Aromatic Annelation by Reaction of Arylimidoyl Radicals with Alkynes: Evidence for the Intervention of a Spirocyclohexadienyl Radical in the Synthesis of Substituted Quinolines

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Arylimidoyl radicals, generated by hydrogen abstraction from *N*-arylideneanilines with di-isopropyl peroxydicarbonate, react with alkynes to give quinolines in good yields. The reaction also involves an intermediate spirocyclohexadienyl radical; the proposed mechanism is discussed.

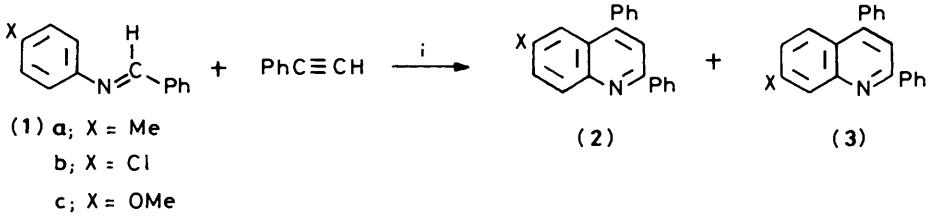
We have recently reported *N*-arylideneanilines react with monosubstituted acetylenes in the presence of di-isopropyl peroxydicarbonate (DPDC) to afford 2,4-disubstituted quinolines in high yields.[1] A similar reaction with *N*-benzylidene-4-X-anilines (**1**) and phenylacetylene gave a mixture of 2,4-diphenyl-6-X-(**2**) and 2,4-diphenyl-7-X-quinoline (**3**) (Scheme 1). The formation of the quinoline (**3**) is somewhat unexpected since the substituent X is not found in the position expected for an intramolecular homolytic substitution by the vinyl radical formed by addition of imidoyl radicals to the phenylacetylene.

Similar results are obtained with *N*-benzylidene-3-methoxy- (**4**) and *N*-(benzylidene-2-methoxy-aniline (**5**): the latter affords 2,4-diphenyl-5-methoxy- (**6**) and 2,4-diphenyl-8-methoxy-quinoline (**7**), whilst compound (**4**) gives four different products, *i.e.* (**6**), (**2c**), (**3c**), and (**7**) (Scheme 2).

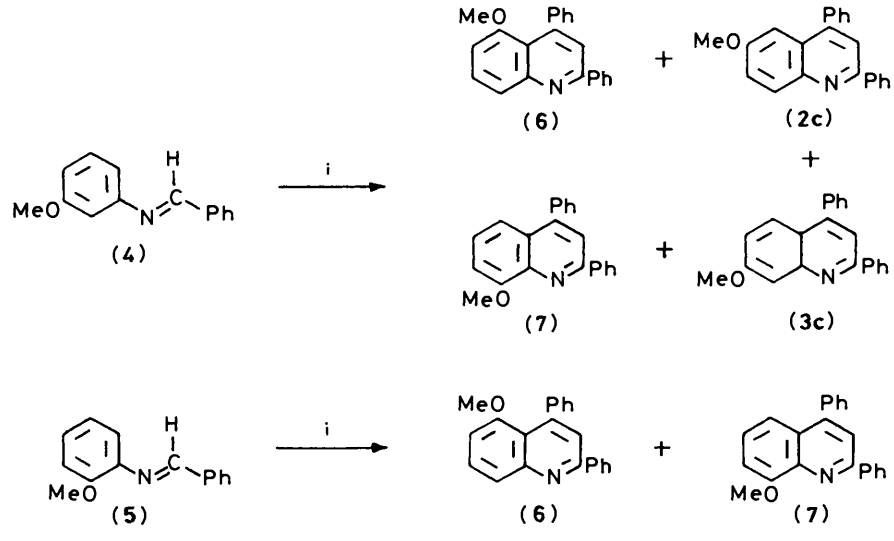
The experimental results can be explained by assuming initial formation of the imidoyl radical (**8**) which generates the vinyl radical (**9**) by addition to the unsubstituted carbon of phenylacetylene. Radical (**9**) may follow two routes giving either (**2**) by an intramolecular homolytic aromatic substitution on the phenyl ring linked to the iminic nitrogen (path a), or (**3**) through an *ipso* cyclization followed by a rearrangement *via* cleavage of the C–N bond of the intermediate spirocyclohexadienyl radical (**10**) (path b, Scheme 3). A similar mechanism also explains the products obtained from the imines (**4**) and (**5**).

Results for the reaction of compound (**1**) (see Table) show that the quinolines (**3**) are always formed in greater amounts than the quinolines (**2**). When the statistical factor has been taken into account, it can be inferred that at 60 °C path b is more important than path a.

The intervention of spirocyclohexadienyl radicals in several intramolecular homolytic aromatic substitutions and gener-



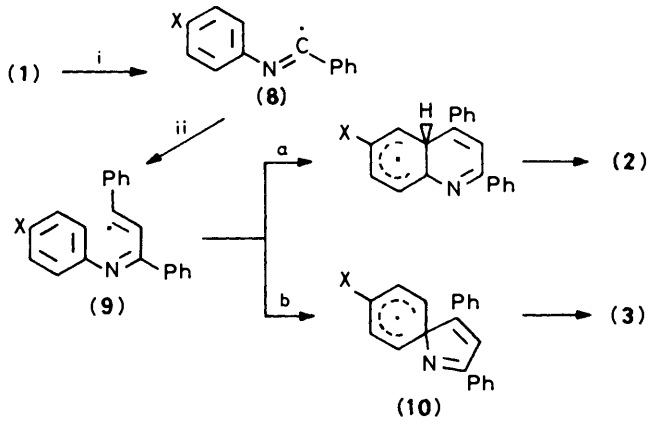
Scheme 1. *Reagents:* i, DPDC, benzene, 60 °C.



Scheme 2. *Reagents:* i, DPDC, PhC≡CH, benzene, 60 °C.

Table. 2,4-Diphenyl-6- (**2**) and 2,4-diphenyl-7-X-quinolines (**3**) obtained from compounds (**1a—c**)

Starting imine	Quinolines obtained (% yield)	
(**1a**)	(**2a**)	(**3a**)
	(22)	(53)
(**1b**)	(**2b**)	(**3b**)
	(17)	(58)
(**1c**)	(**2c**)	(**3c**)
	(35)	(44)

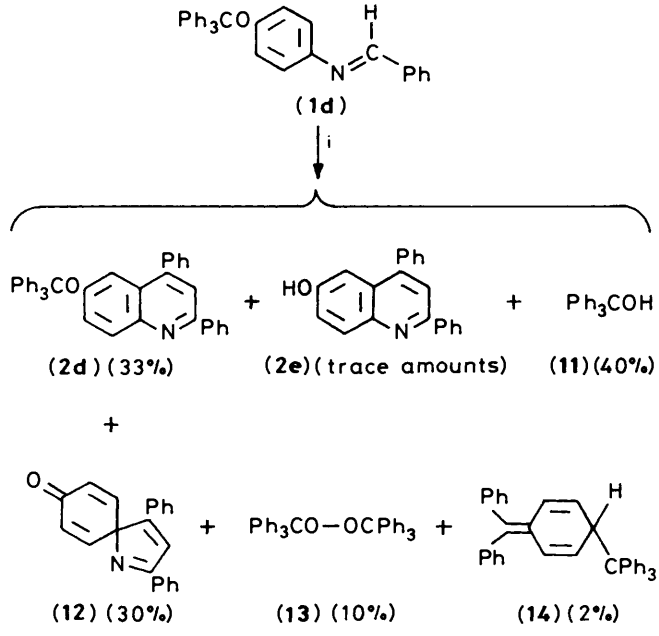


Scheme 3. *Reagents:* i, DPDC, benzene; ii, PhC≡CH.

ation of the implementary iminyl to the vinyl radical (**9**) has been previously described.[2]

The mechanism proposed in Scheme 3 is supported by the following experiment: allowing the imine (**1d**) to react with phenylacetylene and DPDC in benzene at 60 °C under a nitrogen atmosphere, gives the quinoline (**2d**), trace amounts of (**2e**), triphenylmethanol (**11**), the spirodienone (**12**), ditriphenylmethyl peroxide (**13**), and 1,1-diphenylmethylene-4-triphenylmethylcyclohexa-2,5-diene (**14**) (Scheme 4).

Compound (**12**) has been identified by means of spectroscopic methods as follows. ^{1}H N.m.r.: AA′BB′ system detected at



Scheme 4. *Reagents:* i, DPDC, PhC≡CH, benzene, 60 °C, N_2.

δ($CDCl_3$) 6.15—6.65, due to four cyclohexadienyl protons; ^{13}C N.m.r.: one sp^3 carbon detected at δ($CDCl_3$) 80.4; i.r. spectrum: CO stretching at 1 670 cm^{-1} typical for α,β-unsaturated ketones; mass spectrum: molecular ion detected at *m/z* 297 and a fragment ion at *m/z* 269 corresponding to the loss of carbon monoxide, typical for quinonic carbonyl compounds. In the reaction of (**1d**), the formation of the spirodienone (**12**), which was not obtained with the imine (**1c**), can be rationalized on a thermodynamic basis in terms of the lower dissociation energy of the Ph_3C–O bond with respect to the Me–O bond, which renders the elimination of the trityl radical from (**10**) competitive with the C–N bond cleavage. Further points worthy of comment in respect of the reaction shown in Scheme 4 are as follows: (i) the presence in the reaction mixture of (**2d**) together with the absence of the quinoline (**3d**; X = $OCPh_3$) suggests that the quinolines (**2**) directly originate from 6-membered ring cyclization of the vinyl radical (**9**) and that the quinolines (**3**) are formed through the intermediacy of the spirocyclohexadienyl radical (**10**); (ii) the presence of (**13**) and (**14**) indicates that the reaction process leading to the spirodienone (**12**) is a homolytic one; (iii) the 5-membered ring-opening in radical (**10**) occurs exclusively by cleavage of the C–N bond. The latter conclusion arises from the results of the reaction of (**12**) with tributyltin hydride and α,α′-azoisobutyronitrile (1 : 1 : 1 by mol) in boiling benzene, which affords almost quantitatively 7-hydroxy-2,4-diphenylquinoline (**3e**; X = OH); no detectable amounts of quinoline (**2e**), indicative of C–C bond cleavage, were observed.

The formation of triphenylmethanol (**11**) cannot be easily rationalized; it seems that (**11**) may partially arise by hydrolysis on a silica gel column of (**2d**) which also gives the hydroxyquinoline (**2e**).

The quantitative formation of (**3e**) observed in the reaction of (**12**) with tributyltin hydride suggests that the rearrangement of (**10**) might be a synchronous process or, if an intermediate iminyl radical is involved, ring closure is much faster than hydrogen abstraction from the tributyltin hydride by iminyl. No iminyl radicals were detected by photolytically reacting hexabutylditin with (**12**) inside the cavity of an e.s.r. spectrometer in the temperature range from −60 to 25 °C.

Experimental

All m.p.s are uncorrected. Column chromatography was performed on silica gel (Kieselgel 60, 70—230 mesh ASTM, Merck) or aluminium oxide (Aluminiumoxid 90, 70—230 mesh ASTM, Merck).

^{1}H N.m.r. spectra were recorded on a Varian EM 360L instrument, using tetramethylsilane as an internal standard. ^{13}C N.m.r. and i.r. spectra were recorded on a Varian XL100 and on a Perkin-Elmer 257 instrument, respectively.

Mass spectra were performed with a JEOL JMS-D100 spectrometer at an ionization energy of 70 eV. Di-isopropyl peroxydicarbonate (DPDC),[3] *N*-benzylidene-*o*-anisidine,[4] *N*-benzylidene-*m*-anisidine,[5] *N*-benzylidene-*p*-anisidine,[6] *N*-benzylidene-4-chloroaniline,[7] *N*-benzylidene-*p*-toluidine,[8] *N*-benzylidene-4-aminophenol,[9] 1,3,3-triphenylprop-2-en-1-one[10] were prepared according to the literature. The reaction products were identified by mixed m.p. determination and spectral data comparison with authentic specimens.

N-Benzylidene-4-trityloxyaniline (**1d**).—Following the procedure described by Zimmerman[11] for the synthesis of aryl trityl ethers, to *N*-benzylidene-4-hydroxyaniline (9.85 g, 50 mmol) an equimolar amount of sodium ethoxide in ethanol was added. The solvent was removed under reduced pressure and the residue was refluxed in benzene (50 ml) with trityl chloride (13.92 g, 50 mmol) for 1 h. Benzene was evaporated off and the

residue recrystallized from light petroleum (b.p. 70—120 °C) to give the title imine (**1d**) (17.6 g, 80% yield), m.p. 144—146 °C; $\delta_H(CDCl_3)$ 6.59—6.99 (4 H, AA'BB', ArH), 7.00—8.00 (20 H, m, ArH), and 8.33 (1 H, s, olefinic H); *m/z* 439 (M^+, 0.2), 243(100), 197(20), 196(18), and 165(37) (Found: C, 87.20; H, 5.71; N, 3.15. $C_{32}H_{25}NO$ requires C, 87.44; H, 5.73; N, 3.19%).

General Procedure for the Reaction of N-*Benzylideneanilines with Phenylacetylene and DPDC.*—To a solution of *N*-benzylideneaniline (5 mmol) in benzene (20 ml), phenylacetylene (15 mmol) and DPDC (10 mmol) were added and the mixture was kept at 60 °C until the peroxide was completely decomposed (*ca.* 5 h). The disappearance of the peroxide during the reaction was followed by titrating the solution as described in the literature.[12] The solvent was then removed under reduced pressure and the residue chromatographed on silica gel or aluminium oxide (100 g); the products were isolated in the reported yields using light petroleum (b.p. 40—70 °C)–diethyl ether gradient as eluant. Usually the products were recrystallized from light petroleum (b.p. 70—120 °C).

Reaction of N-*Benzylidene*-p-*anisidine* (**1c**) *with Phenylacetylene and DPDC.*—Using the procedure described above, the residue was chromatographed on silica gel; elution with light petroleum–diethyl ether (99.5:0.5 v/v) gave 6-methoxy-2,4-diphenylquinoline (**2c**) (0.55 g, 35%), m.p. 119—121 °C (lit.,[13] m.p. 121—122 °C) and 7-methoxy-2,4-diphenylquinoline (**3c**) (0.69 g, 44%), m.p. 98—100 °C (lit.,[14] m.p. 102 °C).

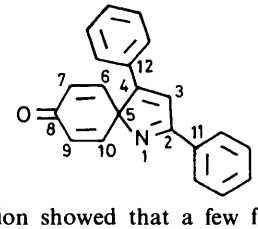
Reaction of N-*Benzylidene*-m-*anisidine* (**4**) *with Phenylacetylene and DPDC.*—Following the procedure previously described, the residue was chromatographed on silica gel; elution with light petroleum–diethyl ether (99.7:0.3, v/v) furnished 5-methoxy-2,4-diphenylquinoline[13] (**6**) (0.15 g, 10%), m.p. 84—85 °C; $\delta_H(CCl_4)$ 3.42 (3 H, s, OMe), 6.50—6.70 (1 H, m, ArH), 7.00—7.85 (11 H, m, ArH), and 8.00—8.33 (2 H, m, ArH); *m/z* 311 (M^+, 100), 310(14), 296(37), 282(5), 281(15), and 280(25) (Found: C, 84.7; H, 5.45; N, 4.45. $C_{22}H_{17}NO$ requires C, 84.86; H, 5.50; N, 4.50%); 6-methoxy-2,4-diphenylquinoline (**2c**) (0.61 g, 39%), m.p. 119—121 (lit.,[13] m.p. 121—122 °C); 7-methoxy-2,4-diphenylquinoline[14] (**3c**) (0.30 g, 19%), m.p. 100—101 °C (lit.,[14] m.p. 102 °C) and 8-methoxy-2,4-diphenylquinoline (**7**) (0.12 g, 8%), m.p. 122—124 °C, $\delta_H(CDCl_3)$ 4.07 (3 H, s, OMe) 6.65—7.65 (11 H, m, ArH), 7.70—7.80 (1 H, s, ArH), and 8.00—8.30 (2 H, m, ArH); *m/z* 311 (M^+, 100), 310(98), 296(2), 282(52), 281(34), and 280(27); (Found: C, 84.58; H, 5.60; N, 4.52. $C_{22}H_{17}NO$ requires C, 84.86; H, 5.50; N, 4.50%).

Reaction of N-*Benzylidene*-o-*anisidine* (**5**) *with Phenylacetylene and DPDC.*—Following the procedure previously described, the residue chromatographed on silica gel and eluted with light petroleum–diethyl ether (99.8:0.2, v/v) afforded 5-methoxy-2,4-diphenylquinoline[13] (**6**) (0.49 g, 32%), m.p. 84—85 °C (lit.,[13] m.p. not reported) and 8-methoxy-2,4-diphenylquinoline (**7**) (0.52 g, 33%), m.p. 121—123 °C.

Reaction of N-*Benzylidene*-p-*toluidine* (**1a**) *with Phenylacetylene and DPDC.*—Using the procedure described above, the residue was chromatographed on aluminium oxide; elution with light petroleum–diethyl ether (95:5, v/v) gave 7-methyl-2,4-diphenylquinoline (**3a**) (0.83 g, 53%), m.p. 71—73 °C (lit.,[13] m.p. not reported) $\delta_H(CCl_4)$ 2.53 (3 H, s, Me), and 7.00—8.43 (14 H, m, ArH); *m/z* 295 (M^+, 100), 294(82), and 280(37) (Found: C, 89.65; H, 5.75; N, 4.65. $C_{22}H_{17}N$ requires C, 89.45; H, 5.80; N, 4.75%) and 6-methyl-2,4-diphenylquinoline[13] (**2a**) (0.34 g, 22%), m.p. 129—131 °C (lit.,[13] m.p. 130—131 °C).

Reaction of N-*Benzylidene*-4-*chloroaniline* (**1b**) *with Phenylacetylene and DPDC.*—Following the procedure previously described, the residue chromatographed on silica gel and eluted with light petroleum–diethyl ether (97:3, v/v) afforded 7-chloro-2,4-diphenylquinoline (**3b**) (0.91 g, 58%), m.p. 94—95 °C; $\delta_H(CDCl_3)$ 7.10—7.90 (12 H, m, ArH) and 8.00—8.30 (2 H, m, ArH); *m/z* 317 (M^+ + 2, 35), 315 (M^+, 100), 314(90), and 280(30) (Found: C, 79.65; H, 4.4; Cl, 11.3; N, 4.6. $C_{21}H_{14}ClN$ requires C, 79.87; H, 4.47; Cl, 11.23; N, 4.43%) and 6-chloro-2,4-diphenylquinoline (**2b**) (0.27 g, 17%), m.p. 127—129 °C (lit.,[15] m.p. 130—131 °C).

Reaction of N-*Benzylidene*-4-*trityloxylaniline* (**1d**) *with Phenylacetylene and DPDC.*—Using the procedure described above under a nitrogen atmosphere, the residue was chromatographed on silica gel and eluted with light petroleum–diethyl ether (90:10, v/v) to give 1,1-diphenylmethylene-4-triphenylmethylcyclohexa-2,5-diene[16] (**14**) (0.05 g, 2%); $\delta_H(CDCl_3)$ 4.65 (1 H, s, aliphatic H), 5.86—6.28 (4 H, AA'BB', olefinic H), and 7.05—7.51 (25 H, m, ArH); *m/z* 486 (M^+, 0.1), 243(100), 165(45), and 77(20); 2,4-diphenyl-6-trityloxyquinoline (**2d**) (0.72 g, 33%), m.p. 170—178 °C, $\delta_H(CDCl_3)$ 6.75—7.70 (27 H, m, ArH), 7.85—8.15 (2 H, m, ArH); *m/z* 539 (M^+, 2), 462(6), 297(20), 243(100), and 165(32) (Found: C, 88.4; H, 5.45; N, 2.55. $C_{40}H_{29}NO$ requires C, 89.02; H, 5.42; N, 2.6%); and triphenylmethanol (**11**) (0.5 g, 40%), m.p. 159—161 °C (lit.,[17] m.p. 158—160 °C). Elution with light petroleum–diethyl ether (80:20, v/v) gave trace amounts of 6-hydroxy-2,4-diphenylquinoline (**2e**), m.p. 222—223 °C (from ethanol) (lit.,[18] m.p. not reported). Further elution with light petroleum–diethyl ether (60:40, v/v) afforded 3',5'-diphenylcyclohexa-2,5-dienespiro-2'-(2'H-pyrrol)-4-one (**12**) (0.4 g, 30%), m.p. 179—180 °C; $\delta_H(CDCl_3)$ 6.15—6.65 (4 H, AA'BB', olefinic H), 7.10—7.78 (9 H, m, ArH), and 7.80—8.25 (2 H, m, ArH); $\nu_{max.}(CHCl_3)$ 1 670 cm^{-1} (CO stretch); *m/z* 297 (M^+, 45), 296(12), 269(100), and 268(15); $\delta_C(CDCl_3)$ (see displayed formula) 185.6 (C-8), 176.2 (C-2), 165.1 (C-4), 145.4 (C-7, C-9), 132.6 and 131.3 (C-11 and C-12), 131.5 (C-3), 131.0 (C-6, C-10), 129.9 (1C, Ph-C), 128.8 (4C, Ph-C), 127.9 (2C, Ph-C), 126.4 (2C, Ph-C), 125.4 (1C, Ph-C), 80.4 (C-5) (Found: C, 84.3; H, 5.1; N, 4.65. $C_{21}H_{15}NO$ requires C, 84.82; H, 5.09; N, 4.71%).



T.l.c. investigation showed that a few fractions contained bistriphenylmethyl peroxide as well. These fractions were therefore rechromatographed on silica gel; elution with carbon disulphide gave bistriphenylmethyl peroxide (**13**) (0.26 g, 10%), m.p. 184—185 °C (from benzene) (lit.,[19] m.p. 185—186 °C).

Reaction of the Spirocyclohexadienepyrrolone (**12**) *with Tributyltin Hydride and α,α'-Azoisobutyronitrile.*—The spirodienone (0.6 g, 2 mmol), tributyltin hydride (0.6 g, 2 mmol) and α,α'-azoisobutyronitrile (0.33 g, 2 mmol) were refluxed in benzene (30 ml) for 4 h after which the solvent was removed under reduced pressure. The residue was chromatographed on silica gel and eluted with light petroleum–diethyl ether (70:30, v/v) to give 7-hydroxy-2,4-diphenylquinoline (**3e**; X = OH) (0.46 g, 78%), m.p. 273—274 °C (from ethanol) (lit.,[20] m.p. 273 °C).

Acknowledgements

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