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In order to find new antimalarial drugs, an exploration about the chemical properties of the starting compounds 3-amino-6-chloro-4-phenyl-1*H*-quinolin-2-one (**1**) and 3-amino-4-methyl-1*H*-quinolin-2-one (**2**) was developed. Acylation with acyl chloride, sulfonyl chloride and acetic anhydride were carried out. Despite a previous report [2], when acetyl chloride or acetic anhydride were assayed on **1**, only the diacetyl derivative **7** was obtained. When this compound was heated at reflux temperature in a mixture of acetic acid and acetic anhydride, it was transformed in the oxazoloquinoline **8**. Further reactions of the acyl derivatives with diazomethane afforded 1-methylated compounds. Compound **2** gave the imine **16** by condensation with 4-nitrobenzaldehyde.

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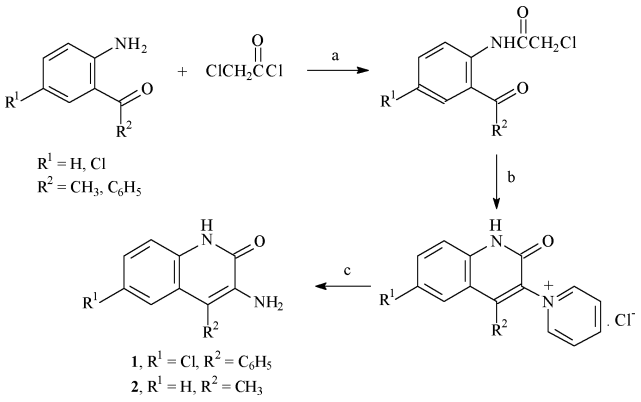
1. Introduction.

Despite efforts to eradicate malaria, the disease still remains in Third World countries. The development of resistance by many strains of *Plasmodium falciparum* to current drugs (quinine, chloroquine) indicates the urgent need for new rather than economic antimalarial compounds.

In an article from 20 years ago, we reported a very useful procedure to synthesize 3-amino-1*H*-quinolin-2-ones [1], Scheme 1. Amino quinolones are valuable substrates for the synthesis of potential biologically active compounds. For this reason we were prompted to avail this substrate for searching a new class of antimalarial drugs possessing a quinoline nucleous. This effort required an exploration of the "chemical plasticity" of the starting compounds (**1** or **2**), in order to determine what kind of derivatives can be achieved from these heads of series.

Scheme 1



a: benzene, reflux; b: pyridine, 115°; c: aniline, reflux

2. Results and Discussion.

2.1 Methylation at Position 1.

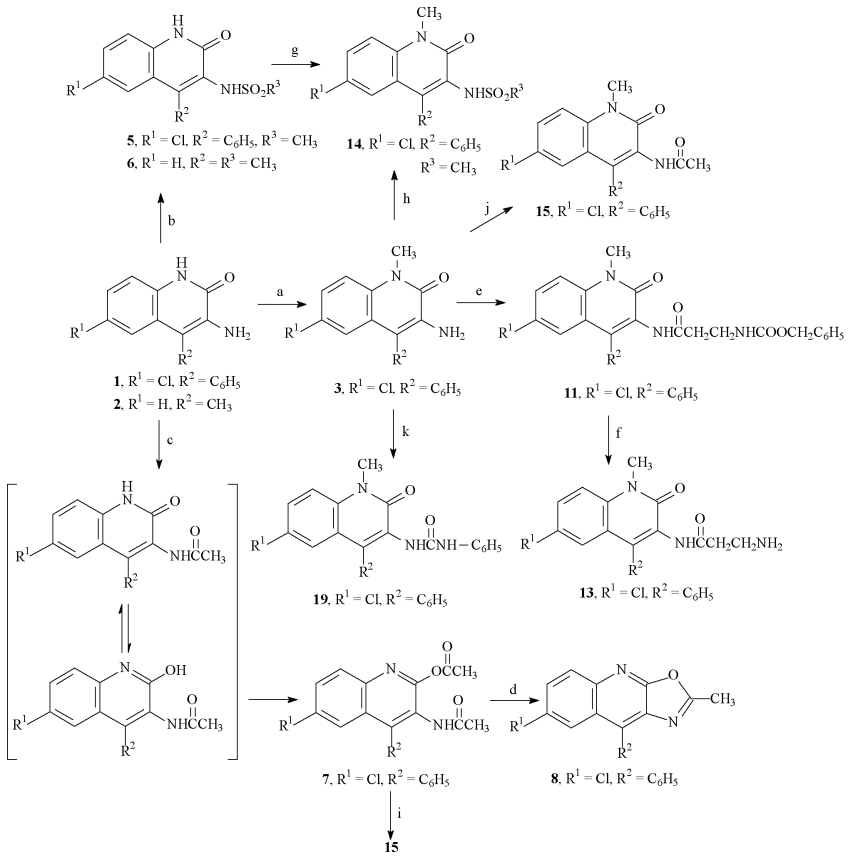
A methylation procedure described before [2] was improved. The sodium salt of 3-amino-6-chloro-4-phenyl-1*H*-quinolin-2-one (**1**) was reacted with methyl iodide in acetone solution to afford the *N*-alkylated compound **3** in good yield (Scheme 2).

2.2 Acylation Reactions at Position 3.

Compounds **4**, **5** and **6** were synthesized from **1** and **2** by reaction with benzoyl chloride under Schotten-Baumann conditions or methanesulfonyl chloride in pyridine, respectively (Schemes 2 and 3). Surprisingly, the reaction of **1** with acetic anhydride turned out to be a specific one. When compound **1** was heated with highly pure acetic anhydride, a white product precipitated rapidly. The analysis agreed with a diacetylated compound **7**, formed by the acetylation of both amino group and lactim form of NHCO group (Scheme 2). The structure of **7** was confirmed in the ^{1}H nmr by the presence of both methyl groups as a singlet signal (δ 2.12) that integrates for six hydrogen atoms. In its mass spectrum, although the expected molecular ion (m/z 355) is not observed, a signal at 312 (12.25 %) for the molecular ion minus one acetyl group and the base peak at m/z 270 (100.00 %) that indicates the loss of two acetyl groups, were found. A third important signal is at m/z 43 (29.83) for the acetyl group. Finally, compound **7** was soluble at the boiling point of a 2:1 ratio acetic anhydride-acetic acid mixture and after prolonged heating, compound **7** was transformed into the oxazoloquinoline **8** with excellent yield (77 %), Scheme 2. This compound had been previously described [3] but no spectroscopical data were reported. It was prepared from different starting materials in low yield (20 %). ^{1}H nmr spectrum of **8** exhibits a singlet signal (δ 2.69) of the methyl group and the mass spectrum has the molecular ion as the base peak at m/z 294 (100.00 %) and also another important peak at m/z 257 (59.39 %) which indicates the loss of a chlorine atom.

Attempts for the synthesis of the 3-acetamido derivative from compound **1** were unsuccessful. Fryer and Sternbach [3] have described the preparation of this amide employing acetyl chloride in refluxing benzene. When this technique

Scheme 2



a: 1. NaOH 4N, acetone, 2. ICH_3, 0-5º; b: CH_3SO_2Cl, pyridine, 5º; c: Ac_2O, reflux; d: Ac_2O, AcOH, reflux; e: $C_6H_5CH_2OCONHCH_2CH_2COCl$, CH_2Cl_2, reflux; f: HCOOH, Pd/C 5 %, MeOH, reflux; g: CH_2N_2, ether, 5º; h: CH_3SO_2Cl, pyridine, 5º; i: CH_2N_2, ether, H_2O, 5º; j: Ac_2O, reflux; k: C_6H_5NCO, CH_2Cl_2, r.t.

was used, the only reaction product was again the diacetyl derivative **7**. Mild hydrolysis of compound **7** was also tried, heating it in ethanol with acid catalysis but it led directly to compound **1**.

Additional attempts based on treating the quinolone **1** with an equimolar amount of acetic anhydride or carrying out the reaction at room temperature, only resulted in the recovery of the starting material. Probably the 3-acetamido derivative is a non-isolated intermediate that easily undergoes further acetylation.

On the other hand, the treatment of 3-amino-4-methyl-2-quinolone (**2**) with acetic anhydride gave the expected monoamide **9** as the unique product (Scheme 3). It can be explained as in the former case (with the 4-phenyl) the hydroxy group of the lactim does not form hydrogen bonding with the carbonyl of the acetamide moiety, while in the 4-methyl derivative (**9**) a hydrogen bonding can be established (Figure 1). This hypothesis is supported on the basis of a conformational study of molecular modeling [4] of the distance between H and O atoms in both structures. When the model has a phenyl ring, the distance is 3.07 Å, but

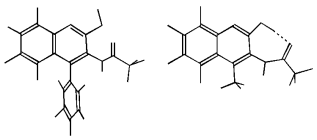


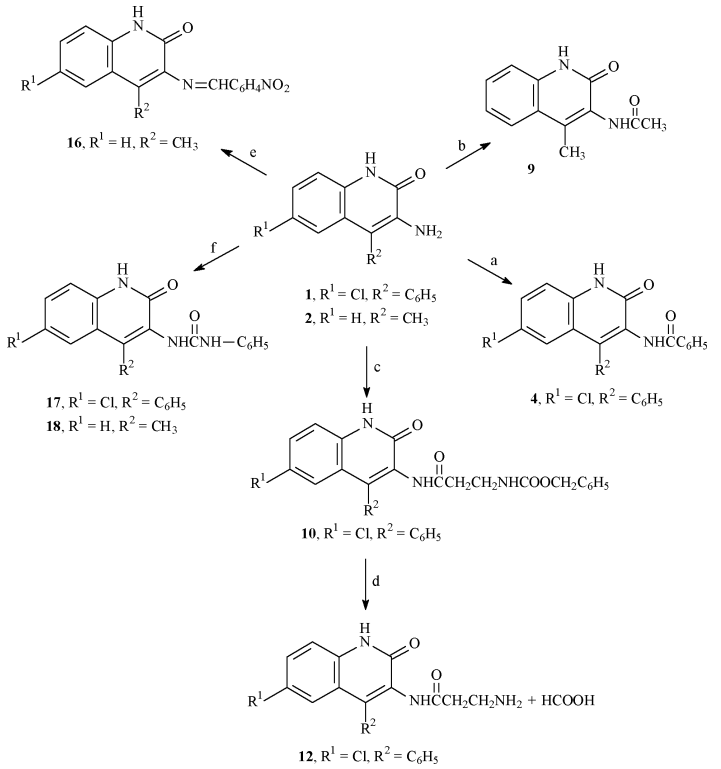
Figure 1. The hydroxy of the lactime model with the phenyl moiety does not form hydrogen bond (left), while it can be established in compound **9** (right).

when there is a methyl group, it is just 1.82 Å. Such a compatible value with the hydrogen bonding formation, stabilizes and blocks the reactivity of that OH group.

In order to protect the amino group, the reactions of **1** and **2** with benzyl chloroformate were intended, but they did not made good progress.

The acylation of the amino group with amino acids is also an attractive target for pharmacological purposes. The reaction of compounds **1** and **3** with *N*-benzyloxycarbonyl-β-alaninyl chloride ($C_6H_5CH_2OCONHCH_2CH_2COCl$) in methylene chloride at reflux temperature, although proceeding slowly, gave the corresponding *N*-benzyloxycar-

Scheme 3



a: aq. Na_2CO_3, C_6H_5COCl, $HCCl_3$, 0-5°; b: Ac_2O, reflux; c: $C_6H_5CH_2OCONHCH_2CH_2COCl$, CH_2Cl_2, reflux; d: HCOOH, Pd/C 5 %, MeOH, reflux; e: 4-$NO_2C_6H_5$, cat., benzene, reflux; f: C_6H_5NCO, CH_2Cl_2 or diglyme, r.t.

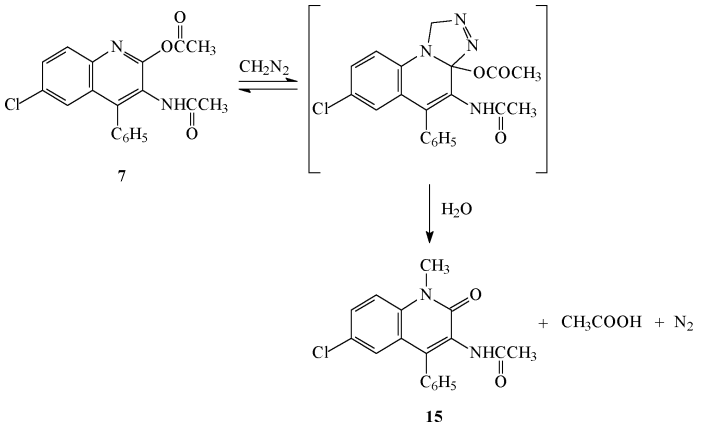
bonyl-β-alaninyl amides **10** and **11** in good yield. Benzyloxycarbonyl protecting group was inert to removal by hydrogenolysis with 10 % palladium on carbon as catalyst at 20 psi at room temperature; was accomplished by heating the amide with formic acid in methanol with a catalytic amount of 10 % palladium on carbon [5], to give compounds **12** and **13** (Schemes 2 and 3).

2.3 Reaction of the Acyl Derivatives with Diazomethane.

Diazomethane reacted slowly with the methanesulfonamide **5** in ether solution at low temperature to give the 1-methyl derivative **14**, which was identical to the product obtained when 1-methyl-3-aminoquinolone (**3**) was reacted with methanesulfonyl chloride, Scheme 2.

Notably, the diacetyl compound **7** also reacted with diazomethane when the ethereal solution was contaminated with a small amount of water as an impurity coming from the synthesis of that reagent. The product of the reaction could be identified as the 3-acetamide-1-methylquinolone **15**, identical to the product obtained when **3** was reacted with acetic anhydride, Scheme 2. According to Scheme 4, the mechanism for the formation of **15** can be explained in terms of addition of diazomethane to the C=N double bond and the consecutive hydrolysis of this intermediate.

Scheme 4



Suggested mechanism for compound **15**.

2.4 Other Reactions.

The preparation of imines with aromatic moieties also constitutes an interesting goal. Then the condensation of quinolones **1** and **2** with 4-nitrobenzaldehyde, a recognized imine forming reagent, was assayed. When compound **1** was heated with 4-nitrobenzaldehyde with acid catalysis at

refluxing temperature in benzene, the starting materials were recovered quantitatively but contaminated with a small amount of a yellow material. The same result was reached starting from the 1-methylated **3**. However, the condensation with the 4-methylquinolone **2** occurred rapidly and the expected imine **16**, which proved to be very insoluble in organic solvents, was achieved (Scheme 3). This behavior implies that the nucleophilicity of the amino group of compound **1** has been diminished because of its partially enaminic nature.

Compounds **1**, **2** and **3** reacted easily with phenyl isocyanate when they were completely dissolved and yielded the corresponding phenylureas **17**, **18** and **19** (Schemes 2 and 3).

All the analytical and spectral data (ir, nmr and ms) were in full agreement with the proposed structures.

EXPERIMENTAL

Melting points were determined on an Electrothermal 9100 apparatus and are uncorrected. Infrared spectra were recorded on a FT Perkin Elmer Spectrum One from KBr discs. ^{1}H and ^{13}C nmr spectra were recorded with a Bruker 200 spectrometer. The mass spectra were obtained on a Trio-2 VG Masslab. Analytical tlc was carried out on precoated (0.2 mm) Merck DC-Plastikfolien Kieselgel 60 F_{254} plates. Elemental analysis were within ±0.4 % of the theoretical values.

3-Amino-6-chloro-1-methyl-4-phenyl-quinolin-2-one (**3**).

A mixture of 5.00 g (18 mmoles) of 3-amino-6-chloro-4-phenyl-1*H*-quinolin-2-one (**1**) and 5.3 ml of 4 *N* sodium hydroxide in 40 ml of acetone was stirred until complete dissolution at room temperature. The solution was then cooled in a water-ice bath and 2.3 ml (37 mmoles) of methyl iodide were added dropwise. The mixture was stirred overnight and then concentrated under reduced pressure. The resulting solid was washed with cold ethanol and then purified by treatment with hot ethanol to afford **3** (3.69 g, 70 %), mp 133-135°. Ir (cm^{-1}): 3473, 3354, 1668, 1575, 1489, 1390, 874, 812, 706. ^{1}H nmr (DMSO-d_6): δ 7.60-7.29 (m, 7H, arom.); 6.78-6.77 (d, 1H, arom.); 5.05 (br s, 2H, NH_2); 3.75 (s, 3H, CH_3).

Anal. Calcd. For $C_{16}H_{13}ClN_2O$: H, 4.60; C, 67.49; N, 9.84. Found: H, 4.68; C, 67.37; N, 9.88.

3-Benzamido-6-chloro-4-phenyl-1*H*-quinolin-2-one (**4**).

Benzoyl chloride (0.3 ml, 2.6 mmoles) was slowly added to a magnetically stirred and cooled to 0-5° mixture of 0.50 g (1.8 mmoles) of compound **1** in 15 ml of chloroform and 0.27 g (2.6 mmoles) sodium carbonate in 5 ml of water. The solution was then allowed to raise to room temperature overnight and after extracting the organic layer was dried with magnesium sulfate and concentrated under reduced pressure to give **4** which was crystallized from benzene: white powder (0.38 g, 57 %), mp 244-246°. Ir (cm^{-1}): 3250, 3000, 1640, 1480, 1260, 820, 750, 700. ^{1}H nmr (DMSO-d_6): δ 12.34 (s, 1H, NHCO); 9.56 (s, 1H, NH); 7.72-7.32 (m, 12H, arom.); 7.00-6.99 (d, 1H, arom.).

Anal. Calcd. for $C_{22}H_{15}ClN_2O_2$: H, 4.03; C, 70.50; N, 7.47. Found: H, 4.10; C, 70.38; N, 7.52.

6-Chloro-3-methanosulfonamido-4-phenyl-1*H*-quinolin-2-one (**5**).

Compound **1** (0.50 g, 1.8 mmoles) was suspended in 5 ml of pyridine and 0.2 ml (2.5 mmoles) of methanesufonyl chloride were added dropwise with stirring at 0-5°. The reaction was allowed to rise to room temperature overnight. The pyridine was evaporated *in vacuo* and 10 ml of ethanol was added. The solid product was collected by filtration and crystallized from pyridine to give **5** (0.30 g, 37 %), mp 317-318°. Ir (cm^{-1}): 3278, 1675, 1489, 1322, 1144, 822. ^{1}H nmr (DMSO-d_6): δ 12.00 (s, 1H, $NHSO_2$); 9.10 (s, 1H, lactam); 7.70-7.15 (m, 8H, arom.); 3.07 (s, 3H, CH_3).

Anal. Calcd. for $C_{16}H_{13}ClN_2O_3S$: H, 3.76; C, 55.10; N, 8.03. Found: H, 3.81; C, 55.03; N, 8.05.

3-Methanosulfonamido-4-methyl-1*H*-quinolin-2-one (**6**).

Compound **2** (1.0 g, 5.7 mmoles) was suspended in 6 ml of pyridine and 0.5 ml (6.5 mmoles) of methanesulfonyl chloride was added dropwise with stirring at 0-5°. A white product precipitated almost immediately and 3 ml of ethanol were added to resuspend the mixture. Compound **6** was collected by filtration *in vacuo* and crystallized from ethanol (0.77 g, 54 %), mp 278-280°. Ir (cm^{-1}): 3206, 1658, 1329, 1153, 750. ^{1}H nmr (DMSO-d_6): δ 11.99 (s, 1H, $NHSO_2$); 8.91 (s, 1H, NH); 7.80-7.25 (m, 4H, arom.); 3.08 (s, 3H, SO_2CH_3); 2.50 (s, 3H, CH_3).

Anal. Calcd. for $C_{11}H_{12}N_2O_3S$: H, 4.79; C, 52.37; N, 11.10. Found: H, 4.83; C, 52.28; N, 11.15.

3-Acetamido-2-acetoxy-6-chloro-4-phenyl-quinoline (**7**).

Compound **1** (4.0 g, 14.8 mmoles) was heated at reflux temperature in 6 ml (54.3 mmoles) of acetic anhydride for 2 h and a white solid precipitated. After cooling, compound **7** was collected by filtration *in vacuo* and recrystallized from methanol-water 2:1 (4.10 g, 78 %), mp 266-267°. Ir (cm^{-1}): 3435, 3000, 1727, 1663, 1485, 1367, 1240, 720. ^{1}H nmr (DMSO-d_6): δ 12.62 (s, 1H, NH); 7.72-6.94 (m, 8H, arom.); 2.12 (s, 6H, CH_3). Ms: m/z 312 (M^+-$COCH_3$); 270 (312-$COCH_3$); 43 ($COCH_3$).

Anal. Calcd. for $C_{19}H_{15}ClN_2O_3$: H, 4.26; C, 64.32; N, 7.90. Found: H, 4.30; C, 64.24; N, 7.94.

7-Chloro-2-methyl-9-phenyl-[1,3]oxazolo[5,4-*b*]quinoline (**8**).

Compound **7** (2.60 g, 7.3 mmoles) was heated at reflux temperature in 30 ml of a mixture acetic anhydride-acetic acid (2:1) for 5 h. Then it was cooled and compound **8** precipitated as yellow needles. After collecting by filtration, the yellow needles were recrystallized from methanol (1.69 g, 78 %), mp 232-233°. Ir (cm^{-1}): 3435, 2923, 1632, 1376, 1245, 828, 703. ^{1}H nmr (DMSO-d_6): δ 8.12 (d, 1H, arom.); 7.80 (d, 2H, arom.), 7.63 (s, 5H, C_6H_5); 2.69 (s, 3H, CH_3). Ms: m/z 294 (M^+); 259 (M^+-Cl); 190 (M^+-$CCH_3C_6H_5$).

Anal. Calcd. for $C_{17}H_{11}ClN_2O$: H, 3.76; C, 69.28; N, 9.50. Found: H, 3.81; C, 69.25; N, 9.48.

3-Acetamido-4-methyl-1*H*-quinolin-2-one (**9**).

A mixture of 0.50 g (2.9 mmoles) of **2** and 1 ml (10.6 mmoles) of acetic anhydride was stirred at room temperature for 2 days. Then 4 ml of ethanol was added and the product was collected by filtration *in vacuo* and washed with ethanol (0.40 g, 64 %), mp 268-270°. Ir (cm^{-1}): 3265, 3015, 1660, 1529, 1400, 1270, 753. ^{1}H nmr (DMSO-d_6): δ 11.90 (s, 1H, NHCO); 9.35 (s, 1H, NH); 7.75-7.18 (m, 4H, arom.); 2.23 (s, 3H, CH_3); 2.05 (s, 3H, $COCH_3$).

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: H, 5.59; C, 66.65; N,12.95. Found: H, 5.65; C, 66.60; N, 12.94.

[2-(6-Chloro-2-oxo-4-phenyl-1,2-dihydro-quinolin-3-ylcarbamoyl)-ethyl]-carbamic Acid Benzyl Ester (**10**).

N-Benzyloxycarbonyl-β-alanine 11.35 g (0.051 mole) was heated at reflux temperature with 37 ml (0.507 mole) of thionyl chloride for 2.5 h to give the acyl chloride (*N*-Benzyloxycarbonyl-β-alaninyl chloride). The excess of thionyl chloride was removed by distillation and the product was used without further purification, 11.06 g (90 % yield). The product was placed in a round bottomed flask with 11.26 g (0.042 mole) of **1** and 140 ml of methylene chloride and the mixture was heated at reflux for 8 h. Upon cooling to room temperature a solid coproduct was collected by filtration and the solvent was concentrated to afford **10**, which was recrystallized from dioxane-methanol (5.40 g, 26 %). Ir (cm^{-1}): 3322, 1687, 1653, 1542, 1483, 1269, 820, 697. ^{1}H nmr (DMSO-d_6): δ 12.33 (s, 1H, NHCO); 9.20 (s, 1H, lactam); 6.98 (d, 1H, CH_2NH); 5.02 (s, 2H, OCH_2Ph); 3.20-3.17 (m, 2H, CH_2NH); 7.63-7.08 (m, 13H, arom.); 2.27-2.20 (t, 2H, CH_2CH_2NH). ^{13}C nmr (DMSO-d_6): δ 170.24 ($NHCOCH_2$); 159.29 (NHCO lactam); 145.68, 137.25, 136.41, 133.74, 130.19, 128.60, 128.46, 127.87, 127.63, 126.01, 125.31, 120.65 (arom.); 117.52 (C=C), 69.34 (OCH_2); 37.09 ($NHCH_2$); 35.58 (CH_2CO). Ms: m/z 367 (M^+-109); 270; 108 ($OCH_2C_6H_5$); 91; 44 (CH_2CH_2NH).

Anal. Calcd. for $C_{26}H_{22}ClN_3O_4$: H, 4.66; C, 65.62; N, 8.83. Found: H, 4.70; C, 65.58; N, 8.83.

[2-(6-Chloro-1-methyl-2-oxo-4-phenyl-1,2-dihydroquinolin-3-ylcarbamoyl)-ethyl]-carbamic Acid Benzyl Ester (**11**).

A solution of 3.00 g (12.4 mmoles) of *N*-Benzyloxycarbonyl-β-alaninyl chloride in 30 ml of methylene chloride was added to a cooled (5º) solution of 3.18 g (11.2 mmoles) of **3** in 45 ml of the same solvent and the mixture was stirred overnight at room temperature. The solvent was evaporated to give a viscous oil which was dissolved in methanol and purified by radial planar chromatography (Chromatotron®) using methylene chloride and methylene chloride:methanol (8:1) as eluents to give **11** (0.84 g, 15 %), mp 169-172º. When the reaction was carried out at reflux temperature for 3 h, compound **11** was obtained in 31 % yield. Ir (cm^{-1}): 3300, 1680, 1650, 1270, 700, 819.

Anal. Calcd. for $C_{27}H_{24}N_3O_4Cl$: H, 4.94; C, 66.19; N, 8.58. Found: H, 5.00; C, 66.15; N, 8.56.

3-Amino-*N*-(6-chloro-2-oxo-4-phenyl-1,2-dihydroquinolin-3-yl)-propionamide (**12**).

Compound **10** (1.00 g, 2.1 mmoles) was dissolved in 20 ml of warm formic acid at which time 40 ml of methanol and 1.00 g of 10 % palladium on carbon was added and the mixture was heated at reflux for 5 h. The catalyst was removed by filtration through a celite bed, and the solvent was evaporated to give a yellow oil that after standing crystallized as a white solid. The product was triturated with methanol to give a water soluble compound, **12** (0.2 g, 25 %), mp 282-288º. The free base could not be isolated because it was highly hygroscopic.

3-Amino-*N*-(6-chloro-1-methyl-2-oxo-4-phenyl-1,2-dihydroquinolin-3-yl)-propionamide (**13**).

This compound was prepared in the same manner as **12** from 0.20 g (0.4 mmole) and 0.20 g of 10 % palladium on carbon, to afford the water soluble compound **13**, which was triturated with methanol (65 mg, 33 %), mp 286-287º. The free base could not be isolated because it was highly hygroscopic.

6-Chloro-3-methanosulfonamido-1-methyl-4-phenyl-quinolin-2-one (**14**).

Route 1.

Compound **5** (0.30 g, 0.86 mmole) was reacted with an ethereal solution of diazomethane prepared from 2.14 g (10 mmoles) of *N*-methyl-*N*-nitroso-4-toluensulfonamide (Diazald®), according to Vogel's technique [6]. A volume of 0.20 ml of methanol was added as catalyst and the mixture was stirred for 2 h at 0-5º and further 20 h at room temperature. The solvent was evaporated and the residual solid was crystallized from methanol to afford **14** (90 mg, 29 %), mp 194-198º. Ir (cm^{-1}): 3010, 2944, 1656, 1589, 1380, 1144, 1067, 833, 710. ^{1}H nmr (DMSO-d_6): δ 8.76 (s, 1H, NH); 7.84-7.32 (m, 8H, arom.); 3.79 (s, 3H, NCH_3); 3.07 (s, 3H, SO_2CH_3).

Anal. Calcd. for $C_{17}H_{15}N_2O_3ClS$: H, 4.17; C, 56.28; N, 7.72. Found: H, 4.23; C, 56.24; N, 7.70.

Route 2.

A solution of 0.50 g (1.76 mmole) of **3** in 3 ml of pyridine was stirred in a water-ice bath and 0.15 ml (1.94 mmole) of methanesulfonyl chloride was added slowly. The yellow mixture was allowed to warm to room temperature and stirred for further 10 h. The solvent was evaporated and a solid product crystallized from the residual oil. It was collected by filtration and recrystallized from ethanol to yield **14** (0.37 g, 57 %), whose properties are identical to those of the product obtained in Route 1.

3-Acetamido-6-chloro-1-methyl-4-phenyl-quinolin-2-one (**15**).

Route 1.

Compound **7** (0.58 g, 1.65 mmole) was reacted with an ethereal solution of diazomethane prepared from 2.14 g (10 mmoles) of *N*-methyl-*N*-nitroso-4-toluensulfonamide (Diazald®), according to Vogel's technique [6]. A volume of 0.02 ml of water was added as catalyst and the mixture was stirred at 0-5º for 2 h and then stored in a refrigerator for 2 days. The solvent was evaporated and the solid residue was recrystallized from ethanol to afford **15** (0.40 g, 74 %), mp 201-203º. Ir (cm^{-1}): 3400, 1720, 1685, 1640, 1360, 1210, 710. ^{1}H nmr (DMSO-d_6): δ 11.47 (s, 1H, NH); 7.78-7.00 (m, 8H, arom.); 3.76 (s, 3H, NCH_3); 2.10 (s, 3H, $COCH_3$).

Anal. Calcd. for $C_{18}H_{15}N_2O_2Cl$: H, 4.63; C, 66.16; N, 8.57. Found: H, 4.71; C, 66.1; N, 8.55.

Route 2.

Compound **3** (0.50 g, 1.76 mmole) and 2 ml (15.9 mmole) of acetic anhydride were heated at reflux for 1.5 h. Upon cooling to room temperature, a white solid was collected by filtration. The solid was triturated with ethanol to give **15** (0.38 g, 66 %), whose properties are identical to those of the product obtained in Route 1.

4-Methyl-3-(4-nitrobenzyliden)amino-1*H*-quinolin-2-one (**16**).

Compound **2** (0.50 g, 2.9 mmole) and 0.48 g (3.2 mmole) of 4-nitrobenzaldehyde were heated at reflux temperature in 10 ml of benzene with a small amount of methansulfonic acid as catalyst. The coloration changed to yellow-orange in 15 min and the resulting suspension was heated and stirred for additional 30 min. The solvent was evaporated and the product was recrystallized

from benzene to give **16** (0.69 g, 76 %), mp 256-260º. Ir (cm^{-1}): 3000, 1644, 1600, 1500, 1339, 833, 756. Ms: m/z 308 (M^{+}+1); 307 (M^{+}); 185 (M^{+}-$C_6H_4NO_2$); 159 ($NCC_6H_4NO_2$).

Anal. Calcd. for $C_{17}H_{13}N_3O_3$: H, 4.26; C, 66.44; N, 13.67. Found: H, 4.32; C, 66.40; N, 13.65.

N-(6-Chloro-2-oxo-4-phenyl-1,2-dihydroquinolin-3-yl)-*N*'-phenylurea (**17**).

To a solution of 0.50 g (1.85 mmole) of **1** in 7 ml of diglyme was added dropwise a solution of 0.24 ml (2.2 mmole) of phenylisocyanate in 1.5 ml of diglyme. The mixture was stirred at room temperature for 40 min at which time a white solid precipitated. The suspension was stirred for further 24 h to complete the reaction. The product was collected by filtration and washed with ethanol to yield **17** (0.38 g, 53 %), mp 228-229º. Ir (cm^{-1}): 3300, 3100, 1680, 1600, 1560, 820, 750. ^{1}H nmr (DMSO-d_6): δ 11.40 (s, 1H, lactam); 8.79 (s, 1H, NHPh); 8.64 (s, 1H, NHCO); 7.69-6.88 (m, 13H, arom.).

Anal. Calcd. for $C_{22}H_{16}ClN_3O_2$: H, 4.14, C, 67.78; N, 10.78. Found: H, 4.22; C, 67.68; N, 10.80.

N-(4-Methyl-2-oxo-1,2-dihydroquinolin-3-yl)-*N*'-phenylurea (**18**).

To a solution of 1.00 g (5.75 mmoles) of **2** in 10 ml of dichloromethane was added dropwise a solution of 0.7 ml (6.42 mmoles) of phenylisocyanate in 2 ml of the same solvent. The mixture was stirred at room temperature overnight and a white solid precipitated. The product was collected by filtration, washed with dichloromethane. The solid was then triturated with ethanol to give **18** (1.50 g, 89 %), mp > 280º. Ir (cm^{-1}): 3303, 3000, 1643, 1552, 1233, 744.

Anal. Calcd. for $C_{17}H_{15}N_3O_2$: H, 5.15; C, 69.61; N, 14.33. Found: H, 5.25; C, 69.52; N, 14.32.

N-(6-Chloro-1-methyl-2-oxo-4-phenyl-1,2-dihydroquinolin-3-yl)-*N*'-phenylurea (**19**).

To a solution of 0.50 g (1.76 mmoles) of **3** in 6 ml of dichloromethane was added dropwise a solution of 0.3 ml (2.75 mmoles) of phenylisocyanate in 2 ml of the same solvent. The mixture was stirred at room temperature for 2 h and concentrated to dryness to give an yellow oil. To this residue was added 2 ml of benzene and the mixture was stirred energically with a glass stick to give a white solid that was collected by filtration and washed with benzene to give **19** (0.46 g, 65 %), mp 207-208º. Ir (cm^{-1}): 3334, 1718, 1608, 1498, 1443, 1217, 815, 752, 693. ^{1}H nmr (DMSO-d_6): δ 8.77 (s, 1H, NHPh); 8.66 (s, 1H, NHCO); 7.67-6.90 (m, 13H, arom.); 3.76 (s, 3H, NCH_3).

Anal. Calcd. for $C_{23}H_{18}ClN_3O_2$: H, 4.49; C, 68.40; N, 10.40. Found: H, 4.57; C, 68.26; N, 10.46.

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