Pergamon

Tetrahedron Vol. 51, No. 33, pp. 9045-9062, 1995
Copyright © 1995 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4020/95 $9.50+0.00

0040-4020(95)00348-7

Radical Annulations and Cyclisations with Isonitriles: the Fate of the Intermediate Imidoyl and Cyclohexadienyl Radicals

Daniele Nanni,[†]* Patrizia Pareschi,[†] Corrado Rizzoli,[‡] Paolo Sgarabotto,[‡] and Antonio Tundo[†]

[†]*Dipartimento di Chimica Organica "A. Mangini", Università di Bologna, Viale Risorgimento 4, I-40136 Bologna, Italy.*

[‡]*Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica,*
Centro di Studio per la Strutturistica Diffrattometrica del C.N.R., Università di Parma, I-43100 Parma, Italy.

Abstract. The reaction of 4-methoxyphenylisonitrile with phenylacetylene and AIBN produces a novel cyclopenta-fused quinoxaline through addition of 2-cyanoprop-2-yl radical to the alkyne; the resulting vinyl radical attacks isonitrile to afford an imidoyl radical, which gives rise to a tandem 5-exo, 6-endo cyclisation. The whole process entails a new example of a rare 4 + 1 radical annulation. The cyanopropyl radical can also attack isonitrile to yield small amounts of quinolines deriving from 4 + 2 and 3 + 2 annulation between the resulting imidoyl radicals and phenylacetylene. The oxidation step leading to the final aromatic products involves the starting isonitrile, which is converted to an α-unsubstituted imidoyl radical and affords 2-unsubstituted quinolines. This behaviour was also found in cyclisations of biphenyl-2-ylisonitrile under various radical conditions. Finally, the title reaction gives small amounts of an α,β-unsaturated nitrile, which can arise from a spirocyclohexadienyl radical through fragmentation and subsequent β-scission of the resulting iminyl. This could be the first, direct evidence of the intermediacy of iminyl radicals in the rearrangements of the spirocyclohexadienyls obtained by 3 + 2 annulation between imidoyl radicals and alkynes.

INTRODUCTION

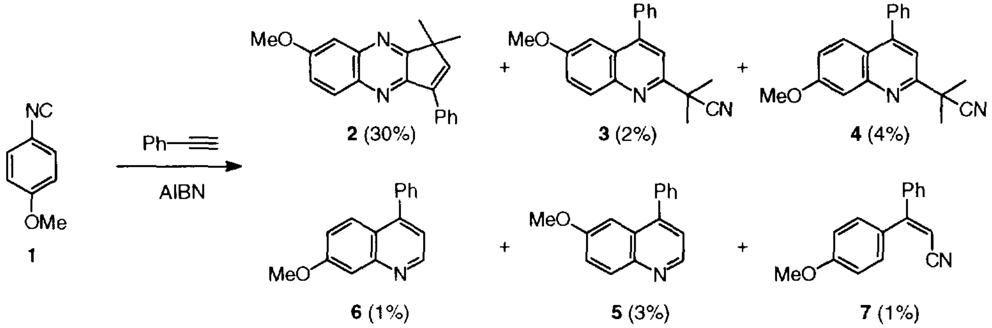
During the last decades imidoyl radicals, generated by abstraction of the aldehydic hydrogen of aldimines[1] or addition of alkyl, alkoxy, thiyl, or silyl radicals to isonitriles,[2] have been studied from a spectroscopic point of view. The reactivity of these intermediates has been also investigated and many examples of fragmentation reactions[3] and intra-[4] or intermolecular[5] additions to unsaturated bonds have been reported, as well as cyclisations onto an aromatic ring[6] or a sulfur atom.[7]

The efficient construction of heterocyclic rings has been accomplished through 4 + 2 annulations involving imidoyl radicals and carbon-carbon[8] or nitrogen-nitrogen[9] multiple bonds; with alkynes,[8b] a 3 + 2 annulation has been also observed, followed by rearrangement of the 5-exo-ring-closure spiranic intermediate. Recently, a new synthesis of cyclopenta-fused quinolines has been reported:[10] in that paper imidoyl radicals have been generated by homolytic addition to isonitriles and the reaction is the first example of a 4 + 1 radical annulation.

We aimed at investigating the behaviour of the imidoyl radicals generated by addition to isonitriles and here we report the reaction between 4-methoxyphenylisonitrile, phenylacetylene, and azo-bis-*iso*-butyronitrile (AIBN), which affords a new cyclopenta-fused quinoxaline derivative as the major product. From this reaction we also got some more insight into the rearrangement of the spiranic 5-membered radical intermediates and the mechanism of oxidation of the cyclohexadienyl radicals precursors of the final aromatic products.

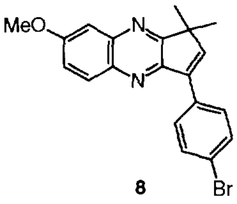
RESULTS AND DISCUSSION

4-Methoxyphenylisonitrile (**1**) was obtained by a literature method[11] and allowed to react (5 mmol) with AIBN (6 mmol) and phenylacetylene (15 mmol) in a refluxing benzene solution to give the products reported in Scheme 1.



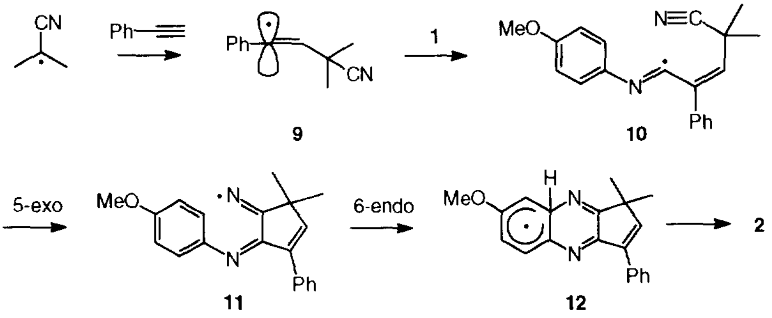
Scheme 1. Reaction of isonitrile **1** with AIBN and phenylacetylene.

The reaction products **3**, **4**, **5**, **6**, and **7** were identified by mixed mp determination and spectral comparison with authentic specimens prepared by literature procedures — when reported — or independent syntheses — for new compounds. To be undoubtedly sure of the major product **2**, particularly the positions of the methoxy- and phenyl substituents, we tried to determine the molecular structure by X-ray crystallography. Unfortunately, attempts to obtain crystals suitable for X-ray analysis were unsuccessful. Therefore, we allowed isonitrile **1** to react under the same conditions with 4-bromophenylacetylene; this reaction afforded, among the other products, quinoxaline **8**, which was recrystallised from ethyl acetate to give crystals fit for structural determination. Taking into account the analogies between MS, ^{1}H NMR, and ^{13}C NMR spectral data of **2** and **8**, the X-ray analysis of **8** confirmed the structural assignments for both derivatives (see X-ray Crystallography Section).



8

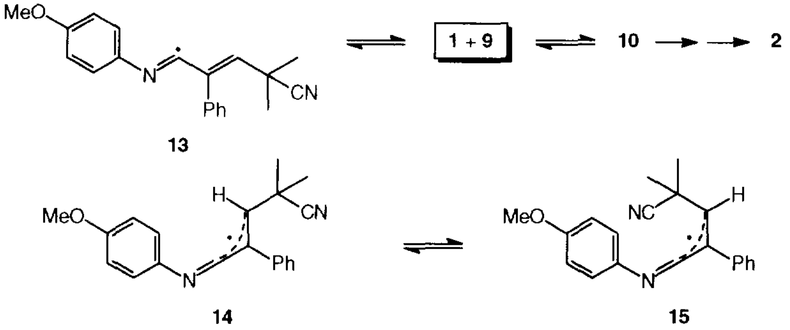
Compound **2**, a novel cyclopenta-fused quinoxaline, was rationalised by assuming addition of the 2-cyanoprop-2-yl radical derived from decomposition of AIBN to phenylacetylene; the resulting vinyl radical **9** can attack the carbon atom of isonitrile **1** giving the imidoyl radical **10**. Tandem 5-exo, 6-endo cyclisation of **10**, through the intermediacy of iminyl radical **11**, and aromatisation of cyclohexadienyl **12** lead to quinoxaline **2** (Scheme 2).



Scheme 2. Mechanism of formation of quinoxaline **2**.

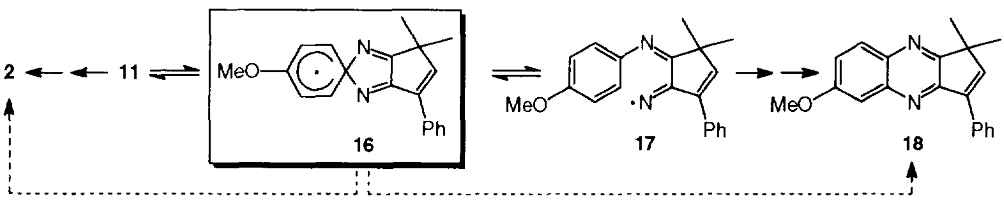
Unexpectedly, we did not find in the literature any kinetic data concerning the addition of the 2-cyanoprop-2-yl radical to phenylacetylene. This notwithstanding, the formation of **9** should be a very feasible process, considering that AIBN has been used as an initiator in the polymerisation of phenylacetylene.[12]

The intermediate **9** is an α-phenyl-substituted vinyl radical, which should have a π-electronic configuration and a linear structure at C_α, in agreement with the characteristics of other styryl radicals.[13] For these species the approach of a scavenger is governed by the steric hindrance of the scavenger itself with the β-substituent, and the approach becomes highly stereoselective with bulky substituents, *e.g.* a *tert*-butyl group.[14] Therefore, in our case radical **9** should attack isonitrile **1** to give radical **13**, kinetically (Scheme 3). As one can see, the intermediate **13** has not the geometry suitable for cyclisation. Hence, to explain the formation of **2** in fair yields we must postulate a mechanism entailing the equilibration between **13** and **10**. First, we might suppose that the addition step to the isonitrile is reversible: in this case, **1** and **9** could be in equilibrium with both the kinetic intermediate **13** and the geometric isomer **10**. Independently of the relative quantities of **13** and **10**, the subsequent cyclisation reactions of **10** should shift the equilibrium towards the formation of quinoxaline **2**.[15] Alternatively, we cannot rule out the possibility that **13** and **10** could interconverte through resonance effects (**14** $\rightleftharpoons$ **15**) without direct intermediacy of **1** and **9**.[16] The absence in the literature of fragmentations providing vinyl radicals suggests that the first possibility could be discarded. It is by no means clear which is the real cyclisation pathway, and further studies are needed to obtain a better understanding of the factors that control the 5-membered ring closure.



Scheme 3. Interconversion pathways for imidoyl radicals.

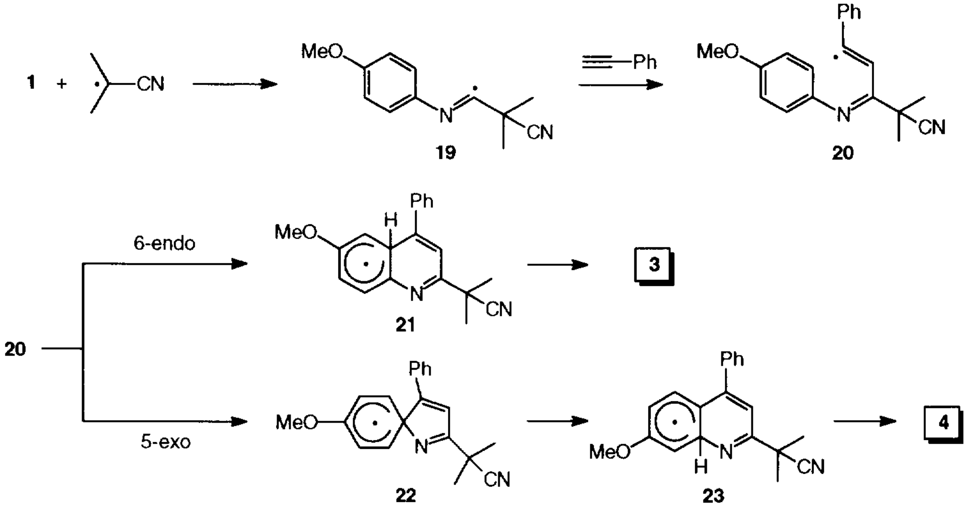
The intramolecular radical addition to the carbon atom of a cyano group is well documented[17] and, in the present case, 5-exo cyclisation of intermediate **10** should be also favored by the nucleophilic character of the imidoyl radicals.[8c] The subsequent 6-endo ring closure entails a homolytic aromatic substitution by iminyl **11**, a well-precedented process.[18] Under FVP (Flash Vacuum Pyrolysis) conditions, iminyls are known to give rise to both 6- and 5-membered cyclisation onto an aromatic ring,[18d-g] affording isomeric products derived also from rearrangement of a spirocyclohexadienyl radical. In our reaction this possibility should be ruled out completely. Indeed, iminyl **11** should afford the spiranic radical **16**, which is very likely to rearrange through fragmentation of either the carbon-nitrogen bonds, also giving the isomeric iminyl **17** and quinoxaline **18**, ultimately (Scheme 4).



Scheme 4. Rearrangement pathways for spirocyclohexadienyl **16**.

Chromatographic, spectroscopic, and crystallographic data indicate that the reaction yielded a single quinoxaline (**2**) and this let us conclude that **2** is not formed by rearrangement of **16**, but through direct 6-endo cyclisation of **11**. It is worth pointing out that this reaction allows simultaneous construction of a cyclopentene- and a pirazine ring, and the 5-membered-ring formation is a novel, rare example of 4 + 1 radical annulation.[19]

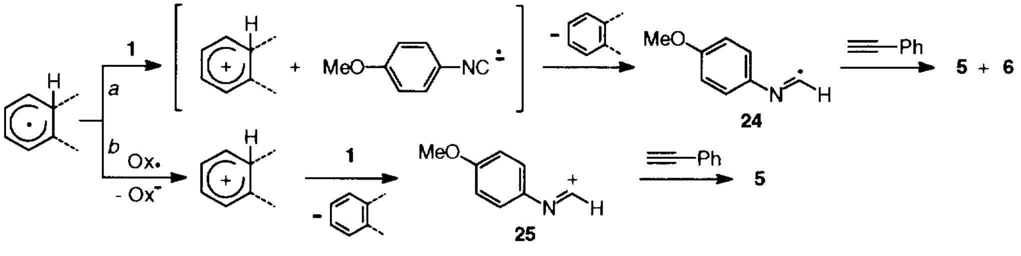
As far as the other reaction products are concerned, quinolines **3** and **4** can arise from the mechanism shown in Scheme 5.



Scheme 5. Mechanism of formation of quinolines **3** and **4**.

The 2-cyanoprop-2-yl radical adds to the carbon atom of isonitrile **1** to give the imidoyl **19** and, after addition to phenylacetylene, vinyl radical **20**; competitive 6-endo and 5-exo ring closure of **20** onto the benzenic ring afford cyclohexadienyls **21** and **22**, respectively. Aromatisation of **21** leads to quinoline **3**, whereas rearrangement of the spiranic radical **22** — through migration of the carbon-nitrogen bond — can give cyclohexadienyl **23** and then the isomeric quinoline **4**. A quite similar mechanism has been undoubtedly demonstrated in the annulations involving phenylacetylene and α-phenyl-substituted imidoyl radicals.[8b]

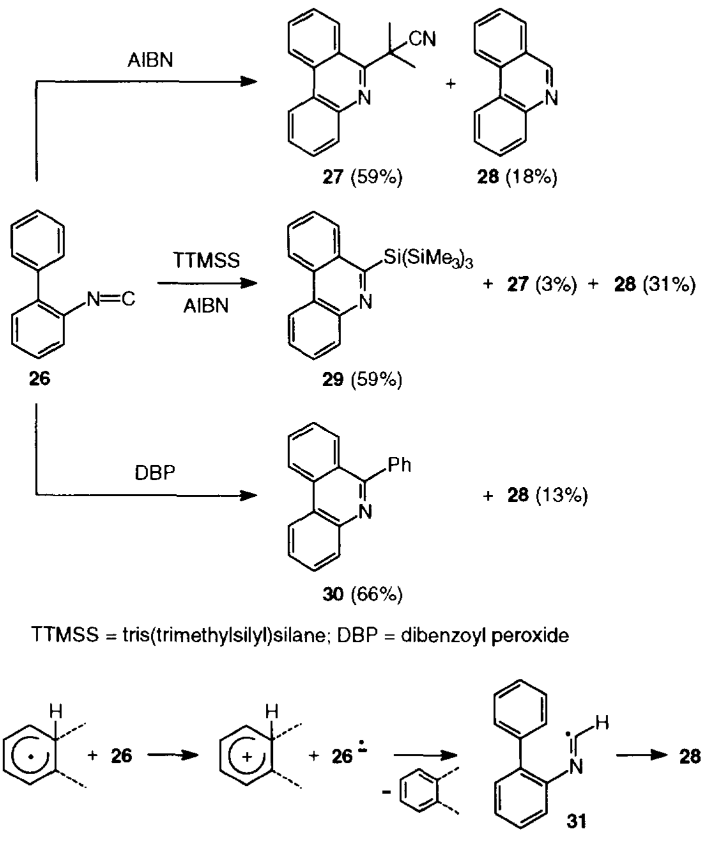
The formation of the 2-unsubstituted quinolines **5** and **6** is rather puzzling, as we cannot conceive any reasonable mechanism — leading to **5** and **6** — that could involve the radical intermediates considered up to this point. A simple reaction of **1** with phenylacetylene must be excluded, for a refluxing benzene solution of these two compounds is stable for many hours in the absence of a radical initiator. Therefore, on the analogy with the mechanism shown in Scheme 5, we suggest that **5** and **6** arise from a radical annulation involving phenylacetylene and the α-unsubstituted imidoyl radical **24** (Scheme 6); formation of **24** might entail an electron-transfer (ET) mechanism in which isonitrile **1** behaves like an aromatising agent of the various cyclohexadienyl radicals that are formed in the course of the reaction.



Scheme 6. Isonitrile-mediated aromatisation of cyclohexadienyl radicals.

The ET reaction of a cyclohexadienyl radical with **1** could afford the corresponding cyclohexadienyl cation and the radical anion of the isonitrile (path *a*). Proton transfer between these ions leads to the aromatic compound and the imidoyl radical **24**, which can then react with the alkyne to give quinolines **5** and **6** according to a mechanism identical to that shown in Scheme 5. We cannot also rule out the possibility that the ET step might be skipped: the isonitrile can direclty abstract a hydrogen from the cyclohexadienyl radical through a mechanism that is the disproportion analog of a radical-radical reaction. In an alternative route, the cyclohexadienyl cation might be generated from the corresponding radical by another oxidative agent, *e.g.* DPDC; isonitrile **1** could then behave like a Brønsted-base, affording imidoyl cation **25** (path *b*). Nevertheless, this pathway should be rejected or, at the most, should be only competitive with route *a*, because the formation of two unsubstituted quinolines (**5** and **6**) clearly indicates the intermediacy of an imidoyl radical.[20]

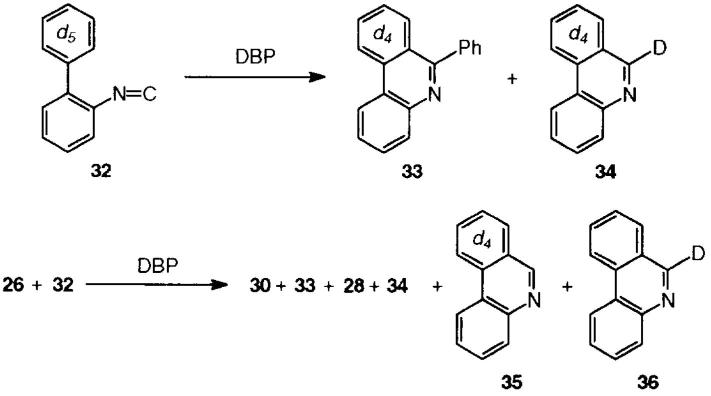
An analogous behaviour was observed in the cyclisations of biphenyl-2-ylisonitrile (**26**) under various radical conditions (Scheme 7). In all of these reactions we found variable amounts of the unsubstituted phenanthridine **28**, arising from homolytic aromatic substitution of the imidoyl radical **31** through a mechanism similar to that described above.[21]



TTMSS = tris(trimethylsilyl)silane; DBP = dibenzoyl peroxide

Scheme 7. Reactions of biphenyl-2-ylisonitrile **26**.

Support to our explanation was obtained by adding to the reaction mixtures of **26** with AIBN variable amounts of oxidising agents, *viz.* quinones and mono-, di-, or trinitrobenzene. Under these conditions, phenanthridine **28** disappeared completely and the yield of **27** increased significantly, as a result of the non-intervention of isonitrile in the aromatisation of the cyclohexadienyls. Furthermore, when the deuterated isonitrile **32** was allowed to react with dibenzoyl peroxide, we obtained phenanthridines **33** and **34** (Scheme 8): this result clearly demonstrates that the hydrogen atom in the 6-position comes from the benzenic ring involved in the cyclisation process. Finally, the reaction of dibenzoyl peroxide with a 1:1 mixture of isonitriles **26** and **32** yielded, besides **30** and **33**, four deuterated phenanthridines, *viz*. **28**, **34**, **35**, and **36**. This let us conclude that the α-unsubstituted imidoyl radicals arise from an intermolecular hydrogen-abstraction reaction from cyclohexadienyls.



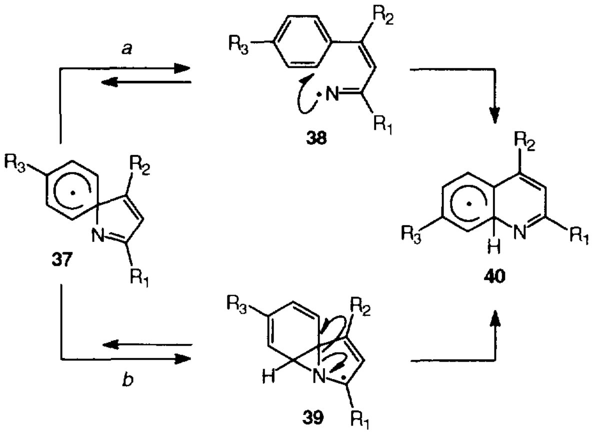
Scheme 8. Reactions of deuterated isonitrile **32**.

We would like to emphasise that this behaviour of isonitriles appears to be unprecedented. In addition, with the above discussion we got some more insight into the mechanism of formation of rearomatised products in radical additions to isonitriles. In these reactions the oxidant of the cyclohexadienyls is not immediately obvious and a definitive explanation of the aromatisation process has not been given yet.[10] Our proposed mechanism could in part give an answer for this problem, although other competitive reactions are of course very likely to take place. We would also remark that radical cyclisation of biphenyl-2-ylisonitrile seems to be a convenient synthetic method for 6-substituted phenanthridines.

On the light of the above discussion, the reaction of Scheme 1 was repeated in the presence of 1,3-dinitrobenzene: under these conditions, we observed complete disappearance of quinolines **5** and **6**. Attempts were also made to improve significantly the yield of quinoxaline **2**, and the best result was obtained by adding dropwise a solution of AIBN (3 mmol) to a refluxing benzene solution of **1** (1 mmol), phenylacetylene (3 mmol), and 1,3-dinitrobenzene (1 mmol). Under these conditions, the yields of by-products **3**, **4**, and **7** remained virtually unchanged (3%, 5%, and 4%, respectively), whereas the yield of **2** raised up to 50%. Therefore, we can conclude that the 4 + 1 radical annulation between isonitrile **1**, AIBN, and phenylacetylene is synthetically interesting, and studies on this general theme are still in progress, through an appropriate choice of isonitriles, alkynes (or alkenes), and radical initiators.

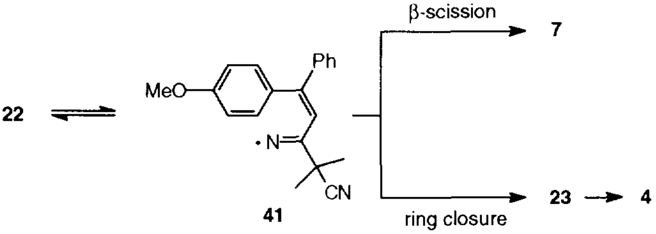
The product that has not been accounted for yet is nitrile **7**. Its low yield notwithstanding, **7** is an important compound, which could resolve a mechanistic problem connected with the rearrangement of **22**-like spirocyclohexadienyl radicals (Scheme 5).

We envisage at least two main pathways by which this isomerisation can occur (Scheme 9). The spiranic radical **37** may afford iminyl **38** through β-fragmentation and consequent ring opening (path *a*): **38** can then give 6-membered ring closure to cyclohexadienyl **40**. Alternatively, **37** undergoes 3-exo closure to **39**, which then rearranges to **40** by homolytic cleavage of the intraannular bond (path *b*).[22] Several experiments have demonstrated that the rearrangement of **37** occurs by migration of the carbon-nitrogen bond, exclusively, and the iminyl **38** is a viable intermediate in the formation of **40**.[8b, 10] Nevertheless, a decisive proof of the real isomerisation mechanism has not been given yet.



Scheme 9. Isomerisation pathways for spirocyclohexadienyl radical **37**.

If the iminyl radical **38** were involved in the rearrangement, we should expect to find products deriving from side-reactions of **38** competitive with ring closure. In particular, β-scission is a viable process for iminyls, especially when it entails opening of a strained ring or release of a stable radical.[23] In our case, the 2-cyanoprop-2-yl radical could be stable enough to allow β-fragmentation of **41** to occur significantly, giving, beside the rearranged quinoline **4**, nitrile **7** (Scheme 10).[24]



Scheme 10. Fate of iminyl radical **41**.

It is worth pointing out that nitrile **7** cannot arise from the alternative rearrangement pathway (Scheme 9, path *b*). Therefore, the finding of **7** is a new, unequivocal evidence of the intermediacy of iminyl radicals in ring enlargement of spirocyclohexadienyls **37**. Obviously, the formation of **7** does not exclude the occurrence of mechanism *b* as well. Studies are in progress to generate suitably-substituted iminyl radicals by an alternative route: the comparison between the cyclisation/fragmentation ratios obtained in the annulation reaction and straight from the corresponding iminyl should remove this last doubt.

X-ray Crystallography. As far as we are aware, this work represents the first example of an X-ray structural analysis of a compound in which a quinoline is condensed with a cyclopentane ring. Bond distances and angles are in line with the hybridisation expected for the atoms. From the study of the conformational geometry by torsion angles and from the analysis of the planarity results that all the single rings are planar in the experimental errors and also the whole molecule is planar, the dihedral angles they form being in the range 1.0-3.1°. So the presence of localised double bonds N(1)=C(2), N(4)=C(3), and C(12)=C(13) (see Table 3) can indicate a possible π-interaction of the p-orbitals of N(4) with that of N(1) and C(12) (Figure 1). Packing is consistent with van der Waals interactions.

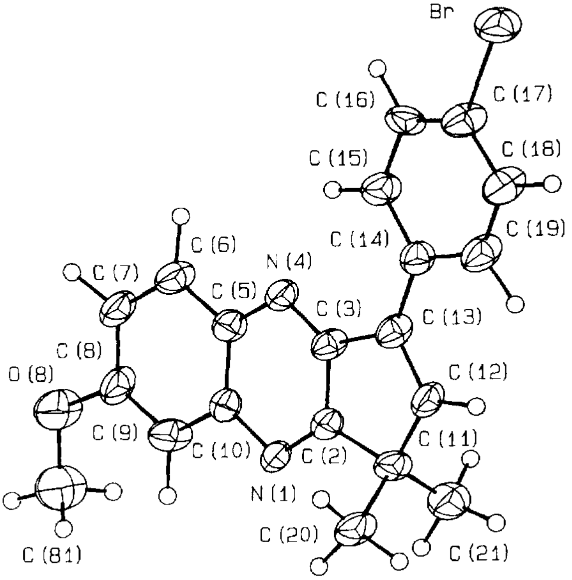


Figure 1. ORTEP plot of 3-(4-bromophenyl)-7-methoxy-1,1-dimethylcyclopenta[*b*]quinoxaline (**8**) with atom-numbering scheme. Thermal ellipsoids for non-H atoms enclose 48% probability.

Table 1. Experimental Data for the X-Ray Diffraction Study on Crystalline Compound **8**.

chemical formula	$C_{20}H_{17}BrN_2O$
a (Å)	10.137 (2)
b (Å)	6.874 (2)
c (Å)	12.603 (3)
α (deg)	90
β (deg)	104.2 (1)
γ (deg)	90
V (Å^3)	851.4 (5)
Z	2
fw	381.3
space group	$P\,2_1$ (no. 4)
t (°C)	21
λ (Å)	1.54178
ρ_{calcd} (g cm^{-3})	1.487
μ (cm^{-1})	33.49
R [a]	0.047
R_w [b]	0.048

---

[a] $R = \sum|\Delta F| / \sum|F_o|$ [b] $R_w = \sum w^{1/2}|\Delta F| / \sum w^{1/2}|F_o|$

Table 2. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters ($\times 10^4$ Å^2) for non - H Atoms with e.s.d.'s in Parentheses for Compound **8**.

$$\underline{U_{eq}} = 1/3\Sigma_i\Sigma_j\Sigma_{ij}a_i{}^*a_j{}^*(\mathbf{a}_i \cdot \mathbf{a}_j)$$

	$\underline{x}$	$\underline{y}$	$\underline{z}$	$\underline{U_{eq}}$
Br	8830 (1)	815 ( )	4541 (0)	627 (3)
O (8)	14221 (4)	780 (52)	14601 (3)	773 (24)
N (1)	9690 (4)	764 (38)	12265 (3)	409 (17)
N (4)	10874 (4)	872 (35)	10415 (3)	389 (18)
C (2)	8985 (5)	781 (43)	11261 (4)	392 (18)
C (3)	9557 (5)	836 (42)	10332 (4)	374 (17)
C (5)	11657 (5)	896 (41)	11472 (5)	373 (20)
C (6)	13090 (6)	917 (40)	11655 (5)	456 (32)
C (7)	13900 (5)	811 (50)	12703 (5)	522 (25)
C (8)	13315 (6)	948 (49)	13606 (5)	487 (29)
C (9)	11923 (5)	860 (46)	13461 (5)	460 (21)
C (10)	11078 (5)	789 (35)	12385 (4)	383 (19)
C (11)	7441 (5)	850 (44)	10900 (4)	419 (22)
C (12)	7256 (5)	815 (47)	9674 (4)	441 (19)
C (13)	8416 (5)	759 (45)	9337 (4)	398 (19)
C (14)	8536 (5)	732 (43)	8197 (4)	394 (20)
C (15)	9795 (5)	867 (36)	7920 (5)	452 (23)
C (16)	9892 (6)	952 (42)	6854 (5)	471 (27)
C (17)	8703 (6)	676 (52)	6022 (5)	464 (29)
C (18)	7451 (6)	830 (52)	6255 (5)	590 (25)
C (19)	7362 (5)	716 (59)	7323 (4)	539 (20)
C (20)	6858 (19)	-1032 (35)	11373 (16)	497 (59)
C (21)	6851 (21)	2636 (35)	11216 (18)	535 (52)
C (81)	13683 (8)	959 (63)	15557 (6)	926 (59)

Table 3. Selected Bond Distances (Å) and Angles (deg) for Compound **8**.

N (1) - C (2)	1.292 (6)	C (2) - C (11)	1.520 (7)
N (1) - C (10)	1.378 (7)	C (3) - C (13)	1.484 (7)
N (4) - C (3)	1.314 (7)	C (5) - C (10)	1.416 (9)
N (4) - C (5)	1.373 (7)	C (11) - C (12)	1.510 (7)
C (2) - C (3)	1.429 (8)	C (12) - C (13)	1.345 (8)

C (2) - N (1) - C (10)	114.3 (4)	N (4) - C (5) - C (10)	122.1 (5)
C (3) - N (4) - C (5)	114.3 (4)	N (1) - C (10) - C (5)	121.8 (5)
N (1) - C (2) - C (3)	124.4 (5)	C (2) - C (11) - C (12)	99.6 (4)
C (3) - C (2) - C (11)	110.4 (5)	C (11) - C (12) - C (13)	115.1 (5)
N (4) - C (3) - C (2)	123.0 (5)	C (3) - C (13) - C (12)	107.0 (5)
C (2) - C (3) - C (13)	107.6 (4)		

CONCLUSIONS

The reaction between 4-methoxyphenylisonitrile, AIBN, and phenylacetylene afforded products derived from attack of 2-cyanoprop-2-yl radical to the isonitrile and subsequent annulation with phenylacetylene, or, predominantly, from addition of the same radical to the alkyne, followed by attack of the resulting vinyl radical to the isonitrile. In this last case, a new quinoxaline derivative was obtained through a tandem 5-exo, 6-endo cyclisation; this is also a new example of a rare 4 + 1 radical annulation. Studies are still underway to extend this reaction to other isonitriles and alkynes (or alkenes) and to explore its synthetic applications. The oxidation step leading to the final aromatic products entails also the intervention of the starting isonitrile: this is converted in an α-unsubstituted imidoyl radical, which is then involved in an annulation reaction with phenylacetylene giving two isomeric quinolines. This behaviour was found also in cyclisations of biphenyl-2-ylisonitrile under various radical conditions and appears to be unprecedented. The reaction also yielded an α,β-unsaturated nitrile, which was rationalised through fragmentation of a spirocyclohexadienyl radical and subsequent β-scission of the resulting iminyl. The finding of this nitrile could be the first evidence of the intervention of iminyl radicals in the rearrangement of spirocyclohexadienyls, although a competitive ring-enlargement mechanism cannot be ruled out completely.

EXPERIMENTAL SECTION

General Procedures.

Melting points were determined on an Electrothermal capillary apparatus and are uncorrected. ^{1}H- and ^{13}C NMR spectra were recorded in deuterochloroform on Varian EM 360L (60 MHz) or Varian Gemini 200 (200 MHz) instruments, using tetramethylsilane as an internal standard. Mass spectra (MS) and high resolution mass spectra (HRMS) were performed with a VG 7070E spectrometer by electron impact with a beam energy of 70 eV. IR spectra were recorded in tetrachloromethane on a Perkin-Elmer 257 spectrophotometer. GC-MS analyses were carried out on a Carlo Erba AUTO/HRGC/MS-QMD 1000 instrument equipped with a Quadrex capillary column (007, 25 m x 0.25 mm I.D.) and a NIST/NBS library. HPLC was performed on a Varian 5000 liquid chromatograph equipped with a C-18 column (Supelcosil LC-18, 5 μ, 25 cm x 4.6 mm I.D.) and a Varian 2050 variable λ detector operating at 254 nm, using acetonitrile/water mixtures as eluant. GC was performed on a Varian Star 3400 CX gas chromatograph equipped with a FID and the same column described for GC-MS analyses.

Column chromatography was carried out on silica gel (ICN Silica, 63-200, 60 A) or basic aluminium oxide (Baker, Activity Grade III), using light petroleum (40-70 °C) and a light petroleum/diethyl ether gradient (from 0 up to 100% diethyl ether) as eluant. Previously reported reaction products were identified by spectral comparison and mixed mp determination with authentic specimens.

Starting Materials.

All reactions were carried out in benzene (Baker). Phenylacetylene, phenanthridine, 1,1'-biphenyl (Aldrich), azo-bis-*iso*-butyronitrile (AIBN), and tris(trimethylsilyl)silane (TTMSS) (Fluka) were commercially available. *n*-Butyllithium (Aldrich) was used as a 1.6 M hexane solution. AIBN was purified by being dissolved in chloroform and reprecipitated with methanol. 4-Methoxyphenylisonitrile (**1**),[11] 2-chloro-6-methoxy-4-phenylquinoline,[25] 1,2-dihydro-7-methoxy-4-phenylquinolin-2-one,[26] 6-methoxy-4-phenylquinoline (**5**),[27] 7-methoxy-4-phenylquinoline (**6**),[28] 4-bromophenylacetylene,[29] and 6-phenylphenanthridine (**30**)[6] were prepared according to the literature. 1,1'-Biphenyl-2-ylisonitrile (**26**) was prepared according to the procedure previously reported for **1**,[11] bp (0.2 mbar) = 98-100 °C [lit.[30] bp (1.5 mmHg) = 113-114 °C].

2-(6-Methoxy-4-phenylquinolin-2-yl)-2-methylpropanenitrile (3). A solution of 2-methyl-2-propanenitrile (0.82 g, 12 mmol) in anhydrous THF (10 mL) was added dropwise during 5 min to a stirred solution of butyllithium (11.4 mmol) in THF (8 mL) kept under nitrogen at -65 °C. The mixture was warmed to 0 °C and, after 15 min, to 10 °C.[31] A solution of 2-chloro-6-methoxy-4-phenylquinoline (1.40 g, 5.2 mmol) in THF (5 mL) was added dropwise. The mixture colored black, red, and finally yellow, and was kept at r.t. for 3 h and then refluxed for 30 min. Then it was poured into water and extracted with diethyl ether. The organic phase was dried over sodium sulfate, the solvent evaporated, and the residue chromatographed on aluminium oxide to give unreacted starting quinoline (0.39 g, 28%), and the title compound (0.16 g, 10%), mp = 114-115 °C (from light petroleum/benzene); ^{1}H NMR (200 MHz) δ 1.88 (6 H, s, $-C(CH_3)_2CN$), 3.80 (3 H, s, $-OCH_3$), 7.18 (1 H, d, J = 2.7 Hz, Ar-*H*), 7.39 (1 H, dd, J_1 = 9.2 Hz, J_2 = 2.7 Hz, Ar-*H*), 7.49-7.61 (6 H, m, Ar-*H*), 8.05 (1 H, d, J = 9.2 Hz, Ar-*H*); MS *m/z* (relative intensity) 302 (M^+, 64), 301 (34), 287 (100), 249 (19), 235 (27); HRMS calcd for $C_{20}H_{18}N_2O$ 302.1419, found 302.1422. Anal. calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.65; H, 6.02; N, 9.29. The reaction also afforded compounds with high molecular weight whose structure was not investigated.

2-Chloro-7-methoxy-4-phenylquinoline. A mixture of 1,2-dihydro-7-methoxy-4-phenylquinolin-2-one (7.12 g, 28.4 mmol), trichloromethane (23 mL), thionyl chloride (5 mL), and N,N-dimethylformamide (5 mL) was kept at 50 °C for 6 h under mechanic stirring. After cooling, the mixture was poured into water/diethyl ether, stirred for a few minutes, and filtered. The aqueous layer was extracted with diethyl ether, the organic phases dried over sodium sulfate, and the solvent evaporated. The residue was chromatographed on aluminium oxide to give the title compound (1.93 g, 25%), mp = 108-108.5 °C (from light petroleum/benzene); ^{1}H NMR (200 MHz) δ 3.92 (3 H, s, $-OCH_3$), 7.11 (1 H, dd, J_1 = 9.2 Hz, J_2 = 2.5 Hz, Ar-*H*), 7.19 (1 H, s, Ar-*H*), 7.39 (1 H, d, J = 2.5 Hz, Ar-*H*), 7.40-7.52 (5 H, m, Ar-*H*), 7.73 (1 H, d, J = 9.2 Hz, Ar-*H*); MS *m/z* (relative intensity) 271 (M^+ + 2, 35), 269 (M^+, 100), 254 (6), 238 (5), 228 (3), 226 (11), 204 (10), 191 (12), 190 (19); HRMS calcd for $C_{16}H_{12}ClNO$ 269.0607, found 269.0609. Anal. calcd for $C_{16}H_{12}ClNO$: C, 71.25; H, 4.48; N, 5.19. Found: C, 71.32; H, 4.47; N, 5.20.

2-(7-Methoxy-4-phenylquinolin-2-yl)-2-methylpropanenitrile (4). Following the procedure previously described for quinoline **3**, 2-chloro-7-methoxy-4-phenyl-quinoline (1.93 g, 7.2 mmol) afforded unreacted chloroquinoline (0.58 g, 30%) and **4** (0.64 g, 30%), mp = 96-97.5 °C (from light petroleum/benzene); ^{1}H NMR (200 MHz) δ 1.88 (6 H, s, $-C(CH_3)_2CN$), 3.95 (3 H, s, $-OCH_3$), 7.13 (1 H, dd, J_1 = 9.2 Hz, J_2 = 2.7 Hz, Ar-*H*), 7.45-7.52 (7 H, m, Ar-*H*), 7.78 (1 H, d, J = 9.2 Hz, Ar-*H*); MS *m/z* (relative intensity) 302 (M^+, 66), 301 (41), 287 (100), 249 (16), 235 (30); HRMS calcd for $C_{20}H_{18}N_2O$ 302.1419, found 302.1423. Anal. calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.57; H, 6.01; N, 9.28.

3-Hydroxy-3-(4-methoxyphenyl)-3-phenylpropanenitrile. Following the procedure previously reported for 3-hydroxy-3,3-diphenylpropanenitrile,[32] a solution of acetonitrile (15 mL, 29 mmol) in anhydrous THF (25 mL) was added dropwise during 7 min to a stirred solution of butyllithium (28 mmol) in THF (17 mL) kept under nitrogen at -65 °C. The mixture was stirred at -65 °C for 1 h. A solution of 4-methoxybenzophenone (5.31 g, 25 mmol) in THF (25 mL) was then added dropwise during 5 min. The resulting yellow solution was warmed to r.t. and poured into cold, aqueous 5% hydrochloric acid (150 mL). The aqueous layer was extracted with diethyl ether and the organic phases dried over sodium sulfate. The solvent was removed and the residue crystallised from ethanol to give the title nitrile (5.88 g, 90%), mp = 134-135 °C; ^{1}H NMR (200 MHz) δ 2.83 (1 H, s, $-OH$), 3.22 (2 H, s, $-CH_2CN$), 3.80 (3 H, s, $-OCH_3$), 6.87 (2 H, d, A part of AA'BB', J = 8.9 Hz, Ar-*H*), 7.25-7.45 (7 H, m + B part of AA'BB', Ar-*H*); IR (ν_{max}, cm^{-1}) 2400 (CN stretch) and 3610 (OH stretch). Anal. calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.79; H, 5.98; N, 5.55.

3-(4-Methoxyphenyl)-3-phenylprop-2-enenitrile (7). Following the procedure previously reported for 3,3-diphenylprop-2-enenitrile,[32] a mixture of the above nitrile (2.53 g, 10 mmol) and 85% phosphoric acid (60 mL) was refluxed for 15 min under mechanic stirring. After cooling, the mixture was poured into ice/water (200 mL) and extracted with diethyl ether. The organic phase was dried over sodium sulfate, the solvent removed, and the residue chromatographed on silica gel to give 1-(4-methoxyphenyl)-1-phenylethylene (0.39 g, 19%), mp = 73.5-75 °C (from light petroleum) (lit.[33] mp = 75 °C) and **7** (1.41 g, 60%) as a 54:46 mixture of (*E*)- and (*Z*)-isomer, mp = 67-69 °C. This mixture was carefully rechromatographed and we succeeded in obtaining little amounts of pure (*E*)- and (*Z*)-isomer. Structural assignment was made on the basis of the chemical shift of the AA'BB' system of the 4-methoxyphenyl group, which is shifted to lower fields when the cyano group is *cis*. Furthermore, the proposed (*Z*)-isomer was found to be identical with the nitrile obtained in the reaction of isonitrile **1** with AIBN and phenylacetylene, which can afford the (*Z*)-isomer, exclusively (see below). (*E*)-**7**: ^{1}H NMR (200 MHz) δ 3.83 (3 H, s, -OCH_3), 5.68 (1 H, s, =C*H*-CN), 6.88 (2 H, d, A part of AA'BB', *J* = 8.8 Hz, Ar-*H*), 7.25 (2 H, d, B part of AA'BB', *J* = 8.8 Hz, Ar-*H*), 7.38-7.52 (5 H, m, Ar-*H*); MS *m/z* (relative intensity) 235 (M$^+$, 100), 234 (15), 220 (15), 219 (9), 204 (14), 195 (15), 190 (17), 165 (23); IR (ν_{max}, cm^{-1}) 2200 (CN stretch); HRMS calcd for $C_{16}H_{13}NO$ 235.0997, found 235.1000. Anal. calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.80; H, 5.58; N, 5.94. (*Z*)-**7**: ^{1}H NMR (200 MHz) δ 3.85 (3 H, s, -OCH_3), 5.60 (1 H, s, =C*H*-CN), 6.95 (2 H, d, A part of AA'BB', *J* = 8.4 Hz, Ar-*H*), 7.25-7.50 (7 H, m + B part of AA'BB', Ar-*H*); MS *m/z* (relative intensity) 235 (M$^+$, 100), 234 (15), 220 (15), 219 (9), 204 (14), 195 (15), 190 (17), 165 (24); IR (ν_{max}, cm^{-1}) 2200 (CN stretch); HRMS calcd for $C_{16}H_{13}NO$ 235.0997, found 235.0998. Anal. calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.79; H, 5.59; N, 5.93.

2-Nitro-2',3',4',5',6'-d_5-1,1'-biphenyl. A solution of 2-nitroaniline (10 g, 72.4 mmol) and amyl nitrite (12.75 g, 109 mmol) in benzene-d_6 (45 mL) was gently warmed until it started refluxing. The flask was kept in an ice-bath until reflux stopped and the solution was then refluxed for 3 h. The solvent was evaporated and the residue chromatographed to give the title biphenyl (3.10 g, 21%), oil;[34] ^{1}H NMR (200 MHz) δ 7.42-7.70 (3 H, m), 7.88 (1 H, dd, J_1 = 7.9 Hz, J_2 = 1.4 Hz); MS *m/z* (relative intensity) 204 (M$^+$, 35), 186 (49), 176 (73), 174 (32), 157 (100), 156 (97), 148 (44), 146 (50), 132 (34), 131 (25), 130 (30), 120 (56), 119 (62), 118 (48), 78 (86); HRMS calcd for $C_{12}H_4D_5NO_2$ 204.0947, found 204.0948.[35]

2-Amino-2',3',4',5',6'-d_5-1,1'-biphenyl. A mixture of 2-nitro-2',3',4',5',6'-d_5-1,1'-biphenyl (6.25 g) and 10% palladium on activated carbon (0.5 g) was stirred under a hydrogen atmosphere (2 atm) for 45 min. After filterin/g, the solvent was removed and the residue chromatographed to give the title amine (3.12 g, 58%), oil;[34] ^{1}H NMR (60 MHz) δ 3.63 (2 H, bs, -NH_2), 6.58-7.40 (4 H, m, Ar-*H*); MS *m/z* (relative intensity) 174 (M$^+$, 100), 173 (37), 172 (39), 171 (19), 170 (7); HRMS calcd for $C_{12}H_6D_5N$ 174.1205, found 174.1205.[35]

N-(2',3',4',5',6'-d_5-1,1'-Biphenyl-2-yl)formamide. A mixture of 2-Amino-2',3',4',5',6'-d_5-1,1'-biphenyl (3.12 g, 18 mmol) and formic acid (5 mL) was refluxed for 75 min. Excess of formic acid was evaporated off and the residue crystallised from light petroleum/benzene to give 2.11 g (58%) of the title compound, mp = 73-75 °C; ^{1}H NMR (200 MHz) δ 7.10-7.40 (8 H, m), 8.27 (1 H, d, *J* = 1.8 Hz), 8.36 (1 H, dd, J_1 = 8.1 Hz, J_2 = 0.6 Hz), 8.67 (0.8 H, d, *J* = 11.6 Hz);[36] MS *m/z* (relative intensity) 202 (M$^+$, 95), 200 (15), 184 (14), 174 (59), 173 (77), 172 (100), 171 (50), 170 (19); HRMS calcd for $C_{13}H_6D_5NO$ 202.1155, found 202.1156.[35]

2',3',4',5',6'-d_5-1,1'-Biphenyl-2-ylisonitrile (32). Following the procedure previously reported for 4-methoxyphenylisonitrile,[11] a solution of diphosgene (0.63 mL, 5.2 mmol) in anhydrous methylene chloride (2 mL) was added dropwise at 0 °C in 1 h to a stirred solution of N-(2',3',4',5',6'-d_5-1,1'-biphenyl-2-yl)formamide (2.11 g, 10.4 mmol) and triethylamine (3 mL) in methylene chloride (10 mL), the reaction vessel being connected to a condenser maintained at -30 °C. The mixture was stirred for 30 min and then warmed to r.t.; water (20 mL) was added and the organic phase separated, washed with aqueous sodium bicarbonate (7.5%), and dried over 5 Å molecular sieves. The solvent was evaporated and the residue distilled to give 1.3 g (68%) of **32**, bp (0.2 mbar) = 98-100 °C; ^{1}H NMR (200 MHz) δ 7.30-7.55 (4 H, m); MS *m/z* (relative intensity) 184 (M$^+$, 100), 183 (33), 182 (25), 157 (16), 156 (25), 155 (18), 154 (12), 78 (24); IR (ν_{max}, cm^{-1}) 2130 (NC stretch); HRMS calcd for $C_{13}H_4D_5N$ 184.1049, found 184.1050.[35]

*Reaction of 4-methoxyphenylisonitrile (**1**) with phenylacetylene and AIBN.* A solution of **1** (1.06 g, 8 mmol), phenylacetylene (2.45 g, 24 mmol), and AIBN (1.57 g, 9.6 mmol) in benzene (40 mL) was refluxed for 6 h. A GC-MS analysis of the reaction mixture showed, besides those indicated in Scheme 1, dimeric products of cyanopropyl radical,[37] and compounds deriving from a reaction between phenylacetylene and AIBN. These products were also found directly by reacting AIBN with the alkyne and their structure was not investigated. In addition, the GC-MS analysis showed the presence of 1,3,5-triphenylbenzene, which arises from phenylacetylene under radical conditions,[12] and a compound containing two molecules of isonitrile and the cyanopropyl moiety [MS *m/z* (relative intensity) 333 (M^+, 58), 318 (7), 265 (100), 250 (6), 222 (8), 160 (6), 92 (17), 77 (22)], probably deriving from attack of radical **19** to **1**.

After column chromatography we obtained a mixture of **3**, **4**, and **7** (0.11 g), 7-methoxy-1,1-dimethyl-3-phenyl-1H-cyclopenta[*b*]quinoxaline (**2**) (0.70 g, 29%), mp = 112-113.5 °C (from light petroleum) [^{1}H NMR (200 MHz) δ 1.52 (6 H, s, -CH_3), 3.98 (3 H, s, -OCH_3), 7.20 (1 H, s, H-2), 7.35 (1 H, dd, J_1 = 8.7 Hz, J_2 = 2.2 Hz, Ar-*H*), 7.40-7.56 (4 H, m, Ar-*H*), 8.04 (1 H, d, *J* = 8.7 Hz, Ar-*H*), 8.17-8.24 (2 H, m, Ar-*H*); ^{13}C NMR δ 23.85 (2 C, -*C*H$_3$, J_{CH} [q] = 126.5 Hz), 45.71 (1 C, *C*-1), 56.20 (1 C, -O*C*H$_3$, J_{CH} [q] = 142.6 Hz), 108.02 (1 C, Ar-*C*, J_{CH} [d] = 161.0 Hz), 121.35 (1 C, Ar-*C*, J_{CH} [d] = 165.6 Hz), 127.90 (2 C, Ar-*C*), 128.94 (3 C, Ar-*C*), 130.76 (1 C), 133.65 (1 C), 137.99 (1 C), 139.47 (1 C), 141.80 (1 C), 148.78 (1 C, *C*-2, J_{CH} [d] = 161.0 Hz), 153.97 (1 C), 160.33 (1 C), 167.47 (1 C); MS *m/z* (relative intensity) 302 (M^+, 100), 301 (16), 287 (66), 272 (5), 259 (5), 244 (21), 243 (17), 242 (10), 151 (7), 143 (16), 122 (20); IR (ν_{max}, cm^{-1}) 1625 (C=N stretch); HRMS calcd for $C_{20}H_{18}N_2O$ 302.1419, found 302.1420. Anal. calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.51; H, 5.99; N, 9.28], and a mixture of **5** and **6** (0.06 g).

The two mixtures (**3** + **4** + **7** and **5** + **6**) were carefully rechromatographed to obtain little amounts of pure compounds, which were identified by GC analysis and spectral comparison with the authentic specimens prepared above. The yields of the reaction products were also determined by GC analysis using indole as an internal standard: the results are reported in Scheme 1.

When the reaction was repeated with **1** (1 mmol), phenylacetylene (3 mmol), AIBN (3 mmol), and 1,3-dinitrobenzene (1 mmol) (6 h of reflux) we obtained — by GC analysis — the following yields: **2** (38%), **3** (3%), **4** (4%), and **7** (1%). Quinoline **6** was completely absent, whereas **5** was present only in unquantifiable trace amounts. The same reaction was performed by adding dropwise AIBN in 1 h to the refluxing solution of **1**, phenylacetylene, and 1,3-dinitrobenzene. The following yields were obtained: **2** (50%), **3** (3%), **4** (5%), and **7** (2%).

*Reaction of **1** with 4-bromophenylacetylene and AIBN.* Following the procedure previously described for phenylacetylene, **1** (0.67 g, 5 mmol), 4-bromophenylacetylene (2.71 g, 15 mmol), and AIBN (0.98 g, 6 mmol) gave 3-(4-bromophenyl)-7-methoxy-1,1-dimethyl-1H-cyclopenta[*b*]quinoxaline (**8**) (0.60 g, 32%), mp = 191-192 °C (from light petroleum/benzene); ^{1}H NMR (200 MHz) δ 1.53 (6 H, s, -CH_3), 4.00 (3 H, s, -OCH_3), 7.19 (1 H, s, H-2), 7.37 (1 H, dd, J_1 = 9.0 Hz, J_2 = 2.8 Hz, Ar-*H*), 7.47 (1 H, d, *J* = 2.8 Hz, Ar-*H*), 7.63 (2 H, d, A part of AA'BB', *J* = 8.6 Hz, Ar-*H*), 8.03 (1 H, d, *J* = 9.0 Hz, Ar-*H*), 8.12 (2 H, d, B part of AA'BB', *J* = 8.6 Hz, Ar-*H*); ^{13}C NMR δ 23.48 (2 C, -*C*H$_3$), 45.54 (1 C, *C*-1), 55.95 (1 C, -O*C*H$_3$), 107.49 (1 C, Ar-*C*), 121.31 (1 C, Ar-*C*), 122.73 (1 C, Ar-*C*), 129.18 (2 C, Ar-*C*), 130.38 (1 C, Ar-*C*), 131.80 (2 C, Ar-*C*), 132.13 (1 C, Ar-*C*), 137.51 (1 C, Ar-*C*), 137.95 (1 C, Ar-*C*), 141.47 (1 C, Ar-*C*), 148.68 (1 C, *C*-2), 153.17 (1 C, Ar-*C*), 160.08 (1 C, Ar-*C*), 166.92 (1 C, Ar-*C*); MS *m/z* (relative intensity) 382 (M^+ + 2, 93), 380 (M^+, 100), 367 (50), 365 (53), 339 (3), 337 (3), 324 (8), 322 (8), 286 (18), 285 (18), 243 (25), 242 (30), 150 (44), 143 (32), 121 (17); HRMS calcd for $C_{20}H_{17}BrN_2O$ 380.0524, found 380.0525. Anal. calcd for $C_{20}H_{17}BrN_2O$: C, 63.00; H, 4.49; N, 7.35. Found: C, 63.18; H, 4.50; N, 7.37.

This reaction was carried out to obtain a sample of **8** suitable for X-ray structural determination. Therefore, the other reaction products were not investigated, although a GC-MS analysis of the reaction mixture showed a composition quite similar to that of the above reaction of **1** with phenylacetylene.

Reaction of 1,1'-biphenyl-2-ylisonitrile (26) with AIBN. A solution of AIBN (1.63 g, 8.75 mmol) in benzene (15 mL) was added dropwise in 1 h to a refluxing solution of **26** (0.90 g, 5 mmol) in benzene (15 mL). The mixture was refluxed for additional 16 h. The solvent was evaporated and the residue chromatographed on silica gel to give 2-methyl-2-(phenanthridin-6-yl)propanenitrile (**27**) (0.66 g, 54%), mp = 98-99.5 °C (from light petroleum) [^{1}H NMR (60 MHz) δ 2.05 (6 H, s, -CH_3), 7.53-8.97 (8 H, m, Ar-*H*); MS *m/z* (relative intensity) 246 (M$^+$, 64), 245 (53), 231 (100), 218 (16), 204 (24), 193 (26), 179 (93), 178 (31), 177 (28), 151 (35); HRMS calcd for $C_{17}H_{14}N_2$ 246.1157, found 246.1157. Anal. calcd for $C_{17}H_{14}N_2$: C, 82.90; H, 5.73; N, 11.37. Found: C, 82.99; H, 5.72; N, 11.38] and phenanthridine (**28**) (0.18 g, 20%), mp = 108-109 °C (from light petroleum/benzene) (mp of a commercial sample 107-109 °C). The reaction was also quantified by HPLC analysis, using acetophenone as an internal standard, to give the following yields: **27** (59%) and **28** (18%).

The reaction was repeated in the presence of variable amounts of oxidising agents. Under these conditions, phenanthridine **28** disappeared completely, and **27** was obtained in the following yields (HPLC): 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (1 equiv): 21%; 3,4,5,6-tetrachloro-1,2-benzoquinone (0.5 equiv): 53%; nitrobenzene (1 equiv): 67%; 1,3-dinitrobenzene (1 equiv): 67%; 1,3-dinitrobenzene (0.5 equiv): 67%; 1,3-dinitrobenzene (0.25 equiv): 62%; 1,3,5-trinitrobenzene (1 equiv): 56%.

Reaction of 26 with tris(trimethylsilyl)silane (TTMSS) and AIBN. A solution of AIBN (0.98 g, 6 mmol) in benzene (15 mL) was added dropwise in 1 h to a refluxing solution of **26** (0.90 g, 5 mmol) and TTMSS[38] (1.49 g, 6 mmol) in benzene (45 mL). The mixture was refluxed for one additional hour; the solvent was evaporated and the residue chromatographed on aluminium oxide to give 6-[tris(trimethylsilyl)silyl]-phenanthridine (**29**) (1.26 g, 59%), mp = 103-106 °C (from absolute ethanol) [^{1}H NMR (60 MHz) δ 0.30 (27 H, s, -CH_3), 7.20-8.53 (8 H, m, Ar-*H*);[39] MS *m/z* (relative intensity) 425 (M$^+$, <1), 424(<1), 410 (100), 352 (28), 294 (29), 278 (14), 264 (5), 250 (10), 236 (22), 220 (10), 206 (48), 179 (8), 73 (22). Anal. calcd for $C_{22}H_{35}NSi_4$: C, 62.05; H, 8.28; N, 3.29. Found: C, 62.12; H, 8.30; N, 3.29], **27** (0.04 g, 3%), mp = 97-99 °C (from light petroleum) [spectroscopic data are identical to those obtained for **27** in the above reaction of **26** with AIBN], and **28** (0.28 g, 31%), mp = 108-109 °C (from light petroleum/benzene) [mp of a commercial sample 107-109 °C].

Reaction of 26 with dibenzoyl peroxide (DBP). A solution of **26** (0.36 g, 2 mmol) and DBP (0.97 g, 4 mmol) in benzene (20 mL) was refluxed for 24 h. The solvent was evaporated and the residue chromatographed on silica gel to give biphenyl (0.18 g, 30% with respect to DBP), mp = 71-73 °C (from light petroleum) (mp of a commercial sample 69-72 °C), 6-phenylphenanthridine (**30**) (0.31 g, 60%), mp = 103-105 °C (from ethanol) (lit.[6] mp = 103-105 °C), and **28** (0.04 g, 10%), mp = 107-109 °C (from light petroleum/benzene) (mp of a commercial sample 107-109 °C). A GC analysis — using phenanthrene as an internal standard — gave: biphenyl (33% with respect to DBP), **28** (13%), and **30** (66%).

Reaction of 32 with DBP. Following the procedure described above for the reaction of **26** with DBP, **32** (0.64 g, 3.5 mmol) afforded, after column chromatography, biphenyl (0.38 g, 36% with respect to DBP), mp = 71-73 °C (from light petroleum), 6-phenyl-7,8,9,10-d_4-phenanthridine (**33**) (0.56 g, 62%), mp = 104-107 °C (from light petroleum/benzene) [^{1}H NMR (200 MHz) δ 7.40-7.80 (6 H, m), 8-06-8.15 (3 H, m); MS *m/z* (relative intensity) 259 (M$^+$, 60), 258 (95), 257 (100), 256 (19), 255 (12), 254 (7), 229 (5), 129 (27), 128 (32); HRMS calcd for $C_{19}H_9D_4N$ 259.1299, found 259.1299][35] and 6,7,8,9,10-d_5-phenanthridine (**34**) (0.03 g, 5%), mp = 107-109 °C (from light petroleum/benzene) [^{1}H NMR (200 MHz) δ 7.64-7.82 (4 H, m), 8.17-8.25 (1 H, m), 8.57-8.64 (1 H, m); MS *m/z* (relative intensity) 184 (M$^+$, 100), 183 (19), 182 (12), 156 (8), 155 (8); HRMS calcd for $C_{13}H_4D_5N$ 184.1049, found 184.1050].[35] The reaction was also quantified by GC analysis, using adamantane as an internal standard, to give: biphenyl (40% with respect to DBP), **34** (7%), and **33** (65%).

Reaction of 26 and 32 with DBP. Following the procedure described above for the reaction of **26** with DBP, a 1:1 mixture of **26** (0.50 g, 2.7 mmol) and **32** (0.49 g, 2.7 mmol) yielded — through quantitative GC analysis using adamantane as an internal standard — biphenyl (42% with respect to DBP), a mixture of **28**, **34**, **35**, and **36** (9%), and a mixture of **30** and **33** (60%). After column chromatography, the fraction containing **28**, **34**, **35**, and **36** was analysed by MS to determine the phenanthridine ratio; from the relative intensities of the mass spectrum we obtained: **28** (43%), **34** (11%), **35** (37%), and **36** (9%) [MS *m/z* (relative intensity) 184 (35), 183 (89), 182 (13), 181 (12), 180 (45), 179 (100), 178 (16), 177 (5), 156 (6), 155 (8), 154 (7), 153 (8), 152 (11), 151 (11), 150 (5), 122 (9), 78 (11), 77 (10), 76 (14)].

X-ray Crystallography. Crystals of 3-(4-bromophenyl)-7-methoxy-1,1-dimethylcyclopenta[*b*]quinoxaline — compound **8** — were colorless flattened prisms (from ethyl acetate). Lattice constants were determined by least-square refinement of angular settings of 30 reflections. Crystal data and details associated with structure refinement are given in Table 1. Data were collected at room temperature — 291 K — on a Siemens AED single-crystal diffractometer in the range $3<\vartheta<70°$. For intensities and background individual reflection profiles were analysed.[40] The structure amplitudes were obtained after the usual Lorentz and polarisation corrections and the absolute scale was established by the Wilson method.[41] No absorption corrections were applied. The structure was solved by direct methods by use of the SHELXS86 program[42] and refined by SHELX-76[43] on the ENCORE 91 computer of the Centro di Studio per la Strutturistica Diffrattometrica del C.N.R. of Parma. The function minimised during the full-matrix least-square refinement (hydrogen atoms isotropically) was $\Sigma w|\Delta F|^2$. A weighting function based on counting statistics of the form $w = 7.2934/(\sigma^2 F_0 + 0.0002 F_0^2)$ was applied. Atomic scattering factors from *International Tables for X-ray Crystallography*.[44]

Acknowledgements. We acknowledge financial support from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST) and CNR (Rome). We also gratefully thank the CIBA-GEIGY S.p.A. Divisione Additivi (Pontecchio Marconi, Italy) for a post-doctoral fellowship given to Dr. Pareschi for part of this work.

REFERENCES AND NOTES

1. Danen, W. C.; West, C. T. *J. Am. Chem. Soc.* **1973**, *95*, 6872-6874. Davies, A. G.; Nedelec, J. -Y.; Sutcliffe, R. *J. Chem. Soc., Perkin Trans. 2* **1983**, 209-211.
2. a) Blum, P. M.; Roberts, B. P. *J. Chem. Soc., Chem. Commun.* **1976**, 535-536. b) Blum, P. M.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1313-1319.
3. Shaw, D. H.; Pritchard, H. O. *Canad. J. Chem.* **1967**, *45*, 2749-2754. Saegusa, T.; Kobayashi, S.; Ito, Y.; Yasuda, N. *J. Am. Chem. Soc.* **1968**, *90*, 4182. Ohta, H.; Tokumaru, K. *J. Chem. Soc., Chem. Commun.* **1970**, 1601. Saegusa, T.; Kobayashi, S.; Ito, Y. *J. Org. Chem.* **1970**, *35*, 2118-2121. Banks, R. E.; Haszeldine, R. N.; Stephens, C. W. *Tetrahedron Lett.* **1972**, 3699-3701. Singer, L. A.; Kim, S. S. *Tetrahedron Lett.* **1974**, 861-863. Kim, S. S. *Tetrahedron Lett.* **1977**, 2741-2744. Meier, M.; Rüchardt, C. *Tetrahedron Lett.* **1983**, *24*, 4671-4674. Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 6765-6766. Wirth, T.; Rüchardt, C. *Chimia* **1988**, *42*, 230-231.
4. Bachi, M. D.; Denenmark, D. *J. Am. Chem. Soc.* **1989**, *111*, 1886-1888. Bachi, M. D.; Denenmark, D. *J. Org. Chem.* **1990**, *55*, 3442-3444. Fukuyama, T.; Chen, X.; Peng, G. *J. Am. Chem. Soc.* **1994**, *116*, 3127-3128.
5. Barton, D. H. R.; Ozbalik, N.; Vacher, B. *Tetrahedron* **1988**, *44*, 3501-3512.
6. Leardini, R.; Tundo, A.; Zanardi, G.; Pedulli, G. F. *Synthesis* **1985**, 107-110.
7. Leardini, R.; Nanni, D.; Santori, M.; Zanardi, G. *Tetrahedron* **1992**, *48*, 3961-3970.

8. a) Leardini, R.; Pedulli, G. F.; Tundo, A.; Zanardi, G. *J. Chem. Soc., Chem. Commun.* **1984**, 1320-1321. b) Leardini, R.; Nanni, D.; Pedulli, G. F.; Tundo, A.; Zanardi, G. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1591-1594. c) Leardini, R.; Nanni, D.; Tundo, A.; Zanardi, G. *Gazz. Chim. Ital.* **1989**, *119*, 637-641.
9. Leardini, R.; Nanni, D.; Tundo, A.; Zanardi, G. *J. Chem. Soc., Chem. Commun.* **1989**, 757-758.
10. Curran, D. P.; Liu, H. *J. Am. Chem. Soc.* **1991**, *113*, 2127-2132. Curran, D. P.; Liu, H. *J. Am. Chem. Soc.* **1992**, *114*, 5863-5864.
11. Skorna, G.; Ugi, I. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 259-260.
12. Amdur, S.; Cheng, A. T. Y.; Wong, C. J.; Ehrlich, P.; Allendoerter, R. D. *J. Polym. Sci., Polym. Chem. Ed.* **1978**, *16*, 407-414.
13. Bennett, J. E.; Howard, J. A. *Chem. Phys. Lett.* **1971**, *9*, 460. Giese, B.; Gonzales-Gomez, J. A.; Lachhein, S.; Metzger, J. O. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 479-480.
14. Journet, M.; Malacria, M. *Tetrahedron Lett.* **1992**, *33*, 1893-1896. Journet, M.; Malacria, M. *J. Org. Chem.* **1992**, *57*, 3085-3093. Curran, D. P.; Kim, D. *Tetrahedron* **1991**, *47*, 6171-6188.
15. Although data on the reversibility of radical addition to isonitriles are not available in the literature, actually we found evidence that, with particularly stable radicals, this reaction appears to be reversible (preliminary, unpublished results). The reaction mixture did not contain, besides those listed in Scheme 1, any other noteworthy compound, except tarry materials and by-products having no relation with this discussion (see Experimental Section). Therefore, side-reactions of **13** are very unlikely or occur to a very small extent.
16. Imidoyl radicals are known to be σ-radicals with a bent structure. In one case, with an α-silyl substituent, a linear geometry has been observed (see Ref. 2b). Spectroscopic data of other imidoyls bearing radical-stabilising substituents at C_α are not available, but we cannot rule out the possibility that these radicals have a linear structure and a π-electronic configuration like styryl radicals. If this were true, resonance should give the carbon-carbon double bond some single-bond character and allow isomerisation. Furthermore, the linear structure of the imidoyl could let us get over the geometrical requirements of the ring closure of **10** to the iminyl **11**, although bent imidoyl radicals have been predicted to adopt just the *E*-configuration that is essential for the 5-exo cyclisation (see Ref. 2b).
17. Clive, D. L. J.; Beaulieu, P. L.; Set, L. *J. Org. Chem.* **1984**, *49*, 1313-1314. Chenera, B.; Chuang, C. P.; Hart, D. J.; Hsu, L. Y. *J. Org. Chem.* **1985**, *50*, 5409-5410. Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 2116-2117. Beckwith, A. L. J.; O'Shea, D. M.; Sendaba, G.; Westwood, S. W. *J. Chem. Soc., Chem. Commun.* **1987**, 666-667. Yeung, B. W.; Contelles, J. L. M.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1989**, 1160-1162. Dickson, J. K., Jr.; Tsang, R.; Llera, J. M.; Fraser-Reid, B. *J. Org. Chem.* **1989**, *54*, 5350-5356. Knapp, S.; Gibson, F. S.; Choe, Y. H. *Tetrahedron Lett.* **1990**, *31*, 5397-5400. Snider, B. B.; Buckman, B. O. *J. Org. Chem.* **1992**, *57*, 322-326. Yang, C. -C.; Chang, H. -T.; Fang, J. -M. *J. Org. Chem.* **1993**, *58*, 3100-3105.
18. a) Forrester, A. R.; Gill, M.; Thomson, R. H. *J. Chem. Soc., Chem. Commun.* **1976**, 677-678. b) Sakuragi, H.; Ishikawa, S. -I.; Nishimura, T.; Yoshida, M.; Inamoto, N.; Tokumaru, K. *Bull. Chem. Soc. Jpn* **1976**, *49*, 1949-1954. c) Forrester, A. R.; Gill, M.; Sadd, J. S.; Thomson, R. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 612-615. d) McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1984**, 371-376. e) McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1984**, 377-380. f) McNab, H.; Smith, G. S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 381-384. g) Hickson, C. L.; McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1569-1572.
19. For radical annulations see Ref. 8, Ref. 9, and Curran, D. P. in *Comprehensive Organic Synthesis*, Pergamon Press: Oxford, **1991**; vol. 4, pp 824-825. For the single example of 4 + 1 radical annulation see Ref 10.
20. Imidoyl cations are known to give 4 + 2 annulations, exclusively; hence, cation **25** is expected to afford the single quinoline **5**. See Ref. 8c and Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1960**, *3*, 804.

For basic behaviour of isonitriles see: March, J. *Advanced Organic Chemistry*, 3rd Edition, Wiley: New York, **1985**; p 870 and references cited therein.

21. Self-reaction of isonitrile **26** must be ruled out, as **26** was found unchanged after prolonged reflux in benzene solution in the absence of a radical initiator.
22. For such ring expansions of β-multiply-bonded alkyl radicals see: Dowd, P.; Choi, S. -C. *Tetrahedron* **1989**, *45*, 77-90. Beckwith, A. L. J.; O'Shea, D. M.; Westwood, S. W. *J. Am. Chem. Soc.* **1988**, *110*, 2565-2575.
23. Griller, D.; Mendenhall, G. D.; Van Hoof, W.; Ingold, K. U. *J. Am. Chem. Soc.* **1974**, *96*, 6068-6070. Boivin, J.; Fouquet, E.; Zard, S. Z. *J. Am. Chem. Soc.* **1991**, *113*, 1055-1057 and references cited therein. Boivin, J.; Fouquet, E.; Zard, S. Z. *Tetrahedron* **1994**, *50*, 1757-1768 and references cited therein.
24. Nitrile **7** was found unchanged after several hours of reflux in benzene solution in the presence of AIBN; hence, we can rule out the intervention of **7** in the formation of unsubstituted quinolines **5** and **6**.
25. Hino, K.; Kawashima, K.; Oka, M.; Uno, H.; Matsumoto, J. *Chem. Pharm. Bull.* **1989**, *37*, 190-192.
26. Venturella, P.; Bellino, A. *J. Heterocycl. Chem.* **1975**, *12*, 669-673.
27. Murphy, S. T.; Taylor, W. C.; Vadasz, A. *Aust. J. Chem.* **1982**, *35*, 1215-1225.
28. Tilak, B. D.; Ravindranathan, T.; Subbaswami, K. N. *Indian J. Chem.* **1968**, *6*, 422-427.
29. Dufraisse, C.; Dequesnes, A. *Bull. Soc. Chim. Fr.* **1931**, *49*, 1880-1882.
30. Boyer, J. H.; DeJong, J. *J. Am. Chem. Soc.* **1969**, *91*, 5929-5930.
31. Yang, S. S.; Dawson, B. T.; Rieke, R. D. *Tetrahedron Lett.* **1991**, *32*, 3341-3344.
32. Kaiser, E. M.; Hauser, C. R. *J. Org. Chem.* **1968**, *33*, 3402-3404.
33. Hurd, C. D.; Webb, C. N. *J. Am. Chem. Soc.* **1927**, *49*, 546-559.
34. Shapiro, B. L.; Mohrmann, L. E. *J. Phys. Chem. Ref. Data* **1977**, *6*, 919-991, bp not reported.
35. Compound purity was confirmed by ^{1}H NMR, HPLC, and GC analysis.
36. This spectrum shows the presence of *cis-* and *trans-*geometric isomers of the formamide, resulting from restricted rotation around the carbon-nitrogen bond. We found in the literature typical J-values of ca. 2 Hz and 11 Hz for the formyl protons of the *cis-* and *trans-*isomer, respectively. Therefore, we assigned the signal at 8.27 δ (J = 1.8 Hz) to the *cis-*isomer, and the doublet at 8.67 δ (J = 11.6 Hz) to the *trans-*form: the two isomers are in a ca. 56:44 ratio. The signal at 8.36 δ is probably due to the 6-aromatic proton of the *cis-*isomer, which is deshielded by the presence of the neighboring carbonyl group. The same behaviour was exhibited by the non-deuterated N-(biphenyl-2-yl)formamide [200 MHz ^{1}H NMR δ 7.07-7.57 (1 H, m), 8.11 (1 H, d, J = 1.9 Hz), 8.27 (1 H, bd, J = 8.0 Hz), 8.45 (0.7 H, d, J = 11.2 Hz)]. See: Bourn, A. J. R.; Gillies, D. G.; Randall, E. W. *Tetrahedron* **1964**, *20*, 1811-1818, for a general discussion, and Siddall, T. H., III; Stewart, W. E. *J. Mol. Spectrosc.* **1967**, *24*, 290-301, for the deshielding effect of the carbonyl group in the *cis-*isomer.
37. Nonhebel, D. C.; Walton, J. C. in *Free-Radical Chemistry*, Cambridge University Press: Cambridge, **1974**; pp 25-26.
38. Kanabus-Kaminska, J. M.; Hawari, J. A.; Griller, D.; Chatgilialoglu, C. *J. Am. Chem. Soc.* **1987**, *109*, 5267-5268. Chatgilialoglu, C.; Griller, D.; Lesage, M. *J. Org. Chem.* **1988**, *53*, 3641-3642. Lesage, M.; Chatgilialoglu, C.; Griller, D. *Tetrahedron Lett.* **1989**, *30*, 2733-2734. Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188-194. Giese, B.; Kopping, B.; Chatgilialoglu, C. *Tetrahedron Lett.* **1989**, *30*, 681-684.
39. The NMR spectrum must be recorded very quickly, since compound **29** readily desilylates (ca. 30 min) in CDCl$_3$ solution — as shown by a GC-MS analysis of the NMR sample.
40. Lehman, M. S.; Larsen, F. K. *Acta Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen. Crystallogr.* **1974**, *A 30*, 580-584.
41. Wilson, A. J. C. *Nature* **1942**, *150*, 151.
42. Sheldrick, G. M. *SHELXS86: Program for the Solution of Crystal Structures*; University of Göttingen: Göttingen, Germany, **1986**.

43. Sheldrick, G. M. *SHELX-76: System of Crystallographic Computer Programs*; University of Cambridge: Cambridge, England, **1976**.
44. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, **1974**.

(*Received in UK* 24 *March* 1995; *accepted* 5 *May* 1995)