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Palladium-catalyzed Heteroannulation with Acetylenic Carbinols as Synthons-Synthesis of Quinolines and 2, 3-Dihydro-4(1H)-quinolones

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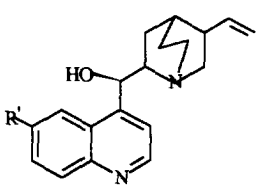
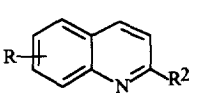
Abstract: *o*-Iodoanilides **4** reacted with terminal acetylenic carbinols **5** under palladium-catalyzed conditions to yield *o*-substituted anilides **6**. Most of the anilides **6** could be cyclized with NaOEt/EtOH to 2-arylquinolines **2**. *o*-Iodoanilines **7** reacted with carbinols **5** leading to **8** which on palladium(II) assisted cyclisation afforded substituted quinolines **2**. An excellent synthesis of the alkaloid dubamine **(2n)** is reported. Also, the anilides **6** on acid-catalyzed rearrangement, deprotection and cyclisation led to the 2-aryl-2, 3-dihydro-4(1H)-quinolones **16**.

INTRODUCTION

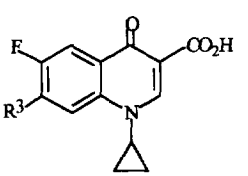
Quinolines, 4(1H)-quinolones and their perhydroderivatives are constituents of several biologically active natural and synthetic compounds.[1] Cinchona alkaloids, for example, quinine **(1a)** and cinchonine **(1b)** are well known antimalarial agents. Recently, *Galiepea longiflora* was found to be a rich source of a number of 2-substituted quinolines, including 2-phenylquinoline[2](**2e**), which was found as effective as the standard antileishmanial drug glucantime. 2-Substituted quinolines have been described as 5-lipoxygenase inhibitors[3],



1a, R' = OMe
1b, R' = H



2e, R = H, $R^2 = C_6H_5$



3, R^3 = pyrrolidine

Dedicated to Professor P. C. Rakshit, our great teacher, on the occasion of his 87th birthday.

leucotriene antagonists[3] and LTD_4 receptor antagonists.[4] The latter may prove useful for control of asthma. 2-Substituted quinolines assume further importance due to the fact that quinine (**1a**) undergoes metabolic hydroxylation at 2-position to give a carbostyril derivative rendering it inactive[5] as antimalarial agent.

On the other hand 4(1H)-quinolone-3-carboxylic acids, e.g. ciprofloxacin (**3**) were reported[6] to inhibit DNA gyrase, a key enzyme in bacterial DNA replication and thereby exhibiting broad spectrum antibacterial activity. Recently, 2-aryl-6, 7-disubstituted 4(1H)-quinolones were evaluated[7] as inhibitors of tubulin polymerization in a variety of tumor cells and were found to be more active than colchicine, a potent antimiotic agent.[8]

As classical methods for the synthesis of quinoline[1a-c, 9] display typical reactivity patterns and selectivities, development of more versatile transition metal catalyzed reactions has drawn considerable interest in recent years. The development of palladium-catalyzed synthesis of quinolines remained closely associated with those of indoles. Several groups of workers have reported formation of quinolines in isolated cases during palladium-catalyzed synthesis of indoles.[10] A few synthetic strategies involving stoichiometric use of palladium catalysts have been reported.[11] In 1991 Larock *et al*[12] reported a one-step palladium catalyzed general method for the synthesis of quinolines from *o*-iodoaniline and alkenols. The reaction appeared to be insensitive to the nature of palladium catalysts, added ligands, bases and solvents. Recently, palladium-catalyzed *in situ* sequential vinylic substitution/annulation have been utilized[13] to synthesize quinolines from the reaction between 4-(*o*-acetamidophenyl)-3-buten-2-one and unsaturated halides or triflates.

One of the most attractive approaches[14] to the indole nucleus involved synthesis of *o*-alkynylanilines and subsequent cyclisation. It appears that while the coupling between *o*-iodoanilines and terminal acetylenes proceeds smoothly under Pd(0) catalysts, the cyclisation which involves intramolecular alkyne amination, requires Pd(II) catalysis.[14b,h,i] However, due to facile alkyne oligomerization, alkyne aminations assisted by Pd(II) are much less common than those in alkenes.[15] On the other hand palladium-catalyzed carbonylative coupling of *o*-aminophenylacetylene and aryl iodides in dialkylamines under a carbon monoxide atmosphere led to 2-aryl-4-dialkylaminoquinolines.[16] For substitutions on preformed quinoline nucleus Suzuki reaction[17] and Stille coupling[18] have been utilized.

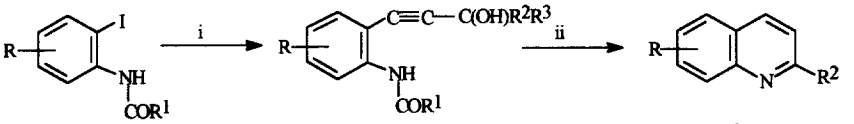
2-Substituted 4(1H)-quinolones have been synthesized by a stoichiometric palladium-induced intramolecular cyclisation of *o*-aminochalcones.[19] Carbonylation of *o*-haloanilines in the presence of terminal acetylenes and Pd(0) also led to 4(1H)-quinolones.[20] Raphael *et al*[21] reported the synthesis of a 2, 3-dihydro-4(1H)-quinolone derivative *via* palladium-catalyzed condensation of an acetylenic alcohol with a substituted *o*-iodoaniline and subsequent acid catalyzed rearrangement accompanied by cyclisation. The synthesis of 2, 3-dihydro-4(1H)-quinolones from *o*-aminochalcones has been reported.[22]

Earlier, we have described a facile and general method for the synthesis of 2- arylquinolines and 2, 3-dihydro-4(1H)-quinolones using protected *o*-aminoarylacetylenic carbinols as the common intermediate.[23] Since

then we developed an alternate procedure which does not require a protecting group for the amino group and involves a Pd(II) induced rearrangement and cyclisation to afford quinolines. This paper presents the details of both procedures and tries to delineate the differences which lead to the formation of six-membered quinolines instead of five-membered indoles.

RESULTS AND DISCUSSION

In recent years, the palladium-catalyzed procedure has emerged as one of the most versatile methodologies for carbon-carbon bond formation and heteroannulation.[15, 24] Mechanisms have been suggested to explain the methodology.[25] We found the procedure very useful for the synthesis of heterocyclic structures.[26] For the synthesis of quinolines we have developed two alternative procedures as shown below in Scheme 1(Method A) and Scheme 2(Method B). Our synthetic strategy involved palladium-catalyzed coupling of *o*-iodoanilides **4**



4a, R = H, $R^1 = CH_3$
4b, R = H, $R^1 = CF_3$

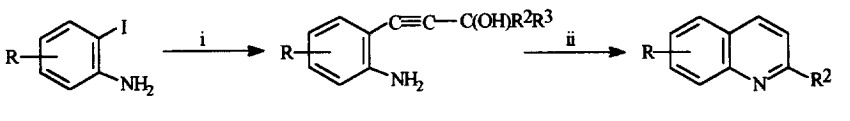
6

2

For legends see Table 1

Reagents and conditions: i) HC≡C-C(OH)R^2R^3 **5**, $(Ph_3P)_2PdCl_2$, Et_3N, DMF, rt, 24h;
ii) NaOEt, in EtOH

Scheme 1



7

8

2

For legends see Table 3

Reagents and conditions: i) HC≡C-C(OH)R^2R^3 **5**, $(Ph_3P)_2PdCl_2$ Et_3N, DMF, rt, 24h;
ii) $Pd(OAc)_2$, LiCl,K_2CO_3, DMF 100 °C, 16h

Scheme 2

or *o*-iodoanilines **7**[27] with terminal acetylenic carbinols **5**[28], under conditions which avoid formation of indoles, to obtain acyclic compounds **6** or **8**. The latter, on base-catalyzed or palladium-catalyzed reaction, underwent simultaneous rearrangement and cyclisation to afford quinolines **2.**

Palladium-catalyzed Synthesis of 2-[(3-Aryl-3-hydroxy)prop-1-ynyl]anilides 6

When a mixture of *o*-iodoanilide **4**, acetylenic carbinol **5** and $(Ph_3P)_2PdCl_2$(1-2 mol% based on **4**) in Et_3N was stirred at room temperature, under N_2 atmosphere for 24h, the acyclic compounds **6** were obtained in moderate to good yields(Table 1). In case of *o*-iodoacetanilide(**4a**) a few drops of DMF was needed to facilitate solution. This reaction, however, could also be carried out using large excess of Et_3N to dissolve **4a**. DMF, with two equivalents of Et_3N which acted as base, could also be used. Yields were comparable to those obtained with Et_3N alone(Table 1, compare entry 6 vs.. 7). An increase in reaction period by two-fold(i.e. 48h entry 8, instead of usual 24h) did not result in any appreciable increase in yield(entry 5 vs. entry 8). Use of temperature higher than room temperature led to lower yields of **6**. When temperature > 60 °C was used, complicated product mixtures were obtained. Use of other palladium catalysts e.g. $Pd(OAc)_2$ in the presence of Et_3N or K_2CO_3 or tetrabutylammonium chloride at 80-100 °C did not give any characterisable product.

We have investigated the necessity of CuI in this coupling reaction. A number of reactions were carried out both in the presence of and in the absence of CuI(see Table 1). The addition of CuI was not found to give any additional advantage. In fact cleaner products were obtained in the absence of CuI by using $(Ph_3P)_2PdCl_2$ alone as catalyst. Apparently, acetylenic carbinols **5**, in the presence of Et_3N could reduce Pd(II) to Pd(0) before oxidative addition of Pd(0) to aryl halide could occur. Furthermore, no coupling occurred when CuI alone was used as catalyst(entry 9).

The use of *o*-iodotrifluoroacetanilide(**4b**) compared to *o*-iodoacetanilide(**4a**) was found to be more advantageous as it gave cleaner and easily characterisable products.

In contrast to the formation of benzofurans[26a] from *o*-iodophenol and acetylenic compounds and phthalides[26b] from *o*-iodobenzoic acid and acetylenic compounds in one step, the substituted acetylenic carbinols **6** did not spontaneously cyclize to the corresponding indoles except in one case (see Table 1, entry 2). In the reaction between **4b** and propargyl alcohol(**5**, $R^2 = R^3 = H$), 2-hydroxymethylindole(**9**) was obtained in 50% yield together with **6b** in 17% yield. The indole **9** was identified from its mp.(71 °C, lit[29] 74 °C), IR spectra(absence of $COCF_3$ at around 1710 cm^{-1}), characteristic UV spectra(λ_{max} 290.7, 282.1, 274.4) and ^1H NMR which showed the presence of C-3H at δ 6.33. Interestingly, the corresponding reaction of propargyl alcohol with **4a**(entry 1) afforded the acyclic compound **6a** as the sole product in 61% yield.

Apparently the results indicate that the acidity of the N-H bond was an important factor in the cyclisation process(compare entry 1 *vs.* 2). Also, in entries 4-14(Table 1) where acetylenic carbinols other than

propargyl alcohol were used, no indole was formed indicating that 'HPdX' elimination process in such cases was faster than the nucleophilic attack by nitrogen.

The compounds **6** were identified from their IR, UV, ^{1}H NMR and elemental analyses. The IR spectra showed the presence of both COR^1 and NH groups ruling out the possibility of any cyclisation. This was

Table 1. Palladium-catalyzed Coupling of *o*-Iodoanilides **4** with Acetylenic Carbinols **5** (Scheme 1)

Entry	*o*-Iodoanilides **4**	HC≡C-C(OH)R^2R^3 **5**		Compound	Yield[a]	Yield[b]
	R^1 = ; R = H	R^2	R^3	**6**	(%)	(%)
1	CH_3 **4a**	H	H	**6a**	61	
2	CF_3 **4b**	H	H	**6b** + **9**[c]	**6b**(17) **9**(50)	
3	CF_3 **4b**	CH_3	CH_3	**6c**	51	
4	CH_3 **4a**	C_6H_5	H	**6d**	62	51
5[d]	CF_3 **4b**	C_6H_5	H	**6e**	65	
6	CF_3 **4b**	C_6H_5	H	**6e**		62
7[e]	CF_3 **4b**	C_6H_5	H	**6e**		65
8	CF_3 **4b**	C_6H_5	H	**6e**	68	
9[f]	CF_3 **4b**	C_6H_5	H	-	-	-
10	CF_3 **4b**	*p*-$CH_3C_6H_4$	H	**6f**	76	63
11	CF_3 **4b**	*m*-$CH_3C_6H_4$	H	**6g**	79	64
12	CF_3 **4b**	*o*-$CH_3C_6H_4$	H	**6h**	77	64
13	CF_3 **4b**	*p*-$CH_3OC_6H_4$	H	**6i**	59	62
14	CF_3 **4b**	*o*-$CH_3OC_6H_4$	H	**6j**	63	65

[a] Reactions were usually carried out with 1-2 mol% $(Ph_3P)_2PdCl_2$ in Et_3N unless mentioned otherwise; [b] 1.4-2 mol% $(Ph_3P)_2PdCl_2$ and 2 mol% CuI in Et_3N was used; [c] **9** is 2-hydroxymethylindole; [d] reaction carried out at rt for 48h; [e] 1.4 mol% $(Ph_3P)_2PdCl_2$ and 2 mol% CuI in DMF with two equivalents of Et_3N used; [f] 2 mol% CuI alone in Et_3N was used

further confirmed by ^{1}H NMR which did not show a peak at around δ 6.3 due to C_3 H of indole. The ^{1}H NMR spectra of compounds **6e-j** showed a broad peak for NH at around δ 8.50-8.80. The presence of $COCF_3$ was confirmed by the fact that one aromatic proton showed downfield shift and occurred as a double-doublet at around δ 8.30. Furthermore, the presence of a singlet at around δ 5.60-5.93 confirmed the presence of benzylic proton.

Base-catalyzed Rearrangement and Cyclisation of 2-[(3-Aryl-3-hydroxy)prop-1-ynyl]trifluoroacetanilides 6e-j to 2-Arylquinolines 2. Method A

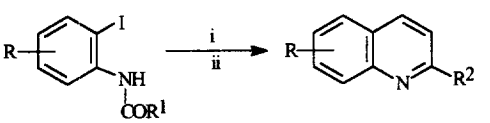
A closer look at compounds **6e-j** showed that these α-acetylenic carbinols should undergo both acid and base-catalyzed rearrangement.[30] Rearrangement[31] of **6e-j** under basic condition would lead to unsaturated ketones with simultaneous removal of the protecting group and subsequent cyclisation to afford the quinolines **2.** Indeed we found that when compounds **6e-j** were refluxed with sodium ethoxide in ethanol for 5h, 2-arylquinolines were obtained in fair to excellent yields(63-90% based on **6**, see Table 2). The products were

Table 2. Synthesis of 2-Arylquinolines **2** by Base-catalyzed Rearrangement and Cyclisation of 2-[(3-Aryl-3-hydroxy)prop-1-ynyl]trifluoroacetanilide **6**(Scheme 1)

Entry	2-Arylquinolines **2** R^2	Yield[a] (%)	Overall yield[b] (%)	Overall yield[c] (%)
1	**2e,** C_6H_5	87	53	59
2	**2f,** *p*-$CH_3C_6H_4$	90	65	65
3	**2g,** *m*-$CH_3C_6H_4$	88.8	65	
4	**2i,** *p*-$CH_3OC_6H_4$	63.5	36	
5	**2j,** *o*-$CH_3OC_6H_4$	73.9	43	

[a] Yield calculated from **6**; [b] yield calculated from *o*-iodoaniline; [c] yield calculated from *o*-iodoaniline in one pot reaction

identified from their spectral data. The IR spectra did not show any peak between 3300-3400 cm^{-1} for NH, while absence of a peak between 1750-1630 cm^{-1} confirmed the absence of $NHCOCF_3$. ^1H NMR spectra gave peaks for aromatic protons at around δ 6.80-8.40 and the corresponding peaks for alkyl substitutents at appropriate positions. The absence of a peak at around δ6.30 ruled out the formation of indoles. Formation of quinolines were confirmed by comparison of their physical constants with known literature values.



4h, $R^1 = CF_3$, R = H
$R^2 = C_6H_5$, *p*-MeC_6H_4, R^3 = H

2

Reagents and conditions: i) HC≡C-C(OH)R^2R^3 **5**, $(Ph_3P)_2PdCl_2$, Et_3N, DMF, rt, 24h; ii) NaOEt, in EtOH

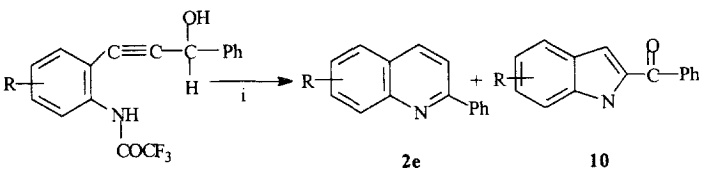
Scheme 3

One Pot Synthesis of 2-Arylquinolines

2-Arylquinolines **2** could be synthesized in a one pot reaction also without isolating the intermediate acyclic compounds **6.** In a typical procedure, after formation of **6**, Et_3N was removed from the reaction flask under reduced pressure and the residue was refluxed with sodium ethoxide in ethanol for 5h to obtain the quinolines **2** (Scheme3). The products were found to be identical with those obtained by the two-step procedure from comparison of mps and spectral data.

Synthesis of Quinolines. Method B

The synthetic methodology described above suffers from two disadvantages-(i) costly trifluoroacetic anhydride is needed to convert *o*-iodoaniline (**7,** R = H) into *o*-iodotrifluoroacetanilide **4b**; (ii) the cyclisation step utilized sodium ethoxide. Initially, we tried to exploit the fact that compounds **6** have an electron rich center in the acetylenic bond, which could be attacked with electron deficient Pd(II) species. It was envisaged that due to the presence of a benzylic proton in the intermediate **6**, this will lead to the ketones by rearrangement and if deprotection of trifluoroacetamido group occurs under the reaction condition it may lead to quinolines. However under Larock's condition[32] [5 mol% $Pd(OAc)_2$, LiCl(1 eq.), K_2CO_3(2.5 eq.), DMF, 100 °C] compound **6e** provided a poor yield of 2-phenylquinoline(**2e**, 15%) and 2-benzoylindole(**10,** 5%) (Scheme 4). It appears that the presence of a free amino group was essential for the cyclisation step.



6e **2e** **10**

Reagents and conditions: i) $Pd(OAc)_2$, LiCl, K_2CO_3, DMF

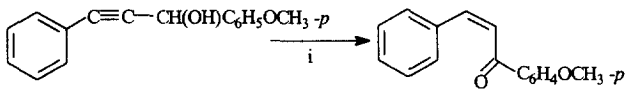
100 °C, 16h

Scheme 4

In order to obviate these difficulties, recently we have developed an alternative and much simpler two-step procedure, which utilized *o*-iodoanilines **7** as starting material, making the procedure more cost-effective and completely palladium-catalyzed.

Palladium(II) Catalyzed Cyclisation of *o*-Aminoarylacetylenic Carbinols to Quinolines

In order to verify our earlier hypothesis that palladium(II) could be used to rearrange α-acetylenic carbinols having structure **6** or **8**, we subjected [3-hydroxy-3-(*p*-methoxyphenyl)prop-1-ynyl]benzene **12** to



12 **13**

Reagents and conditions: i) $Pd(OAc)_2$, LiCl, K_2CO_3, DMF

100 °C, 16h

Scheme 5

Larock's condition for 16h. The compound **12** indeed underwent rearrangement, as evident from the formation of the product **13** - a chalcone(Scheme 5).

Initially, we tried to cyclize compound **8** with $PdCl_2$ in acetonitrile(reflux, 16h). Although cyclisation to quinolines took place, yields were rather poor, for example with **8**(R = H, $R^2 = C_6H_5$, R^3 = H) yield of 2-phenylquinoline(**2e**) was only 14%. Thereafter we cyclized[32] compounds **8** with $Pd(OAc)_2$(3.5-5 mol%), LiCl(1eq.), K_2CO_3(2.5 eq.) in DMF by heating the mixture at 100 °C for 16h to obtain 2-arylquinolines **2** in good yields (Table 3)

Table 3. Palladium-catalyzed Synthesis of Quinolines **2** from *o*-Iodoanilines**7**

Entry	*o*-Iodoanilines[a] **7** R	HC≡C-C(OH)R^2R^3 **5** R^3 = H, R^2 =	Quinolines **2**	Yield[b](%) Method A[c]	Yield[b](%) Method B[d]
1	H	C_6H_5	**2e**	53	60
2	H	*p*-$CH_3C_6H_4$	**2f**	65	60
3	H	*o*-$CH_3C_6H_4$	**2h**		60
4	H	*p*-$CH_3OC_6H_4$	**2i**	36	52
5	H	*o*-$CH_3OC_6H_4$	**2j**	43	47
6	6-CO_2Me	C_6H_5	**2k**		51
7	6-CO_2Me	*p*-$CH_3C_6H_4$	**2l**		45
8	7-CH_3	C_6H_5	**2m**		41
9	H	3,4-OCH_2O	**2n**		44

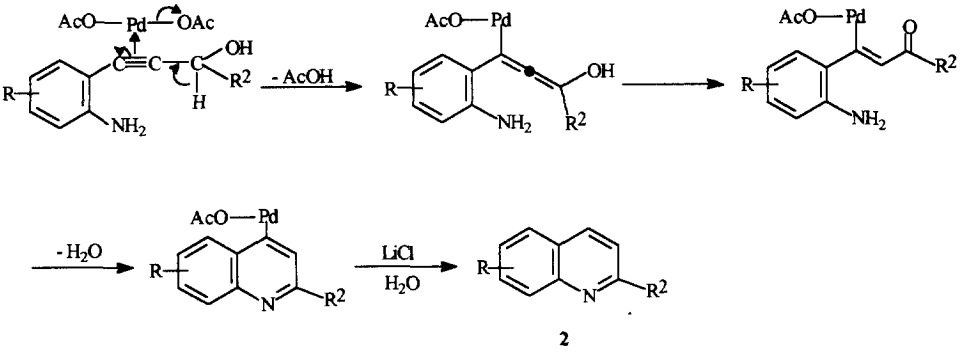
[a] iodoanilines are commercially available or synthesised according to literature procedure; [b] yields based on **7**; [c] see Scheme 1; [d] see Scheme 2

It is to be noted that other workers who utilized *o*-alkynylanilines for palladium(II) catalyzed cyclisation[2b, h-l] obtained indoles. Larock and co-workers[32] also reported formation of indoles in a one-step heteroannulation of *o*-iodoaniline(**7**, R = H) with internal alkynes. However, in our case the presence of a

benzylic CH(OH) group which is α to the acetylenic bond, allowed rearrangement followed by cyclisation which led to the formation of quinolines. A plausible mechanism is depicted in Scheme 6.

We have utilized this methodology for the synthesis of dubamine(Table 3, entry 9), a naturally occurring quinoline alkaloid isolated from *Haplophylum dubium* (Scheme 7).

Our method compares well with the reported synthesis of dubamine by Kozlov *et al*[33](20% yield) and by Kametani *et al*[34] (1% yield). On the other hand the process development of Echavarren & Stille[18a] needs expensive 2-quinolinetriflate and a toxic stannyl reagent whereas we utilized less expensive and readily available starting materials.



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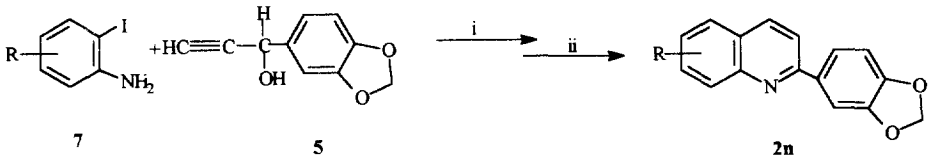
Scheme 6



7 5 2n

Reagents and conditions: i) $(Ph_3P)_2PdCl_2$, Et_3N, DMF, rt, 24h; ii) $Pd(OAc)_2$, LiCl, K_2CO_3, DMF 100 °C, 16h

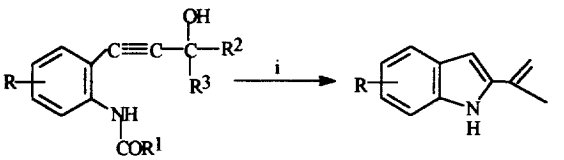
Scheme 7

Palladium(II) catalyzed Cyclisation of 2-[(3-Hydroxy-3,3-dimethyl)prop-1-ynyl]trifluoroacetanilide (6c, R = H, $R^1 = CF_3$, $R^2 = R^3 = CH_3$) to 2-(1-Methylethenyl)indole (14)

Absence of a benzylic proton in compound **6c** (R = H, $R^1 = CF_3$, $R^2 = R^3 = CH_3$) provides an opportunity to look into the role played by it during palladium(II) induced cyclisation. A mixture of compound

6c, anh. K_2CO_3 (2.6 eq.) LiCl (1 eq.) and palladium(II) acetate (5 mol%) in DMF was heated at 100°C for 16h. Removal of solvent followed by usual work-up and column chromatography afforded 2-(1-methylethenyl)indole(**14**, 95%), mp 117-118°C, lit[35] 118-120°C (Scheme 8).

The IR spectra of the product **14** did not exhibit a peak in the carbonyl region which confirmed the absence of $COCF_3$ group. The ^1H NMR spectra showed a doublet (J = 2 Hz) at δ 6.40 which is due to C-3H of the indole nucleus.



6c **14**

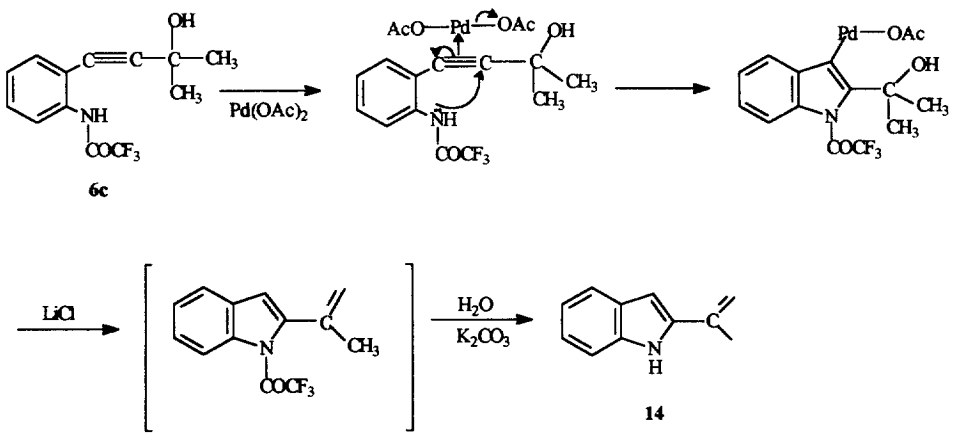
$R = H, R^1 = CF_3, R^2 = R^3 = CH_3$

Reagents and conditions: i) $Pd(OAc)_2$, LiCl, K_2CO_3, DMF 100 °C, 16h

Scheme 8

Evidently, in the absence of a benzylic proton, rearrangement is not possible and nucleophilic attack by lone pair of nitrogen takes place. This shows the differences that could be exploited for the selective formation of 5-membered or 6-membered heterocyclic structures.

A possible mechanism which could explain formation of **14** is depicted in Scheme 9.



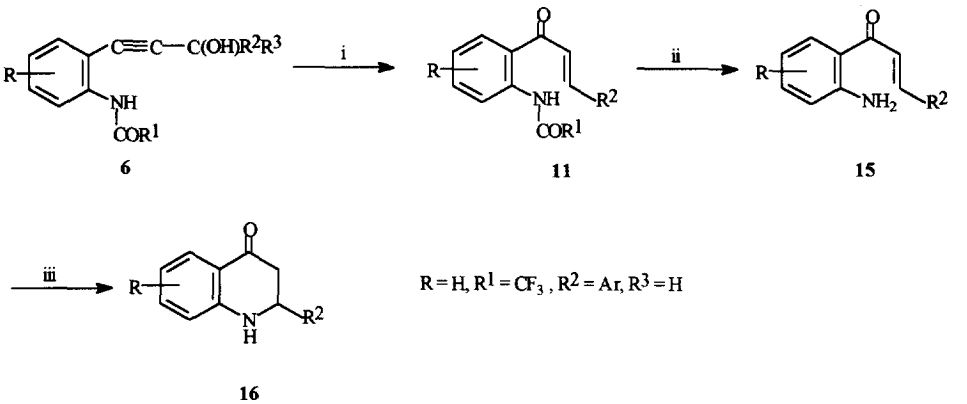
6c **14**

Scheme 9

Acid-catalyzed Rearrangement of 2-[(3-aryl-3-hydroxy)prop-1-ynyl]anilides 6 to N-Substituted 2'-Aminochalcones 11

The α-acetylenic carbinols **6** are ideal substrates for acid-catalyzed Meyer-Schuster rearrangement.[30] Such rearrangement will provide an easy entry into 2'-substituted chalcones, some of which are known[36] to inhibit interleukin-1, a protein, synthesized and released by white blood cells in response to injurious stimuli.

The compounds **6** (R = H, R^1 = CH_3 or CF_3, R^2 = aromatic group, R^3 = H) were stirred with catalytic amounts



Reagents and conditions: i) *p*-TSA, Bz, rt, 48h; ii) NaOH, EtOH, rt, 40h; iii) AcOH, H_3PO_4, 90 °C, 25 min.

Scheme 10

Table 4. Acid-Catalyzed Rearrangement of 2-[(3-aryl-3-hydroxy)prop-1-ynyl]anilides **6** into N-Substituted 2'-aminochalcones **11**(Scheme 10)

Entry	Alkynols, **6** R = R^3 = H		Chalcones, **11**	Yield[a] (%)	Yield[b] (%)
	R^2	R^1			
1	C_6H_5	CH_3	**11d**[c]	73	45
2	C_6H_5	CF_3	**11e**	89	58
3	*p*-$CH_3C_6H_4$	CF_3	**11f**	83	63
4	*o*-$CH_3C_6H_4$	CF_3	**11h**	63	49
5	*p*-$CH_3OC_6H_4$	CF_3	**11i**	65	39

[a] yield based on **6**; [b] yield based on **4**; [c] compound **11d**, mp 77 °C, which agrees well with Batt *et al*[36] (mp 74-76 °C), on the other hand Donnelly *et al*[22c] have reported mp to be 92-93 °C.

of *p*-toluenesulfonic acid in benzene at room temperature for 48h to obtain N-substituted 2'-aminochalcones **11** in 63-89% yields (Scheme 10, Table 4).

In the IR spectra of **11**, the presence of two peaks, one at around 1710 cm^{-1} and the other at around 1640 cm^{-1} showed the presence of the two carbonyl groups. The ^1H NMR spectra showed the presence of NHCOR[1] by giving a broad peak above δ 10. The vinyl protons showed J = 15 Hz in case of compound **11e** at 300 MHz, which confirmed the *E* configuration.

Synthesis of 2-Aryl-2,3-dihydro-4(1H)quinolones 16

Attempts to effect the acid-catalyzed rearrangement of compounds **6** and subsequent cyclisation in a one-pot procedure by treating **6** with *p*-TSA in refluxing benzene for 48h led to the rearranged products **11** only. Evidently, removal of the protecting trifluoroacetamido group of **11** is essential for successful cyclisation. This could be easily achieved by treating compounds **11** with 6N aqueous sodium hydroxide in 95% ethanol at room temperature for 40h to obtain 2'-aminochalcones **15**. Attempts were made to purify compounds **15** by column chromatography followed by crystallization. However, this resulted in development of color on standing and analytical results were not satisfactory. However, IR spectra of **15** did not show any peak around 1710 cm^{-1} which confirmed the absence of $COCF_3$ group. A sharp peak at around 1640 cm^{-1} was due to the keto vinyl group, while two broad peaks, one at around 3320 cm^{-1} and the other at around 3420 cm^{-1} could be assigned to the amino group. In the ^1H NMR spectra the amino group appeared as a broad peak at around δ 6.20-6.40, while the other peaks were consistent with the assigned structures.

The 2'-aminochalcones **15** were cyclized[22a] by treating them with a mixture of glacial acetic acid and phosphoric acid at 90^{0}C for 25 min. to obtain 2-aryl-2, 3-dihydro-4(1H)quinolones **16**. The overall yield of **16** from **11** by two steps was 60-80% (Scheme 10, Table 5).

Table 5. Synthesis of 2-Aryl-2, 3-dihydro-4(1H)-quinolones **16** from N-Substituted 2'-aminochalcones (Scheme 10)

Entry	Aminochalcones **11** $R = R^3 = H$, $R^1 = CF_3$, R^2 =	2-Aryl-2, 3-dihydro-4(1H)-quinolones **16**	Yield (%)
1	**11e**, C_6H_5	**16e**	61
2	**11f**, *p*-$CH_3C_6H_4$	**16f**	79
3	**11h**, *o*-$CH_3C_6H_4$	**16h**	66
4	**11i**, *p*-$CH_3OC_6H_4$	**16i**	72

[a] yield based on **11**

The compounds **16** were characterized from their spectral data and elemental analyses. In the IR spectra, a sharp peak at around 1650 cm^{-1} confirmed the presence of a carbonyl group. A broad peak at around 3320 cm^{-1} was due to NH bond.

The ^1H NMR spectra exhibited a double-doublet for a single proton (N-CH) at around δ 4.72 (J = 12 Hz, J = 6 Hz). This is due to coupling of the C-2 hydrogen with the equatorial and axial hydrogens at C-3. A multiplet due to two protons at around δ 2.50-2.95 accounted for two magnetically non-equivalent hydrogens at C-3. These protons exhibited normal coupling with the C-2 proton and in addition gem coupling between themselves, resulting in the multiplet. Furthermore, the structure could be confirmed by comparison of mp with known literature values e.g. compound **16a**, mp 159 ^0C, lit[22a] mp 159 °C and elemental analyses.

CONCLUSION

In this paper we have described two general and facile methods for the synthesis of quinolines. While the yields were comparable to those reported earlier by Larock *et al*[32], we have used more readily available acetylenic alcohols **6**. We have also reported the synthesis of dubamine, a naturally occurring alkaloid. The available methods for its synthesis either led to poor yields[33, 34] or used costly and toxic starting materials.[18a] Furthermore, we have established the alkynols **6** as versatile intermediates, which could be used to synthesize 2'-aminochalcones **11** in excellent yields. The compounds **11** may inhibit interleukin-1.[36] The 2'-aminochalcones were also cyclized to 2-aryl-2, 3-dihydro-4(1H)quinolones.

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EXPERIMENTAL SECTION

General. All chiral compounds described herein are racemates. Melting points were determined in open capillaries and are uncorrected. Solvents and reagents were reagent-grade materials and were further purified by conventional methods. The acetylenic carbinols[28] and *o*-iodoanilines[27] were synthesized according to literature procedure. The progress of reactions and purity of the products were routinely monitored by TLC on silica gel 60 F_{254} precoated sheets (E. Merck). Column chromatography was carried out on silica gel (60-120 mesh).

The UV spectra were recorded in spectrophotometric grade ethanol (Baker).The IR spectra were taken as KBr plates. ^1H NMR spectra were recorded using CCl_4 or $CDCl_3$ as solvents and TMS as internal standard.

Synthesis of 2-Arylquinolines. Method A. Palladium-catalyzed Cross-coupling Reactions of *o*-Iodo-anilides with Acetylenic Carbinols (General Procedure). A mixture of *o*-iodoanilide (**4**, 1.01 mmol), $(Ph_3P)_2PdCl_2$ (10 mg, 0.014 mmol) in Et_3N (15 mL) was stirred under N_2 atmosphere at room temperature for 15 min. In the case of *o*-iodoacetanilide a few drops of DMF was used to facilitate solution. Freshly distilled propargyl alcohol (Aldrich, USA) (2.50-3.00 mmol) or 1,1-dimethylpropargyl alcohol[28](2.00 mmol) or 1-arylprop-2-yn-1-ol[28] (1.30 mmol) was then added and the mixture was further stirred at room temperature for 24h (TLC). The solvent was then removed under reduced pressure and the residue was purified by column chromatography (silica gel 60-120 mesh) to obtain the substituted alkynols **6**.

2-(3-Hydroxyprop-1-ynyl)acetanilide (6a): yield 61%; white solid; mp 104 °C(petroleum ether-benzene); IR (KBr) υ_{max} 3310, 3250, 1675, 1665, 1610, 1580, 1540, 1475, 1455, 1445 cm^{-1}; UV (EtOH) λ_{max} 297.1 nm (log ε = 3.18), 255.1 nm (log ε = 4.07); ^1H NMR (CCl_4, 60 MHz) δ 2.17 (s, 3H, $COCH_3$), 4.53 (s, 2H, CH_2OH), 6.83-8.40 (m, 5H, Ar H and $NHCOCH_3$); Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; N, 7.40. Found C, 69.70; H, 5.82; N, 7.25.

2-(3-Hydroxyprop-1-ynyl)trifluoroacetanilide (6b) and 2-Hydroxymethylindole (9): column chromatography (silica gel 60-120 mesh) with ethyl acetate in chloform as eluent provides compound **9** as faster moving fractions. The latter chromatographic fractions, after removal of solvents provide **6b**.

6b: yield 17%; white solid; mp 109 °C (benzene-petroleum ether); IR(KBr) υ_{max} 3310, 1710, 1605, 1585, 1545, 1480, 1450 cm^{-1}; UV (EtOH) λ_{max} 300.4 nm (log ε = 2.77), 253.2 nm (log ε = 4.06); ^1H NMR (CCl_4+DMSO-d_6, 60 MHz) δ 4.42 (s, 2H, CH_2OH), 7.00-7.68 (m, 3H, Ar H), 8.08 (app dd, 1H, Ar H), 9.52 (bs, 1H, $NHCOCF_3$); Anal. Calcd. for $C_{11}H_8F_3NO_2$: C, 54.33; H, 3.32; N, 5.56. Found: C, 54.42; H, 3.26; N, 5.60

9: yield 50%; white solid; mp 71 °C (petroleum ether), lit[29] 74 °C; IR (KBr) υ_{max} 3400, 1615, 1455, 1420 cm^{-1}; UV (EtOH) λ_{max} 290.7 nm, 282.1 nm, 274.4 nm; ^1H NMR ($CDCl_3$, 60 MHz) δ 2.63 (bs,1H, CH_2OH), 4.63 (s, 2H, CH_2OH), 6.33 (s, 1H, C-3 H), 6.90-7.73 (m, 4H, Ar H), 8.40 (bs, 1H, NH).

2-(3, 3-Dimethyl-3-hydroxyprop-1-ynyl)trifluoroacetanilide(6c): yield 51%; white solid; mp 72 °C (petroleum ether); IR (KBr) υ_{max} 3420, 3340, 3195, 1720, 1610, 1580, 1505, 1480 cm^{-1}; UV (EtOH) λ_{max} 253.2 nm (log ε = 4.07), 230.0 nm (log ε = 4.26); ^1H NMR ($CDCl_3$, 100 MHz) δ 1.66 (s, 6H, 2 x CH_3), 2.08 (bs, 1H, OH), 7.04-7.56 (m, 3H, Ar H), 8.34 (dd, *J* = 8Hz, 2Hz, 1H, Ar H), 8.74 (bs, 1H, $NHCOCF_3$); Anal. Calcd. for $C_{13}H_{12}F_3NO_2$: C, 57.56; H, 4.46; N, 5.16. Found: C, 57.50; H, 4.41; N, 5.48.

2-[(3-Hydroxy-3-phenyl)prop-1-ynyl]acetanilide(6d): yield 62%; white solid; mp 112-113 °C (benzene-petroleum ether); IR (KBr) υ_{max} 3345, 3270, 1635, 1600, 1575, 1530, 1480, 1450 cm^{-1}; UV (EtOH) λ_{max} 294.0 nm (log ε = 3.36), 257.0 nm (log ε = 4.235), 230.0 nm(log ε = 4.465); ^1H NMR ($CDCl_3$, 100 MHz) δ 2.00 (s, 3H, $COCH_3$), 2.92 (bs, 1H, $CHOH$), 5.76 (s, 1H, $CHOH$), 6.88-8.00 (m, 9H, Ar H and $NHCOCH_3$),

8.32 (d, *J* = 8Hz, 1H, Ar H); Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.08; H, 5.83; N, 5.00.

2-[(3-Hydroxy-3-phenyl)prop-1-ynyl]trifluoroacetanilide(6e): yield 65%; white solid; mp 87 °C (benzene); IR (KBr) υ_{max} 3300, 1710, 1610, 1580, 1550, 1490, 1480, 1450 cm^{-1}; UV (EtOH) λ_{max} 301.2 nm (log ε = 2.85), 255.0 nm (log ε = 4.175), 232.0 nm (log ε = 4.34); ^1H NMR (CCl_4, 60 MHz) δ 2.83 (bs, 1H, CHO*H*), 5.67 (s, 1H, C*H*OH), 6.93-7.67 (m, 8H, Ar H), 8.37 (dd, *J* = 8Hz, 2Hz, 1H, Ar H), 8.67 (bs, 1H, $NHCOCF_3$); Anal Calcd. for $C_{17}H_{12}F_3NO_2$: C, 63.95; H, 3.79; N, 4.39. Found: C, 63.52; H, 3.71; N, 4.70.

2-[3-Hydroxy-3-(*p*-methylphenyl)prop-1-ynyl]trifluoroacetanilide(6f): yield 76%; light yellow solid; mp 103-104 °C (benzene-petroleum ether); IR (KBr) υ_{max} 3300, 1705, 1605, 1580, 1545, 1510, 1480, 1450 cm^{-1}; UV (EtOH) λ_{max} 300.1 mn (log ε = 2.87), 254.9 nm (log ε = 4.205), 230.4 nm (log ε = 4.38); ^1H NMR (CCl_4, 60 MHz) δ 2.40 (s, 3H+1H, $ArCH_3$ and CHO*H*), 5.60 (s, 1H, C*H*OH), 6.93-7.60 (m, 7H, Ar H), 8.33 (d, *J* = 8 Hz, 1H, Ar H), 8.58 (bs, 1H, $NHCOCF_3$); Anal Calcd. for $C_{18}H_{14}F_3NO_2$: C, 64.86; H, 4.23; N, 4.20. Found C, 64.54; H, 4.29; N, 4.20.

2-[3-Hydroxy-3-(*m*-methylphenyl)prop-1-ynyl]trifluoroacetanilide(6g): yield 79%; white solid; mp 82-83 °C (benzene-petroleum ether); IR (KBr) υ_{max} 3300, 1710, 1650, 1580, 1550, 1475, 1450 cm^{-1}; UV (EtOH) λ_{max} 300.6 nm (log ε = 2.90), 255.0 (log ε = 4.21), 232.2 (log ε = 4.38); ^1H NMR ($CDCl_3$ + CCl_4, 60 MHz) δ 2.40 (s, 3H, $ArCH_3$), 5.67 (s, 1H, C*H*OH), 6.93-7.63 (m, 7H, Ar H), 8.37 (dd, *J* = 8 Hz, 2 Hz, 1H, Ar H), 8.63 (bs, 1H, $NHCOCF_3$); Anal Calcd. for $C_{18}H_{14}F_3NO_2$: C, 64.86; H, 4.23; N, 4.20. Found C, 64.99; H, 4.10; N, 4.19

2-[3-Hydroxy-3-(*o*-methylphenyl)prop-1-ynyl]trifluoroacetanilide(6h): yield 77%; white solid; mp 110 °C (benzene-petroleum ether); IR (KBr) υ_{max} 3370, 1750, 1610, 1590, 1580, 1540, 1450 cm^{-1}; UV (EtOH) λ_{max} 255.6 nm (log ε = 4.22), 232.4 nm (log ε = 4.37); ^1H NMR (CCl_4, 60 MHz) δ 2.40 (s, 3H, $ArCH_3$), 2.67 (bs, 1H, CHO*H*), 5.80 (s, 1H, C*H*OH), 6.90- 7.83 (m, 7H, Ar H), 8.30 (dd, *J* = 8 Hz, 2 Hz, 1H, Ar H), 8.63 (bs, 1H, $NHCOCF_3$); Anal Calcd. for $C_{18}H_{14}F_3NO_2$: C, 64.86; H, 4.23; N, 4.20. Found C, 64.91; H, 4.24; N, 4.52.

2-[3-Hydroxy-3-(*p*-methoxylphenyl)prop-1-ynyl]trifluoroacetanilide(6i): yield 59%; white solid; mp 107 °C (benzene); IR (KBr) υ_{max} 3280, 1710, 1610, 1580, 1540, 1515, 1485, 1450 cm^{-1}; UV (EtOH) λ_{max} 252.6 nm (log ε = 4.16), 230.5 nm (log ε = 4.375); ^1H NMR ($CDCl_3$, 100 MHz) δ 2.30 (bs, 1H, CHO*H*), 3.82 (s, 3H, $ArOCH_3$), 5.70 (s, 1H, C*H*OH), 6.84-7.72 (m, 7H, Ar H), 8.34 (dd, *J* = 8Hz, 2 Hz, 1H, Ar H), 8.66 (bs, 1H, $NHCOCF_3$); Anal Calcd. for $C_{18}H_{14}F_3NO_3$: C, 61.89; H, 4.04; N, 4.01. Found C, 61.99; H, 4.09; N, 3.96.

2-[3-Hydroxy-3-(*o*-methoxylphenyl)prop-1-ynyl]trifluoroacetanilide(6j): yield 63%; white solid; mp 87 °C (benzene-petroleum ether); IR (KBr) υ_{max} 3360, 1750, 1610, 1590, 1545, 1490, 1460, 1450, 1440 cm^{-1}; UV (EtOH) λ_{max} 300.4 nm (log ε = 2.97), 255.4 nm (log ε = 4.226), 230.2 nm (log ε = 4.42), 225.2 nm

cm^{-1}; UV (EtOH) λ_{max} 300.4 nm (log ε = 2.97), 255.4 nm (log ε = 4.226), 230.2 nm (log ε = 4.42), 225.2 nm (log ε = 4.42); ^{1}H NMR ($CDCl_3$, 60MHz) δ 3.67 (bs, 1H, CHO*H*), 3.87 (s, 3H, $ArOCH_3$), 5.93 (s, 1H, C*H*OH), 6.77-7.67 (m, 7H, Ar H), 8.30 (dd, *J* = 8 Hz, 2 Hz, 1H, Ar H), 8.78 (bs, 1H, $NHCOCF_3$); Anal. Calcd. for $C_{18}H_{14}F_3NO_3$: C, 61.89; H, 4.04; N, 4.01. Found C, 62.08; H, 4.08; N, 4.02.

2-(1-Methylethenylindole(14): a mixture of compound **6c**(255 mg, 0.94 mmol), K_2CO_3 (340 mg, 2.46 mmol), LiCl (40 mg, 0.94 mmol), Pd $(OAc)_2$ (10 mg, 0.044 mmol) in DMF was heated at 100 °C under N_2 atmosphere for 16h. The solvent was then removed under reduced pressure and to the residue, water (50 mL) was added. It was then extracted with $CHCl_3$ (3X50 mL) and the combined organic layer was washed with water (3X50 mL) and dried (anh. Na_2SO_4). The solvent was then removed and the resulting light brown residue upon column chromatography (silica gel, 60-120 mesh) with $CHCl_3$ afforded compound **14.** Yield 95%; light yellow solid; mp 117-118 °C (ethanol), lit[35] 118-120 °C; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 2.13 (d, *J* = 1 Hz, 3H, CH_3), 4.93 (d, 1H, C=CH_2), 5.13 (s, 1H, C=CH_2), 6.40 (d, *J* = 2Hz, 1H, C-3 H), 6.77-7.57 (m, 4H, Ar H), 7.83 (bs, 1H, NH)

Sodium ethoxide Mediated Cyclization of 2-[(3-Hydroxy-3-aryl)prop-1-ynyl]trifluoroacetanilides 6e-j to 2-Arylquinolines 2 (General Procedure). The procedure for the synthesis of 2-phenylquinoline **2e** is representative: sodium (30 mg, 1.30 mmol) was dissolved in anh. ethanol (3 mL). To this solution, 2-[(3-hydroxy-3-phenyl)prop-1-ynyl]trifluoroacetanilide (**6e**, 90 mg, 0.28 mmol) was added. The reaction mixture was then refluxed under N_2 for 5h. It was then cooled, poured into water (100 mL) and extracted with $CHCl_3$. The combined organic layer was washed with saturated brine (3X50 mL), water (3X50 mL) and dried (anh. Na_2SO_4). The solvent was removed and the resulting light yellow gum upon column chromatography (silica gel 60-120 mesh) with 1:1 chloroform-petroleum ether as eluent afforded compound **2e**. Yield 87%; light yellow solid; mp 83 °C (petroleum ether), lit[17] 84- 85 °C, lit[37] 84 °C; ^{1}H NMR (CCl_4, 60 MHz) δ 7.20-8.33 (m, Ar H).

2-(*p*-Methylphenyl)quinoline (2f): yield 90%; light yellow solid; mp 81-82 °C (petroleum ether), lit[17] 81-82 °C, lit[38] 83-84 °C; ^{1}H NMR (CCl_4, 60 MHz) δ 2.43 (s, 3H, $ArCH_3$), 7.06-8.30 (m, 10H, Ar H).

2-(*m*-Methylphenyl)quinoline (2g): yield 89%; light yellow solid; mp 76-77 °C(petroleum ether) lit[17] 77 °C; ^{1} H NMR (CCl_4, 60 MHz) δ 2.49 (s, 3H, $ArCH_3$), 6.87-8.27 (m, 10H, Ar H).

2-(*p*-Methoxylphenyl)quinoline (2i): yield 64%; light yellow solid; mp 122-123 °C(petroleum ether) lit[17] 120-122 °C, lit[39] 124°C; ^{1}H NMR ($CDCl_3$+ CCl_4, 60 MHz) δ. 3.90 (s, 3H, $ArOCH_3$), 6.73-8.27 (m, 10H, Ar H).

2-(*o*-Methoxylphenyl)quinoline (2j): yield 74%; light yellow viscous oil, lit[17] viscous oil; ^{1}H NMR (CCl_4, 60 MHz) δ 3.80 (s, 3H, $ArOCH_3$), 6.73-8.27 (m, 10H, Ar H).

One Pot Synthesis of 2-Arylquinolines 2. Typical Procedure: Synthesis of 2-Phenyl quinoline(2e). A mixture of compound **4b** (320 mg, 1.01 mmol), $(Ph_3P)_2PdCl_2$ (10 mg, 0.014 mmol) and 1-phenylprop-2-yn-1-ol(**5**, R^2 = Ph, R^3 = H, 170 mg, 1.29 mmol) in Et_3N (15 mL) was stirred under N_2 for 24h (TLC).The solvent was then removed under reduced pressure. The resulting gum was treated in the same pot with sodium ethoxide in ethanol [obtained by dissolving sodium (80 mg, 3.48 mmol) in anh. ethanol (8 mL)] as described above under two-step procedure. After usual work-up and column chromatography compound **2e** was obtained (yield 62.4% light yellow solid). The compound **2e** was found to be identical with the compound obtained by two-step procedure from comparison of IR, UV, ^{1}H NMR spectral data.

Synthesis of 1-*p*-Methoxyphenyl-3-phenylprop-2-en-1-one(13)

The alkynol **12**[40], obtained by palladium-catalyzed coupling between iodobenzene and 1-*p*-methoxyphenylprop-2-yn-1-ol(**5**, R^2 = *p*-$CH_3OC_6H_4$, R^3 = H), was subjected to Larock's condition[32] as described for the synthesis of 2-arylquinolines **2** from compounds **8**, to obtain the title compound **13**. It was identified from its mp 102-104 °C, lit[41] 101-103 °C and comparison of ^{1}H NMR spectra.[41]

Synthesis of 2-Arylquinolines. Method B. (General Procedure). A mixture of *o*-iodoaniline (**7**, 200 mg, 0.91 mmol), $(PPh_3)_2PdCl_2$ (20 mg, 0.028 mmol), CuI (10 mg, 0.053 mmol) in Et_3N (10 mL) was stirred at room temperature for 10 min. To the stirred solution 1- arylprop-2-yn-1-ol (**5**, 1.09 mmol) was added and the mixture was stirred at room temperature for 24h (TLC).The solvent was then removed, the resulting gum was treated with water (50 mL) and was extracted with $CHCl_3$ (3 x 50 mL). The combined organic layer was washed with water (3 x 50 mL) and dried (anh. Na_2SO_4). The crude product was purified by column chromatography (silica gel 60-120 mesh) to obtain 2-(3-hydroxy-3-arylprop-1-ynyl)aniline **8.**

A mixture of compound **8**(o.46 mmol), $Pd(OAc)_2$ (5 mg, 0.022 mmol), K_2CO_3 (160 mg, 1.16 mmol) and LiCl (20 mg, 0.47 mmol) in DMF was heated at 100 °C for 16h. The solvent was then removed under reduced pressure and the residue was treated with water (15 mL) and extracted with $CHCl_3$ (3 x 50 mL). The combined organic layer was washed with water (3 x 50 mL), dried (anh. Na_2SO_4) and the solvent was removed. The residue upon column chromatography (silica gel, 60-120 mesh) afforded 2-arylquinolines **2**.

2-Phenylquinoline (2e), 2-(*p*-Methylphenyl)quinoline(2f), 2-(*p*-Methoxyphenyl)quinoline(2i) and 2-(*o*-Methoxyphenyl)quinoline (2j): comparison of mp, IR, UV, and ^{1}H NMR spectral data showed these compounds to be identical with those obtained by Method A. The isolated yields are given in Table 3.

2-(*o*-Methylphenyl)quinoline (2h): 60%, light brown viscous oil; lit[42] viscous oil, ^{1}H NMR (CCl_4, 60 MHz) δ 2.46 (s, 3H, $ArCH_3$), 7.06-8.29 (m, 10 H, Ar H).

6-Carbomethoxy-2-phenylquinoline(2k): 51%; white solid; mp 166-168 °C (petroleum ether); IR (KBr): υ_{max} 1720, 1600, 1440 cm^{-1}; UV (EtOH) λ_{max} 302.7 nm (logε = 4.21), 262.6 nm (logε = 4.57); ^{1}H NMR

($CDCl_3$ + CCl_4, 60 MHz) δ 3.93 (s, 3H, $COOCH_3$) 7.43-8.67 (m, 10H, Ar H); Anal. Calcd. for $C_{17}H_{13}NO_2$ C: 77.55; H, 4.98; N, 5.32. Found: C, 77.38; H, 5.11; N, 5.20.

6-Carbomethoxy-2-(*p*-methylphenyl)quinoline(2l): 45%; white solid; mp 180 °C (petroleum ether); IR (KBr): υ_{max} 1720, 1600, 1470 cm^{-1}; UV (EtOH) λ_{max} 308.8 nm (log ε = 4.29) 267.4 nm (log ε = 4.57); ^1H NMR ($CDCl_3$ + CCl_4, 60 MHz) δ 2.43 (s, 3H, $ArCH_3$), 3.93 (s, 3H, $COOCH_3$), 7.23-8.60 (m, 9H, Ar H). Anal. Calcd. for $C_{18}H_{15}NO_2$: C,77.96; H, 5.45; N, 5.05. Found: C, 77.84; H, 5.66; N, 4.85.

7-Methyl-2-phenylquinoline(2m): 41%; light yellow solid; mp 82 °C; IR (KBr) υ_{max} 1620, 1600, 1510 ,1450, 1440 cm^{-1}; UV (EtOH) λ_{max} 325.2 nm (log ε = 3.86) 257 nm (log ε = 4.54) ^1H NMR (CCl_4, 60 MHz) δ 2.53 (s, 3H, $ArCH_3$), 7.26-8.33 (m, 10H, Ar H); Anal Calcd. for $C_{16}H_{13}N$: 87.64; H, 5.98; N, 6.39. Found: C, 87.69; H, 6.20; N, 6.57.

Dubamine (2n): 44%; white solid; mp 93-94 °C (petroleum ether) lit[18a] 95 °C; IR (KBr): υ_{max} 1600, 1500, 1490 cm^{-1}; UV (ethanol) λ_{max} 337 nm (log ε = 4.15), 217.8 nm (log ε = 4.56); ^1H NMR (CCl_4, 60 MHz) δ 6.03 (s, 2H, OCH_2O), 6.80-8.43 (m, 9H, Ar H).

Acid-catalyzed Rearrangement of 2-[(3-Hydroxy-3-aryl)prop-1-ynyl]anilides 6 to N-Substituted 2'-Aminochalcones 11. General Procedure. A mixture of 2-[(3-hydroxy-3-aryl)prop-1-ynyl]anilide (**6**, 0.56 mmol) and p-toluenesulfonic acid (10 mg, 0.05 mmol) in benzene (5 mL) was stirred at room temperature for 48h (TLC). The solvent was then removed under reduced pressure and the residue was treated with water (25 mL). It was extracted with $CHCl_3$ (3 x 50 mL) and the combined organic layer was washed with water (3 x 50 mL) and then dried (anh. Na_2SO_4). The residue after removal of solvent was chromatographed (silica gel, 60-120 mesh) and the product was further purified by crystallization.

[E]-3-Phenyl-1-(2-acetamidophenyl)prop-2-en-1-one (11d): yield 73%; light yellow solid; mp 77 °C (petroleum ether); lit[36] 74-76 °C, lit[22c] 92-93 °C; IR (KBr): υ_{max} 3300, 1710, 1645, 1595, 1585, 1515, 1450 cm^{-1}; UV(EtOH) λ_{max} 316.5 nm (log ε = 4.29), 237.0 nm (log ε = 4.28); ^1H NMR ($CDCl_3$, 100 MHz) δ 2.24 (s, 3H, $NHCOCH_3$), 7.04-8.16 (m, 10H, Ar H and CH=CHCO), 8.76 (dd, *J*=8 Hz, 2 Hz, 1H, Ar H), 11.60 (bs, 1H, $NHCOCH_3$); Anal. Calcd. for $C_{17}H_{15}NO_2$ C, 76.96; H, 5.70; N, 5.28. Found: C, 77.08; H, 5.83; N, 5.00.

[E]-3-Phenyl-1-(2-trifluoroacetamidophenyl)prop-2-en-1-one(11e): yield 89 %; faint yellow solid, mp 120 °C (petroleum ether); IR (KBr): υ_{max} 3020, 1725, 1645. 1585, 1575, 1535, 1495, 1450 cm^{-1} UV (EtOH) λ_{max} 324.8 nm (log ε = 4.38), 237.6 nm (log ε = 4.31); ^1H NMR (CCl_4, 60 MHz) δ 7.13-8.23 (m, 10H, Ar H and CH=CHCO), 8.83 (dd, *J* = 8 Hz, 2 Hz, 1H, Ar H), 13.06 (bs, 1H, $NHCOCF_3$); Anal. Calcd. for $C_{17}H_{12}F_3NO_2$: C, 63.95; H, 3.79; N, 4.39. Found: C, 63.92; H, 3.75; N, 4.36.

[E]-3-(*p*-Methylphenyl)-1-(2-trifluoroacetamidophenyl)prop-2-en-1-one (11f): yield 83%; faint yellow solid; mp 135-136 °C (benzene-petroleum ether); IR (KBr): υ_{max} 3000, 1710, 1650, 1585, 1580, 1530, 1510, 1460, 1415 cm^{-1}; UV (EtOH) λ_{max} 339.4 nm (log ε = 4.45), 240 nm (log ε = 4.39); ^1H NMR (CCl_4, 60

MHz) δ 2.43 (s, 3H, $ArCH_3$), 6.93-8.17 (m, 9H, Ar H and CH=CHCO), 8.73 (dd, J = 8 Hz, 2 Hz, 1H, Ar H), 12.93 (bs, 1H, $NHCOCF_3$); Anal. Calcd. for $C_{18}H_{14}F_3NO_2$: C, 64.86; H, 4.23; N, 4.20. Found: C, 64.87; H, 4.33; N, 4.05.

[E]-3-(*o*-Methylphenyl)-1-(2-trifluoroacetamidophenyl)prop-2-en-1-one (11h): yield 63%; light yellow solid; mp 132-133 °C (benzene-petroleum ether); IR (KBr): υ_{max} 3020, 1720, 1640, 1585, 1530, 1455 cm^{-1}; UV (EtOH) λ_{max} 335.0 nm (log ε = 4.276), 240.8 nm (log ε = 4.25); ^1H NMR (CCl_4, 60 MHz) δ 2.53 (s, 3H, $ArCH_3$), 7.00-8.30 (m, 9H, Ar H and CH=CHCO), 8.67 (d, J = 8 Hz, 1H, Ar H), 14.00 (bs, 1H, $NHCOCF_3$); Anal. Calcd. for $C_{18}H_{14}F_3NO_2$: C, 64.86; H, 4.23; N, 4.20. Found: C, 64.83; H, 4.28; N, 4.04.

[E]-3(*p*-Methoxyphenyl)-1-(2-trifluoroacetamidophenyl)prop-2-en-1-one (11i): yield 65%; light yellow solid; mp 144 °C (ethylacetate-petroleum ether, 1:9); IR (KBr): υ_{max} 3010, 1725, 1645, 1585, 1575, 1535, 1495, 1450 cm^{-1}; UV (EtOH) λ_{max} 365.4 nm (log ε = 4.455), 243.6 nm (log ε = 4.41); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.88 (s, 3H, $ArOCH_3$), 6.92-7.02 (m, 2H, Ar H), 7.30-7.37 (m, 1H, Ar H), 7.50 (d, J = 15 Hz, 1H, CH=CHCO), 7.60-7.69 (m, 3H, Ar H), 7.88 (d, J = 15 Hz, 1H, CH=CHCO), 8.08 (app dd, J = 8 Hz, 1H, Ar H), 8.70 (app dd, J = 8 Hz, 1H, Ar H), 13.03 (bs, 1H, $NHCOCF_3$), Anal. Calcd. for $C_{18}H_{14}F_3NO_3$: C, 61.89; H, 4.04; N, 4.01. Found: C, 62.01; H, 3.95; N, 3.95.

Synthesis of 2-Aryl-2,3-dihydro-4(1H)quinolones 16 (General Procedure): To a solution of [E]-3-aryl-1-(2-trifluoroacetamidophenyl)prop-2-en-1-one (**11**, 1.41 mmol) in ethanol (10 mL) 6N aqueous sodium hydroxide solution (7.2 mL) was added and stirred at room temperature for 40h (TLC). The solvent was removed at reduced pressure. To the residue water (50 mL) was added and it was extracted with $CHCl_3$ (3 x 100 mL). The combined organic layer was washed with water (2 x 50 mL), dried (anh. Na_2SO_4) and the solvent was removed to obtain [E]-3-aryl-1-(2-aminophenyl)prop-2-en-1-one **15** as a brown solid. The latter was dissolved in glacial acetic acid and to it was added phosphoric acid (2.4 mL). The mixture was stirred at 90°C for 25 min and then cooled to room temperature before pouring over crushed ice. It was extracted with $CHCl_3$ (3 x 75 mL). The combined chloroform layer was washed (H_2O, 2 x 50 mL), dried (anh. Na_2SO_4) and the solvent was removed. The residue upon column chromatography (silica gel 60-120 mesh) with 1:1 chloroform-petroleum ether as eluent affords compound **16.**

2-Phenyl-2, 3-dihydro-4(1H)-quinolone (16e): yield 61%; light yellow solid; mp 159 °C (petroleum ether); lit[22a] 159 °C; ^1H NMR ($CDCl_3$, 60 MHz) δ 2.70-3.18 (m, 2H, C-3 H_a and H_b), 4.52 (bs, 1H, NH), 4.76 (dd, J = 12 Hz, 10 Hz, 1H, C-2 H), 6.63-7.00 (m, 2H, Ar H), 7.23-7.63 (m, 6H, Ar H), 7.93 (dd, J = 8 Hz, 2 Hz, 1H, Ar H).

2-(*p*-Methylphenyl)2, 3-dihydro-4(1H)-quinolone(16f): yield 79%; mp 159 °C(petroleum ether); IR(KBr): υ_{max} 3310, 1650, 1600, 1510, 1480 cm^{-1}; UV(EtOH): λ_{max} 377.4nm(log ε = 3.52), 259.6nm (log ε =

3.86), 235.2nm(logε = 4.37); ^{1}H NMR($CDCl_3$, 100 MHz): δ 2.36(s, 3H, $ArCH_3$), 2.53-2.83(m, 2H, C-3 H_a and H_b), 4.48(bs, 1H, NH), 4.72(dd, J = 12 Hz, 6 Hz, 1H, C-2 H), 6.64-6.94(m, 2H, Ar H), 7.14-7.44(m, 3H, Ar H), 7.90(dd, J = 8Hz, 2Hz, 1H, Ar H); Anal. calcd. for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.88; H, 6.43; N, 5.82

2-(*o*-Methylphenyl)2, 3-dihydro-4(1H)-quinolone(16h): yield 66%, light yellow solid; mp 139 °C(benzene-petroleum ether); IR(KBr): υ_{max} 3320, 3300, 1650, 1600, 1510, 1480 cm^{-1}; UV(EtOH): λ_{max} 377.4nm(logε = 3.66), 258.8nm(logε = 3.95), 235.2nm (logε = 4.46): ^{1} H NMR($CDCl_3$, 100 MHz): δ 2.36(s,3H, $ArCH_3$), 2.60-3.04(m, 2H, C-3 $H_a$and H_b), 4.40(bs, 1H, NH), 5.04(dd, J = 10 Hz, 8 Hz, 1H, C-2 H), 6.64-6.94(m, 2H, Ar H), 7.18-7.48(m, 4H, Ar H), 7.56-7.78(m, 1H, Ar H), 7.88(dd, J = 8 Hz, 2Hz, Ar H); Anal. Calcd. for $C_{16}H_{15}$ NO:C, 80.98; H, 6.37; N, 5.90. Found: C, 80.86; H, 6.30; N, 5.87

2-(*p*-Methoxyphenyl)-2, 3-dihydro-4(1H)quinolone (16i): yield 72%; light yellow solid; mp 135 °C (benzene-petroleum ether); IR (KBr): υ_{max} 3340, 1660, 1610, 1510, 1480 cm^{-1}; UV (EtOH) λ_{max} 378.4 nm (logε = 3.43), 267.4 nm (logε = 3.88), 233.2 nm (logε = 4.42); ^{1}H NMR ($CDCl_3$, 100 MHz) δ 2.57-2.90 (m, 2H, C-3 H_a and H_b), 3.82 (s, 3H, $ArOCH_3$), 4.46 (bs, 1H, NH), 4.72 (dd, J = 16 Hz, 6 Hz, 1H, C-2 H), 6.64-7.04 (m, 3H, Ar H), 7.20-7.52 (m, 2H, Ar H), 7.90 (dd, J = 8 Hz, 2 Hz, 1H, Ar H).; Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.77; H, 6.01; N, 5.44.

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