Journal of Organometallic Chemistry 696 (2011) 87–98

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Tandem imination/annulation of γ- and δ-ketoalkynes in the presence of ammonia/amines

Antonio Arcadi [a,*], Giorgio Abbiati [b], Elisabetta Rossi [b]

[a] Dipartimento di Chimica, Ingegneria Chimica e Materiali, Università degli Studi di L'Aquila, Via Vetoio, Coppito Due, I-67100 L'Aquila, Italy
[b] DISMAB, Sezione di Chimica Organica Alessandro Marchesini, Università degli Studi di Milano, Via Venezian 21, 20133 Milano, Italy

ARTICLE INFO

Article history:
Received 15 July 2010
Received in revised form
6 August 2010
Accepted 10 August 2010
Available online 18 August 2010

Keywords:
Ketoalkynes
Heterocycles
Dual role catalysts
Domino reactions
Hydroamination
Aminobenzannulation

ABSTRACT

In this account, we summarize the peculiar effects and advantages of gold, silver, and titanium dual role catalysis over the uncatalyzed tandem imination/annulation processes of γ- and δ-ketoalkynes.

1. Introduction

Domino reactions are proven to play a pivotal role for the assembly of simple or polyfunctionalized organic molecules from readily accessible organic compounds. [1] Unactivated alkynes are not very reactive toward nucleophiles. This behavior changes significantly as soon as the triple bond is activated by complexation with a suitable metal catalyst. On the other hand, transition metals can operate as bifunctional Lewis acids activating either (or both) carbon–carbon multiple bonds via π-binding or make the σ-complexes with heteroatoms. [2] The determination of the relative ability for making π- and σ-complexes with appropriate substrates is a valuable tool for the choice of catalysts for the desired transformations, especially in the cases when bi- or polyfunctional substrates are involved. Computed enthalpies of formation for various Lewis acid and metal salt complexes [3] with aldehydes, imines, styrene and phenylacetylene have been reported to help to evaluate what kind of Lewis acids (and metal salts) is more suitable to activate selectively individual functional group [4]. Here our own results associated with the selective transformations of γ- and δ-ketoalkyne derivatives with ammonia/amines by means of transition metals catalysis are summarized and discussed in the context of current status of designing intelligent synthetic strategies on the way to the desired products by the knowledge of organometallic Lewis acids properties. Moreover, the role of transition metal catalysis on accomplishing transformations that were previously impractical due the severe conditions required will be highlighted.

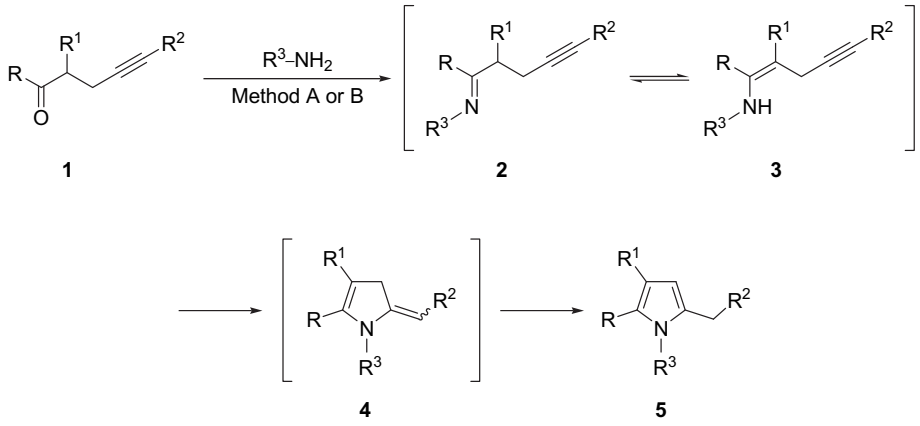
2. Results and discussion

During the last years, we focused our attention on the uncatalyzed and catalyzed domino addition-annulation reaction of of γ- and δ-ketoalkynes in the presence of ammonia/amines. In particular, the sequential addition/elimination/cycloamination of 4-pentynones **1** in the presence of benzylamine or ammonia produced 1,2,3,5-substituted and 2,3,5-substituted pyrroles and fused pyrrole systems in good to high yields (Scheme 1). [5] The reaction mechanism probably involves the formation of imine/enamine intermediates **2**/**3** that undergo a regioselective *5-exo-dig* cyclization followed by isomerization to give pyrroles **5**. We previously published the synthesis of simple and polycondensed furans starting from different substituted pentynones and described for these compounds unusual base catalyzed reactions [5b,6].

Surprisingly, under the same reaction conditions 2-propynyl-1,3-dicarbonyl compounds **6** failed to give the pyrrole derivatives

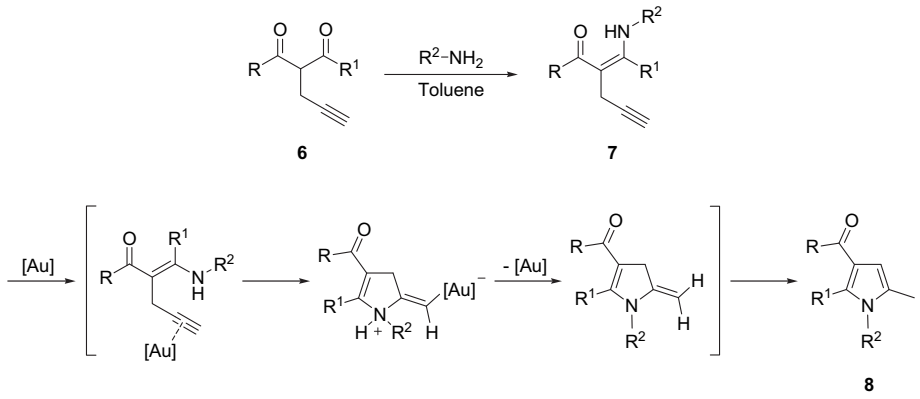
* Corresponding author. Tel.: +390862433773; fax: +390862434203.
E-mail address: antonio.arcadi@univaq.it (A. Arcadi).

0022-328X/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2010.08.011



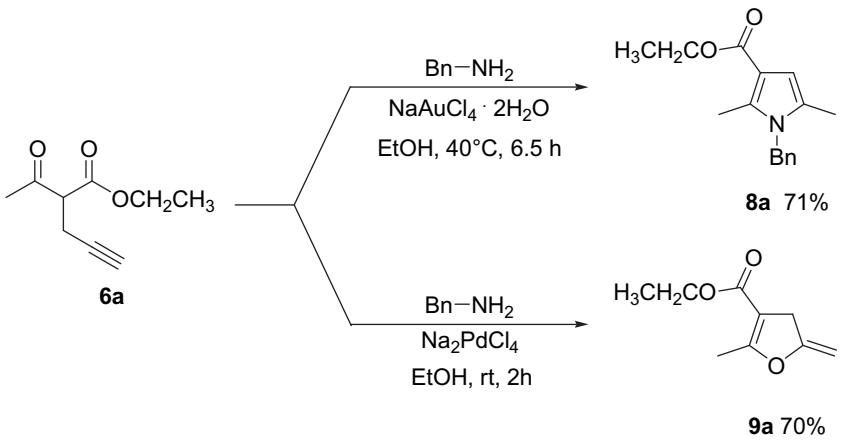
Method A: R^3 = Bn, toluene or xylene, ΔT, 2-23h, 76-97%
Method B: R^3 = H, 2M in MeOH, 120 °C, 9-24 h, 50-89%

Scheme 1.

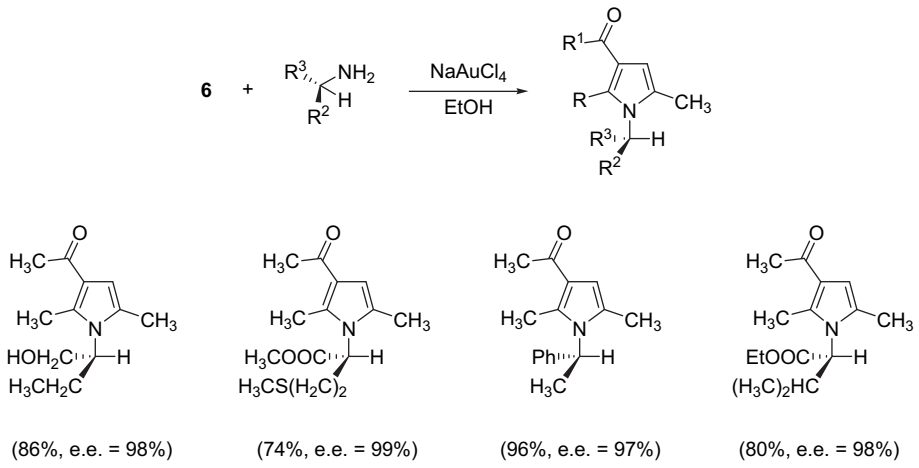


Scheme 2.

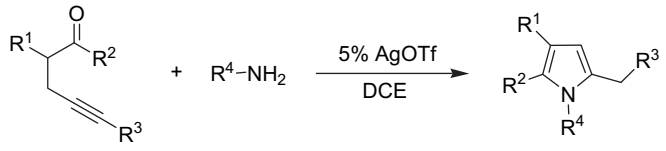
allowing for the isolation of enaminones **7** (Scheme 2). Very likely, the *5-exo-dig* annulation reaction of **7** as well as of a variety of alkynes containing nucleophiles near the alkyne moiety is dependent on intriguing combination of electronic, coordinating, and medium factors. Among them, the strength of the nucleophile appears to play a prominent role. The presence of the electron-withdrawing acyl group in **7** implies that the electron density of the NH–Ph group is lower than it would be if there were no –M resonance effects of the β-substituent of the enamine. Consequently, the intramolecular nucleophilic attack of the NH–Ph on the carbon–carbon triple bond was hampered by the weakness of the nucleophile.



Scheme 3.



Scheme 4.



Scheme 5.

Although the regioselective intramolecular cyclization of **7** to pyrrole can be easily accomplished under the catalytic action of various metal salts, $NaAuCl_4$ resulted the catalyst of choice for the conversion of the 2-propynyl-1,3-dicarbonyl compounds **6** into pyrroles **8** because of its further specific quality of accelerating the condensation of ketones with primary amines determining the prevalence of the formation of the pyrrole over that of the 5-methylene-4,5-dihydrofuran scaffold **9** derived by a competitive tandem intramolecular oxymetalation/protonolysis reaction (Scheme 3).

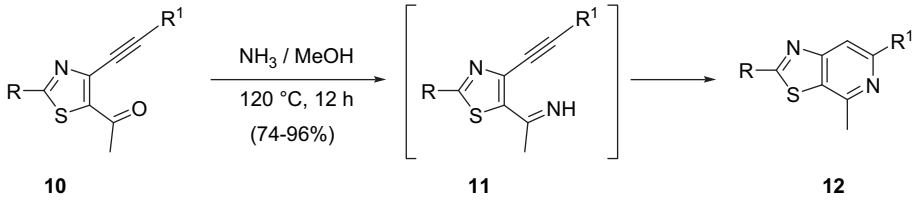
These results clearly point out that the condensation reaction of **6** with primary amines must be faster than the oxymetalation reaction to allow the chemoselective formation of the pyrrole nucleus. Because of the simple experimental procedure, mild conditions, easy availability of the starting materials, and ability to incorporate a variety of functional groups, the method represents a valuable tool for the synthesis of 1,2,3,5-tetrasubstituted pyrroles. [7] On the basis of the assumption that stereogenic center in the starting amine is not affected during this transformation, subsequent extension of the procedure to enantiomerically pure amines, β-amino alcohols and α-aminoesters led to the formation of the trisubstituted pyrroles in homochiral form (Scheme 4) [8]. The oxo- and alkynophilicity of gold(III) derivatives [9] makes possible to activate both C = X (X = O, N,…) unsaturated bonds and C–C multiple bonds in a single transformation. [10] Interestingly, further exploration of Au-catalyzed condensation reaction of ketones with amines allowed the overcoming of the drawbacks caused by more vigorous reagents and drastic reaction conditions [11].

More recently the research group of Dake reported that, also, silver salts can efficiently promote a similar path to pyrroles (Scheme 5) [12]. Silver salts have been shown to increase the speed of the reaction and gave better yields than gold(I) precatalyst. The activation of common C═O and C═N electrophiles by using gold, platinum, silver and copper complexes are beneficial for the design of new catalysts triggering annulation processes. Recent progress in this field has been highlighted [13].

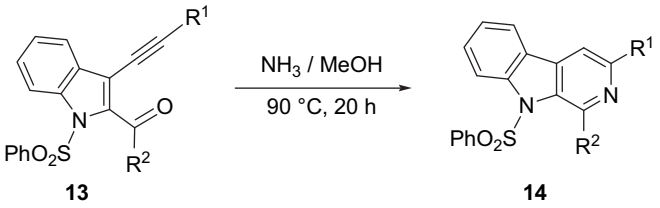
Interestingly, the regioselective outcome of the annulation reaction (6-*endo-dig* cyclization vs. 5-*exo-dig* cyclization) seemed to be directed by a suitable choice of the starting γ-ketoalkyne derivative. Indeed, by contrast with the above results, the presence of the γ-ketoalkyne moiety in an aromatic framework determines the formation of the 6-*endo-dig* cyclization derivatives. The treatment, under metals free conditions, of the readily available 2-substituted-5-acetyl-4-alkynylthiazoles **10** with ammonia in MeOH led to the formation of the pyrido[3,4-*c*]thiazoles **12**. Probably the formation of the products **12** occurs via the regioselective 6-*endo-dig* cyclization of the imine intermediate **11** (Scheme 6) [14].

Analogously, the 6-*endo-dig* annulation reaction of 2-acyl-3-alkynyl-1-benzenesulphonyl-1H-indoles and 3-alkynyl-1-benzenesulphonyl-1H-indole-2-carbaldehydes **13** in the presence of ammonia gave the corresponding 9H-pyrido[3,4-*b*]indoles **14** in satisfactory yields (Scheme 7) [15].

2-Alkynylbenzaldehydes **15** have also been reported by Sakamoto et al. to undergo thermal annulation in the presence of ammonia to give isoquinolines **16** [16]. A more comprehensive study showed that microwaves heating gave comparable or better yields in reduced reaction times (Scheme 8) [17]. The product derived from a 5-*exo-dig* cyclization mode has never isolated or



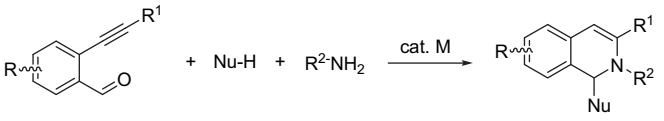
Scheme 6.



Scheme 7.

detected in the reaction crude, even when the alkyne was substituted with an aromatic ring potentially able to stabilize the α-anion of the zwitterionic intermediate **18**. The regiospecificity achieved is probably due to the zwitterionic intermediate **17** and the resulting isoquinoline **16**, arising from a 6-*endo*-*dig* mechanism, being more thermodynamically stable than the hypothetical intermediate **18** and consequent isoindole, derived from a 5-*exo*-*dig*cyclization mode.

Isoquinoline heterocycles have been also prepared in excellent yields via copper-catalyzed cyclization of *tert*-butylimine derivatives of 2-alkynylbenzaldehydes [18]. Dirhodium acetate and silver triflates cooperatively catalyzed tandem cyclization/three-component reactions of 2-alkynylarylaldimines with diazo compounds and water or alcohols afforded 1,2-dihydroisoquinolines bearing α-hydroxyl-β-amino carboxylate skeleton in high yield [19]. AgOTf-catalyzed addition of pronucleophiles to 2-alkynylarylaldimines led functionalized 1-substituted-1,2-dihydroisoquinoline skeletons [20]. With related substrates, bis(2,4,6-trimethylpyridine) silver(I) hexafluorophosphate proved to be a more powerful catalyst for challenging nucleophiles such as the substituted silyl enol ethers. Compounds possessing the main structural features of karachine, a berberine alkaloid have been accessed as well as the pyrroloisoquinoline core after dipolar additions to isoquinoline ylide intermediates [21]. Silver catalysis, also, allowed the synthesis of isoquinolines from *ortho*-alkynylarenecarbaldehyde oxime derivatives [22]. Coinage metal salts [copper(I), gold(I), gold(III), silver] and palladium(II) salts have been tested as catalysts for the cyclization of *ortho*-alkynylarenecarbaldehyde hydrazones. However, only silver nitrate gave good results [23]. Copper(I)-catalyzed domino four-component coupling-cyclization using 2-ethynylbenzaldehydes, paraformaldehyde, secondary amine, and *t*-BuNH$_2$ in DMF leads to direct and efficient formation of 3-(aminomethyl)isoquinolines in good to high yields [24]. Moreover, a concise synthesis of 1,2-dihydroisoquinolines was established via three-component reactions of 2-alkynylbenzaldehydes, amines and various nucleophiles or pronucleophiles in the absence of a catalyst [25] or in the presence of carbophilic Lewis acid catalysts such as AgOTf [26], In(OTf)$_3$, or AuClPPh$_3$/AgNTf$_2$ [27] and Cu(I) or Pd(II) salts [28] CuSO$_3$/C$_{12}$H$_{25}$SO$_3$Na [29] and Mg(ClO$_4$)$_2$/Cu(OTf)$_2$ [30] (Scheme 9).

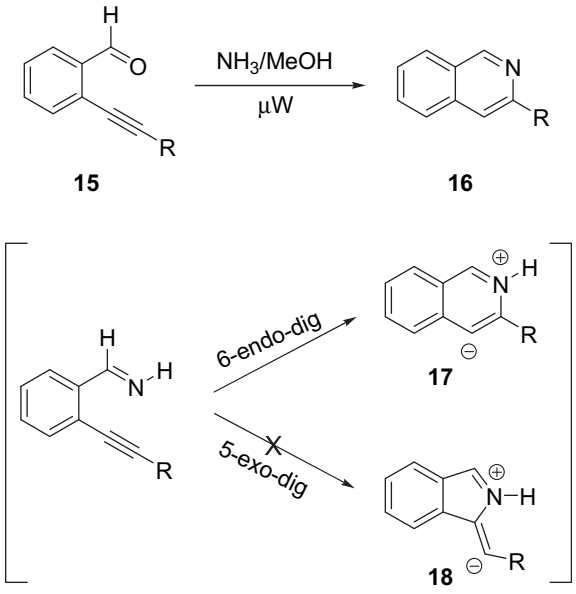


Scheme 9.

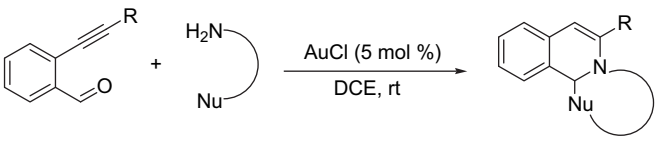
A two-component activation system that combines metal catalysis (AgOTf) and the employment of catalytic amount of organocatalyst (PPh$_3$) has been successfully employed in the three-component reaction of 2-alkynylbenzaldehyde, amine, and α,β-unsaturated ketone. This reaction proceeds smoothly in THF under mild conditions leading to the functionalized 1,2-dihydroisoquinolines in moderate to good yields [31]. A highly efficient silver triflate-catalyzed three-component reaction of 2-alkynylbenzaldehyde, sulfonohydrazide, and α,β-unsaturated carbonyl compound gave H-pyrazolo[5,1-a]isoquinoline-1-carboxylates in good yield [32]. For the possible mechanism, after condensation of 2-alkynylbenzaldehyde derivative with sulfonohydrazide, the corresponding N'-(2-alkynylbenzylidene)hydrazide would be obtained. In the presence of AgOTf, the triple bond would be activated and then the 6-endo-cyclization occurred to afford an isoquinolinium-2-yl amide intermediate. Subsequently, acrylate would be involved in a [3+2] cycloaddition process to generate after release of tosyl group and aromatization H-pyrazolo[5,1-a] isoquinoline-1-carboxylates.

More recently, a gold(I)-catalyzed, operationally simple coupling-cyclization technique was developed for the synthesis of isoquinoline-fused polycyclic compounds. The reaction makes use of two coupling partners such as *o*-alkynylbenzaldehydes and aromatic amines bearing tethered nucleophiles (Scheme 10) [33].

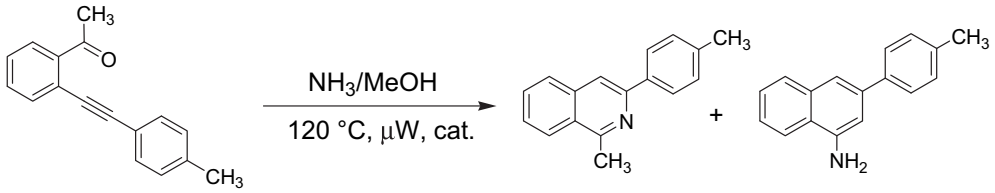
AuCl acts as a dual role catalyst [34] allowing rapid preparation of biologically important polycyclic derivatives through gold-catalyzed cascade cyclizations. According to the concept of a single-metal complex which exhibits dual roles in a single transformation, metal species which can act simultaneously as a Lewis acid and as a transition metal are beneficial for this process and have been reported to be indispensable catalysts in a variety of sequential amination/cyclization reaction [35]. Indeed, by switching to the less reactive 2-alkynyl-acetophenones as substrates their reaction with ammonia is not observed at all in the absence of a catalyst. By choosing as model system the reaction of 1-{2-[(4-methylphenyl)ethynyl]phenyl} ethanone **19a** with ammonia, we tried some metal catalysts potentially able to promote both the imine formation and the intermolecular hydroamination step (Scheme 11) [36]. In the literature there are many examples of the double activity exerted by metals like



Scheme 8.



Scheme 10.



19a **20a** **21a**

Entry	t (min)[a]	Catalyst	**20** Yield (%)[b]	**21** Yield (%)[b]
1	15	$TiCl_4$ (10 mol %)	-	-
2	80	$TiCl_4 \cdot 2$ THF (10 mol %)	11 [18][c]	-
3	100	$Pd(OAc)_2$ (10 mol %)	46	25
4	120	$Cu(OTf)_2$ (10 mol %)	23 [8]	13
5	120	CuI (10 mol %)	38	20
6	120	AgF (10 mol %)	15 [17]	14
7	120	Ag_2O (10 mol %)	10 [18]	10
8	60	$AgNO_3$ (10 mol %)	46 [7]	35
9	45	AgOTf (10 mol %)	54	37
10	120	$NaAuCl_4 \cdot 2 H_2O$ (10 mol %)	11 [31]	6
11	30	PPh_3AuCl (10 mol %)	41 [10]	34
12	120	$InCl_3$ (10 mol %)	5 [18]	-

[a] Not including 11 min "ramp time" (10 °C/min).

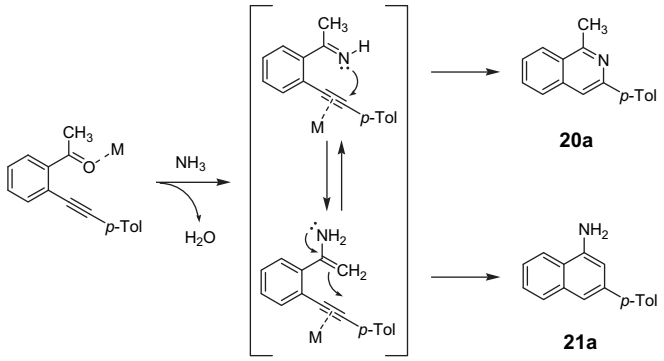
[b] Yields referred to pure isolated products.

[c] In brackett the yields of **19** recovered.

Scheme 11.

palladium [34c,d], copper [34c], silver [37], gold [38] and indium [39], in the intramolecular annulation reactions involving alkynes bearing a proximate nucleophile.

As reported in Scheme 11, a catalytic amount of $TiCl_4$ gave rise to a complex mixture of unidentified products (Scheme 11, entry 1) whereas the less acidic complex $TiCl_4 \cdot 2THF$ gave very poor result also after an extended reaction time (Scheme 11, entry 2). After 100 min of microwaves irradiation in the presence of a palladium (II) catalyst the expected isoquinoline **20a** was isolated in 46% yields, beside a moderate amount of the isomeric naphthalen-1-amine **21a** (Scheme 11, entry 3). Cu(II) based catalyst gave poorer results (Scheme 11, entry 4), whereas in the presence of Cu(I) salts the yields and ratio between **20a** and **21a** are comparable to those observed using palladium (Scheme 11, entry 5). Among the four silver based catalysts tested (Scheme 11, entries 6–9), silver fluoride and silver oxide gave scarce results even after a protracted reaction time (Scheme 11, entries 6 end 7). On the other hand, silver nitrate seemed to be a little more active than palladium despite the ratio of products was slightly shifted toward the naphthalen-1-amine **21a** (Scheme 11, entry 8). The best result was obtained using silver triflate with an overall reaction yield of 91% in a relative short reaction time and a ratio **20a**/**21a** equal to 1.5 (Scheme11, entry 9). Gold(III) salt was not effective (Scheme 11, entry 10) whereas cationic gold was active as silver nitrate (Scheme 11, entry 11).



Scheme 12.

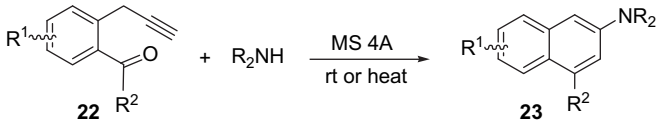
Finally, indium trichloride seemed to be absolutely unsuited to the purpose (Scheme 11, entry 12). The formation of the isomeric naphthalen-1-amine **21a** is the consequence of the conceivable equilibrium imine/enamine of reaction intermediate which can reacts with triple bond respectively as nitrogen nucleophile to give **20a** as well as carbon-nucleophile to give **21a** (Scheme 12).

The results clearly indicate that at the beginning of the cyclization the triple bond should coordinate to a π-Lewis acid. Silver has been intensively used for this purpose [40]. Subsequent attack of the nitrogen- or carbon nucleophile at the electron-deficient triple bond could represent the rate determining step in the present reaction. Analogously, the reaction proceeded smoothly with aliphatic alkyne **19b** (Scheme 13).

Further work is in progress to evaluate the product selectivity control [41] in the sequential amination/annulation reaction of 2-alkynyl-acetophenones. The selective synthesis of different products from the same starting materials by simple modification of the reaction conditions is an attractive challenge for chemists. The goal to successful address the amine-triggered benzannulation, so-called aminobenzannulation has been achieved through reaction of 2-(prop-2-ynyl)(oxo)benzenes **22** with various dialkylamines (Scheme 14) [42]. This efficient and general synthesis of 2-dialkylaminonaphthalenes proceeds under mild reaction conditions without metal promoters and catalysts.

A proposed reaction mechanism is shown in Scheme 15. Initially, rapid isomerization of **22** in the presence of a dialkylamine leads to the allene **24**. Subsequent nucleophilic addition of dialkylamine to the central carbon of the allene **24** followed by the cycloaddition onto the iminium moiety probably forms the intermediate **25**. Finally the formation of the 2-dialkylaminonaphthalene **23** is allowed by the aromatization reaction of **25**.

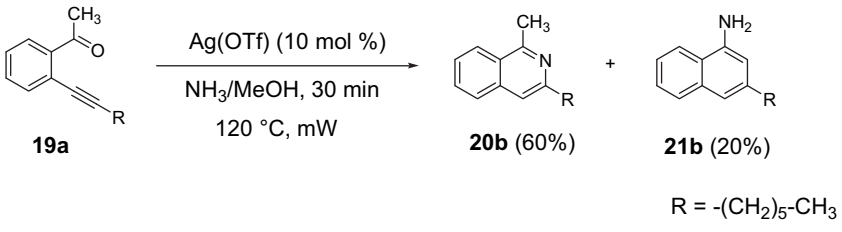
We have, also, been involved in depth investigation on the tandem imination/annulation of δ-ketoalkynes. In this field, we reported the synthesis of the pyrazino[1,2-*a*]indole nucleus through the sequential imination/annulation of 2-carbonyl-*N*-propargylindoles **26** in the presence of ammonia in methanol. The reaction worked well with *N*-propargylindole-2-carbaldehydes, but yields and selectivity were



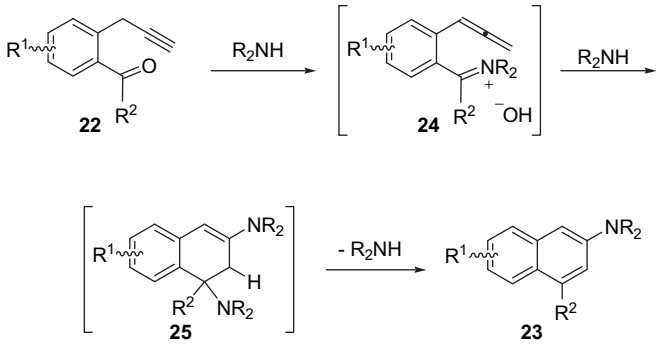
Scheme 14.

unsatisfactory using 2-acetyl-*N*-propargylindoles. Moreover, the reaction totally failed with 2-benzoyl-*N*-propargylindoles [43]. The suggested reaction mechanism involves the formation of an imine intermediate **27** that undergoes a stereoselective 6-*exo-dig* cyclization to 3,4-dihydropyrazinoindole **28** followed by partial isomerization to give pyrazinoindole **29** (Scheme 16).

With the aim to maximize the efficiency of this synthetic approach in terms of reaction times (2-acetyl and 2-benzoyl derivatives), overall yields (2-benzoyl derivatives), and the internal ratio between dihydro derivatives **28** and fully conjugated compounds **29**, we customized the methodology according by the employment of a microwave and the support of catalysts. Thus, a solution of the appropriate alkynyl indole in 2 M ammonia in methanol was heated in a multi-mode microwave oven at 150 °C until no more starting product was detectable by TLC analysis. The microwave-assisted reaction took place quicker than conventional heated ones, and overall yields were incremented. The ratio between dihydropyrazinoindoles **28** and pyrazinoindoles **29** was shifted toward the fully conjugated system. Moreover, it is interesting to note that the synthesis of a single pyrazino isomer is achieved through longer reaction times, while the dehydro derivatives **28** can be isolated after shorter times. As depicted in Scheme 17, the cyclization reactions of 1-propargyl-2-carbonylindole derivatives proceed in two key steps: (1) the formation of an imine intermediate and (2) the addition of the nitrogen nucleophile to the triple bond. It is well-known that ketones (in particular if aromatic and/or sterically hindered) react with amines and ammonia more slowly than aldehydes to form imines. This process can be accelerated by protons and Lewis acid catalysts and/or by water removal from the reaction mixture [44]. On the other hand, considering the annulation step, a number of metal complexes of group 4 and organolanthanides as well as various metal salts of group 9, 10, and 11 have been reported to successfully catalyze the intramolecular addition of nitrogen nucleophiles to alkynes [45]. Based on these accounts, we tested a variety of water scavengers/catalytic systems. The obtained results show that titanium tetrachloride, under mild conventional heating conditions, accelerates the cyclization of 2-acetylindoles and allowed the cyclization of 2-benzoylindoles with good yields and reasonable reaction times. Reaction times were further reduced by microwave heating. On the whole, the overall yields on pyrazinoindoles **28**/**29** appeared improved with respect to reactions performed without catalyst. Finally, titanium tetrachloride catalyzed cyclization of internal alkynes gave preferentially and sometimes exclusively the dihydropyrazino derivatives **28**. On the basis of these findings, we hypothesize that titanium tetrachloride affects both critical steps of pyrazinoindole formation.



Scheme 13.

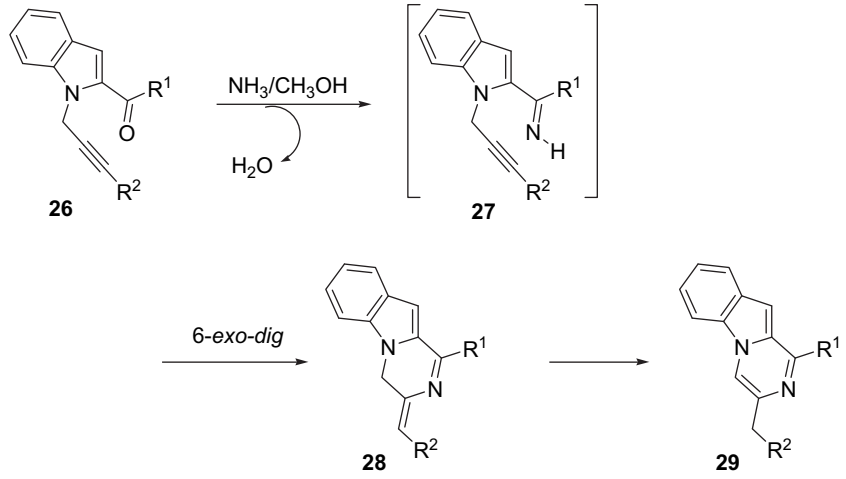


Scheme 15.

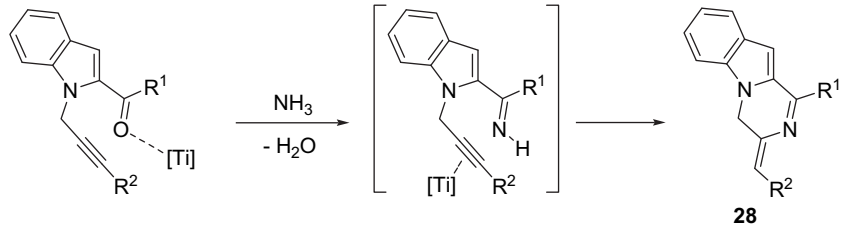
First, it can promote the imine intermediate formation through the double activity of vigorous water scavenger as well as useful Lewis acid [46]. In the second instance, $TiCl_4$ or a catalytically active species generated in situ from $TiCl_4$ and ammonia can promote the cyclization step through the coordination between the triple bond [47] and imine. Moreover, this dual activity of $TiCl_4$ justifies the high catalyst/substrate ratio required. Through a similar approach, we synthesized the 3-substituted 1-methylpyrrolo[1,2-*a*]pyrazines **21** from 2-acetyl-*N* propargylpyrroles **19** (Scheme 18) [17].

Following the procedure previously optimised for the imination/annulation of 2-acetyl and 2-benzoyl *N*-alkynylindoles, we dissolved alkynylpyrroles **26** in 2 M ammonia in methanol (20 equiv. of NH_3) in a sealed microwave test tube. Three equiv. of $TiCl_4$ were slowly added to the solution (caution!), and the reaction mixture was heated in a multi-mode microwave oven at 130 °C. The reactions gave the corresponding pyrrolo[1,2-*a*]pyrazines **33**, in some cases beside the isomeric dihydropyrrolo[1,2-*a*]pyrazine **32**. The isomeric products **32** and **33** were easily separated by flash column chromatography. The dihydro isomers **32** can be converted, in almost quantitative yields, into the corresponding fully conjugated isomers **33** under basic conditions by treatment with NaOMe/MeOH (10%) at reflux. Furthermore, the cleverness of $TiCl_4$ to perform a variety of tasks allowed a new synthetic route to pyrrolo[1,2-*a*]indole-2-carbaldehydes **32** through a divergent $TiCl_4$/*t*-$BuNH_2$ mediated hydroamination/annulation reaction starting from 2-acyl-1-propargyl-1H-indoles **26′a**–**g** containing a terminal alkyne moiety (Scheme 19) [48].

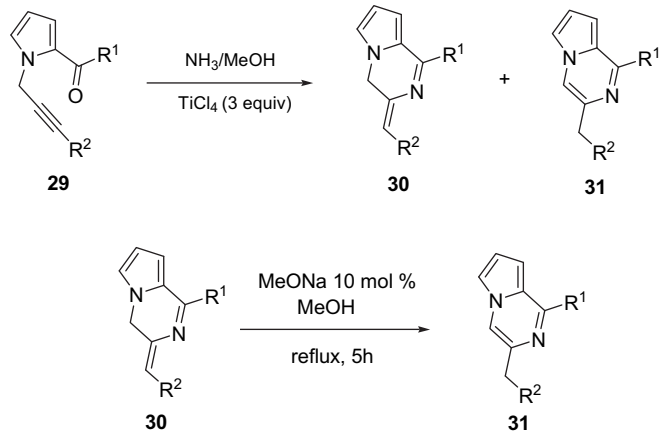
Better results were observed in toluene by increasing the ratio among the reagents; in particular, a ratio of substrate/$TiCl_4$/*t*-$BuNH_2$ of 1:1.5:9 gave the best results already at room temperature. A rise in temperature gave a dropout of overall yield, maybe as a consequence of a thermal degradation of products. A different titanium salt as well as the use of polar protic and aprotic solvents gave a complex mixture of unidentified products. The reaction of 2-acetyl derivative **26′a** took place quickly and gave the corresponding 3*H*-pyrrolo[1,2-*a*]indole-carbaldehyde **32a** in moderate yields (Scheme 19, entry 1). Better yields were obtained using 2-benzoyl-1-propargylindoles (Scheme 19, entries 2–4). The reaction allows also a heteroaryl substituent on C=O (Scheme 19, entries 5–7), but when reacting thiophen-2-yl and furan-2-yl derivatives **26′f-g**, only the isomeric 9*H*-pyrrolo[1,2-*a*]-indole-carbaldehydes **33f-g** (fluorazene form) were isolated (Scheme 19, entries 6 and 7). All 3*H*-pyrrolo[1,2-*a*]indole-carbaldehyde derivatives **32** were isomerised in the more stable tautomeric fluorazene form **33** standing in a $CDCl_3$ solution at room temperature for 24 h. The same result was obtained by stirring at room temperature a solution of **32b** in toluene for 40 min in the presence of a catalytic amount of *p*-TSA. Similarly, the reaction of 2-acetyl-1-propargyl



Scheme 16.



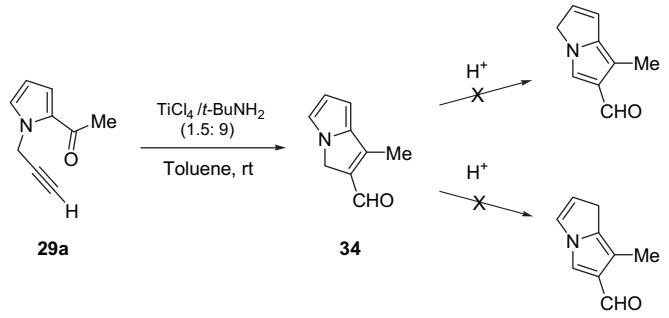
Scheme 17.



Scheme 18.

pyrrole **29a** under optimized conditions gave the corresponding 1-methyl-3*H*-pyrrolizin-2-carbaldehyde **34** in moderate yields as a single product; interestingly, the treatment of **34** with *p*-TSA acid did not give any of the possible tautomers (Scheme 20).

The proposed reaction mechanism involves three steps in which $TiCl_4$ has a multiplicity of activities (Scheme 21).



Scheme 20.

The first step is a $TiCl_4$ catalyzed hydroamination of alkyne with the formation of an enamine intermediate **35**. The addition is highly regioselective in anti-Markovnikov fashion, due to the steric hindrance of the *tert*-butyl moiety of amine [49]. According to recent Ackermann studies, the catalytically active species is probably generated in situ by reaction between $TiCl_4$ and *t*-$BuNH_2$ [50]. The second step is an aldol type intramolecular reaction: the nucleophilic addition of the β-carbon of enamine on the carbonyl group gave the intermediate **36**. The carbonyl group is activated by $TiCl_4$ as a Lewis acid catalyst. It is worth noting that the carbonyl group

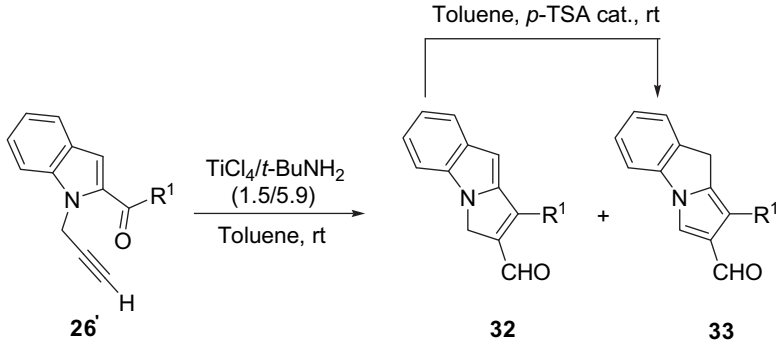
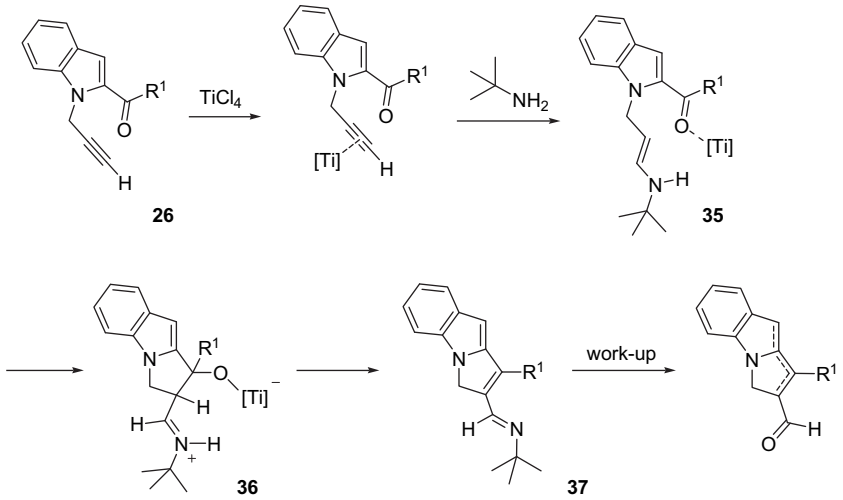


Table 1. Synthesis of Pyrrolo[1,2-*a*]indole-2-carbaldehydes

entry	**26'**	R^1	t (h)	yield %[a] **32**	yield %[a] **33**
1	**a**	methyl	0.3	50	-
2	**b**	phenyl	6	87	-
3	**c**	*p*-tolyl	6	75	-
4	**d**	*m*-tolyl	6	91	-
5	**e**	thiophe-3-yl	2	89	-
6	**f**	thiophe-2-yl	2	-	75
7	**g**	furan-2-yl	2	-	77

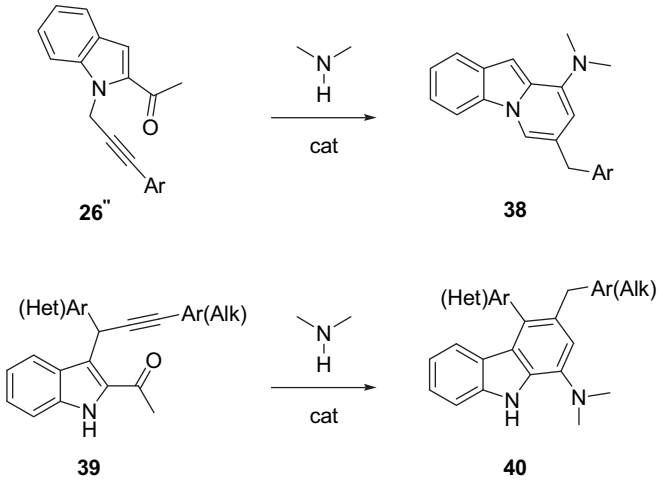
[a] Yields refer to isolated products

Scheme 19.



Scheme 21.

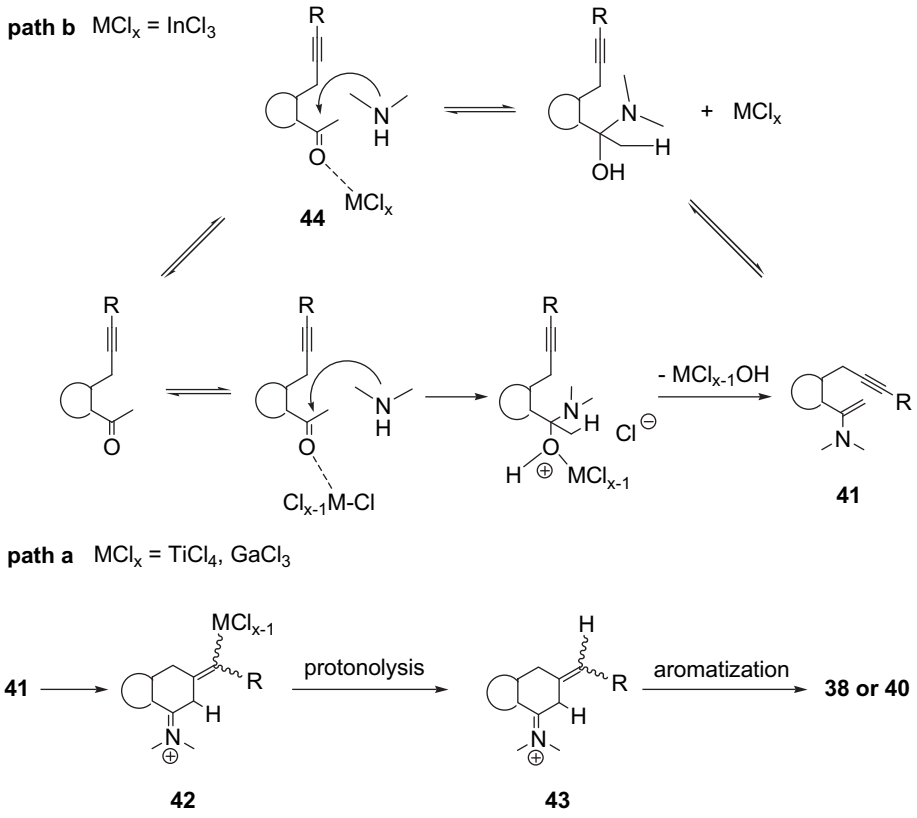
reacts in preference with enamine in regard to its direct reaction with *t*-BuNH$_2$. This behavior is related to the well known inertia of ketones toward bulky amines. In the third step, the imine **37** could be formed by intramolecular elimination of HOTiCl$_3$ and deprotonation or by an N–O proton shift followed by elimination of water and TiCl$_4$. Either way, the driving force of this step is the formation of a new C=C double bond stabilized by the conjugation with the heterocyclic ring. Also in this case, TiCl$_4$ could play a central role, avoiding the release of water in the reaction medium thus preventing the hydrolysis of enamine/imine intermediates [51]. Besides, the excess of amine buffers the reaction solution scavenging the acid chloride. Afterward, the usual workup leads to the hydrolysis of the imine intermediate to give the pyrrolo[1,2-*a*]indole-2-carbaldehydes **32** or **33**. This mechanism that involves a plethora of different activities of TiCl$_4$-catalyst/Lewis acid/water scavenger-well explains the need to use an excess of this reagent. The ^{1}H and ^{13}C NMR spectra of the reaction crude validate the final step of the suggested mechanism highlighting the presence of the characteristic signals of the *tert*-butylimine group of compound **37**. A divergent domino process involving the initial formation of an enamine intermediate followed by a regioselective 6-*exo*-*dig* intramolecular nucleophilic attack of the β-carbon of the enamino moiety to the C–C triple bond has been accomplished by the reaction of internal alkynes **26″** and **39** with secondary amines in the presence of an appropriate Lewis acid (Scheme 22) [52]. The Lewis acid mediated aminobenzoannulation reactions of 2-acyl-N-propargylindoles **26″** and 2-acyl-3-propargylindoles **39** give 9-amino-pyrido[1,2-*a*]indoles **38** and 1-aminocarbazoles **40**, respectively.



Scheme 22.

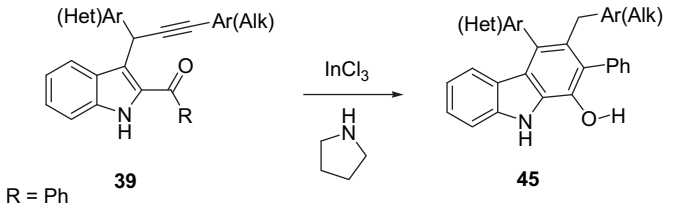
Both δ-ketoalkynes **26″** and **39** contained a heteroaromatic scaffold undergo two sequential inter and intramolecular nucleophilic attacks at the two electrophilic sites, that is, the carbonyl group and C–C triple bond. The reactions proceed in the presence of the appropriate catalytic system through a proposed dual activation sequence. 2-Acyl-*N*-propargylindoles **26″** give rise to 9-amino-pyrido[1,2-*a*]indoles **38** in good yield in the presence of TiCl$_4$ or GaCl$_3$ as catalysts. Probably in this case both catalysts operate as Lewis acids and water scavengers in the first step of the reaction to give rise to enamine intermediate **41** (Scheme 23, path a). Enamine **41** regioselectively attacks the activated alkyne to give rise to carbometalation adduct **42** which after deprotonation, protonolysis of the carbon–metal bond (**42**), and aromatization affords 6-*exo*-*dig* adduct **38**. The ability of TiCl$_4$ and GaCl$_3$ to activate carbonyl groups and carbon–carbon triple bonds towards nucleophiles is well documented. In particular, the catalytic interaction of carbon–oxygen double bonds and carbon–carbon triple bonds with GaCl$_3$ and TiCl$_4$ has been proven by ^{1}H and ^{13}C NMR spectroscopic measurements [53]. The intermediacy of vinyltitanium [54] and vinylgallium [55] species like **42** is supported by literature references. Moreover it is worth noting that, as reported in the reactions performed in the presence of GaCl$_3$ and TiCl$_4$ require 1.2 and 0.5 equiv. of catalyst, respectively. This experimental evidence could be ascribed to the high stability of the vinylgallium intermediate that does not undergo direct protonolysis in the reaction medium, thus regenerating the catalyst, but only during the final acidic workup. 2-Acyl-3-propargylindoles **39** gave rise to 1-(pyrrolidin-1-yl)-9*H*-carbazoles **40** under InCl$_3$ catalysis. The proposed mechanism (Scheme 23, path b) parallels in part that proposed for gallium- and titanium-catalyzed reactions with a single difference. The indium salt is a water-tolerant Lewis acid, stable under hydrolytic conditions and does not work as a water scavenger in the first step of the reaction [56]. Thus, enamine **41** is formed through a reversible process involving nucleophilic attack of the secondary amine on InCl$_3$ complex **44** [57] followed by loss of water.

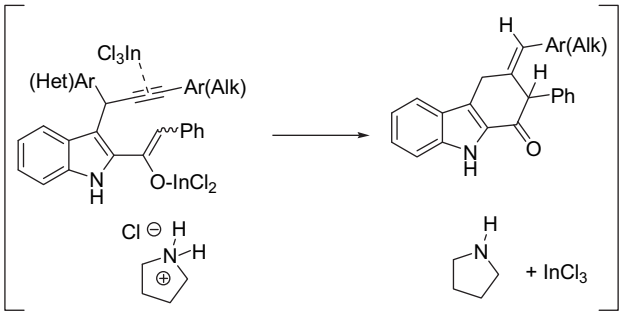
Moreover, the fastest formation of indium enolate **45** (Scheme 24) stabilized by the adjacent phenyl ring could be the driving force for the intramolecular cyclization that gives rise to



Scheme 23.

1-hydroxy-9*H*-carbazoles **45**. The reaction proceeds only in the presence of a base (pyrrolidine) able to act as a proton acceptor/proton donor. The intermediacy of vinylindium species [58] and indium enolates [59] has been reported by several authors. Moreover, the dual role exerted by the catalyst was demonstrated by IR, ^{1}H NMR, and ^{13}CNMR spectroscopic measurements [60]. Actually, $InCl_3$ seems to act as a weak σ- and π-electrophilic Lewis acid, whereas $TiCl_4$ acts as a weak π-electrophilic catalyst and as a strong σ-electrophilic catalyst [57]. Several reports dealing with related reactions of γ-ketoalkynes have been, also, published. In particular, a 6-*endo-dig* aminobenzannulation reaction of *o*-alkynylacetophenones with pyrrolidine or diethylamine takes place in the presence of a catalytic amount of palladium chloride, copper iodide, and triphenylphosphane to give rise to aminonaphthalene derivatives [61]. The reaction is strongly substrate dependent and works only with alkynylsubstituted acetophenone and in the presence of the above mentioned amines. Moreover, the 6-*endo-dig* aminobenzannulation reaction has been reported to occur starting from 2-alkynyl-3-acetylquinolines, 2-alkynyl-3-acetylindoles, 2-alkynyl-3-acetylpyridines, and 2-alkynyl-3-acetylbenzofuranes and pyrrolidine in the presence of 4 Å molecular sieves, yielding, respectively, 1-aminoacridines, 4-aminocarbazoles, 5-aminoquinolines, and 1-aminobenzofurans [62]. For some other secondary amines, neutral Al_2O_3 or $PtCl_2$ catalysts are required [63].





Scheme 24.

3. Conclusion

In this account, we report a summary of recent progress in the field of tandem imination/annulation reactions of γ- and δ-ketoalkynes in the presence of ammonia/amines. Main focus has been devoted to the peculiar effects and advantages of the transition metal catalysis over the uncatalyzed processes for the construction of functionalized aromatics and polycyclic aromatics through the reaction of the carbon-tethered acetylenic carbonyls with ammonia/amines. Notably, it was shown that the proper choice of a Lewis acid which may exhibit dual roles catalysis makes it possible to activate both C—C multiple bonds and C = X unsaturated bonds in a single transformation. In recent years, these catalysts have gained much attention owing to their ability to enhance selectivity and reactivity in tandem reactions. Those

processes are not only efficient but also they can achieve the direct construction of complex molecules, without isolating any intermediates, from readily accessible starting materials under mild conditions and with high atom economy. A continuation of progressive research is thus anticipated in this area.

4. Experimental

General details. All chemicals and solvents are commercially available and were used after distillation or treatment with drying agents. Silica gel F_{254} thin-layer plates were employed for thin-layer chromatography (TLC). Silica gel 40-63 micron/60A was employed for flash column chromatography. Infrared spectra were recorded on an FT-IR spectrophotometer using KBr tablets for solids and NaCl disks for oils. Proton NMR spectra were recorded at room temperature in $CDCl_3$, at 200 or 500 MHz, with residual chloroform as the internal reference (δ_H = 7.27 ppm). ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ at 50.3 or 125.75 MHz, with the central peak of chloroform as the internal reference (δ_C = 77.3 ppm). The APT or DEPT sequences were used to distinguish the methine and methyl carbon signals from those due to methylene and quaternary carbons. Data for ^1H NMR are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintuplet, m = multiplet, b = broad. Coupling constants (*J*) are reported as values in hertz. All ^{13}C NMR spectra were recorded with complete proton decoupling. Two-dimensional NMR experiments (NOESY and HMBC) were used, where appropriate, to aid in the assignment of signals in proton and carbon spectra. The ammonia in methanol 2 M solution was purchased from standard chemical suppliers. Microwave assisted reactions were performed in a MILESTONE microSYNT multi-mode labstation, using 12 mL sealed glass vessels. The internal temperature was detected with an optical fibres sensor.

4.1. General procedure for microwave-assisted/AgOTf-catalyzed reaction of 2-alkynylacetophenones with ammonia: reaction of 1-(2-(oct-1-ynyl)phenyl)ethanone (**19b**)

A stirred solution of the 1-(2-(oct-1-yn-1-yl)phenyl)ethanone **19b** (0.100 g, 0.438 mmol), and AgOTf (11.3 mg, 0.044 mmol) in dry ammonia in methanol (NH_3/MeOH 2 M solution, 4.34 mL, 8.68 mmol) was heated at 120 °C in a sealed tube for 30 min in a multi-mode microwave oven (ramp time = 10 min). The internal temperature was detected with a fiber optic sensor. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography over a silica gel column (hexane/EtOAc, 97:3) yielding progressively 3-hexyl-1-methylisoquinoline **20b** (0.060 g, 60% yield) and 3-hexylnaphthalen-1-amine **21b** (0.021 g, 20% yield).

4.2. 3-p-Tolyl-1-methylisoquinoline (**20a**)

IR (neat): ν = 3056, 2920, 1621 cm^{-1} ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.43 (s, 3H, CH_3), 3.04 (s, 3H, CH_3), 7.30 (d, 2H, arom. *J* = 8.1 Hz), 7.05–7.69 (m, 2H, arom.), 7.86 (t, 2H, arom. *J* = 7.0 Hz), 8.07 (t, 2H, arom. *J* = 8.4 Hz), 8.14 (s, 1H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 200 MHz): δ = 21.5, 22.9, 114.9, 125,9, 126.7, 126.8, 127.0, 127.8, 129.7, 130.2, 137.0, 137.3, 138.4, 150.3, 158.7 ppm. ESI-MS *m*/*z*: 234 ($(M + 1)^+$, (100)). Calcd for $C_{17}H_{15}N$ (233.31): C, 87.52; H, 6.48; N, 6.00. Found: C, 87.45; H, 6.42; N, 6.03.

4.3. 3-p-Tolylnaphthalen-1-amine (**21a**)

IR (KBr): ν = 3425, 3024, 2915, 2855 cm^{-1} ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.43 (s, 3H, CH_3), 4.22 (bs, 2H, NH_2), 7.05 (d, 1H, arom, *J* = 1.1 Hz), 7.28 (d, 2H, arom, *J* = 8.4 Hz), 7.44–7.50 (m, 2H, arom), 7.52 (s, 1H, arom), 7.61 (d, 2H, arom, *J* = 8.1 Hz), 7.79–7.89 (m, 2H, arom) ppm. ^{13}C NMR ($CDCl_3$, 200 MHz): δ = 21.4, 109.5, 117.1, 120.9, 123.1, 125.0, 126.5, 127.4, 129.1, 129.7, 134.9, 137.3, 138.7, 139.3, 142.6 ppm. ESI-MS *m*/*z*: 234 ($(M + 1)^+$, (100)). Calcd for $C_{17}H_{15}N$ (233.31): C, 87.52; H, 6.48; N, 6.00. Found: C, 87.44; H, 6.43; N, 6.08.

4.4. 3-Hexyl-1-methylisoquinoline (**20b**)

Yellow-green oil. IR (neat): ν = 2953, 2925, 2855, 1692, 1625, 1590, 1568, 1444, 1390, 747 cm^{-1} ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, 3H, CH_3, *J* = 7.0), 1.35 (m, 6H, 3 CH_2), 1.79 (qt, 2H, CH_2, *J* = 7.6), 2.88 (t, 2H, CH_2, *J* = 7.6), 2.95 (s, 3H, CH_3), 7.32 (s, 1H, arom), 7.50 (ddd, 1H, arom, *J* = 8.2, 6.8, 1.5 Hz), 7.61 (ddd, 1H, arom, *J* = 8.2, 6.8, 1.3 Hz), 7.72 (d, 1H, arom, *J* = 7.5), 8.07 (d, 1H, arom. *J* = 7.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 200 MHz): δ = 14.3, 22.6, 22.9, 29.4, 30.2, 32.0, 38.5, 116.7, 125.8, 126.1, 126.2, 127.0, 129.9, 136.9, 154.9, 158.2 ppm. ESI-MS *m*/*z*: 228 ($(M + 1)^+$, (100)). Calcd for $C_{16}H_{21}N$ (227.343): C, 84.53; H, 9.31; N, 6.16. Found: C, 84.41; H, 9.22; N, 6.19.

4.5. 3-Hexylnaphthalen-1-amine (**21b**)

Yellow-orange oil. IR (neat): ν = 3369, 2954, 2926, 2854, 1626, 1597, 1576, 1512, 1460, 1408, 741 cm^{-1} ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.90 (t, 3H, CH_3, *J* = 6.8), 1.27–1.41 (m, 6H, 3 CH_2), 1.61–1.76 (m, 2H, CH_2), 2.68 (t, 2H, CH_2, *J* = 7.6), 3.82 (bs, 2H, NH_2), 6.66 (s, 1H, arom.), 7.12 (s, 1H, arom.), 7.35–7.46 (m, 2H, arom.) 7.70–7.79 (m, 2H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 200 MHz): δ = 14.4, 22.9, 29.3, 31.5, 32.0, 36.5, 111.5, 118.0, 120.9, 122.6, 124.2, 126.1, 128.3, 134.9, 141.4, 142.0 ppm. ESI-MS *m*/*z*: 228 ($(M + 1)^+$, (100)), 144 (40). Calcd for $C_{16}H_{21}N$ (227.343): C, 84.53; H, 9.31; N, 6.16. Found: C, 84.36; H, 9.28; N, 6.12.

References

[1] (a) K.C. Nicolaou, D.J. Edmonds, P.G. Bulger, Angew. Chem. Int. Ed. 45 (2006) 7134–7186;
(b) L.F. Tietze, G. Brasche, K. Gericke, Domino Reactions in Organic Synthesis. Wiley-VCH, Weinheim, 2006;
(c) R.A. Sheldon, Pure Appl. Chem. 72 (2000) 1233–1246;
(d) B.M. Trost, Angew. Chem. Int. Ed. Engl. 34 (1995) 259–281.
[2] Y. Yamamoto, I.D. Gridnev, N.T. Patil, T. Jinab, Chem. Commun. (2009) 5075–5087.
[3] Y. Yamamoto, J. Org. Chem. 72 (2007) 7817–7831.
[4] (a) H. Yamamoto, Lewis Acids in Organic Synthesis, vols. 1, 2, Wiley-VCH, Weinheim, Germany, 2000;
(b) S. Kobayashi, K. Manabe, Acc. Chem. Res. 35 (2002) 209–217;
(c) A.D. Dilman, S.L. Ioffe, Chem. Rev. 103 (2003) 733–772.
[5] (a) A. Arcadi, E. Rossi, Synlett (1997) 667–668;
(b) A. Arcadi, E. Rossi, Tetrahedron 54 (1998) 15253–15272.
[6] A. Arcadi, F. Marinelli, E. Pini, E. Rossi, Tetrahedron Lett. 37 (1996) 3387–3390.
[7] A. Arcadi, S. Di Giuseppe, F. Marinelli, E. Rossi, Adv. Synth. Catal. 343 (2001) 443–446.
[8] A. Arcadi, S. Di Giuseppe, F. Marinelli, E. Rossi, Tetrahedron Asymmetry 12 (2001) 2715–2720.
[9] R. Balamurugan, V. Gudla, Org. Lett. 11 (2009) 3116–3119.
[10] T. Jin, Y. Yamamoto, Org. Lett. 10 (2008) 3137–3139.
[11] (a) A. Arcadi, G. Bianchi, S. Di Giuseppe, F. Marinelli, Green Chem. 5 (2003) 64–67;
(b) A. Arcadi, M. Chiarini, S. Di Giuseppe, F. Marinelli, Synlett (2003) 203–207.
[12] T.J. Harrison, J.A. Kozak, M. Corbella-Pané, G.R. Dake, J. Org. Chem. 71 (2006) 4525–4529.
[13] A. Das, S. Md Abu Sohel, R.-S. Liu, Org. Biol. Chem. 8 (2010) 960–979.
[14] (a) A. Arcadi, O.A. Attanasi, B. Guidi, E. Rossi, S. Santeusanio, Eur. J. Org. Chem. (1999) 3117–3126;
(b) A. Arcadi, O.A. Attanasi, B. Guidi, E. Rossi, S. Santeusanio, Chem. Lett. (1999) 59–60.
[15] G. Abbiati, E.M. Beccalli, A. Marchesini, E. Rossi, Synthesis (2001) 2477–2483.
[16] T. Sakamoto, A. Numata, Y. Kondo, Chem. Pharm. Bull. 48 (2000) 669–672.
[17] M. Alfonsi, M. Dell'Acqua, D. Facoetti, A. Arcadi, G. Abbiati, E. Rossi, Eur. J. Org. Chem. (2009) 2852–2862.
[18] K.R. Roesch, R.C. Larock, J. Org. Chem. 67 (2002) 86–94.
[19] Z. Guo, M. Cai, J. Jiang, L. Yang, W. Hu, Org. Lett. 12 (2010) 652–655.

[20] N. Asao, S. Yudha, T. Nogami, Y. Yamamoto, Angew. Chem. Int. Ed. 44 (2005) 5526–5528.
[21] (a) S. Su, J.A. Porco Jr., Org. Lett. 9 (2007) 4983–4986;
(b) S. Su, J.A. Porco Jr., J. Am. Chem. Soc. 129 (2007) 7744–7745.
[22] H. Gao, J. Zhang, Adv. Synth. Catal. 351 (2009) 85–88.
[23] N. Ghavtadze, R. Frölich, E.-U. Würthwein, Eur. J. Org. Chem. (2010) 1767–1797.
[24] Y. Ohta, S. Oishi, N. Fujii, H. Ohno, Chem. Commun. (2008) 835–837.
[25] N. Asao, K. Iso, S. Yudha, Org. Lett. 8 (2006) 4149–4151.
[26] X. Yu, J. Wu, J. Comb. Chem. 12 (2010) 238–244.
[27] S. Obika, H. Kono, Y. Yasui, R. Yanada, Y. Takemoto, J. Org. Chem. 72 (2007) 4462–4468.
[28] (a) M. Yu, Y. Wang, C.-J. Li, X. Yao, Tetrahedron Lett. 50 (2009) 6791–6794;
(b) H. Zhou, H. Jin, S. Ye, X. He, J. Wu, Tetrahedron Lett. 50 (2009) 4616–4618;
(c) Q. Ding, B. Wang, J. Wu, Tetrahedron 63 (2007) 12166–12171.
[29] Y. Ye, Q. Ding, J. Wu, Tetrahedron 64 (2008) 1378–1382.
[30] K. Gao, J. Wu, J. Org. Chem. 72 (2007) 8611–8613.
[31] S. Ye, J. Wu, Tetrahedron Lett. 50 (2009) 6273–6275.
[32] S. Ye, X. Yang, J. Wu, Chem. Commun. 46 (2010) 5238–5240.
[33] N.T. Patil, A.K. Mutyala, P.G.V.V. Lakshmi, P.V.K. Raju, B. Sridhar, Eur. J. Org. Chem. (2010) 1999–2007.
[34] Selected examples: (a) A.G. Pérez, C.S. López, J.M. Contelles, O.N. Faza, E. Soriano, A.R. de Lera, J. Org. Chem. 74 (2009) 2982–2991;
(b) Y. Xiao, J. Zhang, Angew. Chem. Int. Ed. 47 (2008) 1903–1906;
(c) N.T.P. Patil, Y. Yamamoto, J. Org. Chem. 69 (2004) 5139–5142;
(d) N. Asao, T. Nogami, K. Takahashi, Y. Yamamoto, J. Am. Chem. Soc. 124 (2002) 764–765.
[35] G. Abbiati, A. Arcadi, G. Bianchi, S. Di Giuseppe, F. Marinelli, E. Rossi, J. Org. Chem. 68 (2003) 6959–6966.
[36] M. Alfonsi, M. Dell'Acqua, A. Arcadi, G. Abbiati, E. Rossi, in preparation.
[37] T. Godet, C. Vaxelaire, C. Michel, A. Milet, P. Belmont, Chem. Eur. J. 13 (2007) 5632–5641.
[38] T. Yao, X. Zhang, R.C. Larock, J. Am. Chem. Soc. 126 (2004) 11164–11165.
[39] R. Yanada, S. Obika, H. Kono, Y. Takemoto, Angew. Chem. Int. Ed. 45 (2006) 3822–3825.
[40] P. Belmont, E. Parker, Eur. J. Org. Chem. (2009) 6075–6089.
[41] G. Bianchi, M. Chiarini, F. Marinelli, L. Rossi, A. Arcadi, Adv. Synth. Catal. 352 (2010) 136–142.
[42] T. Jin, F. Yang, Y. Yamamoto, Org. Lett. 12 (2010) 388–390.
[43] (a) G. Abbiati, A. Arcadi, A. Bellinazzi, E. Beccalli, E. Rossi, S. Zanzola, J. Org. Chem. 70 (2005) 4088–4095;
(b) G. Abbiati, A. Arcadi, E. Beccalli, E. Rossi, Tetrahedron Lett. 44 (2003) 5331–5334.
[44] G. Borg, D.A. Cogan, J.A. Ellman, Tetrahedron Lett. 40 (1999) 6709–6712.
[45] T.E. Müller, K.C. Hultzsch, M. Yus, F. Foubelo, M. Tada, Chem. Rev. 108 (2008) 3795–3892.
[46] H. Weingarten, J.P. Chupp, W.A. White, J. Org. Chem. 32 (1967) 3246–3249;
[47] D. Facoetti, G. Abbiati, L. d'Avolio, L. Ackermann, E. Rossi, Synlett (2009) 2273–2276.
[48] G. Abbiati, A. Casoni, V. Canevari, D. Nava, E. Rossi, Org. Lett. 8 (2006) 4839–4842.
[49] A. Tillack, I. Garcia Castro, C.G. Hartung, M. Beller, Angew. Chem. Int. Ed. 41 (2002) 2541–2543.
[50] L. Ackermann, Organometallics 22 (2003) 4367–4368.
[51] R.W. Layer, Chem. Rev. 63 (1963) 489–510.
[52] D. Facoetti, G. Abbiati, E. Rossi, Eur. J. Org. Chem. (2009) 2872–2882.
[53] (a) G.W. Kabalka, Y. Ju, Z. Wu, J. Org. Chem. 68 (2003) 7915–7917;
(b) G.W. Kabalka, Y. Ju, Z. Wu, Org. Lett. 4 (2002) 3415–3417;
(c) P.G. Cozzi, E. Solari, C. Floriani, A. Chiesi-Villa, C. Rizzoli, Chem. Ber. 129 (1996) 1361–1368;
(d) M. Oshita, T. Okazaki, K. Ohe, N. Chatani, Org. Lett. 7 (2005) 331–334;
(e) M. Yamaguchi, Y. Nishimura, Chem. Commun. (2008) 35–48.
[54] (a) T. Takeda, N. Saeki, Y. Takagi, T. Fujiwara, Chem. Lett. 10 (2000) 1198–1199;
(b) O. Kitagawa, T. Suzuki, T. Inoue, Y. Watanabe, T. Taguchi, J. Org. Chem. 63 (1988) 9470–9475.
[55] (a) M. Arisawa, K. Akamatsu, M. Yamaguchi, Org. Lett. 3 (2001) 789–790;
(b) H. Zhou, C. Zeng, L. Ren, W. Liao, X. Huang, Synlett (2006) 3504–3506;
(c) K. Kobayashi, M. Arisawa, M. Yamaguchi, J. Am. Chem. Soc. 124 (2002) 8528–8529.
[56] T.-P. Loh, G.-L. Chua, Chem. Commun. (2006) 2739–2749.
[57] M. Anniyappan, D. Muralidharan, P.T. Perumal, J.J. Vittal, Tetrahedron 60 (2004) 2965–2969.
[58] (a) T. Tsuchimoto, T. Maeda, E. Shirakawa, Y. Kawakami, Chem. Commun. (2000) 1573–1574;
(b) T. Tsuchimoto, K. Hatanaka, E. Shirakawa, Y. Kawakami, Chem. Commun. (2003) 2454–2455;
(c) K. Miura, N. Fujisawa, S. Toyohara, A. Hosomi, Synlett (2006) 1883–1886.
[59] (a) P. Angell, P.G. Blazecka, M. Lovdahl, J. Zhang, J. Org. Chem. 72 (2007) 6606–6609;
(b) J. Zhang, P.G. Blazecka, P. Angell, M. Lovdahl, T.T. Curran, Tetrahedron 61 (2005) 7807–7813;
(c) T. Fujimoto, K. Endo, H. Tsuji, M. Nakamura, E. Nakamura, J. Am. Chem. Soc. 130 (2008) 4492–4496;
(d) M. Nakamura, K. Endo, E. Nakamura, J. Am. Chem. Soc. 125 (2003) 13002–13003.
[60] R. Takita, Y. Fukuta, R. Tsuji, T. Ohshima, M. Shibasaki, Org. Lett. 7 (2005) 1363–1366.
[61] J.W. Herndon, Y. Zhang, K. Wang, J. Organomet. Chem. 634 (2001) 1–4.
[62] P. Belmont, M. Tiano, J. Org. Chem. 73 (2008) 4101–4109.
[63] P. Belmont, T. Belhadj, Org. Lett. 7 (2005) 1793–1795.