alkyl group on the NH-ring, in order to better facilitate the solubility of these compounds in non polar solvents. The *N*-methylation of the ring nitrogen was achieved using conventional chemistry, from the NH-3-acetyl-4-hydroxyquinolin-2-one **4**, involving *N*-methylation with sodium hydride and methyl iodide in tetrahydrofuran with a yield of 81%.

Treatment of the quinolinones **4** and **5** (1 equivalent) with an excess of hydrazine hydrate (2 equivalents) in

boiling ethanol (2 hours) gave the corresponding hydrazones **6** and **9** in good yields (65-89%) (Scheme 1), whereas the *N*-methylquinolinone **5** (2 equivalents) when treated with hydrazine hydrate (1 equivalent) in boiling ethanolic solution (2 hours) gave the "azine" **12**. Further evidence for the structure of **12** was derived from the mass spectral data.

Scheme 1

(i) (AcO)$_2$O, 120-130°; (ii) MeCOCH$_2$CO$_2$Et, *t*-BuOK, *t*-BuOH, rt.; (iii) NaOH/Na$_2$CO$_3$, rt.; (iv) NaH, MeI, tetrahydrofuran, reflux; (v) H$_2$NNR$_2$R$_3$, EtOH, reflux; (vi) H$_2$NNH$_2$•H$_2$O, EtOH, reflux; (vii) YNH$_2$•HCl, Et$_3$N, MeOH, reflux.

Similar reactions of **4** and **5** (1 equivalent) with an excess of substituted hydrazines (2 equivalents), such as phenylhydrazine and 1,1-dimethylhydrazine, in boiling ethanol resulted the corresponding hydrazones **7, 8, 10** and **11**. The reactions of compound **4** (1 equivalent) with 1,1-diphenylhydrazine hydrochloride, hydroxylamine hydrochloride or methoxyamine hydrochloride (1.1 equivalents) were carried out in a methanolic solution at reflux (2 hours) in the presence of triethylamine (1.1 equiva-

lents) to afford the hydrazone **13** and the corresponding oxime **14** or the *O*-methyl oxime **15** in 64-69% yield.

In an attempt to establish the tautomeric forms of the isolated products in solution, a detailed comparison of their nmr spectra with those of the enol form of the precursors **4** and **5** was carried out [7]. Only one set of signals was observed in the ^{1}H and ^{13}C nmr spectra of these compounds indicating that the tautomeric equilibrium shown in Scheme 2 is fast on the nmr time scale. The ^{1}H nmr

spectroscopic data for all the compounds are presented in the experimental section. Overall we believe that the spectral data are fully in accord with the enolized form of hydrazone tautomers. All the spectra lacked any resonance characteristic of an sp^3-CH group (methinyl proton), corresponding to the keto form at position-3. The aromatic protons are differentiated with H-5 being observed at 7.8-8.2 ppm as doublet of doublets signal, H-7 at 7.4-7.6 as pseudotriplet, H-8 at 7.1-7.3 as doublet and H-6 at 7.0-7.2 as pseudotriplet. Integration of these signals gave the ratio 1:1:1:1.

Scheme 2
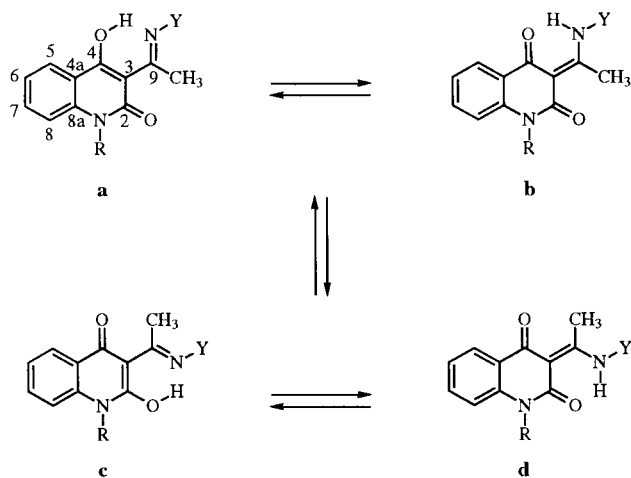
The ^{13}C nmr assignments of compounds **4-15**, presented in Table 1, are based on the off-resonance decoupling. The signals of the carbon atoms of 3-acetylhydrazones have been assigned by comparison with the established values of these carbon atoms reported for 3-acetyl-quinolinone derivatives **4** and **5** [1,7]. The "carbonyl" car-

bons C-9, C-4 and C-2 of 3-acetylquinolinones **4** and **5** resonate at approximately the region of δc 206, 174 and 161 ppm, respectively, whereas the resonance of the C-9 (C=N) hydrazone grouping appears at higher field, in the region of δc 157-163 ppm. The absence of C-9 resonance absorption in the region of 205 ppm of the spectra for hydrazones establishes uniquivocally that in the reaction of substituted hydrazines with 3-acetylquinolinones, nucleophilic attack occurs at the C-9 of the 3-position. This effect is clearly illustrated by the data in Table 1 and also helps to estimate the C-9 electrophilicity of 3-acetyl-quinolinone molecules.

In order to confirm the structure and tautomerism of the coupling compound **14** in the solid state, an X-ray crystal structure determination was carried out. Figure 1 shows the molecular structure together with the numbering scheme of **14**. The partial double bond character of the N(1)-C(9) and C(7)-C(8) bonds in this compound is evident. Interatomic distances and selected bond angles are given in Tables 2 and 3. The results confirm that condensation has taken place in the carbonyl at the acetyl side chain at the 3-position, and they support the oxime tautomer **a** (Scheme 2, Y = OH) of the product. Thus, the C(8)-C(9), C(7)-C(8) and C(8)-C(10) bond lengths are 1.446 Å, 1.389 Å and 1.484 Å, respectively, indicating that the bond C(7)-C(8) has partial double bond character. The length of the O(2)-C(7) bond [1.333 Å] is longer than the normal carbonyl bond length O(1)-C(9) [1.259 Å]. The length of N(1)-C(9) bond [1.384 Å] is significantly shorter than that of the normal C-N bond [1.48 Å], presumably because of some delocalization of the ring-nitrogen atom's lone pair [8], whereas the length of the N(2)-C(10) bond [1.293 Å] is very similar to that of the normal C=N double bond.

Table 1

^{13}C NMR Chemical Shifts for Compounds **4-15**
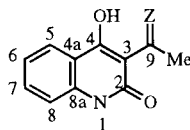
Compound		C-2	C-3	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	C-9
4	(Dimethyl-d$_6$ Sulfoxide)	161.1	105.7	174.7	113.3	124.7	122.0	134.8	115.5	140.5	205.7
5	(Deuteriochloroform)	161.4	105.9	173.8	115.8	126.5	122.3	135.2	114.5	142.0	206.6
6	(Dimethyl-d$_6$ Sulfoxide)	165.0	98.9	176.8	119.6	126.1	120.5	131.7	114.7	138.9	164.0
7	(Dimethyl-d$_6$ Sulfoxide)	162.9	102.4	169.6	116.7	124.2	120.2	132.0	114.8	138.5	159.0
8	(Deuteriochloroform)	174.9	99.6	181.2	120.5	126.1	120.6	132.7	114.9	139.2	164.5
9	(Dimethyl-d$_6$ Sulfoxide)	164.8	99.6	175.1	120.7	125.8	121.2	132.5	114.5	140.4	163.1
10	(Dimethyl-d$_6$ Sulfoxide)	166.9	108.0	171.3	117.4	125.3	122.1	134.5	117.8	133.8	161.7
11	(Deuteriochloroform)	169.7	94.7	174.1	116.6	121.7	116.7	128.7	110.0	136.2	159.0
12	(Deuteriochloroform)	168.9	103.3	172.6	114.0	126.2	121.9	133.5	117.9	140.8	162.8
13	(Deuteriochloroform)	178.5	101.0	182.3	122.0	124.7	120.5	133.5	115.0	139.7	165.6
14	(Dimethyl-d$_6$ Sulfoxide)	162.2	103.1	163.4	114.9	123.8	121.6	132.0	115.0	138.5	159.0
15	(Dimethyl-d$_6$ Sulfoxide)	161.9	104.5	162.0	114.4	123.7	121.6	131.9	115.1	138.5	157.4
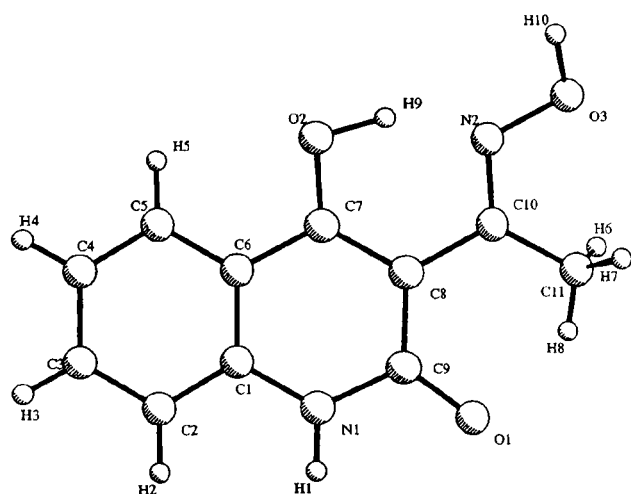
Figure 1. Crystal structure of compound **14** with the atom numbering scheme.

Table 2

Interatomic Distances (Å) in **14** with
Standard Deviations in Parentheses

Atom	Atom	Distance
O(1)	C(9)	1.259(3)
O(2)	C(7)	1.333(3)
O(2)	H(9)	1.043
O(3)	N(2)	1.404(3)
O(3)	H(10)	1.020
N(1)	C(1)	1.386(3)
N(1)	C(9)	1.384(3)
N(1)	H(1)	0.950
N(2)	C(10)	1.293(4)
C(1)	C(2)	1.395(4)
C(1)	C(6)	1.398(4)
C(2)	C(3)	1.375(4)
C(2)	H(2)	0.962
C(3)	C(4)	1.393(4)
C(3)	H(3)	0.965
C(4)	C(5)	1.370(4)
C(4)	H(4)	0.970
C(5)	C(6)	1.402(4)
C(5)	H(5)	0.974
C(6)	C(7)	1.438(4)
C(7)	C(8)	1.389(4)
C(8)	C(9)	1.446(4)
C(8)	C(10)	1.484(4)
C(10)	C(11)	1.493(4)
C(11)	H(7)	0.953
C(11)	H(6)	0.957
C(11)	H(8)	0.952

Table 3

Selected Bond Angles (°) in **14** with
Standard Deviations in Parentheses

Atom	Atom	Atom	Angle
C(7)	O(2)	H(9)	104.17
N(2)	O(3)	H(10)	101.34
C(1)	N(1)	C(9)	123.3(2)
O(3)	N(2)	C(10)	114.1(2)
N(1)	C(1)	C(2)	119.2(2)
N(1)	C(1)	C(6)	119.6(2)
C(2)	C(1)	C(6)	121.1(3)
C(1)	C(2)	C(3)	118.9(3)
C(3)	C(4)	C(5)	120.5(3)
C(4)	C(5)	C(6)	120.1(3)
C(1)	C(6)	C(5)	118.6(3)
C(1)	C(6)	C(7)	118.0(3)
C(5)	C(6)	C(7)	123.4(3)
O(2)	C(7)	C(6)	114.5(2)
O(2)	C(7)	C(8)	123.0(3)
C(6)	C(7)	C(8)	122.5(3)
C(7)	C(8)	C(9)	117.8(3)
C(7)	C(8)	C(10)	121.3(3)
C(9)	C(8)	C(10)	120.9(3)
O(1)	C(9)	N(1)	116.6(2)
O(1)	C(9)	C(8)	124.8(3)
N(1)	C(9)	C(8)	118.7(2)
N(2)	C(10)	C(8)	114.8(3)
N(2)	C(10)	C(11)	121.3(3)
C(8)	C(10)	C(11)	123.9(3)

Table 4

Fractional Atomic Coordinates for **14**

Atom	X	Y	Z
O(1)	-0.1301(3)	-0.1569(2)	0.2490(3)
O(2)	-0.3334(3)	0.0443(2)	-0.2992(3)
O(3)	-0.2925(3)	-0.2985(2)	-0.5329(3)
N(1)	-0.1801	0.0464	0.3113
N(2)	-0.2739(4)	-0.1790(3)	-0.3825(4)
C(1)	-0.2237(4)	0.1578(3)	0.2537(5)
C(2)	-0.2099(4)	0.2714(3)	0.4071 (5)
C(3)	-0.2473(5)	0.3841(3)	0.3503(5)
C(4)	-0.2995(5)	0.3846(3)	0.1428(5)
C(5)	-0.3149(4)	0.2724(3)	-0.0087(5)
C(6)	-0.2768(4)	0.1563(3)	0.0445(5)
C(7)	-0.2851(4)	0.0368(3)	-0.1041 (4)
C(8)	-0.2454(4)	-0.0767(3)	-0.0479(4)
C(9)	-0.1845(4)	-0.0684(3)	0.1718(4)
C(10)	-0.2581(4)	-0.1998(3)	-0.2056(4)
C(11)	-0.2578(5)	-0.3399(3)	-0.1702(5)
H(1)	-0.1453	0.0487	0.4539
H(2)	-0.1724	0.2715	0.5508
H(3)	-0.2366	0.4637	0.4560
H(4)	-0.3280	0.4638	0.1043
H(5)	-0.3522	0.2733	-0.1537
H(6)	-0.3803	-0.4245	-0.2750
H(7)	-0.1505	-0.3522	-0.1813
H(8)	-0.2442	-0.3358	-0.0318
H(9)	-0.3353	-0.0505	-0.3848
H(10)	-0.2529	-0.2476	-0.6301

EXPERIMENTAL

Melting points were determined on a Gallenkamp MFB-595
melting point apparatus and are uncorrected. The ir spectra were
recorded on a Perkin Elmer 267 spectrometer. The nmr spectra
were recorded on either Varian Gemini-2000 300 MHz or

Bruker AC-300 300 MHz spectrometers, using tetramethylsilane as the internal reference. Chemical shifts are quoted in ppm (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad); J values are given in Hz. Elemental analyses were obtained from the University of Liverpool, Chemistry Department, and the microanalytical laboratory of CNRS (France).

Preparation of 2-Methyl-3,1-benzoxazin-4-one 2.

Anthranilic acid (6.86 g, 0.05 mole) was added to acetic anhydride (60 ml) and the mixture was stirred at 130° for 1 hour, until all the solid dissolved. The solution after being cooled to <80°, was evaporated under reduced pressure. The crude product was dissolved in dichloromethane (40 ml) and the solution washed with aqueous 1N sodium hydroxide (3 x 30 ml), then with water (3 x 30 ml) and dried with sodium sulfate. Evaporation of the dried solution afforded a solid residue which was treated with light petroleum and filtered. The title compound 2 was obtained as a white solid (6.8 g, 80%), mp 77-79° (lit [1] mp 74-78°). The product thus obtained was stable under storage at room temperature for several weeks; ^{1}H nmr (deuteriochloroform): 2.44 (3H, s, CH$_3$), 7.47 (1H, pseudotriplet, 6-H), 7.51 (1H, d, J$_{7,8}$ = 7.3, 8-H), 7.77 (1H, pseudotriplet, 7-H), 8.15 (1H, dd, J$_{5,6}$ = 7.8, J$_{5,7}$ = 1.5, 5-H); ^{13}C nmr (deuteriochloroform): 21.2 (CH$_3$), 116.7 (C-4a), 126.4 (C-8), 128.2 (C-6), 128.5 (C-5), 136.6 (C-7), 146.5 (C-8a), 159.7 (C-2), 160.3 (C-4).

Ethyl [(2-Acetylaminophenyl)hydroxymethylidene]acetoacetate 3.

The product was prepared as described in reference [1b].

3-Acetyl-4-hydroxyquinolin-2(1H)-one 4.

The product was prepared as described in reference [1b]; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 2.72 (3H, s, CH$_3$), 7.23 (1H, pseudotriplet, 6-H), 7.30 (1H, d, J$_{7,8}$ = 8.3, 8-H), 7.65, (1H, pseudotriplet, 7-H), 7.99 (1H, d, J$_{5,6}$ = 8.0, 5-H), 11.53 (1H, s, NH), 17.04 (1H, s, OH).

1-Methyl-3-acetyl-4-hydroxyquinolin-2(1H)-one 5.

Sodium hydride (55-60% sodium hydride in oil; 0.81 g, 0.018 mole) was added portionwise to a stirred solution of compound 4 (1.25 g, 0.006 mole) and iodomethane (3.1 ml, 0.049 mole) in tetrahydrofuran (30 ml). The reaction was allowed to warm to room temperature and the reaction mixture was refluxed for 1 hour, after which it was stirred overnight at room temperature. The residue was concentrated under reduced pressure, diethyl ether (30 ml) was added and the evaporation was repeated. Water and diethyl ether were then added to the reaction mixture, after which the aqueous layer was separated, extracted with diethyl ether and acidified with 10% hydrochloric acid in an ice-water bath. The resulting precipitate was filtered to give a yellowish solid (1.07 g, 80%) mp 145-146° (lit [7] mp 143-146°) after recrystallization (ethanol).

General Method for the Preparation of Hydrazones 6-11.

A solution of hydrazine derivative R$_2$R$_3$NNH$_2$ (0.02 mole) in absolute ethanol was added in portions to a suspension of compound 4 (or solution of compound 5) (0.01 mole) in ethanol and the reaction mixture was refluxed for 1-2 hours. The solid product was either formed directly in the reaction mixture or precipitated after concentration of the solution under reduced pressure.

3-(1-Hydrazonoethyl)-4-hydroxyquinolin-2(1H)-one 6.

A suspension of compound 4 (2.03 g, 0.01 mole) in ethanol (70 ml) and a solution of hydrazine hydrate (80% in water, 1.25 g, 0.02 mole) in ethanol (5 ml) were mixed and refluxed for 2 hours. The hydrazone 6 was isolated as a yellow solid, formed directly from the reaction mixture (1.94 g, 89%), mp >320° (from methanol) (lit [2] mp 308°); ir (Nujol): ν max cm^{-1} 3290 w (NH), 3180 w (NH sym), 1650 s (CO lactam and C=N), 1600 m (C=C ring stretching) and 1550 w; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 2.70 (3H, s, CH$_3$), 6.00 (2H, s, NH$_2$), 7.05 (1H, pseudotriplet, 6H), 7.14 (1H, d, J$_{7,8}$ = 8.1, 8-H), 7.43, (1H, pseudotriplet, 7-H), 7.93 (1H, d, J$_{5,6}$ = 7.9, 5-H), 10.60 (1H, s, NH), 16.12 (1H, s, OH).

Anal. Calcd. for C$_{11}$H$_{11}$N$_3$O$_2$: C, 60.82; H, 5.10; N, 19.35. Found: C, 60.95; H, 5.08; N, 19.31.

3-[1-(2-Phenylhydrazono)ethyl]-4-hydroxyquinolin-2(1H)-one 7.

A suspension of compound 4 (2.03 g, 0.01 mole) in ethanol (70 ml) and a solution of phenylhydrazine (2.16 g, 0.02 mole) in ethanol (5 ml) were mixed and refluxed for 2 hours. The hydrazone 7 was isolated as a white solid, formed directly in the reaction mixture (2.41 g, 82%), mp 235-236° (from methanol) (lit [2] mp 222-229°); ir (Nujol): ν max cm^{-1} 3180 w (NH sym), 1650 s (CO lactam and C=N), 1600 s (C=C ring stretching) and 1550 w; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 2.70 (3H, s, CH$_3$), 6.89 (1H, t, J$_{4',3'}$ = 7.3, 4'-H), 7.00, (2H, d, J$_{2',3'}$ = 7.9, 2'-H), 7.13 (1H, pseudotriplet, 6-H), 7.22 (1H, d, J$_{7,8}$ = 8.1, 8-H), 7.30 (2H, pseudotriplet, 3'-H), 7.49, (1H, pseudotriplet, 7-H), 7.95 (1H, d, J$_{5,6}$ = 7.3, 5-H), 9.24 (1H, s, NHPh), 11.12 (1H, s, NH), 16.09 (1H, s, OH).

3-(1-Dimethylhydrazonoethyl)-4-hydroxyquinolin-2(1H)-one 8.

A suspension of compound 4 (2.03 g, 0.01 mole) in ethanol (70 ml) and a solution of 1,1-dimethylhydrazine (1.20 g, 0.02 mole) in ethanol (5 ml) were mixed and refluxed for 1 hour. The hydrazone 8 was isolated as a white solid, after evaporation under reduced pressure (1.97 g, 75%), mp 185-186°; ir (Nujol): ν max cm^{-1} 3180 w (NH sym),1640 s (CO lactam and C=N), 1600 s (C=C ring stretching) and 1560 w; ^{1}H nmr (deuteriochloroform): δ 2.72 [6H, s, N(CH$_3$)$_2$], 2.99 (3H, s, CH$_3$) 7.0-7.2 (2H multiplet, 6-H, 8-H), 7.46 (1H, pseudotriplet, 7-H), 8.11 (1H, d, J$_{5,6}$ = 7.8, 5-H), 10.23 (1H, s, NH), 15.58 (1H, s, OH).

Anal. Calcd. for C$_{13}$H$_{15}$N$_3$O$_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.39; H, 6.29; N, 16.98.

1-Methyl-3-(1-hydrazonoethyl)-4-hydroxyquinolin-2(1H)-one 9.

A solution of compound 5 (0.60 g, 0.003 mole) in ethanol (40 ml) and a solution of hydrazine hydrate (80% in water, 0.18 g, 0.0055 mole) in ethanol (5 ml) were mixed and refluxed for 2 hours. The hydrazone 9 was isolated as a yellowish solid, which was filtered (0.41 g, 65%), mp 335°, dec (lit [2] mp 300°); ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 2.49 (3H, s, C-CH$_3$), 3.46 (3H, s, N-CH$_3$), 6.08 (2H, s, NH$_2$), 7.56 (1H, pseudotriplet, 6-H), 7.33 (1H, d, J$_{7,8}$ = 8.4, 8-H), 7.15 (1H, pseudotriplet, 7-H), 8.05 (1H, dd, J$_{5,6}$ = 7.5, J$_{5,7}$ = 1.5, 5-H), 16.32 (1H, s, OH).

Anal. Calcd. for C$_{12}$H$_{13}$N$_3$O$_2$: C, 62.32; H, 5.67; N, 18.17. Found: C, 62.20; H, 5.68; N, 18.04.

1-Methyl-3-[1-(2-Phenylhydrazono)ethyl]-4-hydroxyquinolin-2(1H)-one 10.

A solution of compound 5 (0.22 g, 0.001 mole) in ethanol (30 ml) and a solution of phenylhydrazine (0.21 g, 0.002 mole)

in ethanol (10 ml) were mixed and refluxed for 2 hours. The hydrazone **10** was isolated as a yellow solid, which was filtered (0.22 g, 70%), mp 222-223°, (lit [2] 211-212°); ^{1}H nmr (dimethyl-d_6 sulfoxide, tetramethylsilane): δ 2.62 (3H, s, C-CH$_3$), 3.55 (3H, s, N-CH$_3$) 6.86 (1H, t, $J_{4',3'}$ = 7.5, 4'-H), 7.02, (2H, d, $J_{2',3'}$ = 8.1, 2'-H), 7.24 (1H, pseudotriplet, 6-H), 7.45 (1H, d, $J_{7,8}$ = 8.4, 8-H), 7.29 (2H, pseudotriplet, 3'-H), 7.64, (1H, pseudotriplet, 7-H), 8.07 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,7}$ = 1.5, 5-H), 9.33 (1H, s NHPh), 15.84 (1H, s, OH).

Anal. Calcd. for C$_{18}$H$_{17}$N$_3$O$_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.39; H, 5.57; N, 13.66.

1-Methyl-3-(1-dimethylhydrazonoethyl)-4-hydroxyquinolin-2(1*H*)-one **11**.

A solution of compound **5** (0.18 g, 0.00083 mole) in ethanol (30 ml) and a solution of 1,1-dimethylhydrazine (0.10 g, 0.00166 mole) in ethanol (10 ml) were mixed and refluxed for 2 hours. The hydrazone **11** was isolated as a yellowish-green solid after evaporation under reduced pressure (0.12 g, 55%), mp 120-121°; ir (Nujol): ν max cm^{-1}, 1640 m (CO lactam and C=N), 1620 s (C=C ring stretching) and 1580 w; ^{1}H nmr (deuteriochloroform, tetramethylsilane): δ 2.64 [6H, s, N(CH$_3$)$_2$], 2.79 (3H, s, C-CH$_3$), 3.42 (3H, s, N-CH$_3$), 7.13 (1H, pseudotriplet, 6-H), 7.30 (1H, d, $J_{8,7}$ = 8.5, 8-H), 7.56 (1H, pseudotriplet, 7-H), 8.04 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,7}$ = 1.5, 5-H), 15.21 (1H, s, OH).

Anal. Calcd. for C$_{14}$H$_{17}$N$_3$O$_2$: C, 64.56; H, 6.63; N, 15.95. Found: C, 64.56; H, 6.63; N, 15.95.

1,1'-Azino-di-(1-methyl-3-ethylidene-4-hydroxyquinoline-2(1*H*)one (**12**).

A solution of hydrazine hydrate (80% in water, 0.04 g, 0.001 mole) in ethanol (10 ml) was added in portions to a solution of compound **5** (0.43 g, 0.002 mole) in ethanol (30 ml) and the mixture was refluxed for 2 hours. The precipitate which formed was filtered and washed with ethanol to afford compound **12** as a bright yellow solid (0.30 g, 70%) mp >320° dec (lit [2] mp 342° dec); ms: m/z [FB+(3-NOBA)] 431 ([M+H]$^+$ 94%), 273 (56) 215 ([M/2]$^+$ 110).

Anal. Calcd. for C$_{24}$H$_{22}$N$_4$O$_4$: C, 66.57; H, 5.11; N, 13.09. Found: C, 66.96; H, 5.15; N, 13.02.

General Procedure for the Preparation of Compounds **13-15**.

Triethylamine (0.16 g, 0.0016 mole) and YNH$_2$•HCl (0.0016 mole) were added to a suspension of compound **4** (0.31 g, 0.0015 mole) in methanol (30 ml) and the mixture was refluxed for 2-3 hours. The reaction mixture was allowed to cool at room temperature and the precipitated solid was collected by filtration and washed with small amounts of methanol.

3-(1-Diphenylhydrazonoethyl)-4-hydroxyquinolin-2(1*H*)-one **13**.

1,1-Diphenylhydrazine hydrochloride (0.35 g, 0.0016 mole) and compound **4** (0.31 g, 0.0015 mole) were refluxed in methanol in the presence of triethylamine (0.16 g, 0.0016 mole) to afford compound **13** as a greenish yellow solid (0.41 g, 75%) mp 238-240° (from methanol) ir (Nujol): ν max cm^{-1} 3300 w (NH), 3210 w (NH sym), 1630 m (CO lactam and C=N), 1600 m (C=C ring stretching) and 1580 s; ^{1}H nmr (deuteriochloroform): δ 2.96 (3H, s, CH$_3$), 7.03 (1H, d, $J_{7,8}$ = 7.7, 8-H), 7.1-7.2 (7H, multiplet, 6-H, 2'-H, 4'-H), 7.35 (4H, pseudotriplet, 3'-H), 7.45 (1H, pseudotriplet, 7-H), 8.13 (1H, d, $J_{5,6}$ = 8.1, 5-H), 10.29 (1H, s, NH), 16.56 (1H, s, OH).

Anal. Calcd. for C$_{23}$H$_{19}$N$_3$O$_2$: C, 74.78; H, 5.18; N, 11.38. Found: C, 74.48; H, 5.17; N, 11.29.

3-(1-Hydroxyiminoethyl)-4-hydroxyquinolin-2(1*H*)-one **14**.

Hydroxylamine hydrochloride (0.11 g, 0.0016 mole) and compound **4** (0.31 g, 0.0015 mole) were heated at reflux in methanol (30 ml) in the presence of triethylamine (0.16 g, 0.0016 mole). After standing at room temperature for 12 hours the white crystalline solid formed was filtered and air dried to afford compound **14** as white prisms (0.21 g, 64%) mp 204°, (lit [2] mp 199-200°); ir (Nujol): ν max cm^{-1} 1650 s (CO lactam and C=N), 1610 m (C=C ring stretching), 1550 w and 1490 s; ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 2.41 (3H, s, CH$_3$), 7.14 (1H, pseudo-triplet, 6-H), 7.23 (1H, d, $J_{7,8}$ = 7.9, 8-H), 7.49, (1H, pseudotriplet, 7-H), 7.87 (1H, d, $J_{5,6}$ = 8.1, 5-H), 11.33 (1H, s, NH), 11.48 (1H, s, NOH),14.49 (1H, s, OH).

Anal. Calcd. for C$_{11}$H$_{10}$N$_2$O$_3$: C, 60.54; H, 4.62; N, 12.84. Found: C, 60.51; H, 4.63; N, 12.86.

3-(1-Methoxyiminoethyl)-4-hydroxyquinolin-2(1*H*)-one **15**.

Methoxyamine hydrochloride (0.13 g, 0.0015 mole) and compound **4** (0.31 g, 0.0015 mole) were heated in the presence of triethylamine (0.16 g, 0.0016 mole) to afford compound **15** as a white solid (0.24 g, 69%) mp 224°; ir (Nujol): ν max cm^{-1} 3200 w (OH), 1640 s (CO lactam and C=N), 1610 m (C=C ring stretching) and 1580; ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 2.27 (3H, s, CH$_3$), 3.91 (3H, s, NOCH$_3$), 7.17 (1H, pseudotriplet, 6H), 7.25 (1H, d, $J_{7,8}$ = 8.0, 8-H), 7.52, (1H, pseudotriplet, 7-H), 7.87 (1H, d, $J_{5,6}$ = 8.1, 5-H), 11.45 (1H, s, NH), 12.59 (1H, s, OH).

Anal. Calcd. for C$_{12}$H$_{12}$N$_2$O$_3$: C, 62.00; H, 5.21; N, 12.06. Found: C, 62.07; H, 5.19; N, 11.97.

X-Ray Crystallographic Analysis of Compound **14**.

Crystallographic Data.

Molecular formula: C$_{11}$H$_{10}$N$_2$O$_3$, M = [218.21], triclinic, a = 8.125(3) Å, b = 10.187(3) Å, c = 7.198(2) Å, α = 99.97(2)°, β = 112.00(2)°, γ = 110.46(2)°, V = 484.8(3) Å^3 (by least-squares refinement on twenty five carefully centered reflections in the range 37.37 < 2θ < 44.23°), λ = 0.71069Å, space group P$_1$ (No 2), Z = 2, Dx = 1.495 g cm^{-3}, colorless prisms, dimensions of crystals used 0.200 x 0.150 x 0.300 mm, μ (MoKα) = 1.04 cm^{-1}.

Data Collection and Processing.

Rigaku AFC6S diffractometer, graphite monochromated MoKα radiation, ω-2θ scans to maximum 2θ value of 50.0° with ω scan width (1.47 + 0.30 tan θ)°; 1840 reflections collected of which 1710 were unique (R$_{int}$ = 0.015). The intensities of three representatives reflections which were measured after every 150 reflections remained constant throughout data collection indicating crystal and electronic stability. An empirical absorption correction, based on azimuthal scans of several reflections, was applied which resulted in transmission factors ranging from 0.82 to 1.00. The data were corrected for Lorenz and polarization effects.

Structure Solution and Refinement.

The structure was solved by direct methods [9]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the structure factor calculation in idealized position (d$_{C-H}$ = 0.95 Å), and were assigned isotropic thermal parameters which are 20% greater than the B$_{equivalent}$ value of the atom to which they were bonded. The final cycle of

full-martrix least-squares refinement was based on 1216 observed reflections ($I > 3.00\sigma$ (I)) and 142 variables parameters and converged (largest parameter shift was 0.01 times its esd) with unweighted and weighted agreement factors of R, Rw = 0.048, 0.062, respectively. The standard deviation of an observation of unit weight was 2.38. The maximum and minimum peaks of the final difference Fourier map corresponded to 0.51 and -0.41e$^-$/Å^3. TEXSAN-TEXRAY software package was used [10] including atomic scattering factors and weighting scheme. The diagram was produced using PLUTO [11]. A list of atomic coordinates for **14** is given in Table 4.

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REFERENCES AND NOTES

[1a]   A. Detsi, J. Markopoulos and O. Igglessi-Markopoulou, *Chem. Commun.*, 1323 (1996); [b] A. Detsi, V. Bardakos, J. Markopoulos and O. Igglessi-Markopoulou, *J. Chem. Soc., Perkin Trans. 1*, 2909 (1996).

[2]   T. Kappe, R. Aigner, M. Jöbstl, P. Hohengassner and W. Stadlbauer, *Heterocyclic Commun.*, **1**, 341 (1995).

[3]   T. Kappe and B. Schnell, *J. Heterocyclic Chem.*, **33**, 663 (1996).

[4]   S. Gelin, B. Chantegrel and M. Chabannet, *Synth. Commun.*, **12**, 431 (1982).

[5]   R. C. F. Jones, A. D. Bates, J. Crane and C. J. Hayes, *J. Chem. Res. (S)*, 444 (1994).

[6]   A. Jackson and O. Meth-Cohn, *J. Chem. Soc., Perkin Trans. 1*, 1319 (1995).

[7]   G. M. Coppola, A. D. Kahle and M. J. Shapiro, *Org. Magn. Reson.*, **17**, 242 (1981).

[8]   M. J. Nolte, P. S. Steyn and P. L. Wessels, *J. Chem. Soc., Perkin Trans. 1*, 1057 (1980).

[9]   C. J. Gilmore, MITHRIL, *J. Appl. Crystallogr.*, **17**, 42 (1984).

[10]   TEXSAN-TEXRAY Structure Analysis Package, Molecular Structure Corporation (1985).

[11]   S. Motherwell, W. Clegg; PLUTO, Program for plotting molecular and crystal structures, Univ. of Cambridge, England (1978).