Synthesis of indole derivatives *via* isocyanides†

J. Campo,[a] M. García-Valverde,*[a] S. Marcaccini,[b] M. J. Rojo[a] and T. Torroba[a]

Received 20th October 2005, Accepted 23rd November 2005
First published as an Advance Article on the web 20th December 2005
DOI: 10.1039/b514946k

Fast and convenient approaches to the indole nucleus from isocyanides are reviewed as a means for the tailored preparation of conveniently functionalized indoles by using the unique reactivity of isocyanides in one-pot multicomponent and cascade reactions.

1. Introduction

Isocyanides belong to a unique class of stable organic compounds with a formally divalent carbon that offers a wide range of reactions.[1] The chemistry of isocyanides is characterized by three distinct reactions, the α-addition, the α-metallation and the easy formation of radicals. These characteristics are perfectly suited for the synthesis of indole systems, one of the most widespread systems in nature. Common methods for the synthesis of indole systems have been reviewed.[2] Several nitrogenated groups such as hydrazones, amides, amines, imines and nitrenes, have been used as starting materials in diverse syntheses of indole derivatives. The scope of this review is to show the enormous versatility of isocyanides as starting materials for the rapid synthesis of the indole nucleus.

2. α-Addition reactions

The most important synthetic property of isocyanides is the possibility of reactions with nucleophiles and electrophiles at the same carbon atom, in contrast to several other functional groups in organic chemistry that react in only one way. This characteristic explains the effectiveness of the isocyano group in multicomponent reactions (MCR),[3] in which three or more starting materials react to form a product, where all the reagents contribute to the newly formed product.

One of the first multicomponent reactions to use isocyanides was the Passerini reaction (Scheme 1). The mechanism of this reaction is based on the ambident reactivity of the isocyanide group.

The substrates of the Passerini reaction may be diversified to give different products. This is well illustrated by an indole synthesis performed by this methodology. In this case, it is necessary to carry out a series of post-condensation transformations (Scheme 2).[4]

This synthesis illustrates the possibilities of multicomponent reactions followed by post-condensation processes.[5] But the synthetic possibilities of the isocyano group in the construction

Javier Campo obtained his MSc in Chemistry from the University of Burgos in 2005. He is currently pursuing a PhD degree under Dr María García-Valverde working on the study of multicomponent reactions.

María García-Valverde obtained her MSc in chemistry from the University of Valladolid where she received a doctorate with Professor Rafael Pedrosa and Martina Vicente in 1995. In 1995 she moved to the University of Burgos, first as Assistant Professor and currently as Associate Professor. She has been a postdoctoral fellow at the Universities of Graz with Dr Oliver Kappe and Florence with Dr Stefano Marcaccini. Her current interests include multicomponent reactions and the synthesis of natural products.

J. Campo

M. García-Valverde

---

[a] *Departamento de Química, Facultad de Ciencias, Universidad de Burgos, Pza. Misael Bañuelos, s/n 09001, Burgos, Spain. E-mail: magaval@ubu.es; Fax: +34947258087*
[b] *Dipartimento di Chimica Organica "Ugo Schiff", Università degli Studi di Firenze, 50121, Firenze, Italy*

† This paper is dedicated to the memory of Ricardo Bossio.

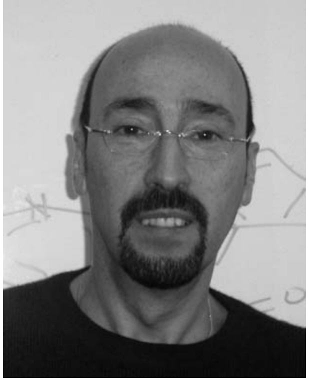
Stefano Marcaccini performed his career in organic chemistry at the University of Florence, where he got a doctoral degree in 1982 under the supervision of Dr Roberto Pepino. During 1983–1986 he was granted as postdoctoral researcher in the University of Florence, then he became a full time researcher at the same university. His research interest is the multicomponent reactions of isocyanides in the synthesis of heterocycles.

M. José Rojo obtained her MSc in chemistry from the Universidad de Valladolid. She received a doctoral degree in 1987 from the Universidad Autónoma de Madrid. Currently she is Associate Professor at the University of Burgos. Her current interests include the synthesis of nitrogenated heterocycles.

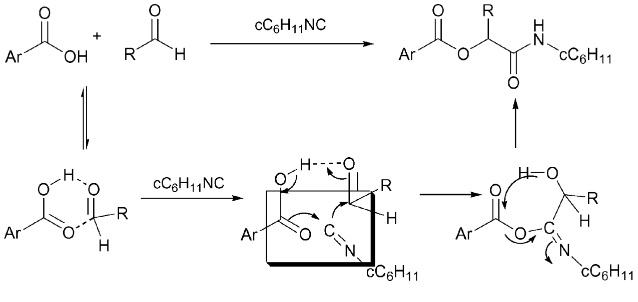
Tomás Torroba performed his undergraduate career in chemistry at the University of Valladolid, where he got a doctoral degree in 1983 under the supervision of Professor Angel Alberola. During 1978–1982 he was Assistant Professor at the Universidad de Valladolid, then he became Associate Professor at the University of Extremadura (1983–1998). Since 1998 he has been Full Professor at the University of Burgos. His research interest is the chemistry of poly-sulfur–nitrogen heterocycles.

S. Marcaccini

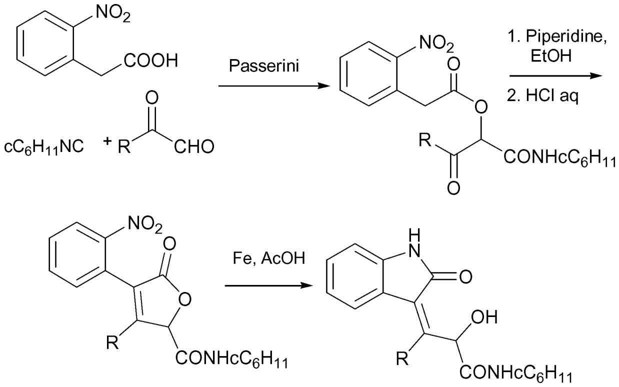
M. J. Rojo



T. Torroba



Scheme 1



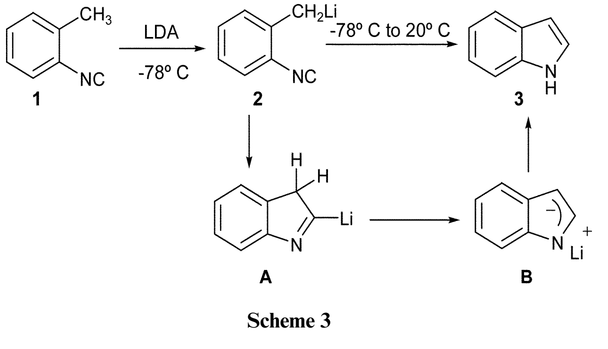
Scheme 2

of the indole nucleus may be successfully performed in one-pot reactions.

Although the process of α-addition implies that nucleophiles and electrophiles add onto the same carbon of the isocyano group, the completion of α-addition is usually a rapid process no matter the reactivity of the generated intermediates, however the order of addition of reagents is not always the same because it depends on the characteristics of the species selected.

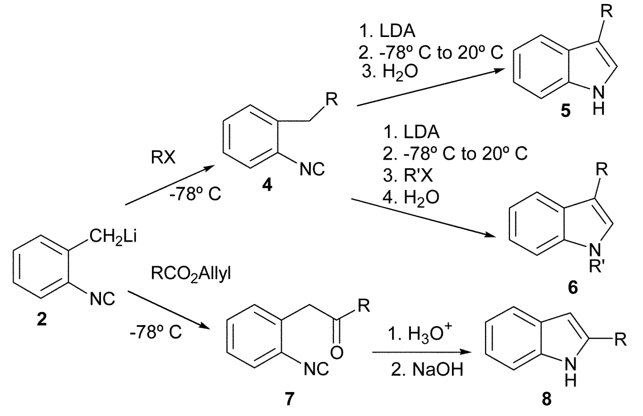
2.1. Isocyanide as an electrophile

One of the first indole syntheses using isocyanides as precursors was described by Saegusa *et al.* in 1977.[6] Thus, the selective ortholithiation of the alkyl group in *o*-alkylphenylisocyanides followed by subsequent intramolecular 5-*endo*-digonal ring closure afforded indole **3** (Scheme 3).



Scheme 3

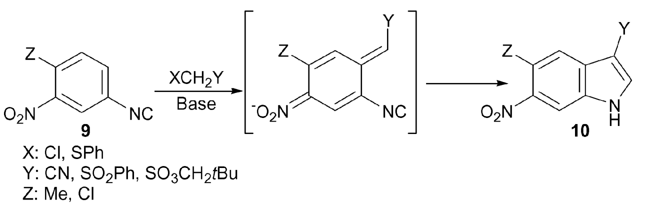
Solvent and temperature were critical for the obtained results. The lithiation on the alkyl group of *o*-tolyl isocyanide **1** was achieved in almost quantitative yield by lithium diisopropylamide (LDA) in diglyme at −78 °C. The lithiation of **1** in ether or THF as the solvent generated the *o*-(lithiomethyl)phenyl isocyanide **2** in low yields, being substantially accompanied by an adduct of LDA to the isocyano carbon of **1**, while the reaction at −25 °C afforded *C*-lithioaldimines resulting in the attack on the isocyanide group.[7] According to this behaviour Saegusa and co-workers synthesized 3-substituted indoles. However, attempts to trap the *C*-lithioaldimine **A** were not successful because this derivative rapidly converted to the stabilized α-lithioaldimine **B**, leading to 1-substituted indoles **6**, after addition of alkyl halides (Scheme 4).



Scheme 4

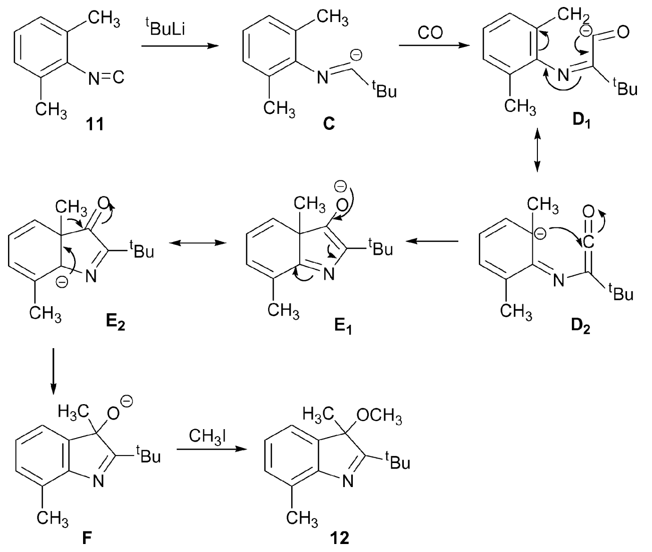
Consequently, only 1- and 3-substituted indoles were obtained by this method. Alternatively, Saegusa and co-workers synthesized 2-substituted indoles **8** from *o*-lithioalkylphenylisocyanides, although in this case the isocyanide group was only used as a protecting group.[8]

Applying a similar strategy, Makosza and Wojciechowski synthesized indoles *via* vicarious nucleophilic substitution (VNS) of hydrogen in *m*-isocyanonitrobenzenes. Products of VNS were formed as nitrobenzylic carbanions which cyclized rapidly *via* intramolecular nucleophilic addition to the isocyano group, as in the Saegusa synthesis of indoles (Scheme 5).[9]



Scheme 5

Another interesting reaction was described by Murai *et al.*, where isocyanides and carbon monoxide showed their parallelism in their reactivity as species with divalent carbon atoms (Scheme 6).[10] The reaction of carbon monoxide with *C*-lithioaldimine **C** prepared by α-addition of *tert*-butyllithium to xylylisocyanide **11** yielded the 3*H*-indole derivative **12** through a formal [4 + 1] cyclic coupling.



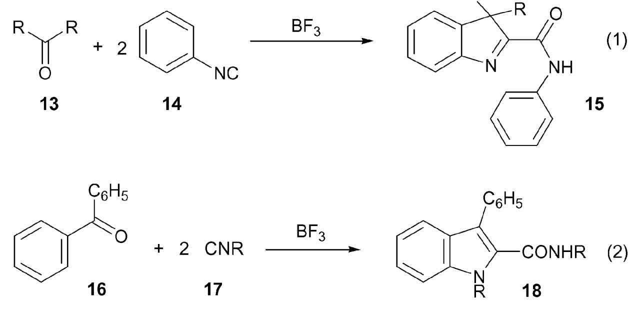
Scheme 6

Like isocyanides, carbon monoxide undergoes α-addition reactions. The reaction of *C*-lithioaldimine **C** with carbon monoxide generates the carbonyl anion D_1; these species are very reactive and they immediately convert to other reactive species such as lithium enolate D_2 which, by an intramolecular reaction, cyclizes to intermediate **E**. The aromatization energy favours the rearrangement of the alkyl group from the bridged carbon atom to the electron deficient adjacent carbonyl atom.

Attempts to synthesize aromatic indoles through this method were unfruitful. Thus, when the starting substrates were unsubstituted phenyl isocyanides, *ortho*-lithiation was an important side reaction.

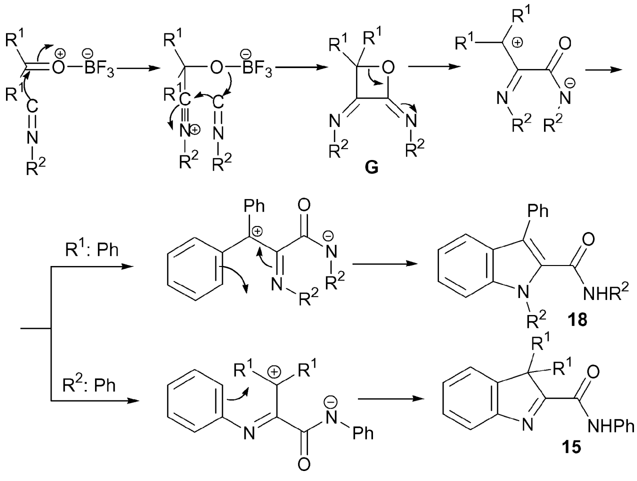
2.2. Isocyanide as a nucleophile

The order in the addition of a nucleophile or electrophile over the divalent carbon in carbon monoxide and the isocyano group depends on the species present in the reaction environment. The high versatility of these systems is explained by the different intermediates generated in every case. As seen above, the addition of nucleophiles as organolithium reagents allows reaching highly reactive species as acyllithium[10,11] and *C*-lithioaldimines,[10] respectively. The umpolung in these carbons was achieved by the addition to an electrophile which gives acylium[12] and nitrilium intermediate cations.[13] This behaviour is well illustrated by the reaction of alkyl ketones **13** and phenylisocyanide **14** in the presence of boron trifluoride to yield 3*H*-indole derivatives **15**[14] or by the analogous reaction of aromatic ketone **16** and *tert*-butylisocyanides **17** to yield aromatic indoles **18**[15] (Scheme 7). The



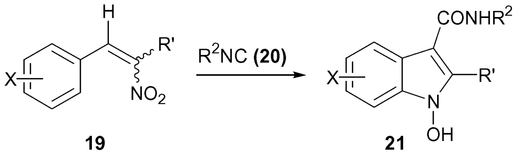
Scheme 7

proposed mechanism implied the formation of 2,3-diiminooxetane **G**, followed by rearrangement to a cationic intermediate and electrophilic aromatic substitution (Scheme 8).



Scheme 8

The synthesis of 1-hydroxyindoles **21** was achieved by a [1 + 4] cycloaddition reaction of isocyanides with aryl nitroalkenes **19** (Scheme 9).[16] However, in this case the nitrogen of the indole nucleus arose from the nitro group and not from the isocyano group.

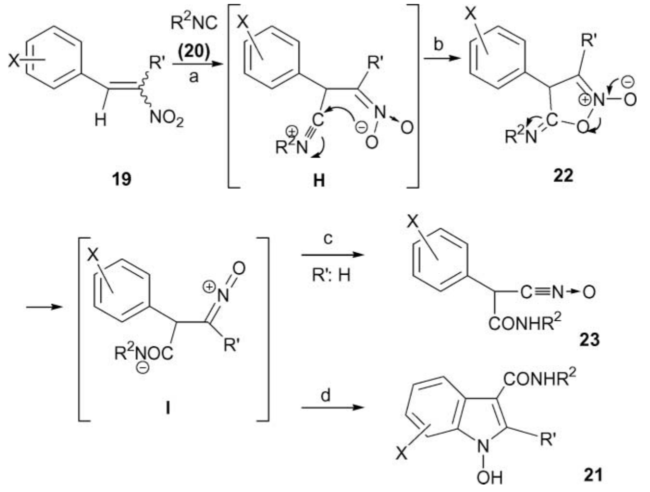


Scheme 9

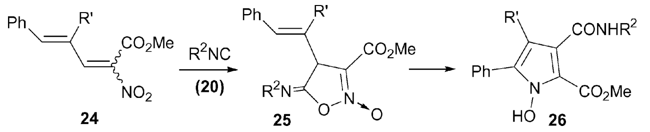
The reaction took place through a domino process. The initially produced isoxazoline *N*-oxide **22** rearranged *via* the rupture of the N–O bond to the intermediate **I**; the evolution of this intermediate depended on the nature of R′. When it was a hydrogen atom, its shift gave the nitrile oxide **23**, whereas if R′ was an alkyl group an intramolecular electrophilic substitution took place yielding the 1-hydroxyindole **21** (Scheme 10).

The mechanism proposed was in agreement with the experimental results; the increase of electrophilic character of the initial alkene (R′ = CO_2Me *vs.* Me) resulted in faster reactions (stage a); isomeric alkenes gave the same reaction (stage b); when R′ was a hydrogen atom the resulting product was a nitrile oxide (stage c); when two non-equivalent positions for the ring closure were available, the reactions involved preferentially the position of highest reactivity for the electrophilic substitution reaction (stage d). However, when the ring had donor substituents, the yield was considerably reduced in comparison to the unsubstituted or electron poor rings.

Alternatively, this methodology has been used to synthesize 1-hydroxypyrroles **26** from butadiene-nitro derivatives **24** (Scheme 11). In this case, the ring closure to the pyrrole ring was achieved by an electrophilic addition.



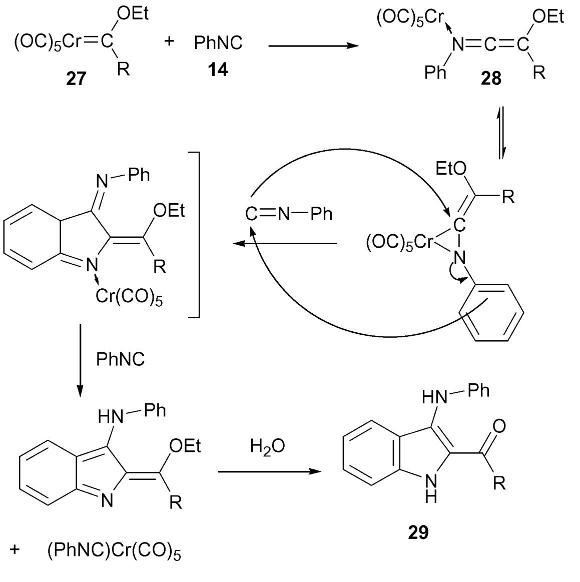
Scheme 10



Scheme 11

2.3. α-Addition to carbenes

The known reaction of carbenes and carbenoids with isocyanides to give iminoketenes has been applied to the synthesis of indoles.[17] Carbene complexes reacted with isocyanides to give ketimine complexes **28** in which the ligand was coordinated through the lone pair of the nitrogen atom; these complexes have been proven as versatile synthons in the synthesis of heterocyclic systems. When ketimine complexes were prepared from aromatic isocyanides, they rapidly added two further molecules of aryl isocyanide; the cycloaddition by *ortho*-attack at the *N*-aryl groups leads to the formation of 3-aminoindole derivatives **29** in the presence of water (Scheme 12).[18]



Scheme 12

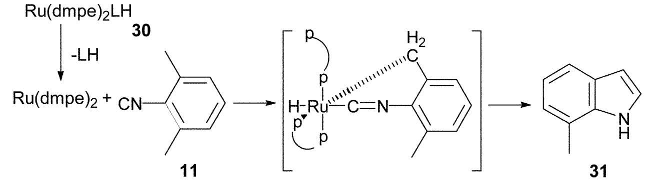
The results depended on the aromatic substitution of the isocyanide, thus, electron-rich aryl isocyanides favoured the formation of indoles, while electron-poor aryl isocyanides favoured the formation of azetidines.[19]

2.4. α-Addition catalyzed by transition metals

The insertion reactions of carbon monoxide into metal–carbon σ-bonds have received much attention because they constitute one of the best ways to introduce a carbonyl group in organic substrates. The relationship between carbon monoxide and isocyanides has provided a rapid development of similar chemistry on the isocyano group. Moreover, the isocyano group has an *N*-substituent which constitutes an additional advantage for the synthesis of nitrogen heterocyclic systems such as indoles.

In the group of isocyanides employed in the synthesis of indolic systems, *o*-functionalized arylisocyanides are the most valuable precursors. This is well illustrated in the indole synthesis mediated by transition metal complexes.

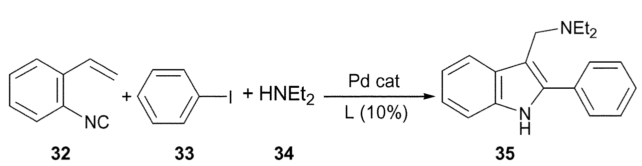
In the synthesis of indoles from *o*-alkylphenylisocyanides catalyzed by transition metals, the key stage is the activation of the C–H bond achieved by ruthenium complexes [$Ru(dmpe)_2LH$] **30**. The intramolecular oxidative addition of ruthenium, previously coordinated to the isocyano group, allowed the activation of the C–H bond, as it is shown in Scheme 13.[20]



Scheme 13

The catalytic formation of indoles from less hindered isocyanides took a slightly different course. Heating a solution of *o*-tolyl isocyanide with the catalyst at 140 °C resulted in isocyanide decomposition. When the reaction temperature was decreased to 60 °C RuH(indole-C^2)$(dmpe)_2$ was formed; the sustained heating of this complex gave the more stable RuH(indole-*N*)$(dmpe)_2$ complex, which constituted a non-catalytic process. This different behaviour between more or less hindered isocyanides was explained by the destabilization of N–H insertion products from the *cis* C–H activation products when the indole nucleus possessed an alkyl group in the 7-position.[20]

o-Alkenylphenyl isocyanide **32** reacted with aryl iodide **33** and amine **34** through palladium iminoacyl complexes in an intramolecular cyclization reaction producing indole **35**. Depending on the nature of the catalyst, the reaction needed stoichiometric[21] or catalytic[22] amounts of the organopalladium complex (Scheme 14).



Scheme 14

Analogous methodology tried on *o*-((trimethylsilyl)ethynyl)phenyl isocyanide gave the indolidenemethyl palladium complex **J** (Fig. 1).[23] The impossibility of 1,3-hydrogen shift explained the lack of aromatisation of the product.

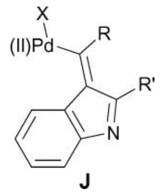
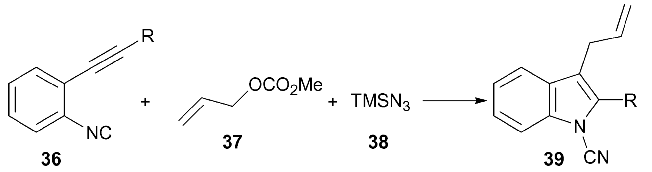


Fig. 1 Indolidenemethyl palladium complex **J**.

The same substrates have been employed in the synthesis of *N*-cyanoindoles **39** in a multicomponent coupling reaction (MCR) of arylisocyanides **36**, allylmethyl carbonate **37** and trimethylsilyl azide **38** (Scheme 15).[24]



Scheme 15

The isocyanide is inserted between the Pd–N_3 bond in the π-allylpalladium azide **K**, generated in the reaction of Pd(0) with allylmethyl carbonate and $TMSN_3$. A π-allylpalladium mimic of the Curtius rearrangement gave the palladium–carbodiimide complex **M** in equilibrium with the palladium–cyanamide complex **N**. The *N*-cyanoindoles were formed *via* insertion of the alkyne moiety into the Pd–N bond in the intermediate **N** (Scheme 16).

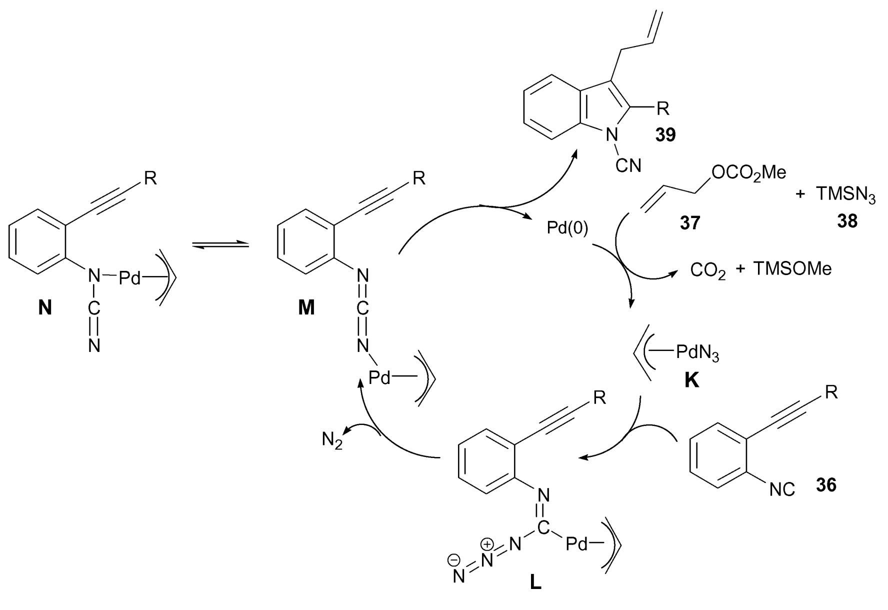
The key step in the proposed mechanism was the formation of the π-allylpalladium–carbodiimide complex through a palladium mimic of the Curtius rearrangement, that explained why in this case the insertion took place in the Pd–N bond in an opposite way to the Pd–C isocyanide insertion, which occurred in previous reactions.

Less clear was the mechanism of the formation of indolenine derivatives **43** from dicobalt octaisocyanides **40** and carbon tetrahalides (Scheme 17). The authors proposed two different pathways, the first going through the dihaloketimine and the second going through an oxidative addition of the polyhalogen compound to $Co(RNC)_8$ and double insertion of isocyanide molecules into the cobalt–carbon bond.[25]

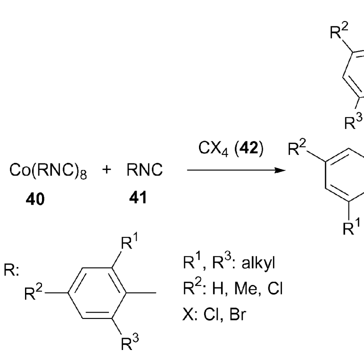
3. Radical reactions

Radical reactions have become an important tool in organic chemistry, thereby radical carbonylation has become a useful method for the preparation of carbonyl compounds.[26] Similarly, the ability of the isocyano group to form imidoyl radicals has been known since 40 years ago,[27] however the easy cleavage of the carbon–nitrogen bond in alkylimidoyl radicals has restricted their synthetic application to deamination reactions.[28]

Nevertheless, the scope of more stable *N*-arylimidoyl radicals for the synthesis of nitrogen heterocyclic systems has been

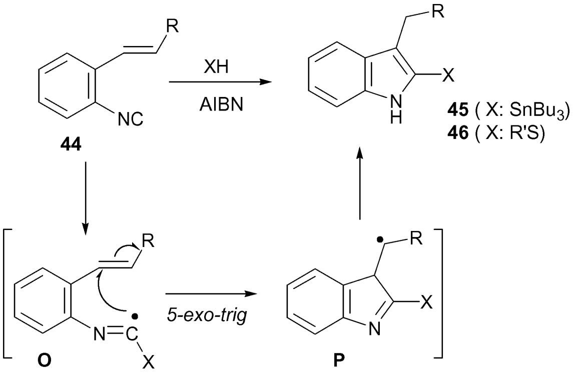


Scheme 16



Scheme 17

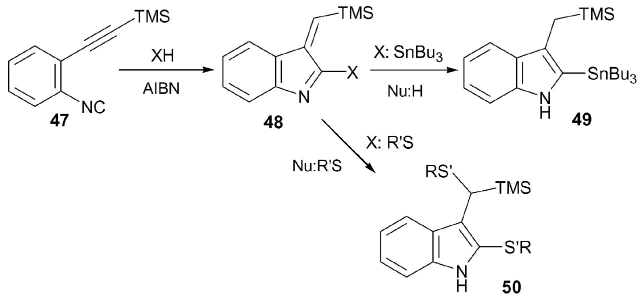
recently developed.[29] The α-imidoyl radicals **O** obtained from *o*-isocyanostyrene derivatives **44** are added to the carbon–carbon double bond in a 5-*exo*-trig fashion to furnish indoles **45–46** (Scheme 18).



Scheme 18

The nature of R in **44** was very important for the obtained results. While radical-stabilizing substituents, as carboxymethyl or phenyl groups, gave indoles in good yields, the substrates bearing alkyl groups gave a mixture of indole and tetraquinoline derivatives.[30]

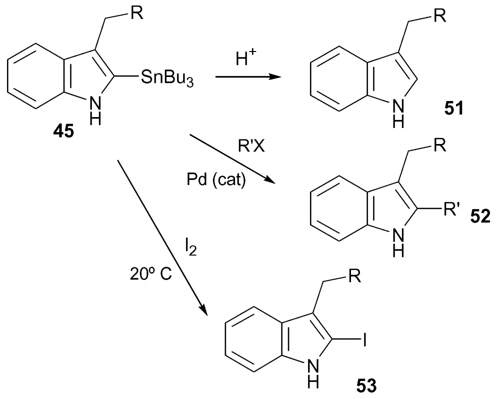
Alternatively, the same methodology has been developed for alkynyl starting materials. The intramolecular alkyne–isocyanide free-radical reaction took place in a 5-*exo*-dig fashion when the substituent in the unsaturated carbon–carbon bond was the TMS group. The indolenines generated in the cyclization reaction were attacked by different nucleophiles depending on the source of the free-radical in the initial cyclization (Bu_3SnH or thiols) (Scheme 19).[31]



Scheme 19

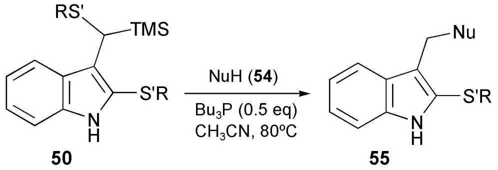
The scope of these syntheses goes further to the indole nucleus. The 2-stannylindole intermediate **45** generated by tin-mediated cyclizations could be destannylated by treatment with mild acid to 3-substituted indoles. In addition, it could be used as an intermediate in the straight synthesis of 2,3-disubstituted indoles **52** by Stille's palladium-mediated coupling reactions. After oxidation of the tin–carbon bond with iodine, the corresponding 2-iodoindole **53** was also obtained (Scheme 20). These 2-iodoindoles underwent smooth palladium-catalyzed coupling reactions with substrates such as acetylenes (Sonogashira coupling), acrylates (Heck reaction), vinyl tin reagents (Stille coupling), and phenylboronic acid (Suzuki coupling).[30]

The synthetic possibilities associated with bis-thioindoles generated by sulfur-mediated radical cyclizations on *o*-((trimethylsilyl)ethynyl)phenyl isocyanide have been studied. The coupling of



Scheme 20

dithioindoles **50** with active hydrogen-containing compounds was achieved utilizing Somei's conditions (Scheme 21).[32]

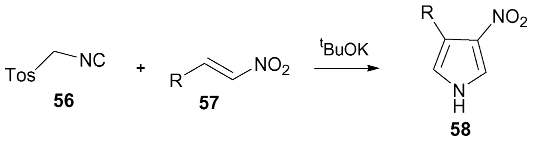


Scheme 21

The synthesis of indole systems by radical cyclization reactions has several advantages such as high chemo- and regioselectivity, functional group tolerance, and possibilities of diverse transformations of the products because of the diverse functionalization resulting in these reactions. These advantages are well illustrated by the synthesis of some indolic alkaloids such as vindoline[30] and aspidophytine (Scheme 22).[33]

4. α-Metallation

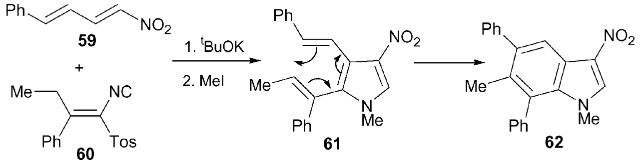
As mentioned above, one distinction between isocyanides and carbon monoxide is the *N*-substituent. This characteristic is important for carrying out intramolecular cyclizations, but also because of the possibility of anionization of the α-position.[34] α-Metallated isocyanides can add to polar double bonds forming heterocycles. This was illustrated in the van Leusen pyrrole synthesis based on the reaction of tosylmethyl isocyanide (TosMIC, **56**) with electron-deficient alkenes (Scheme 23). The toluenesulfinate ion was eliminated at the final stage.[35]



Scheme 23

Although the indole syntheses are usually based on the construction of a pyrrole ring onto the benzene nucleus, as in the methods described above, the methodology followed in this case implies the building of a benzene ring onto a pyrrole. The precursors were synthesized following the van Leusen pyrrole synthesis, through a base-induced cycloaddition of 1-tosylalk-1-enyl isocyanide **60** to Michael acceptors. Thermal or photochemical electrocyclization of the 2,3-dialk-1′-enylpyrrole **61**, followed by dehydrogenation gave indole **62** in excellent yields.[36]

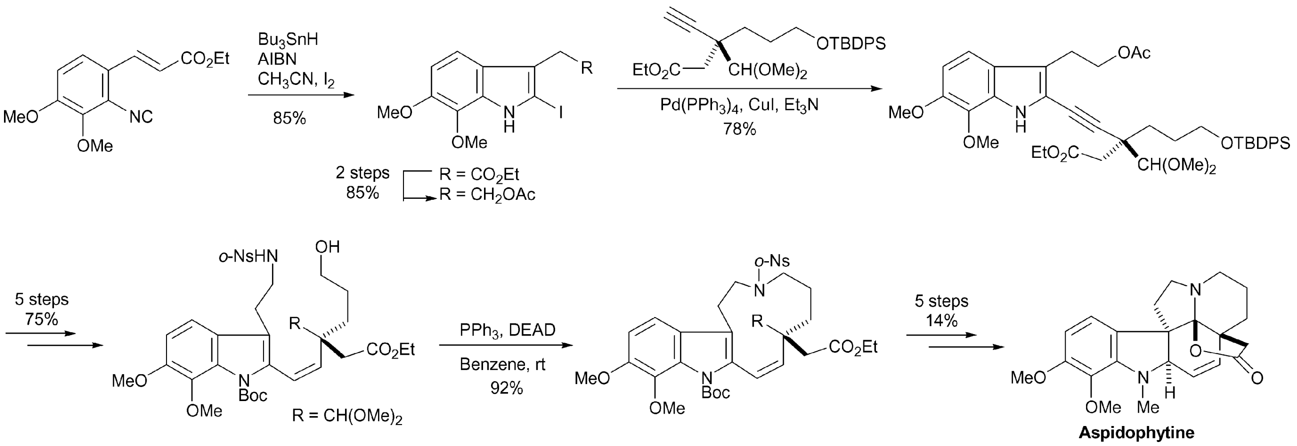
The above example illustrates another isocyanide characteristic. Isocyanides are examples of the few organic compounds with two nucleophile sites, that explain the different results obtained when a reaction with similar reagents takes place in the presence (Scheme 24) or absence of base (Scheme 11).



Scheme 24

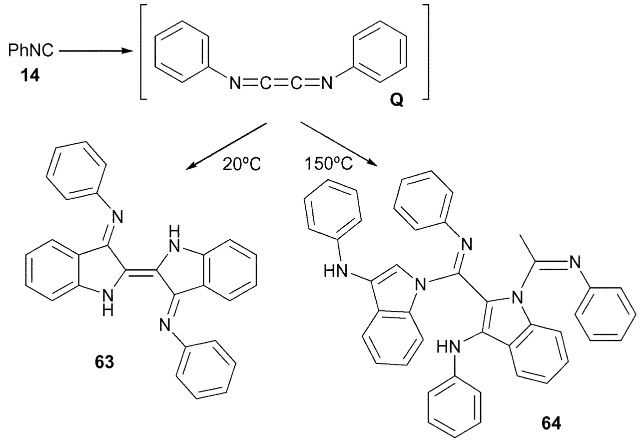
5. Oligomerization of aryl isocyanides

The first known reaction of isocyanides for the preparation of the indole nucleus was the oligomerization of phenyl isocyanide. Aryl isocyanides rapidly became blue at ambient temperature, this colour arose from the indolic tetramer **63**.[37] However at



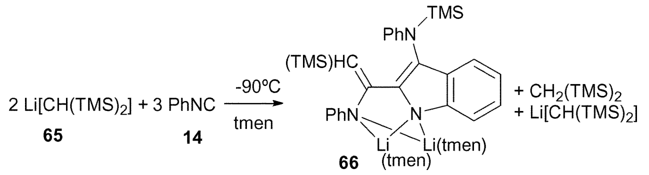
Scheme 22

temperatures above 200 °C isocyanides isomerized into the corresponding nitriles[38] and when aryl isocyanides were heated at 150 °C for several hours a stable hexamer **64** was obtained.[39] All mechanistic proposals for these oligomerization processes proposed the dimeric intermediate **Q** as the key intermediate (Scheme 25).



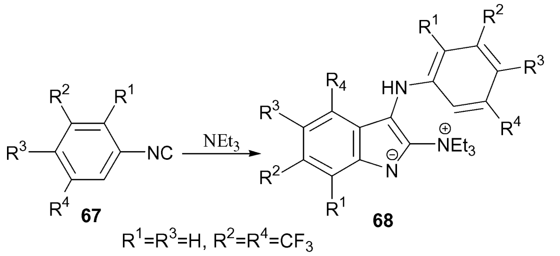
Scheme 25

The presence of an appropriate base in the reaction environment has been useful for the oligomerization process. In this way, alkyl lithium reagents and phenyl isocyanide reacted at −78 °C in the presence of TMEDA to yield products of α-addition and *ortho*-lithiation,[40] while lower temperatures (−90 °C) and the presence of $LiCH(TMS)_2$ **65** as a base afforded the trimeric *N*-lithioindole **66** (Scheme 26).[41]



Scheme 26

The presence of electron-withdrawing substituents on the aromatic nucleus of aryl isocyanides allowed the synthesis of indolates **68** in the presence of a weak base such as triethylamine (Scheme 27).[42]



R^1=R^3=H, R^2=R^4=CF_3

R^1=Br, R^2=R^4=H, R^3=NO_2

R^1=R^4=H, R^2=CF_3, R^3=Cl

R^1H, R^2=R^3=R^4=Cl

Scheme 27

6. Conclusions

Among the many approaches to the construction of the indole nucleus, those starting from isocyanide derivatives are characterized by experimental simplicity and wide versatility. The complexity of the indole derivatives obtained by these methodologies, the ready availability of the starting materials and the simple manipulation of the reagents, usually involving one-pot reactions, constitute attractive reasons for the use of isocyanides in the synthesis of indole derivatives that are useful in further synthetic manipulations on the way to highly elaborated structures.

Acknowledgements

We gratefully acknowledge financial support from the Junta de Castilla y León, Consejería de Educación y Cultura, y Fondo Social Europeo (Project ref. BU01/03).

References

1 M. Suginome and Y. Ito, in *Science of Synthesis*, *Houben-Weyl Methods of Molecular Transformations*, Georg Thieme Verlag, Stuttgart, 2004, vol. 19, pp. 445–530.
2 (*a*) G. W. Gribble, *Contemp. Org. Synth.*, 1994, 145–172; (*b*) G. W. Gribble, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1045–1075.
3 (*a*) A. Dömling and I. Ugi, *Angew. Chem., Int. Ed.*, 2000, **39**, 3168; (*b*) V. Nair, C. Rajesh, A. U. Vinod, S. Bindu, A. R. Sreekanth, J. S. Mathen and L. Balagopal, *Acc. Chem. Res.*, 2003, **36**, 899.
4 S. Marcaccini, R. Pepino, C. F. Marcos, C. Polo and T. Torroba, *J. Heterocycl. Chem.*, 2000, **37**, 1501–1503.
5 S. Marcaccini, T Torroba, in *Multicomponent reactions*, ed. J. Zhu and H. Bienaymé, Wiley-VCH, Weinheim, 2005, ch. 2, pp. 33–75.
6 Y. Ito, K. Kobayashi and T. Saegusa, *J. Am. Chem. Soc.*, 1977, **99**, 3532–3534.
7 Y. Ito, K. Kobayashi, N. Seko and T. Saegusa, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 73–84.
8 Y. Ito, K. Kobayashi and T. Saegusa, *J. Org. Chem.*, 1979, **44**, 2030–2032.
9 K. Wojciechowski and M. Makosza, *Tetrahedron Lett.*, 1984, **25**, 4793–4794.
10 A. Orita, M. Fukudome, K. Ohe and S. Murai, *J. Org. Chem.*, 1994, **59**, 477–481.
11 (*a*) M. Ryang and S. Tsutsumi, *Bull. Chem. Soc. Jpn.*, 1962, **35**, 1121–1124; (*b*) N. S. Nudelman and A. A. Vitale, *J. Org. Chem.*, 1981, **46**, 4625–4626.
12 M. Koch and W. Haaf, *Org. Synth.*, 1964, **44**, 1–3.
13 (*a*) B. Henkel, B. Beck, B. Westner, B. Mejat and A. Dömling, *Tetrahedron Lett.*, 2003, **44**, 8947–8950; (*b*) O. T. Kern and W. B. Motherwell, *Chem. Commun.*, 2003, 2988–2989.
14 (*a*) B. Zeeh, *Chem. Ber.*, 1968, **101**, 1753–1760; (*b*) B. Zeeh, *Chem. Ber.*, 1969, **102**, 1876–1882.
15 B. Zeeh, *Chem. Ber.*, 1969, **102**, 678–685.
16 A. Foucaud, C. Razorilalana-Rabearivony, E. Loukakou and H. Person, *J. Org. Chem.*, 1983, **48**, 3639–3644.
17 (*a*) K. A. Hofmann, *Chem. Ber.*, 1907, **40**, 1777; (*b*) R. Aumann and E. O. Fischer, *Chem. Ber.*, 1968, **101**, 954; (*c*) C. G. Kreiter and R. Aumann, *Chem. Ber.*, 1978, **111**, 1223–1227; (*d*) R. Aumann, *Angew. Chem., Int. Ed. Engl.*, 1988, **100**, 1456–1467.
18 (*a*) R. Aumann, E. Kuckert and H. Heinen, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 978–980; (*b*) R. Aumann, H. Heinen, C. Krüger and Y.-H. Tsay, *Chem. Ber.*, 1986, **119**, 3141–3149.
19 R. Aumann and H. Heinen, *Chem. Ber.*, 1986, **119**, 2289–2307.
20 G. C. Hsu, W. P. Kosar and W. D. Jones, *Organometallics*, 1994, **13**, 385–396.
21 K. Onitsuka, S. Suzuki and S. Takahashi, *Tetrahedron Lett.*, 2002, **43**, 6197–6199.
22 K. Onitsuka, M. Yamamoto, S. Suzuki and S. Takahashi, *Organometallics*, 2002, **21**, 581–583.
23 K. Onitsuka, M. Segawa and S. Takahashi, *Organometallics*, 1998, **17**, 4335–4337.

24 S. Kamijo and Y. Yamamoto, *J. Am. Chem. Soc.*, 2002, **124**, 11940–11945.

25 Y. Yamamoto and H. Yamazaki, *Organometallics*, 1988, **7**, 2411–2413.

26 (*a*) I. Ryu and N. Sonoda, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1050–1066; (*b*) I. Ryu, N. Sonoda and D. P. Curran, *Chem. Rev.*, 1996, **96**, 177–194; (*c*) I. Ryu, *Chem. Soc. Rev.*, 2001, **30**, 16–25; (*d*) I. Ryu, *Chem. Rec.*, 2002, **4**, 249–258; (*e*) M. Tojino, Y. Uenoyama, T. Fukuyama and I. Ryu, *Chem. Commun.*, 2004, 2482–2483.

27 T. Saegusa, S. Kobayashi, Y. Ito and N. Yasuda, *J. Am. Chem. Soc.*, 1968, **90**, 4182.

28 D. H. R. Barton, G. Bringmann, G. M. Lamotte, R. S. H. Motherwell and W. B. Motherwell, *Tetrahedron Lett.*, 1979, 2291–2294.

29 R. Leardini, G. F. Pedulli, A. Tundo and G. Zanardi, *J. Chem. Soc., Chem. Commun.*, 1984, 1320–1321.

30 (*a*) H. Tokuyama and T. Fukuyama, *Chem. Rec.*, 2002, 37–45; (*b*) S. Kobayashi, T. Ueda and T. Fukuyama, *Synlett*, 2000, 883–886.

31 (*a*) J. D. Rainier and A. R. Kennedy, *J. Org. Chem.*, 2000, **65**, 6213–6216; (*b*) J. D. Rainier, A. R. Kennedy and E. Chase, *Tetrahedron Lett.*, 1999, **40**, 6325–6327.

32 M. Somei, Y. Karasawa and C. Kaneko, *Heterocycles*, 1981, **16**, 941–949.

33 S. Sumi, K. Matsumoto, H. Tokuyama and T. Fukuyama, *Org. Lett.*, 2003, **5**, 1891–1893.

34 U. Schöllkopf, *Angew. Chem., Int. Ed. Engl.*, 1977, **16**, 339–422.

35 A. M. van Leusen, H. Siderius, B. E. Hoogenboom and D. van Leusen, *Tetrahedron Lett.*, 1972, **13**, 5337–5340.

36 (*a*) J. Moskal and A. M. van Leusen, *J. Org. Chem.*, 1986, **51**, 4131–4139; (*b*) R. ten Have and A. M. van Leusen, *Tetrahedron*, 1998, **54**, 1913–1920.

37 C. Grundmann, *Chem. Ber.*, 1958, **91**, 1380–1387.

38 (*a*) A. W. Hofmann, *Justus Liebigs Ann. Chem.*, 1867, **144**, 114; (*b*) J. U. Nef, *Justus Liebigs Ann. Chem.*, 1892, **270**, 267; (*c*) G. Gross and C. Wentrup, *J. Chem. Soc., Chem. Commun.*, 1982, 360–361.

39 J. C. A. Boeyens, L. M. Cook, Y. Ding, M. A. Fernandes and D. H. Reid, *Org. Biomol. Chem.*, 2003, **1**, 2168–2172.

40 H. M. Walborsky and P. Ronman, *J. Org. Chem.*, 1978, **43**, 731–734.

41 M. A. Fernandes, M. F. Lappert, M. Layh and B. Omondi, *Chem. Commun.*, 2003, 656–657.

42 M. A. Mironov and V. S. Mokrushin, *Mendeleev Commun.*, 1998, 242–243.