NMR Analysis of Restricted Internal Rotation in 2-Substituted-2,3-Dihydro-3-*o*-tolyl(chlorophenyl)-4(1*H*)-quinazolinones

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Received January 31, 1996

Steric interactions between aryl and heterocyclic moieties in 2-substituted-2,3-dihydro-3-*o*-tolyl(chlorophenyl)-4(1*H*)-quinazolinones **1a-j** produce sufficient restriction to rotation about the aryl C-N bond that the presence of torsional isomers may be detected at room temperature. Diastereomeric population and free energy of activation for rotation have been calculated by ^{1}H nmr spectra. Probably due to a preferred axial position of R^2 substituent no dramatic variation both in **A/B** ratio and in $\Delta G^{\neq}$ value has been observed for **1a-f**. The comparison between **1a** and **1j** $\Delta G^{\neq}$ values allows to formulate a hypothesis on the structure of the transition state.

J. Heterocyclic Chem., **33**, 1067 (1996).

Introduction.

Restricted rotation about the C-N bond in *N*-aryl heterocycles is well known since 1931 [1] and some classes of these compounds have been studied with reference to their stereostructures [2] and to separation of stereoisomers [3].

Aryl heterocycles as well as biheteroaryl systems are of great interest in the study of restricted rotation because they provide a large variety of geometrical situations in addition to the differences in conjugation which are impossible in carbocyclic analogues [4].

In connection with our recent research [5] we synthesized the 2-methyl-2,3-dihydro-3-*o*-tolyl-4(1*H*)-quinazolinone **1a** [6]. Compound **1a** is the dihydro form of the methaqualone **2**, a well known anticonvulsive and hypnotic agent [7].

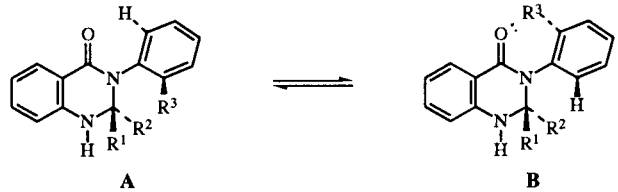
The ^{1}H (Figure) and ^{13}C nmr spectra of compound **1a** taken at room temperature showed many signals that were consistent, for example, with the hypothesis of a non planar ground state and restricted rotation about the C-N bond. It is worthwhile to note that R^1 in diastereomer [8] **A** and R^1 in **B** may exhibit, depending on the entity of the rotation barrier, different shifts, the same being true for R^2 and R^3. In contrast, the axial-equatorial equilibrium of groups on C-2 is surely fast due to great flexibility [9] of the heterocyclic ring in the quinazolinone moiety of **1a**, so it does not give rise to splitting of ^{1}H nmr signals for R^1, R^2 and R^3 at room temperature.

Since derivatives as **1a** may be of some pharmaceutical interest and conformational data are more and more useful in the above area, it seemed reasonable to study restricted rotation that occurs in **1** and to collect data about the height of the rotation barrier. Some compounds **1** were synthesized and their ^{1}H nmr spectra at variable temperature were performed. Compounds **1** were chosen in such a way as to have a variable steric hindrance on C-2 carbon atom or on *ortho* position of the *N*-aryl ring.

Results and Discussion.

The ^{1}H and ^{13}C nmr spectra of compound **1a** taken at room temperature showed that the signals relative to HC2 moiety were split ($\Delta\nu$). The same behaviour was observed for signals for both the methyl groups in the ^{1}H nmr spectrum while in the ^{13}C spectrum it could be observed that the signal relative to the methyl group on the C-2 was not split. The ^{1}H nmr spectra of **1a** taken at higher than room temperature showed a broadening of the signal to coalescence of the signals (Figure). This is consistent with the fact that **1a**, like sterically hindered aryl *N*-substituted heterocyclic compounds [4,11], adopts a non planar ground state at room temperature corresponding to two diastereomeric rotamer

Scheme 1



A ⇌ **B**

1 [10]

a, R^1 = H; R^2 = Me; R^3 = Me **b**, R^1 = H; R^2 = Et; R^3 = Me **c**, R^1 = H; R^2 = Pr^i; R^3 = Me
d, R^1 = H; R^2 = Bu^t; R^3 = Me **e**, R^1 = H; R^2 = Ph; R^3 = Me **f**, R^1 = H, R^2 = 2-Th; R^3 = Me
g, R^1 = R^2 = H; R^3 = Me **h**, R^1 = R^2 = R^3 = Me **i**, R^1 = R^3 = Me; R^2 = Et
j, R^1 = H; R^2 = Me; R^3 = Cl

forms. At higher temperature rotation about the single bond connecting the two rings is fast and coalescence of signals may be observed. By analysis of the ^1H nmr splitting signal intensities the ratio (46:54 at room temperature) was calculatd between the two diastereomeric forms of **1a** with **A** probably predominating because of a minor steric interaction between the two methyl groups. The ^1H nmr spectra of compounds **1b-j** duplicated qualitatively what was been seen for **1a** but variations both in the **A/B** ratio and in the coalescence temperature were observed. These values are listed in Table 1 where they are also reported literature values for methaqualone **2** [12] and for 5-methyl-1-*o*-tolylimidazolidine-2,4-dione **3** [13].

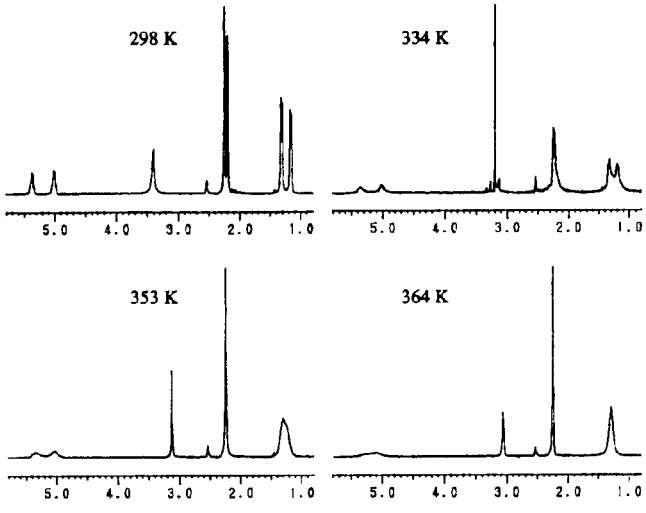
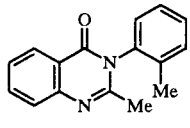
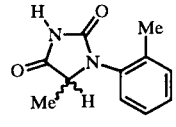


Figure. Selected ^1H nmr of **1a** at different temperatures.

Scheme 2



2



3

The **A/B** ratio values show that an increase in steric bulk of R^2 causes a parallel variation in differences in energy between diastereomeric forms. Presumably a variable substituent on C-2 carbon atom should mainly influence, increasing, the energy of the diastereomer **B** because of its interaction with the methyl group linked to aryl moiety and to a lesser extent the energy of the diastereomer **A**.

In Table 1 are also reported the free energy of activation ($\Delta G^{\neq}$) values for the rotation process observed in compounds **1-3**. $\Delta G_A^{\neq}$ and $\Delta G_B^{\neq}$ values for **A** $\rightleftharpoons$ **B** equilibrium were estimated from equations 1-3 [9,14]

$$k = \sqrt{2}\pi\Delta\nu/2 \quad \text{(eqn. 1)}$$

$$k_A = (1 + \Delta n)k \text{ and } k_B = (1 - \Delta n)]k \quad \text{(eqn. 2)}$$

$$\Delta G_A^{\neq} = RT_c[\log_e(RT_c/Nhk_A)] \quad \text{(eqn. 3)}$$

where k is the average rate constant, k_A and k_B are, respectively, the forward and reverse rate constants, Δn is the difference in mole fractions of the two species **A** and **B** at equilibrium, T_c and $\Delta\nu$ are, respectively, the coalescence temperature and the difference in frequencies [15] expressed in Hertz relative to a split signal.

The comparison between the values of free energy of activation for compounds **1a** and **2** shows that the barrier to internal rotation about the C-N pivot bond is higher (≈20 kJmol^{-1}) for compound **2** than for **1a**, *i.e.* the rotation about the C-N bond is faster for compound **1a** than for **2**. Assuming that most of the influence on the values of $\Delta G^{\neq}$ arises from interactions in transition state [13], it is possible that steric effects can be responsible for the difference in energy between the transition states relative to **1a** and **2**.

In compound **2** the methyl group on C-2 is forced by trigonal hybridisation of the C-2 carbon atom to reside in the plane of the heterocyclic ring, consequently it exerts the greatest steric hindrance possible. In contrast, in compound **1a**, as it can be seen with Dreiding models, the methyl group on C-2 may adopt an axial position so the repulsive interaction, between methyl and tolyl, decreases

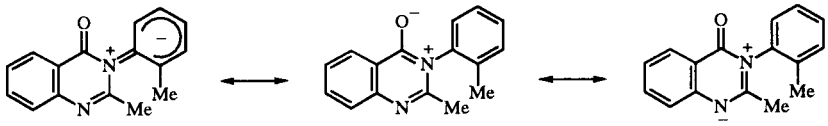
Table 1

Data Relative to **A** $\rightleftharpoons$ **B** Equilibrium for Compounds **1-3**.

Compound	A/B	Δν/Hz [a]	T_c/K [a]	$\Delta G_A^{\neq}$ /kJmol^{-1} [b]	$\Delta G_B^{\neq}$ /kJmol^{-1} [b]
1a	54/46	90.5	364	73.5	73.9
1b	64/36	114.0	358	71.0	72.7
1c	68/32	117.9	340	67.0	69.1
1d	69/31	124.1	374	73.8	76.3
1e	60/40	116.1	341	67.6	68.8
1f	66/34	104.0	344	68.3	70.2
1g		76.5	315	63.8	63.8
1h			>400	>80	>80
1i	87/13	110.8 [c]	>400	>80	>80
1j	64/36	49.5	329	67.3	68.9
2				131.6	131.6
3				52.7 [d]	

[a] $\Delta\nu$ and T_c were taken on the 2-H signals. [b] Very similar barriers were estimated from $\Delta\nu$ and T_c values relative to other splitted signals. [c] Taken on 2-CH_3. [d] Average value.

Scheme 3



C D E

and parallely steric hindrance to rotation exercised by the methyl group also decreases. A preferred axial position of the substituent on C-3 in alkylpiperazine-2,5-dione derivatives has been reported [16]. An axial position for the R^2 group in **1a-f** compounds can explain the observed lack of dramatic variation both in the diastereomeric population (from 46:54 for **1a** up to 31:69 for **1d**) and in $\Delta G^{\neq}$ values (fewer than 10 kJmol^{-1}) induced by steric bulk of the substituent. A more significant variation in the **A/B** ratio was observed for **1i** which has two different alkyl substituents on C-2. The importance of steric effects on the rotational barrier and the axial position of R^2 group for **1a-f** seems confirmed by quite high (> 400 K) coalescence temperature relative to compounds **1h,i** which have necessarily an equatorial methyl group on C-2.

Since nonsteric contributions may affect the energy barriers [4] it must be noted that also electronic effects can explain the faster rotation about the C-N bond for compound **1a** than for **2**. Compound **2** may be depicted as resonance hybrid of the canonical stuctures **C-E.** For **1a** only structures corresponding to **C** and **D** are possible. The lack of form **E** has the effect of increasing the contribution of **C** and so reducing the barrier to rotation about the C-N bond. Indeed the stronger the partial double bond character for the C-N bond in a planar conformation, *i.e.* the transition state, the less the $\Delta G^{\neq}$ value.

The $\Delta G^{\neq}$ values for compounds **1** and **3** show that the barrier for the internal rotation about the C-N pivot bond is higher (≈20 kJmol^{-1} for compound **1** than for **3**. In this case the difference in energy can be caused mainly by a different role played by steric effects in the two transition states relative to **1** and **3** [17]. Steric interactions between the groups in the transition state are less for compound **3** than for **1** because of the different geometry of five and six-membered heterocyclic rings, indeed the interacting groups in the transition state of **3** are more distant than in **1**.

Two diastereomeric planar transition states are possible for the rotation about the C-N bond in compounds **1**. In fact, the *o*-methyl substituent can pass either to the carbonyl group or R^1. As it has been suggested [13] for compounds like **1** the variation of the $\Delta G^{\neq}$ value observed when the methyl group (R^3) is replaced with a chloro atom (**1a** and **1j** respectively in our case) allows us to put forward a hypothesis about the configuration of the preferred transition state. The energy of transition states in which the bulky *ortho*-substituent passes near to the 2-position should be determined by the steric effects of the methyl group and the chloro atom and then it should be parallel with the relative size of these two groups [18]. The energy of the other two transition states in which an *ortho*-substituent passes near the carbonyl group should be mainly affected by polar interactions and it should be in the order **1j>1a** as it has been found for arylthiazolinones [3b] arylquinolones [3c] and arylthiohydantoins [13]. Therefore the $\Delta G^{\neq}$ values for **1a** and **1j** (**1a>1j**) seem to indicate that the preferred transition state is one in which the bulky *ortho*-substituent passes the 2-position rather than the carbonyl group.

EXPERIMENTAL

Melting points were determined with a Kofler hot stage and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer 1310 infrared spectrophotometer. The ^{1}H nmr spectra were recorded using a Bruker AC-E Series 250 MHz in DMSO-d_6 solutions. The ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to tetramethylsilane (TMS) as the internal standard. Variable temperature ^{1}H and ^{13}C nmr spectroscopy were conducted on dilute solutions in DMSO-d_6. Spectra were recorded at 5 or 2 K intervals. Measurements were taken on the 2-H or *o*-CH_3 signal. All compounds were prepared by reacting the 2-amino-*N*-(*o*-tolyl)benzamide or the 2-amino-*N*-(*o*-chlorophenyl)benzamide, obtained by reduction of the corresponding nitro-compounds, with carbonyl compounds. All 2,3-dihydro-4(1*H*)-quinazolinones **1a-j** were crystallized from ethanol.

General Method for the Preparation of the 2,3-Dihydro-4(1*H*)-quinazolinones **1a-j**.

To a solution of the amide (5 mmoles) in ethanol (20 ml), the carbonyl compound (7 mmoles) and few drops of acetic acid were added. The reaction mixture was stirred and heated for a few minutes then allowed to stand at room temperature without stirring. After a period of 1-3 days, depending on the carbonyl compound, a precipitate was formed and filtered to give compounds **1a-j**. Further material was recovered from mother liquors.

2-Methyl-3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1a**.

This compound had mp 176° (88%); ir (Nujol): 3290, 1625, 1605 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.18 (d, 3H, J = 5.8 Hz, 2-CH_3, **B**), 1.33 (d, 3H, J = 5.8 Hz, 2-CH_3, **A**), 2.22 (s, 3H, *o*-CH_3, **B**), 2.27 (s, 3H, *o*-CH_3, **A**), 5.03 (q, 1H, J = 5.8 Hz, 2-H, **A**), 5.39 (q, 1H, J = 5.8 Hz, 2-H, **B**), 6.77-6.87 (m, 2H), 6.99 (s, 1H, NH, **B**), 7.02 (s, 1H, NH, **A**), 7.22-7.43 (m, 5H), 7.70-7.75 (m, 1H); ^{13}C nmr (DMSO-d_6): δ 17.7 (*o*-CH_3, **A**), 18.3 (*o*-CH_3, **B**), 20.2 (2-CH_3, **A+B**), 66.8 (C-2, **A**), 67.6 (C-2, **B**), 114.7 (CH), 115.1 (CH), 115.3 (Cq), 115.6 (Cq), 117.6 (CH), 117.7

(CH), 126.5 (CH), 127.0 (CH), 127.6 (CH), 127.9 (CH), 128.0 (CH), 128.1 (CH), 128.2 (CH), 130.3 (CH), 130.6 (CH), 131.0 (Cq), 133.6 (Cq), 135.8 (Cq), 137.1 (Cq), 139.1 (Cq), 147.7 (Cq), 148.3 (Cq), 161.9 (C=O), 162.2 (C=O).

Anal. Calcd. for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.36; H, 6.27; N, 11.04.

2-Ethyl-3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1b**.

This compound had mp 156-158°, (81%); ir (Nujol): 3310, 1628, 1605, 1570 cm^{-1}; ^1H nmr (DMSO-d_6): δ 0.82-0.90 (m, 3H, CH_2CH_3, **A+B**), 1.42-1.94 (3m, 2H, CH_2CH_3, **A+B**), 2.23 (s, 3H, *o*-CH_3, **B**), 2.30 (s, 3H, *o*-CH_3, **A**), 4.68 (m, 1H, 2-H, **A**), 5.14 (m, 1H, 2-H, **B**), 6.76 (t, 1H, J = 7.6 Hz, 6-H, **A+B**), 6.88-6.94 (2d, 1H, J = 8.0 Hz, **A+B**), 7.04 (s, 1H, NH, **B**), 7.20 (d, 1H, J = 2.3 Hz, NH, **A**), 7.29-7.43 (m, 5H), 7.71 (d, 1H, J = 7.2 Hz); ^{13}C nmr (DMSO-d_6): δ 8.93 (2-CH_3, **B**), 9.47 (2-CH_3, **A**), 17.6 (*o*-CH_3, **A**), 18.7 (*o*-CH_3, **B**), 26.0 (CH_2, **A**), 26.3 (CH_2, **B**), 71.8 (C-2, **A**), 73.1 (C-2, **B**), 114.8 (Cq), 114.9 (CH), 115.5 (Cq), 117.2 (CH), 117.4 (CH), 126.4 (CH), 127.0 (CH), 127.4 (CH), 127.7 (CH), 127.8 (CH), 128.0 (CH), 128.1 (CH), 130.5 (CH), 130.6 (CH), 131.1 (CH), 133.6 (CH), 135.2 (Cq), 137.1 (Cq), 139.7 (Cq), 139.8 (Cq), 147.1 (Cq), 147.6 (Cq), 161.5 (C=O).

Anal. Calcd. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.51; H, 6.88; N, 10.63.

2-Isopropyl-3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1c**.

This compound had mp 182-185° (91%); ir (Nujol): 3280, 1625, 1610 cm^{-1}; ^1H nmr (DMSO-d_6): δ 0.84-0.94 [m, 6H, $CH(CH_3)_2$, **A+B**], 1.80-1.90 [m, 1H, $CH(CH_3)_2$, **B**], 2.00-2.11 [m, 1H, $CH(CH_3)_2$, **A**], 2.26 (s, 3H, *o*-CH_3, **B**), 2.31 (s, 3H, *o*-CH_3, **A**), 4.69 (m, 1H, 2-H, **A**), 5.16 (s, 1H, 2-H, **B**), 6.64-6.70 (m, 1H), 6.84-6.91 (m, 1H), 6.95 (s, 1H, NH, **B**), 7.10 (d, 1H, J = 2.3 Hz, NH, **A**), 7.25-7.43 (m, 5H), 7.65 (d, 1H, J = 7.7 Hz); ^{13}C nmr (DMSO-d_6): δ 16.0 (CH_3, **B**), 16.5 (CH_3, **A**), 17.4 (CH_3, **A**), 18.4 (CH_3, **A**), 18.5 (CH_3, **B**), 18.8 (CH_3, **B**), 33.2 [$CH(CH_3)_2$, **B**], 33.6 [$CH(CH_3)_2$, **A**], 74.8 (C-2, **A**), 76.8 (C-2, **B**), 113.7 (CH), 113.8 (Cq), 114.6 (CH), 116.4 (CH), 116.6 (CH), 126.2 (CH), 127.1 (Cq), 127.2 (CH), 127.7 (CH), 130.7 (CH), 131.1 (CH), 131.2 (CH), 133.6 (CH), 134.8 (CH), 140.0 (Cq), 148.2 (Cq), 148.3 (Cq), 161.7 (C=O).

Anal. Calcd. for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.03; H, 7.24; N, 10.06.

2-*tert*-Butyl-3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1d**.

This compound had mp 146-148° (54%); ir (Nujol): 3310, 1625, 1615 cm^{-1}; ^1H nmr (DMSO-d_6): δ 0.81 [s, 9H, $C(CH_3)_3$, **B**], 0.87 [s, 9H, $C(CH_3)_3$, **A**], 2.36 (s, 3H, *o*-CH_3, **A**), 2.38 (s, 3H, *o*-CH_3, **B**), 4.60 (d, 1H, J = 3.1 Hz, 2-H, **A**), 5.10 (d, 1H, J = 3.1 Hz, 2-H, **B**), 6.63-6.69 (m, 1H), 6.85-6.90 (2d, 1H, J = 7.9 Hz, **A+B**), 7.10 (d, 1H, J = 3.1 Hz, NH, **B**), 7.24-7.51 (m, 5H), 7.60-7.65 (m, 1H); ^{13}C nmr (DMSO-d_6): δ 17.7 (*o*-CH_3, **A**), 20.2 (*o*-CH_3, **B**), 25.8 [$C(CH_3)_3$, B], 26.9 [$C(CH_3)_3$, **A**], 41.7 [$C(CH_3)_3$, **B**], 42.1 [$C(CH_3)_3$, **A**], 77.7 (C-2, **A**), 80.3 (C-2, **B**), 113.4 (CH), 115.5 (CH), 115.8 (CH), 116.3 (CH), 116.6 (CH), 125.3 (CH), 126.1 (CH), 126.5 (CH), 126.9 (CH), 127.7 (CH), 127.8 (CH), 130.8 (CH), 131.2 (CH), 132.6 (CH), 133.6 (CH), 136.8 (Cq), 142.2 (Cq), 143.7 (Cq), 147.9 (Cq), 148.0 (Cq), 162.3 (C=O).

Anal. Calcd. for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.63; H, 7.49; N, 9.48.

2-Phenyl-3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1e**.

This compound had mp 177-179° (lit mp 173-175° [19]), (72%); ir (Nujol): 3300, 1620, 1610, 1580 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.91 (s, 3H, *o*-CH_3, **B**), 2.36 (s, 3H, *o*-CH_3, **A**), 5.96 (s, 1H, 2-H, **A**), 6.42 (s, 1H, 2-H, **B**), 6.76-6.92 (m, 4H), 7.08-7.44 (m, 10H), 7.58 (s, 1H, NH), 7.76-7.80 (m, 1H); ^{13}C nmr (DMSO-d_6): 18.0 (*o*-CH_3, **A**), 18.2 (*o*-CH_3, **B**), 73.0 (C-2, **A**), 74.8 (C-2, **B**), 114.5 (CH), 114.9 (CH), 115.3 (Cq), 117.6 (CH), 126.3 (CH), 126.5 (CH), 126.8 (CH), 127.2 (CH), 127.7 (CH), 128.0 (CH), 128.2 (CH), 128.7 (CH), 129.1 (CH), 129.3 (CH), 130.2 (CH), 131.1 (CH), 133.9 (CH), 135.6 (Cq), 136.9 (Cq), 139.4 (Cq), 139.9 (Cq), 141.1 (Cq), 147.0 (Cq), 148.4 (Cq), 162.0 (C=O).

Anal. Calcd. for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91. Found: C, 80.21; H, 5.68; N, 8.99.

2-(2-Thienyl)-3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1f**.

This compound had mp 165-167° (95%); ir (Nujol): 3240, 1625, 1610, 1575 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.89 (s, 3H, *o*-CH_3, **B**), 2.35 (s, 3H, *o*-CH_3, **A**), 6.22 (d, 1H, J = 2.4 Hz, 2-H, **A**), 6.64 (s, 1H, 2-H, **B**), 6.81-7.45 (m, 10H), 7.59 (s, 1H, NH, **B**), 7.65 (d, 1H, J = 2.4 Hz, NH, **A**), 7.79 (d, 1H, J = 7.6 Hz); ^{13}C nmr (DMSO-d6): δ 17.8 (*o*-CH_3, **A**), 18.1 (*o*-CH_3, **B**), 69.2 (C-2, **A**), 70.4 (C-2, **B**), 114.9 (CH), 115.3 (CH), 115.6 (Cq), 118.1 (CH), 118.2 (CH), 125.9 (CH), 126.2 (CH), 126.3 (CH), 126.6 (CH), 127.4 (CH), 127.6 (CH), 127.8 (CH), 127.9 (CH), 128.1 (CH), 129.2 (CH), 130.2 (CH), 131.0 (CH), 133.8 (CH), 135.4 (Cq), 137.3 (Cq), 139.4 (Cq), 142.7 (Cq), 144.4 (Cq), 146.7 (Cq), 147.5 (Cq), 161.3 (C=O).

Anal. Calcd. for $C_{19}H_{16}N_2OS$: C, 71.22; H, 5.03; N, 8.74. Found: C, 71.09; H, 5.03; N, 8.68.

3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1g**.

This compound had mp 175-176° (75%); ir (Nujol): 3270, 1625, 1605 cm^{-1}; ^1H nmr (DMSO-d_6): δ 2.25 (s, 3H, *o*-CH_3), 4.71 and 5.01 (d, each 1H, J = 9.0 Hz, 2-H), 6.81-6.91 (m, 2H), 6.98 (s, 1H, NH), 7.30-7.42 (m, 5H), 7.79 (dd, 1H, J = 7.6 and 1.4 Hz); ^{13}C nmr (DMSO-d_6): δ 17.9 (*o*-CH_3), 61.5 (C-2), 115.1 (CH), 116.4 (Cq), 117.9 (CH), 126.9 (CH), 127.2 (CH), 127.5 (CH), 128.3 (CH), 130.7 (CH), 133.4 (CH), 135.3 (Cq), 140.5 (Cq), 149.4 (Cq), 162.3 (C=O).

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 76.06; H, 6.02; N, 11.70.

2,2-Dimethyl-3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1h**.

This compound had mp 234-235° (85%); ir (Nujol): 3280, 1620 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.21 (s, 3H, 2-CH_3), 1.62 (s, 3H, 2-CH_3), 2.16 (s, 3H, *o*-CH_3), 6.76-6.84 (m, 2H), 7.02 (s, 1H, NH), 7.24-7.41 (m, 5H), 7.69 (d, 1H, J = 7.5 Hz); ^{13}C nmr (DMSO-d_6): δ 18.2 (*o*-CH_3), 27.0 (2-CH_3), 27.7 (2-CH_3), 72.1 (C-2), 114.8 (CH), 115.3 (Cq), 117.4 (CH), 126.6 (CH), 127.8 (CH), 128.0 (CH), 129.3 (CH), 130.7 (CH), 133.5 (CH), 137.0 (Cq), 138.2 (Cq), 147.0 (Cq), 161.8 (C=O).

Anal. Calcd. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.77; H, 6.85; N, 10.59.

2-Methyl-2-ethyl-3-(*o*-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone **1i**.

This compound had mp 217-219° (lit mp 223-225° [20]), (85%); ir (Nujol): 3300, 1625 cm^{-1}; ^1H nmr (DMSO-d_6): δ 0.83-0.92 (m, 3H, CH_2CH_3, **A+B**), 1.13 (s, 3H, 2-CH_3, **A**), 1.57 (s, 3H, 2-CH_3, **B**), 1.84-1.92 (m, 2H, $CHHCH_3$, **A+B**), 2.19 (s, 3H, *o*-CH_3, **A+B**), 2.30-2.36 (m, 2H, $CHHCH_3$, **A+B**), 6.75-6.81 (m, 1H), 6.87-6.91 (m, 1H), 7.17 (s, 1H, NH), 7.22-7.40 (m, 5H), 7.68-7.72 (m, 1H); ^{13}C nmr (DMSO-d_6): δ 8.04 (CH_2CH_3, **B**), 8.82 (CH_2CH_3, **A**), 18.2 (*o*-CH_3, **A**), 18.6 (*o*-CH_3, **B**), 23.6 (2-CH_3, **A**),

25.9 (2-CH_3, **B**), 31.8 (CH_2, **B**), 32.1 (CH_2, **A**), 74.7 (C-2, **A**), 74.9 (C-2, **B**), 114.4 (CH), 115.0 (CH), 115.3 (Cq), 115.7 (Cq), 117.1 (CH), 117.3 (CH), 126.3 (CH), 126.6 (CH), 127.6 (CH), 127.8 (CH), 127.9 (CH), 128.0 (CH), 129.4 (CH), 130.7 (CH), 130.8 (CH), 133.5 (CH), 137.0 (CH), 137.3 (Cq), 137.9 (Cq), 138.4 (CH), 146.6 (Cq), 146.9 (Cq), 161.9 (C=O), 162.1 (C=O)

Anal. Calcd. for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.06; H, 7.24; N, 10.03.

2-Methyl-3-(*o*-chlorophenyl)-2,3-dihydro-4(1*H*)-quinazolinone **1j**.

This compound had mp 199-201° (85%); ir (Nujol): 3300, 1630, 1610 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.23 (d, 3H, J = 5.8 Hz, 2-CH_3, **B**), 1.29 (d, 3H, J = 5.8 Hz, 2-CH_3, **A**), 5.22 (q, 1H, J = 5.8 Hz, 2-H, **A**), 5.42 (q, 1H, J = 5.8 Hz, 2-H, **B**), 6.78-6.87 (m, 2H), 7.06 (s, 1H, NH, **B**), 7.11 (s, 1H, NH, **A**), 7.36-7.57 (m, 4H), 7.63-7.75 (m, 2H); ^{13}C nmr (DMSO-d_6): δ 20.1 (2-CH_3, **B**), 20.2 (2-CH_3, **A**), 66.3 (C-2, **A**), 67.5 (C-2, **B**), 114.7 (CH), 114.9 (CH), 115.0 (Cq), 117.6 (CH), 127.9 (CH), 128.2 (CH), 128.4 (CH), 129.3 (CH), 129.7 (CH), 129.9 (CH), 130.1 (CH), 130.6 (CH), 132.3 (Cq), 132.7 (CH), 133.6 (CH), 133.7 (CH), 133.9 (CH), 137.0 (Cq), 137.6 (Cq), 148.0 (Cq), 148.3 (Cq), 162.4 (C=O).

Anal. Calcd. for $C_{15}H_{13}ClN_2O$: C, 66.06; H, 4.80; N, 10.27. Found: C, 66.00; H, 4.81; N, 10.38.

Acknowledgements.

This research was supported by a research grant from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST), Italy. Authors wish to thank Mr. Marco Cascino for technical assistance in nmr spectroscopy.

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