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# One-Pot Synthesis of 2,3-Dihydro-2,3-disubstituted Benzo[g]-quinazolin-4(1H)ones

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# SYNTHETIC COMMUNICATIONS, 22(17), 2499-2508 (1992)

### ONE-POT SYNTHESIS OF 2,3-DIHYDRO-2,3-DISUBSTITUTED BENZO[g]-QUINAZOLIN-4(1H)-ONES

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#### ABSTRACT

Condensation of 2H-naphth[2,3-d][3,1]oxazin-2,4 (1H)-dione (1) with schiff bases (2) in acetic acid resulted in the formation of 2,3-dihydro-2,3-diarylbenzo[g]quinazolin-4(1H)-ones (3). Reaction of 1 with ketoanils generated in situ results in 2,3-dihydro-2,2-substituted-3-phenylbenzo[g]quinazolin-4(1H)-ones (6) and the spiroalkanes (5). Dehydrogenation of 3 gave 2,3-diaryl benzo[g]quinazolin-4(3H)-ones (7).

 $2H-Naphth[2,3-d][3,1]oxazin-2,4(1H)-dione (1)^{1,2}$  is a reactive molecule of great value in the synthesis of heterocycle systems. Though 1 has been reported in literature decades back, its utility in the synthesis of heterocyclic systems has scarcely been explored<sup>3</sup>. We report here in one pot synthesis of 2,3-dihydro-2,3-diarylbenzo[g]quinazolin-4(1H)-ones (3) and their heteroaromatic analogues from 1.

The reaction of 2H-naphth[2,3-d][3,1]oxazin-2,4(1H)-dione (1) with N-benzylidene-4-methylaniline (2b) in equimolar proportions

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in hot acetic acid gave 2,3-dihydro-3-(4-methylphenyl)-2-phenyl benzo[g]guinazolin-4(lH)-one (3b, Scheme, l Table) as a light yellow crystalline compound, m.p. 212°C. The mass spectrum of compound 3b exhibited the molecular ion at m/z 364. The IR spectrum (KBr) of 3b revealed the presence of  $\sqrt[7]{NH}$  (3340 cm<sup>-1</sup>) and  $\hat{\gamma}_{\text{C}=0}$  (1650 cm<sup>-1</sup>). Its <sup>1</sup>H-NMR spectrum (DMSO-d<sub>6</sub>) revealed a doublet at 56.2 due to C<sub>2</sub>-H which became a singlet after deuterium exchange indicating its coupling with the proton on adjacent nitrogen. Thus it is clear that 3b is formed by the loss of carbondioxide from 1 and insertion of C-N unit of the schiff base. The reaction has been extended to nine other arylideneanilines to ascertain the generality of the reaction and the products obtained in each case have been characterised as the corresponding 2,3-dihydro-2,3-diarylbenzo[g]quinazolin-4(1H)-ones (3a-j, Scheme, 1 Table) by analogy, spectral (1 Table) and microanalytical data. It has been generally observed that compounds 3 separate out from acetic acid solution in high yields within an hour. Thus, simple reaction conditions and high yields of the products make this reaction a facile one-step method for synthesis of a variety of 3.

Compounds 3 were also obtained by an alternate route involving reaction of 1 with aromatic primary amines in acetic acid followed by the treatment of resulting 3-amino-2-(N-aryl)carbamyl



d CH3

C6H5

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<pre>1 Table 0 2,3-dihydro-2,3-diarylbenzo[g]quinazolin~4(1H)-ones (3)</pre>	<sup>1</sup> н-имг (б)	6.4(d,1H,C <sub>2</sub> -H),6.8-7.9(m,16H,15Ar-H & 1N~H), 8.5(s,1H,periproton)	2.3(s,3H,CH <sub>3</sub> ),6.1(d,1H,C <sub>2</sub> -H),7.0-8.0(m,15H,14Ar-H & 1N-H),8.4(s,1H, periproton)	6.2(d,lH,C <sub>2</sub> -H),7.0-7.9(m,l5H,l4Ar-H&lN-H),8.6(s,lH,periproton)	2.3(s,3H,CH <sub>3</sub> ),6.1(d,1H,C <sub>2</sub> -H),6.9-7.9(m,15H,14Ar-H&IN-H),8.5(s,1H,peri- proton)	3.7(s,3H,0CH <sub>3</sub> ),6.3(d,lH,C <sub>2</sub> -H),7.1-8.0(m,15H,14Ar-H&lN-H),8.4(s,1H, periproton)	6.3(d,1H,C <sub>2</sub> -H),7.1-8.0(m,15H,14Ar-H&lN-H),8.6(s,1H,periproton)	6.2(d,1H,C <sub>2</sub> -H),7.0-8.1(m,15H,14Ar-H&1N-H),8.6(s,1H,periproton)	6.2(d,1H,C <sub>2</sub> -H),6.9-7.9(m,14H,13Ar-H&lN-H),8.6(s,1H,periproton)	2.3(d,3H,CH <sub>3</sub> ),6.0(d,1H,C <sub>2</sub> -H),6.9-8.1(m,14H,13Ar-H&lN~H),8.6(s,1H,peri- proton)	6.2(d,1H,C <sub>2</sub> -H),7.0-8.0(m,14H,13Ar~H&IN-H),8.6(s,1H,periproton)	$1 \xrightarrow{1} C=0$ around 1620 and $3N-H$ around 3300 cm <sup>-1</sup> .
ı data	Yield (%)	80	85	74	78	80	84	81	82	76	74	libited
haracterisation	Mol.fprmula (M <sup>•</sup> )	C <sub>24</sub> H <sub>18</sub> N <sub>2</sub> 0 (350)	C <sub>25</sub> H <sub>20</sub> N <sub>2</sub> 0 (364)	C <sub>24</sub> H <sub>17</sub> N <sub>2</sub> 0Br (428)	C <sub>25</sub> H <sub>20</sub> N <sub>2</sub> 0 (364)	C25 <sup>H20N20</sup> 2	$C_{24}H_{17}N_{2}0C1$ (384)	C <sub>24</sub> H <sub>17N3</sub> 0 <sub>3</sub> (395)	$C_{24H_{16}N_{2}}^{H_{16}N_{2}}^{OC1_{2}}$ (418)	C <sub>25</sub> H <sub>19</sub> N <sub>2</sub> 0Br (442)	C <sub>24</sub> H <sub>16</sub> N <sub>3</sub> 0 <sub>3</sub> Br (473)	tra of <b>3a-j e</b> xt pounds gave sat
<u>ช</u>	а.р. (°С)	186	212	221	190	175	205	161	228	165	222	spect comp
	Compd	, , ,	م	υ	q	Ø	ч	σ	ч	·н	·	The IR All th

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naphthalenes (4) with aromatic aldehydes under the same experimental conditions.

Condensation of 1 with cyclohexylideneaniline, generated <u>in</u> <u>situ</u>, in acetic acid at steam bath temperature resulted in 2,3-dihydro-2-spirocyclohexane-3-phenylbenzo[g]quinazolin-4(1H)one (5b), characterised on the basis of spectral data. This reaction has been extended to five other anils derived from one cyclic and four acyclic ketones (5 and 6, Scheme, 2 Table).

Reaction of 1 with 2 in hot acetic acid resulted in 3 with spontaneous evolution of carbondioxide. The stability of arylideneanilines in hot acetic acid and the absence of evolution of carbondioxide when 1 was heated alone in acetic acid rule out the possibility of step-wise formation of 3 from 1 and 2. Thus initial nucleophilic attack by the nitrogen of 1 on the electrophilic carbon of schiff base (2), followed by the formation of a six-membered cyclic intermediate and subsequent expulsion of carbondioxide appears to be the pathway for the formation of 3.

Schiff bases are known to function as source of carbonyl carbon and as hydrogen acceptor in the synthesis of benzimidazoles<sup>4,5</sup>, quinazolinones<sup>6</sup> and quinazolinoquinazolinones<sup>7</sup>. To explore the possibility of directly obtaining the heteroaromatic analogue (7) of 3, compound 1 was treated with 2 in 1:2 molar proportions. The reaction, however, resulted in only 3 and not 7. Downloaded by [Purdue University] at 22:01 20 March 2013

Characterisation data of 2,3-dihydro-2-spirocycloalkane-3-phenylbenzo[q]quinazolin-4(1H)-ones (5a&b) **2 Table** 

	and 2,3-dihydr	o-2,2-disubstituted-3-	henyl be	nzo[g]quinazolin-4(1H)-ones (6a to d)
Compd	п.р. (°С)	Mol. formula (M <sup>+</sup> )	Yield (%)	<sup>1</sup> H-NMR (§)
5a	236	C <sub>22</sub> H <sub>20</sub> N <sub>2</sub> 0 (328)	74	
5b	242	$C_{23}H_{22}N_{2}0$ (342)	78	1.2-2.5(m,10H,cyclohexyl protons),7.1-8.2 (m, 11H,10Ar-H&IN-H), 8.6(s,1H,periproton)
ସେ	252	C20 <sup>H</sup> 18 <sup>N</sup> 2 <sup>0</sup> (302)	64	ł
6b	234	C <sub>21</sub> H <sub>20</sub> N <sub>2</sub> 0 (316)	81	1.0(t,3H,CH <sub>3</sub> ),1.4(s,3H,CH <sub>3</sub> ),1.7-1.9(q,2H,CH <sub>2</sub> ), 7.0-7.9(m,11H,10Ar-H&IN-H),8.5(s,1H,periproton)
ęc	233	C <sub>23</sub> H <sub>24</sub> N <sub>2</sub> 0	80	I
ସେ	194	C <sub>25</sub> H <sub>2</sub> 0 <sup>N</sup> 2 <sup>0</sup>	76	1.5(s,3H,CH <sub>3</sub> ),7.1-7.9(m,16H,15Ar-H&lN-H),8.4 (s,1H,periproton)
The IR	spectra of <b>5a s</b>	5b and 6a-d exhibited	C=0 arou	Ind 1620 and $\frac{1}{2}$ N-H around 3300 cm <sup>-1</sup> .
All the	compounds gave	satisfactory C, H and I	l analyse	. ç.

# CONDENSATION WITH SCHIFF BASES IN ACETIC ACID

Compounds **3a-j** on dehydrogenation with potassium permanganate in acetone under refluxing conditions afforded colourless crystalline products having two mass units less than starting material. These compounds have been characterised as 2,3-diaryl benzo[g]quinazolin-4(3H)-ones (**7a-j**, Scheme, 3 Table) on the basis of spectral data and elemental analysis.

#### EXPERIMENTAL

Melting points are uncorrected. I.R. spectra were recorded in KBr on Perkin-Elmer 283 B spectrophotometer, PMR spectra on JEOL FX 90Q instrument using TMS as internal standard and mass spectra on Micromass 7070 H instrument.

# 2H-Naphth[2,3-d][3,1]oxazin-2,4(1H)-dione (1)

A mixture of 2-amino-3-naphthalene carboxylic acid (500 mg) and ethylchloroformate (4 ml) was refluxed for 6 hours. To the resulting solution acetyl chloride (4 ml) was added and refluxed for additional 1 hour. Compound that separated out was filtered, m.p. above 290°C, yield 430 mg (76%).

# 2,3-Dihydro-2,3-diarylbenzo[g]quinazolin-4(1H)-ones (3) General procedure

To a solution of 1 (1 mmol) in acetic acid (2 ml) was added the schiff base (2, 1 mmol) and the reaction mixture heated

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**3 Table** 

ompđ	m.p. (°C)	Characterisation Mol.formula Y (M <sup>1</sup> )	data of ; /ield (%)	2,3-diaryl benzo[g]quinazolin-4(3H)-ones (7) <sup>1</sup> H-NMR (§)
ъ	196	C <sub>24</sub> H <sub>16</sub> N <sub>2</sub> 0	85	7.2-8.7(m,15H,Ar-H),9.1(s,1H,periproton)
þ	236	(348) $C_{25}H_{18}N_{2}^{0}$	87	2.1(s,3H,CH <sub>3</sub> ),7.5-8.5(m,14H,Ar-H),9.1(s,1H,periproton)
υ	248	(362) C <sub>24</sub> H <sub>15</sub> N <sub>2</sub> 0Br	80	7.0-8.4(m,14H,Ar-H),8.9(s,1H,periproton)
ъ	228	(426) $C_{25}H_{18}N_{20}$	92	2.3(s,3H,CH <sub>3</sub> ),7.9-8.9(m,14H,Ar-H),9.1(s,1H,periproton)
Ø	230	(362) $C_{25}H_{18}N_{2}O_{2}$	84	3.8(s,3H,0CH <sub>3</sub> ),6.8-8.4(m,14H,Ar-H),9.1(s,1H,periproton)
Чн	255	(378) C <sub>24</sub> H <sub>15</sub> N <sub>2</sub> 0C1	87	7.2-8.5(m,14H,Ar-H),9.1 (s,1H,periproton)
σ	257	(382) C24 <sup>H</sup> 15 <sup>N30</sup> 3	89	7.3-8.4(m,14H,Ar-H), 9.1(s,1H,periproton)
ч	245	(393) C <sub>24</sub> H <sub>14</sub> N <sub>2</sub> 0C1 <sub>2</sub>	85	7.3-8.6(m,l3H,Ar-H), 9.2(s,lH,periproton)
. <del>г</del>	235	(416) C <sub>25<sup>H</sup>17<sup>N</sup>2<sup>0Br</sup></sub>	88	2.3(s,3H,CH <sub>3</sub> ),7.0-8.4(m,13H,Ar-H),9.0(s,1H,periproton)
· <b>-</b> -	259	(440) C <sub>24</sub> H <sub>14</sub> N <sub>3</sub> O <sub>3</sub> Br (471)	84	7.0-8.4(m,13H,Ar-H), 9.0(s,1H,periproton)
the J	R spectra the compou	t of <b>7a-j</b> exhibited Inds gave satisfact	Ac=0 ar	ound 1680 cm 1. and N analyses.

2506

# CONDENSATION WITH SCHIFF BASES IN ACETIC ACID

on a steam bath for 1 hr. and left aside for few minutes. Comppounds 3 separated out in each case were filtered, washed with a few drops of methanol and characterised on the basis of spectral data given in 1 Table.

#### Condensation of 1 with ketoanils : General procedure

To a solution of aniline (0.093 ml, 1 mmol) in acetic acid (2 ml) was added the appropriate ketone (1 mmol) and the reaction mixture, kept on a steam bath for 30 minutes. To the ketoanil thus generated <u>in situ</u>, 1 (1 mmol) was added and heated for 1 hr. and left aside. 2,3-Dihydro-2-spiro cycloalkane (5) and 2,3-dihydro-2,2-substituted-3-phenylbenzo[g]quinazolin-4(1H)ones (6) thus obtained were filtered, washed with few drops of methanol (2 Table).

#### 2,3-Diaryl benzo[g]quinazolin-4(3H)-ones (7)

Compound 3 (2 mmol) was dissolved in acetone (250 ml) and  $KMn0_4$  (1 g) added to it and refluxed on a steam bath. Slowly the pink colour of  $KMn0_4$  disappeared. Addition of  $KMn0_4$  (about .5 g each time) and refluxing was continued until the pink colour persisted. The hot acetone solution was filtered, excess of acetone was distilled off and excess  $KMn0_4$  in the filtrate destroyed with sodium sulphite. The resulting solution was extracted with chloroform and the solvent eliminated from the dried extracts to yield the pure 7 (3 Table).

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