Gold(I) catalyses the intermolecular hydroenamination of alkynes with imines and produces α, α´,*N*-triarylbisenamines: studies on their use as intermediates in synthesis.

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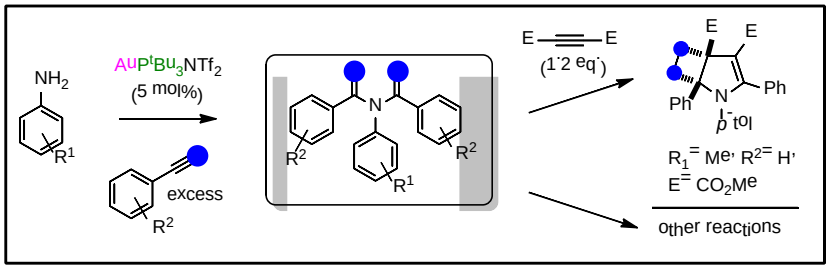


Abstract. α,α´,*N*-triarylbisenamines have been efficiently formed and isolated for the first time. The synthesis is based on an unprecedented gold(I)-catalysed double intermolecular hydroamination between *N*-arylamines and aryl alkynes. This reaction constitutes a new example of the intriguing behaviour of gold as catalyst in organic synthesis. The reactivity of these bisenamines for three different reactions, leading to potentially useful intermediates, is also shown. In particular, hindered azabicycles [3.2.0], which present excellent UVA and UVB absorption properties, are obtained by addition of triarylbisenamines to propiolates following an unexpected mechanism.

Keywords. Gold catalysis, bisenamines, hydroamination, intermolecular addition, UV screener.

Introduction.

Enamines are important molecules in organic synthesis[1] and constitute the key intermediates in organocatalysis.[2] However, bisenamines (Figure 1) are elusive compounds since the corresponding imine form is generally more stable.[3]

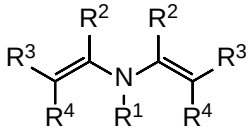


Figure 1. Structure of bisenamines.

Bisenamines having a terminal vinyl group (R^3=R^4=H) are particularly rare and only a few methods to form this kind of compounds have been reported.[4-6] These bisenamines present a carbonyl-type group in the α position (R^2= CO, CN) which shifts the equilibrium towards the enamine by an electronic withdrawing (EW) effect and scarce examples of molecules without this stabilising effect can be found.[7] Consequently, the number of bisenamines reported up to date is quite limited and there is not a general method for their synthesis. To this respect, the synthesis of bisenamines with substituents other than carbonyl-type in the α position would open access to new stable bisenamines.[8]

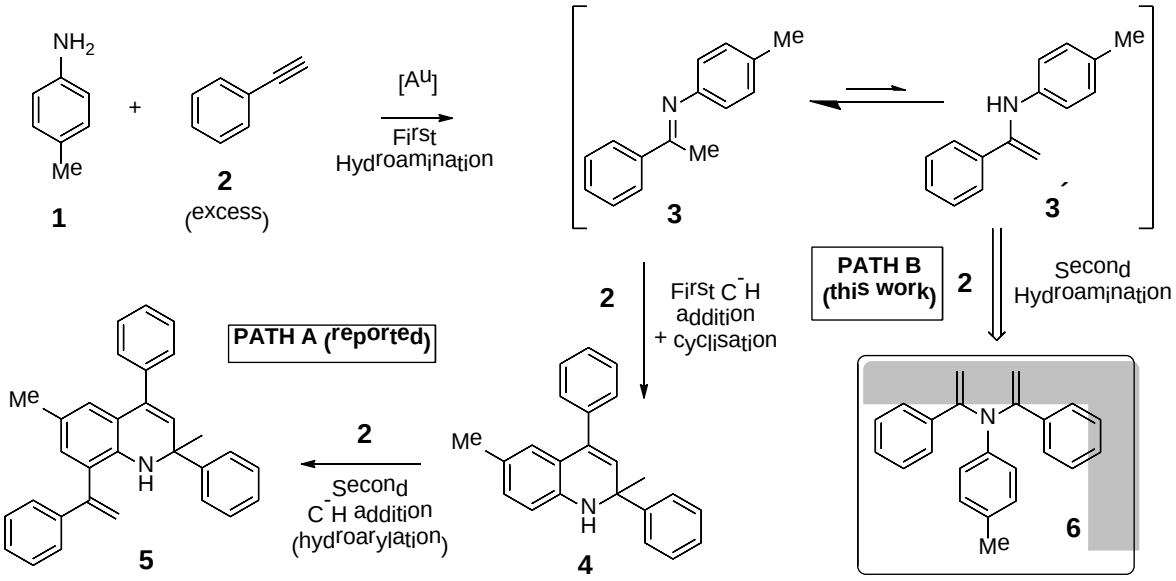
Gold catalysis has emerged in the last years as a powerful tool in organic synthesis.[9] The particular Lewis acidity of gold[10] makes this metal unique as catalyst, in terms of reactivity and selectivity, and unexpected reaction pathways have been found. Up to now, gold salts,[11] gold complexes,[12a-b] gold metal-organic frameworks[12c] or supported gold nanoparticles[13] have been used as catalysts. In particular, highly acidic, bench-stable complexes of general formula $AuPR_3NTf_2$ (R= Phenyl, ^{t}Bu, SPhos; NTf_2: triflimide)[14-15] have been shown to catalyse the addition of water (hydration) and amines (hydroamination) to alkynes at room temperature.[14] Here, we report the first gold(I)-catalyzed intermolecular hydroenamination of terminal alkynes to form aryl bisenamines. The reactivity of these

new bisenamines is also studied, obtaining, for instance, new azobicycles with photochemical properties.

Results and discussion.

- ***Gold(I)-catalyzed synthesis of aryl bisenamines.***

In the course of our work on hydroaminations,[16] we have observed that the addition of an excess of alkyne **2** to the amine **1** gives the unexpected highly symmetric product **6** (Scheme 1).



Scheme 1 Mechanistic pathways for the gold(I)-catalysed reaction of **1** with **2.**

Che and co-workers[17] and Bertrand and co-workers[18] have reported the obtention of the 1,2-dihydroquinoline **4** by using gold(I) carbene complexes at temperatures above 100 ºC (pathway A). The reaction sequence involves a hydroamination to get **3**, addition of the alkyne to the imine and later cyclisation. When forcing the reaction conditions, a hydroarylation occurs to form product **5**.[17,19] It has to be remarked that a second hydroamination of **3** has not been observed since the equilibrium imine-enamine (**3**-**3´**) is mainly shifted towards **3**. In fact, when using ^{13}C-marked phenylacetylene, ~17 % of enamine **3'** respect to imine can be observed by ^{13}C-NMR spectroscopy in $CDCl_3$ solution (see ahead

imine **34**). In our case, when using AuSPhosNTf$_2$ **7a** as catalyst, **6** is the main product of the reaction (see Scheme 1). Product **6** was detected by ^{1}H- and ^{13}C-NMR, and **4** and **5** were not present in the final reaction mixture. This bisenamine **6** comes from the intermolecular hydroamination of **2** with **3´**, as confirmed by isotopic experiments (see Scheme S1 in SI). To our knowledge, this reaction has no precedent.

Li and co-workers[20] have reported a gold(III)-catalysed double-hydroamination of *o*-alkynylanilines with terminal alkynes, in which they showed that the addition of the in-situ formed enamine to the alkyne occurs only intramolecularly. In the work reported here, this addition is *intermolecular* and bisenamine **6** is obtained in good yields under solventless conditions at temperatures between 50-100 ºC (Table 1, entries 2-4). The cyclised products **4** and **5** are obtained in low yields in all cases. Catalyst **7a** could be recovered and reused (entries 4 and 5). The use of gold(I) complex **7a** as catalyst rather than other gold(I) species seems to be preferable. As it can be seen in Table 1, the presence of the phosphine (compare entries 2 and 9) and a low-coordinating counteranion (compare entries 2 and 8 with 7) are necessary. Carbene gold(I) complexes with non-coordinating counteranions also worked as catalysts (entries 10-13) as well as AuP^{t}Bu$_3$OTf (entry 14).

Table 1 Formation of the bisenamine **6** from *p*-toluidine **1** and phenylacetylene **2** under different conditions and catalysts.

entry	**Catalyst**	**2 (eq.)**	**T (ºC)**	**1 (%, s.m.)[a]**	**3 (%)[a]**	**4 + 5 + others (%)[a]**	**6 (%)[a]**
1	**7a**	2	25	3	**86**	3	9
2		4	50	8	10	5	**76**
3		2	80	10	25	-	**65**
4		3.5	100	3	3	11	**83**
5[b]				10	8	-	**82**
6[c]				7	39	-	54
7	AuSPhosCl	4	50	87	13	-	-
8	AuSPhosOTf[d]	4	50	-	8	2	**90**

9	$AuNTf_2$[e]	4	50	65	35	10	-
10	$IPrAuNTf_2$[f]	3.5	100	-	18	5	**77**
11	IPrAuOTf[g]	3.5	100	-	10	5	**85**
12	IPrAuOTf[h]	5	80	-	9	5	**86**
13	IPrAuCl	3.5	100	65	30	5	-
14	AuP^tBu_3OTf[i]	4	80	-	35	-	65

[a] GC yield. [b] Reuse of entry 4. [c] Reuse of entry 5. [d] Isolated from AuSPhosCl and AgOTf. [e] Generated *in-situ* from AuCl and $AgNTf_2$. [f] Generated *in-situ* from chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) complex and $AgNTf_2$; see ref. 17 in the main text. [g] Generated *in-situ* from chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) complex and AgOTf; see ref. 17. [h] Using a similar protocol to that in ref. 17: CD_3CN as solvent (1 M in **1**), AgOTf (5 mol%), KPF_6 (25 mol%). [i] Generated *in-situ* from AuP^tBu_3Cl and AgOTf, CH_3CN as solvent (1 M in **1**).

At this point, we prepared and studied the catalytic activity of different gold(I)-NTf_2 complexes where the nature of the corresponding phosphine was varied (Table 2, phosphines are roughly ordered from more to less donor from left to right). It can be seen there that the better donor and hindered the phosphine, the higher the activity is. Catalysts containing Buchwald-type phosphines (**7a-b**, entries 1-2) or alkyl phosphines (**7c-d**, entries 3-5) gave the best yields of **6**. The optimum result in terms of both activity and selectivity was observed for complex **7c**, which contains the bulky *tert*-butylphosphine (entry 3, the corresponding triflate derivative did not work so well, see entry 14 in Table 1). On the contrary, catalysts containing EW phosphines (**7e-g**, entries 6-8) gave mainly **3**, which means that the reaction is still in progress and uncompleted. The yield of the cyclised products **4** and **5** is low even for the most active catalysts and the formation of one or another seems to depend on the nature of the phosphine (compare entries 1-2 to 6-8).

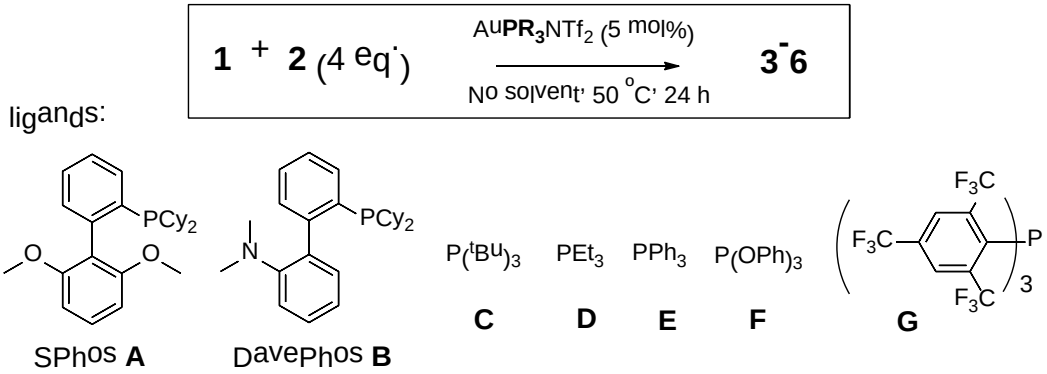


Table 2 Catalyst screening for the formation of bisenamine **6.**

Entry	Catalyst	Ligand	1[a]	3[a]	4[a]	5[a]	6[a]	Others[a]
1	**7a**	A	8	10	-	5	76	-
2	**7b**	B	7	5	-	4	84	-
3	**7c**	**C**	**7**	**3**	**-**	**-**	**90**	**-**
4	**7d**	D	8	35	-	-	52	6
5	**7d**[b]	D[b]	13	8	-	-	74	5
6	**7e**	E	10	60	11	-	19	-
7	**7f**	F	12	48	15	-	26	-
8	**7g**	G	7	57	19	-	16	-

[a] GC yield, in percentage. [b] 10 mol% of catalyst.

The influence of the electronic density of the aniline ring on the catalytic activity was also studied (Table S1, SI). It was observed that electronically poor rings improve the formation of the corresponding bisenamines (entries 1 and 2) while electronically rich aniline rings hamper its formation (entry 4). The results are in agreement with those found by Tanaka and co-workers on gold(I)-catalysed hydroamination of alkynes.[21]

Bisenamines containing different functionalities can be formed in good to excellent yields (Table 3) including amides (entry 2), α,,β-unsaturated esters (entry 3), nitriles (entries 4 and 6) and halogens (entries 5, 8-10). Isolation was not trivial since the bisenamines decomposed largely on silica (column

or preparative TLC)[22] and on neutral alumina. However, the purification was possible on basic alumina, affording bisenamines **6**, **9**, **11**, **13** and **18** in moderate to good yields after column chromatography. Non-symmetric bisenamines can also be formed (entry 8). Amines having an *o*-substituent reacted sluggishly (compare entry 7 to 4 and 6), possibly due to steric effects (see DRX for **13** in SI). The alkyl alkyne **23** is also reactive, obtaining the α-substituted bisenamines **24** (entry 9) and **25** (entry 10) in high yields, as a mixture of *Z,E*-isomers. Unfortunately, **24** decomposed under chromatographic conditions and **25** after the work-up. The only product recovered from the decomposition of **25** was the corresponding aromatic imine, which comes from the tautomerisation of the alkyl enamine functionality to the imine and subsequent hydrolysis. This degradation pathway confirms the results showed in the isotopic experiments (see Scheme S1). In those, the bisenamines **59** and **60** were obtained as equimolecular mixtures of the *Z*/*E* isomers, coming from the rapid imine-enamine equilibrium. This was assessed by GC-MS (different isomers) and by ^{1}H-NMR spectroscopy (different vinylic H peaks. Although the natural tendency of the enamime to tautomerise to the imine form indeed occurs, the triarylbisenamines here prepared are enough stable and isolable.

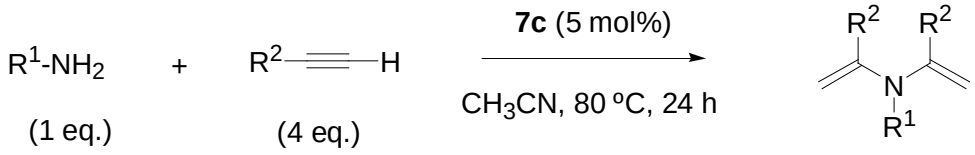
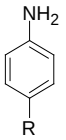
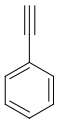
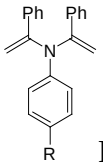
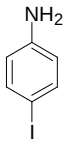
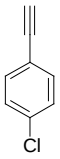
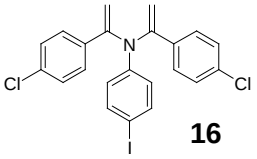
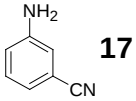
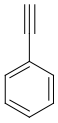
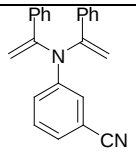
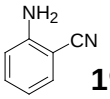
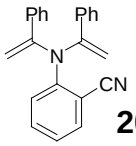
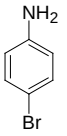
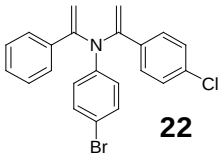
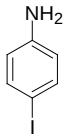
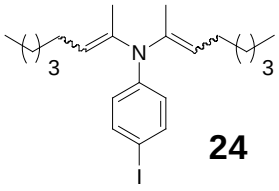
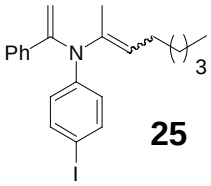


Table 3 Formation of different bisenamines catalysed by **7c**.

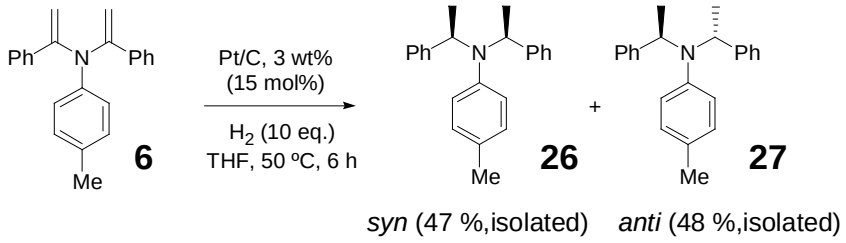
Entry	Amine	Alkyne(s)	Product	Yield (%)[a]
1	 R= Me **1**	 **2**	 R= Me **6**	99 [90][b]
2	R= $CONH_2$ **8**		R=$CONH_2$ **9**	83[c] [56]

3	R=CH:CH-COOEt **10**		R=CH:CHCOOEt **11**	95 [77]
4	R= CN **12**		R= CN **13**	57[c] [47]
5	 **14**	 **15**	 **16**	58[c]
6	 **17**	 **2**	 **18**	[95]
7	 **19**		 **20**	25[d]
8	 **21**	**15** (1.1 eq.) then **2** (3 eq.)	 **22**	65[e]
9	 **14**	 **23**	 **24**	95[b,c,f]
10		**2** (1.1 eq.) then **23** (3 eq.)	 **25**	90[g]

[a] GC yield, isolated yield between brackets. [b] **7b** (5 mol%) as catalyst, 60 ºC, solventless. [c] ^{1}H-NMR yield of the crude. [d] 20 mol% catalyst, 8 eq. alkyne, 48 h. [e] r.t. for 24 h, then 80 ºC for 24 h. [f] 60 ºC, solventless; **24** decomposes under chromatographic purification. [g] **7b** (1 mol%), 60 ºC for 24 h, then **7b** (4 mol%), 60 ºC for 24 h; **25** could be detected by GC-MS; the aromatic imine was the only product recovered after the work-up.

- ***Studies on the reactivity of aryl bisenamines.***

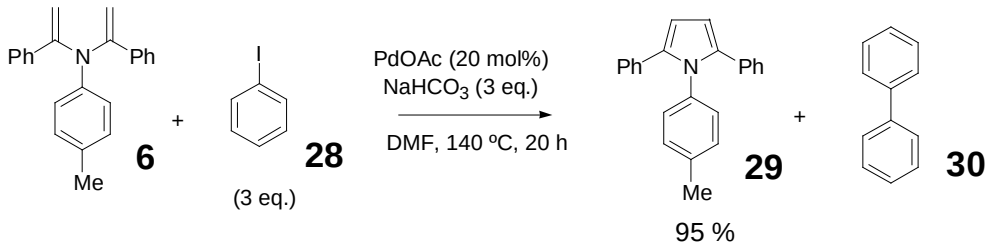
The reactivity of these novel compounds was explored. Bisenamine **6** was chosen as substrate for three different reactions: a catalytic hydrogenation, a palladium-catalyzed sp^2 C-C coupling of the two terminal double bonds and an addition to propiolates. Firstly, **6** was reduced with H_2 over Pt/C to form the corresponding racemic mixture of the diastereoisomers **26** and **27** (Scheme 2).



Scheme 2 Catalytic hydrogenation of **6**.

Gratifyingly, the *syn*- and the *anti*- isomers could be separated on preparative TLC in quantitative yield. As far as we know, these are the first examples of diastereopure compounds of this kind and they could work as diastereoselective inductors in basic and metal- catalysed reactions. The enantioselective version was then tried. Unfortunately, neither Noyori-Takaya´s ruthenium catalyst[23a] nor Buchwald´s titanium complex[23b] (specific for enamine hydrogenation) were active in our hands, under standard conditions.

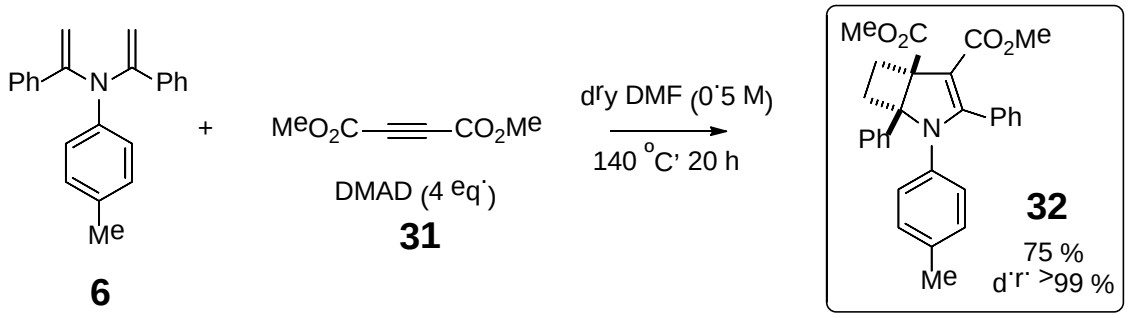
Secondly, the Pd-catalyzed Heck-Mizoroki coupling between the terminal bonds in **6** and PhI was attempted. For our surprise, the product recovered in quantitative yield after separation of biphenyl was the pyrrole **29**, corresponding to the intramolecular oxidative coupling of the double bonds (Scheme 3).[24]



Scheme 3 Pd-catalyzed intramolecular oxidative coupling of **6**.

It was checked that the presence of PhI as sacrificial oxidant to form **30** is necessary, playing the role of hydroquinone or O_2 in related reactions.[24a] This unusual C-C coupling constitutes a new method to obtain 2,5-diarylpyrroles.[25]

Finally, the reaction between triarylbisenamine **6** and dimethylacetylenedicarboxylate (DMAD) **31**, an excellent Michael-type acceptor, was studied (Scheme 4).[26]



Scheme 4 Synthesis of the azabicyclo **32** from bisenamine **6** and DMAD **31**.

According to the nucleophilia of the enamime groups in **6**, we should expect a double addition to **31**. However, a single isolated product whose structure corresponds to the highly crowded compound **32** was obtained in good yields. DRX analysis (Figure 2) confirmed this structure with four different quaternary centers and a cyclobutane-pyrroline bicyclic ring. Overall, four new C-C bonds are formed in the reaction, with complete diastereoselectivity.

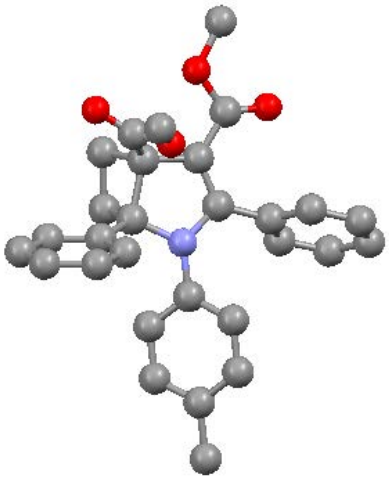


Figure 2. DRX structure of the azabicyclo **32** (N: purple, O: red, C: grey, hydrogens omitted for clarity).

Given the inherent instability of bisenamines, a one-pot procedure to form the azobicycle from the corresponding amine and alkyne would be desirable. In fact, **32** could be directly obtained from *p*-toluidine **1** and phenylacetylene **2** (Table 4), using $AuP^tBu_3NTf_2$ **7c** as catalyst. After optimization of the reaction conditions, an excellent atom economy was obtained, since the excess of **2** can be recovered by distillation.

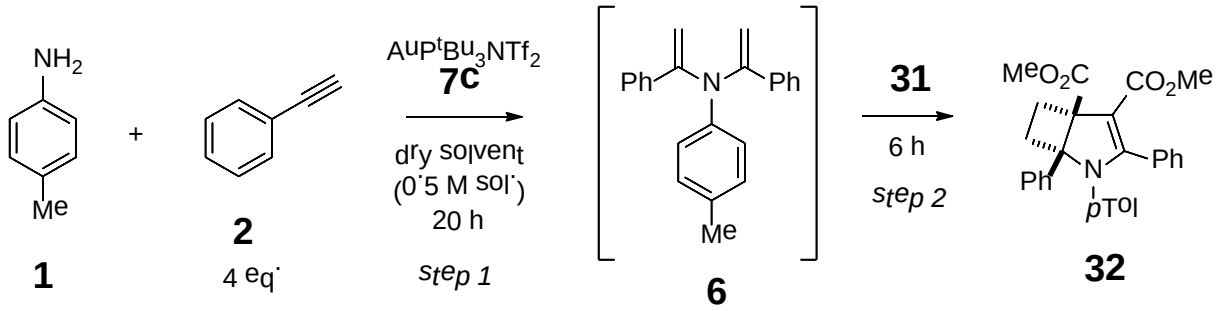


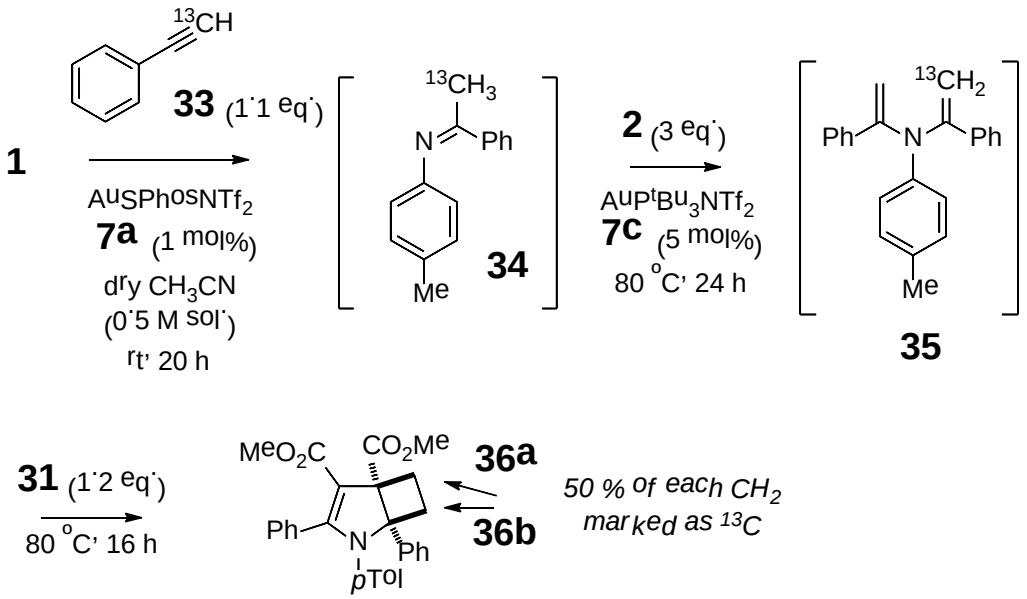
Table 4. One-pot formation of azabicycle **32** from **1** and **2**, catalysed by gold(I) complex **7c**.

Entry	7c (mol%)	Solvent[a] (step 1)	T (*step 1*, °C)	31 (eq.)	T (*step 2*, °C)	32 (%)[b]
1	5	CH_3CN	80	4	80	75
2	5	CH_3CN	80	1.2	80	73
3	5	CH_3CN	80	1.2	rt	8

4	2	CH_3CN	80	1.2	80	56
5	2	CH_3CH_2CN	95	1.2	95	34
6	**3**	**CH_3CN**	**80**	**1.2**	**80**	**75**

[a] DMF and 1,4-dioxane are also suitable solvents. [b] GC yield.

This cyclobutapyrroline system is quite unusual[27] and may present pharmacological activity.[28] In order to shed light on the mechanism of this reaction, isotopic experiments were carried out. Firstly, bisenamine **35**, having one of the vinyl carbons marked as ^{13}C, was prepared and reacted with **2** under the optimized conditions in Table 4 (Scheme 5).[14]



Scheme 5 Formation of the azabicycles **36a** and **36b**, marked with ^{13}C.

The degree of isotopic incorporation in each step was quantitative, as determined by GC-MS. It was found that the marked carbon eventually appears in both CH_2 of the cyclobutane ring, equimolarly, thus giving two different isotopic products **36a** and **36b**. This can be clearly assessed by comparing the different ^1H- and ^{13}C-NMR spectra of **32** and **36a**+**36b** (see SI). For the sake of illustration, the DEPT spectra of **32** and **36a**+**36b** are compared in Figure 3, showing clearly how the two CH_2s in **32** are now recorded as four different carbons in **36a**+**36b**: one more intense signal corresponding to the enriched

^{13}C (intense singlets) and another lesser intense signals corresponding to the ^{12}C coupled with the neighboring ^{13}C (doublets, J= 29. 1 Hz).

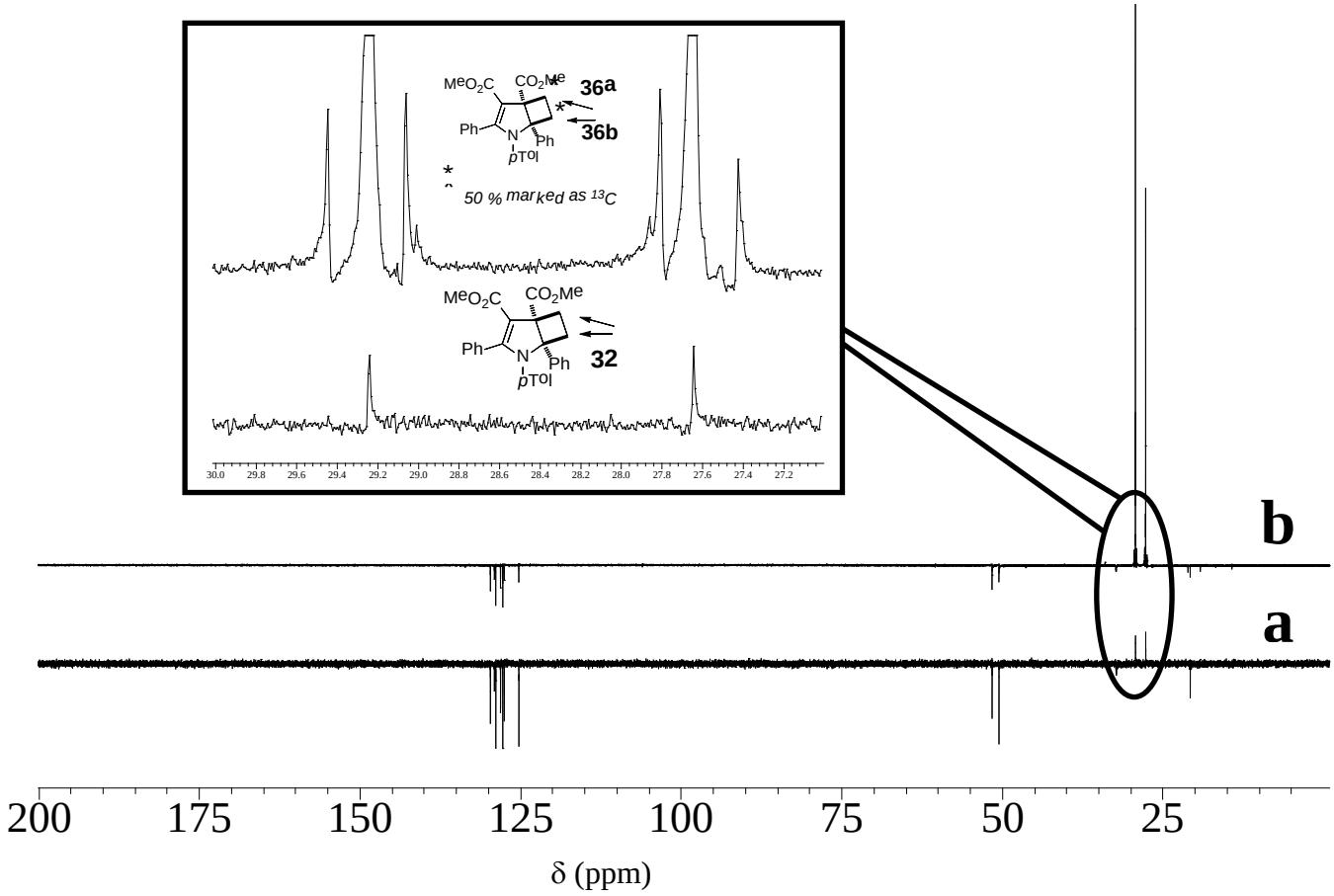
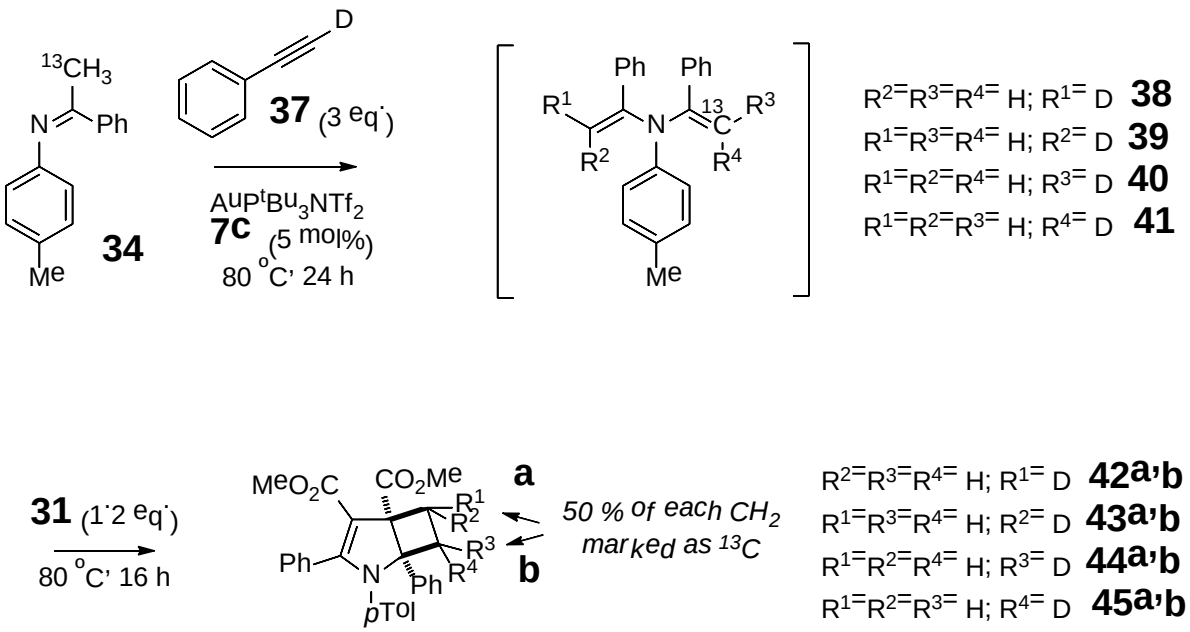


Figure 3 DEPT spectra of the azabicycles **32** (**a**) and **36a+b** (**b**); CH_2s upside.

A new isotopic experiment was carried out with deuterated phenylacetylene **37** as vinylating agent of **34** (Scheme 6).



Scheme 6 Formation of the azabicycles **42-45a** and **42-45b**, marked with ^{13}C and ^{2}H.

It was found that scrambling of the deuterium atom occurs in bisenamine **38**,[3] leading to the other three different deuterated bisenamines **39-41** in equimolecular ratio. Comparison of the ^{1}H-NMR spectra of these bisenamines **38-41** and that corresponding to bisenamine **35** (see Scheme 5) clearly shows the appearance of two different signals for each hydrogen on both marked and unmarked carbons (Figure 4), indicating one geminal deuterium by molecule. This is also confirmed by ^{13}C-NMR and DEPT (see SI), since one $^{13}CH_2$ and one ^{13}CH signals are recorded in a similar ratio.

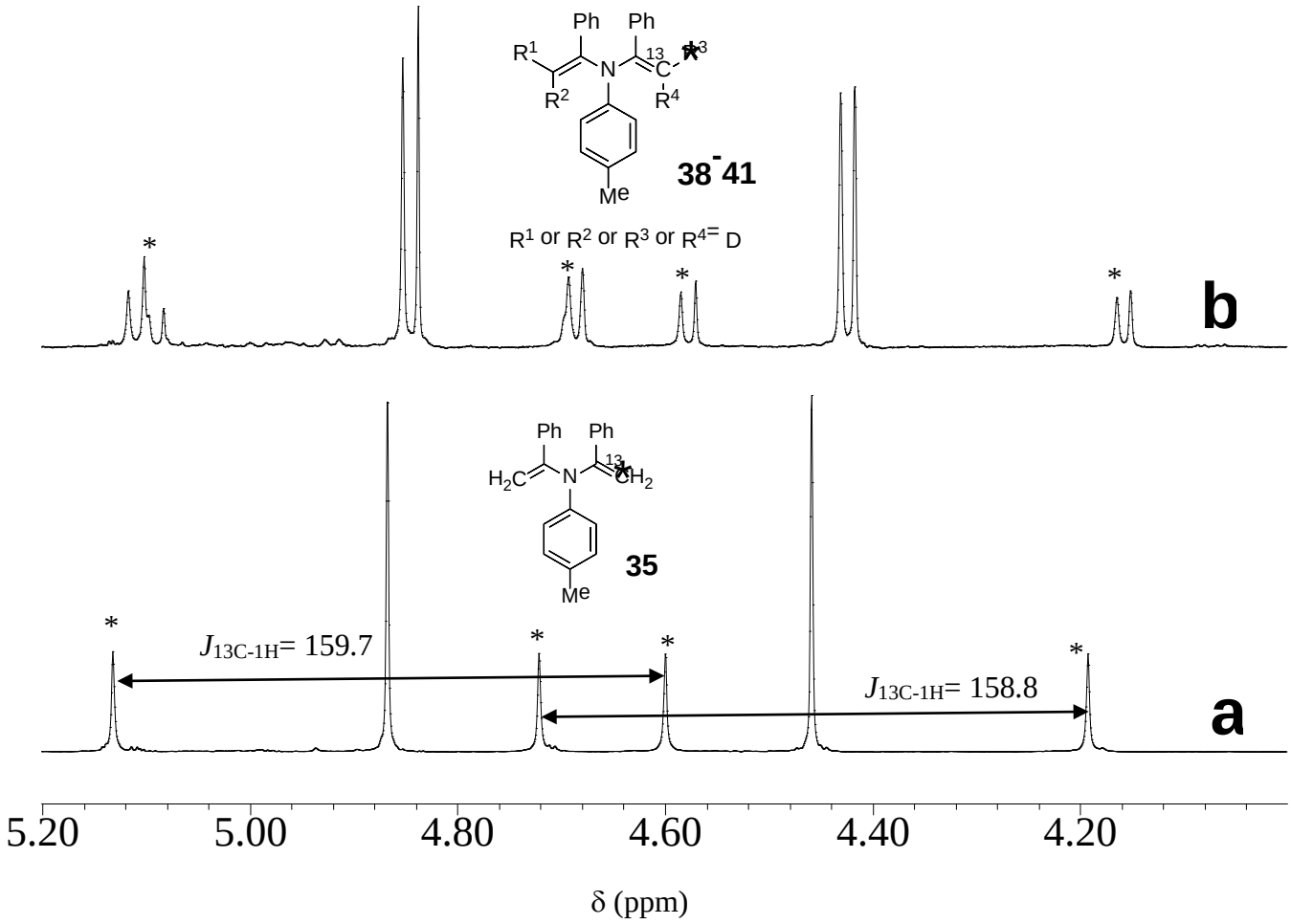


Figure 4 Vinylic region of the ^{1}H-NMR spectra of the azabicycles **35** (**a**) and **38-41** (**b**).

With the mixture **38-41** in hand, it was expected that reaction with **31** would give a mixture of eight different azabicycles **42-45a,b**, according to the results in Scheme 5. Indeed, the ^{1}H- and ^{13}C-NMR spectra of the isolated mixture confirmed the presence of one deuterium per molecule bounded to the outer carbons of the cyclobutane ring, having an equimolecular mixture of ^{13}C. For illustration, the ^{13}C-NMR spectra of **32**, **36a,b** and **42-45a,b** are compared in Figure 5, showing how 50 % of the CH_2s in **32** are marked as ^{13}C in **36a,b** (see also Figure 3) and finally split again as triplet by deuterium incorporation in 50 % of those; DEPT experiments confirmed that the latest corresponds to a mixture of CH_2s and CHs (see SI).

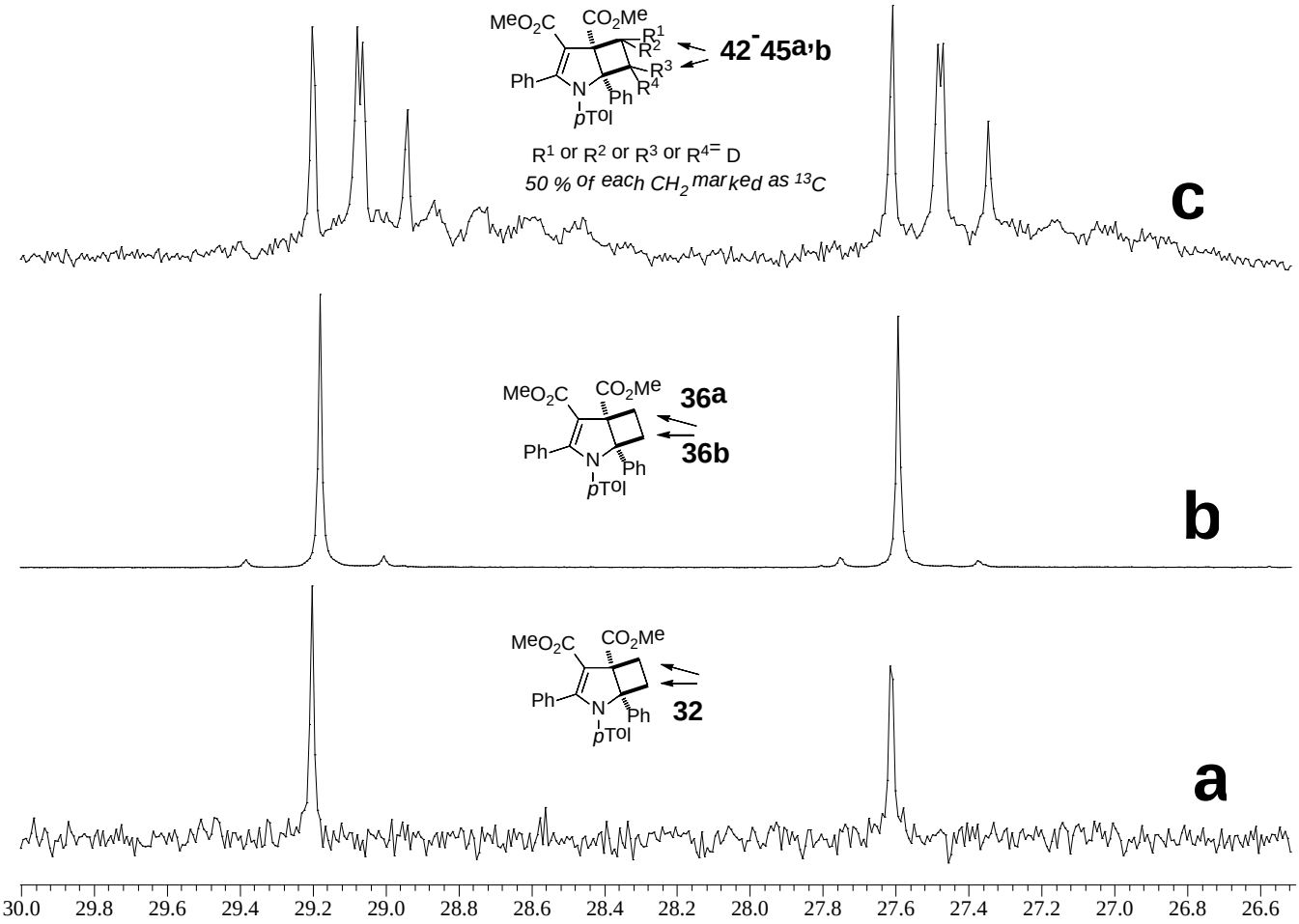
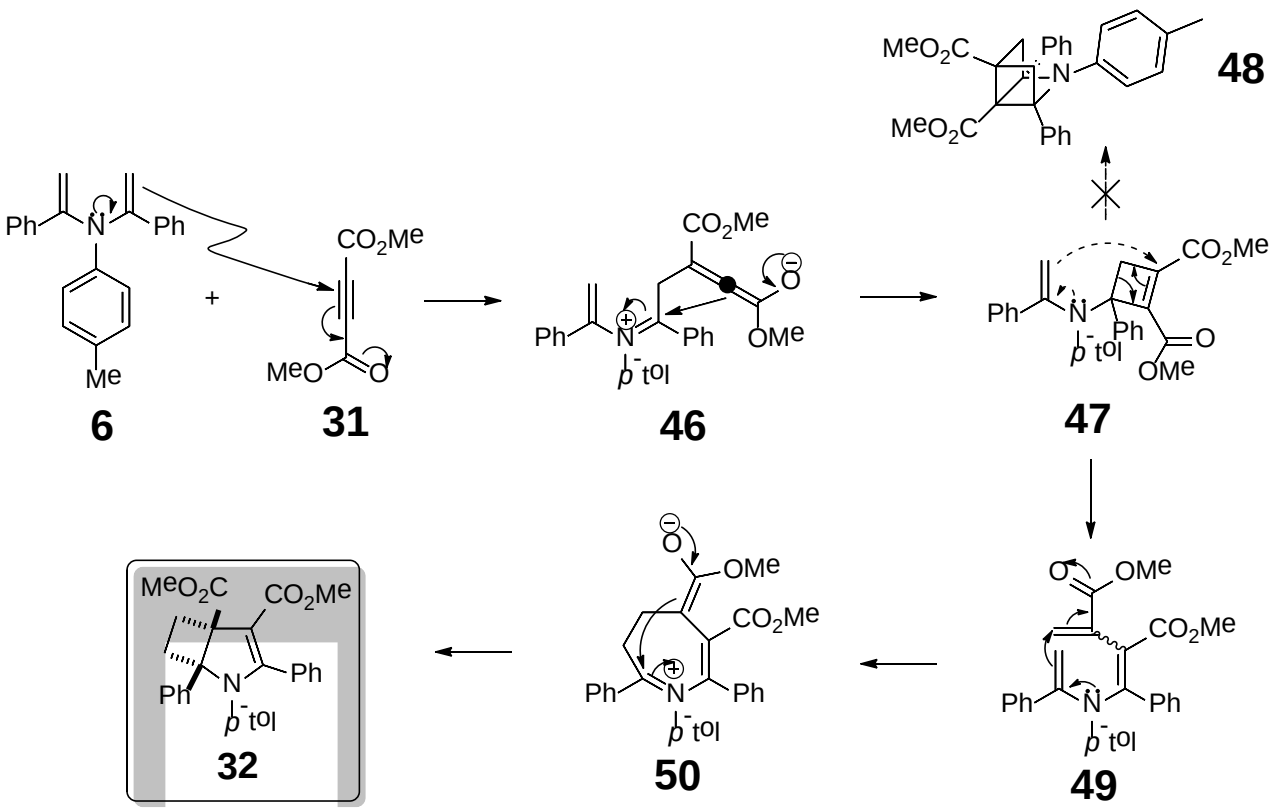


Figure 5 Part of the ^{13}C-NMR spectra of the azabicycles **32** (**a**), **36a,b** (**b**) and **42-45a,b** (**c**).

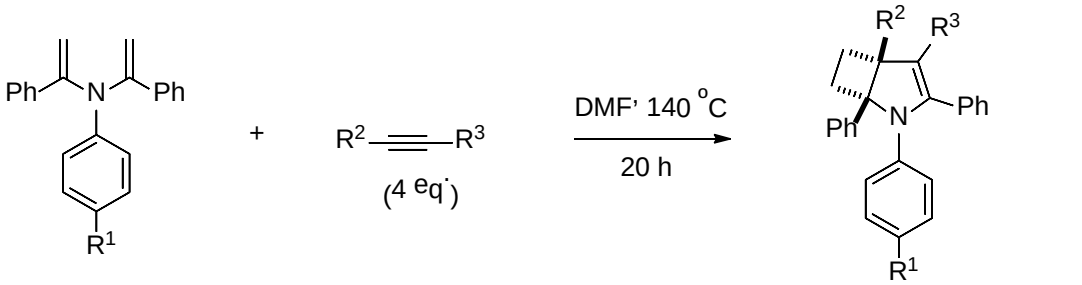
From these results it can be concluded that the carbons of the cyclobutane ring in **32** are originally the terminal vinyl carbons of the bisenamine **6**. This implies that at least one vinyl C=C bond is broken during the process.[29] A plausible mechanism is depicted in Scheme 7.



Scheme 7 Proposed mechanism for the addition of DMAD **31** to bisenamine **6**.

According to this mechanistic proposal, a first [2+2] cycloaddition occurs to form the cyclobutene adduct **47**. At this point, a second intramolecular addition to the formed alkene does not occur but ring opening to form **49**. This fragmentation has been well reported for the addition of alkyl enamines from ketones to **31**[26] and other propiolates.[30] The failed intramolecular addition of the second bisenamime group in **47** can be explained by steric and electronic factors on the cyclobutene ring, since a tertiary carbon must act as electrophile.[31] Moreover, the high steric hindrance in the hemiazacubane **48** would also hamper this reaction pathway. But once **49** is formed, the second intramolecular Michael-type addition *can proceed without steric impediments* to form the seven-membered cycle adduct **50**, which rapidly cyclizes back to form **32**.[30-32] The Michael-type addition of **6** to acrylate esters only works intramolecularly, since reaction of **6** with α-methyl acrylate or other activated double bonds did not proceed under any experimental conditions tested, including metal-catalyzed (see Scheme S2 in SI). The planarity of adduct **50** and the rigidity of the bicylic ring in **32** forces the ester and the phenyl moieties

to be in *cis* position, conferring complete diastereoselectivity to the process. The proposed diionic nature[33] of the intermediates instead of a possible radical mechanism is supported by three facts: a) slight variations in the polarity of the solvent produce an important change in the reaction rate (Table 4, entries 4 and 5) and, in general, polar solvents are more suitable (see footnote in Table 4); b) the nucleophilicity of the bisenamine and/or the electrophilicity of the Michael acceptor determines dramatically the reaction yield (Scheme 8 and Scheme S2 in SI) and c) addition of the radical AIBN (50 mol%) to the reaction mixture does not stop the formation of **32**, although a slowdown in the reaction rate is observed.



R^1		R^2	R^3		Product	Isolated Yield (%)
Me	**6**	CO_2Me	CO_2Me	**31**	**32**	75
Me	**6**	COMe	H	**53**	**54**	25[a]
CN	**51**	CO_2Me	CO_2Me	**31**	**55**	30
$CONH_2$	**52**	CO_2Me	CO_2Me	**31**	**56**	35

Scheme 8 Influence of the electronic nature of both bisenamine and alkyne in the reaction. [a] GC yield

As it can be seen, the better donor the aryl ring of the bisenamine (**6**) and the more electron acceptor the alkyne are (**31**), the higher the reaction yield. Although other factors such as the polymerization rate of the alkyne and the stability of the bisenamine under the reaction conditions cannot be overridden, these results point to diionic charged intermediates in the reaction.

- ***Azobicycles as UV sunscreeners.***

UV sunscreen organic chemicals are delocalized compounds such as, for instance, *p*-octyl methoxycinnamate and bisoctrizole. The azobicycles here synthesized posses similar functionalities to

those and, in principle, they could absorb strongly in the whole range of the UV-A and UV-B rays. The UV-Vis spectra for compounds **32**, **55** and **56** are shown in Figure 6.

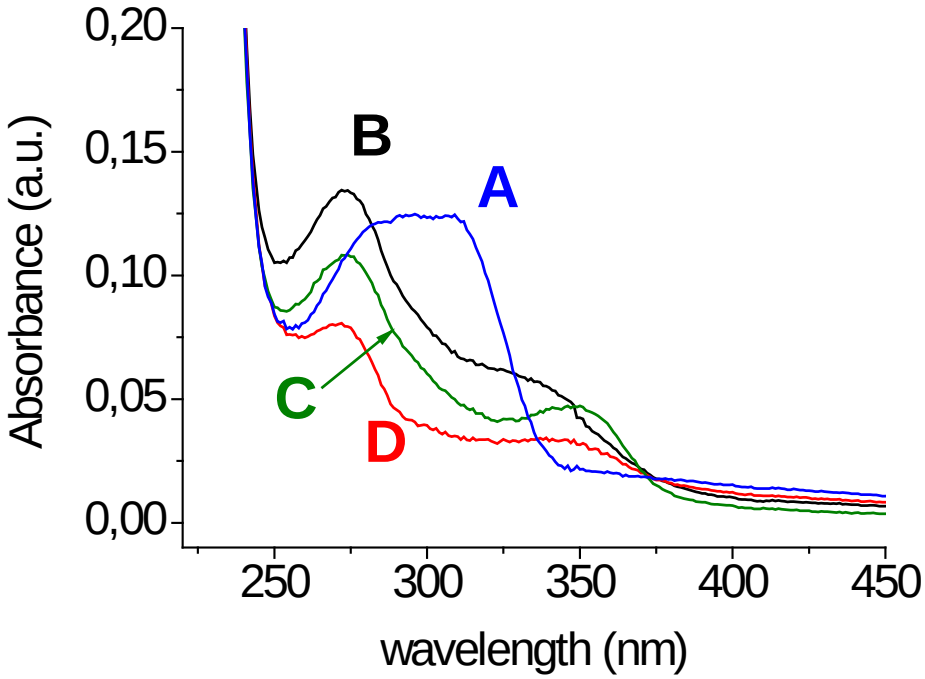


Figure 6 UV-Vis spectra of *p*-octyl methoxycinnamate (**A**), compound **32** (**B**), compound **55** (**C**) and compound **56** (**D**), measured at 1 μM concentration in CH_2Cl_2.

As it can be seen, azobicycles **32**, **55** and **56** indeed absorb in the UVA and UVB ranges at similar concentrations than the commercial *p*-octyl methoxycinnamate. Although, in general, the latter absorbs stronger over the UVB region, the azobicycles absorb more strongly in the UVA region and even in the far UVB. These results indicate the potential interest of these molecules for manufacturing sunscreen products.

Conclusions.

In conclusion, the first intermolecular hydroamination of alkynes with imines have been shown, $AuPR_3NTf_2$ complexes acting as catalysts. α,α´,*N*-triarylbisenamines have been formed and isolated for the first time. These novel compounds could open new synthetic pathways for other chemicals. As proof of reactivity, a catalytic hydrogenation, an intramolecular oxidative C-C coupling of the two terminal

double bonds and an addition to propiolates have been performed, giving access to useful intermediates. In particular, the latter allows the synthesis of UV absorbers azabicycles [3.2.0], creating four new quaternary centers with complete diastereoselectivity in a single step. The terminal vinyl carbons of the bisenamine eventually form the cyclobutane ring and this carbon rearrangement can be explained by successive [2+2] cycloaddition-cycloreversion reactions.

Experimental section.

*General double-hydroamination procedure (bisenamine **6**).* Complex **7b** (22 mg, 5 mol %) and *p*-toluidine **1** (54 mg, 0.5 mmol) were placed into a vial. Then, dry CH_3CN (0.25 mL) and phenylacetylene **2** (220 μL, 2 mmol) were sequentially added (alternatively, the reaction can be run without solvent). The vial was sealed and the mixture was magnetically stirred in a pre-heated oil bath at 80 ºC for 24 h. After cooling, an aliquot was taken for GC analysis. The CH_3CN was removed under *vacuo* and CH_2Cl_2 (1 mL) was added to re-dissolve the mixture. Then, *n*-hexane (10-20 mL) was added and the mixture was vigorously stirred for 15 min and filtered over celite.™ The resulting filtrates were concentrated under reduced pressure and analysed by NMR. The crude was purified by column chromatography on basic alumina (2-5 % AcOEt in *n*-hexane) to achieve bis-(1-phenylvinyl)-*p*-tolylamine **6** as a yellow oil (140 mg, 0.45 mmol, 90 %). This oil solidifies in a fridge at -14 ºC as yellow crystals, which were washed with *n*-hexane and dried.

*Addition of bisenamine **6** to DMAD **31***. Bisenamine **6** (15.6 mg, 0.05 mmol) was placed into a vial. Dry DMF (0.25 ml) and DMAD (24.6 μl, 4 eq.) were added and the vial was sealed and magnetically stirred in a pre-heated oil bath at 140 ºC for 20 h. After cooling, the resulting solution was analysed by GC and GC-MS and the product was purified by TLC on silica (10 % AcOEt in hexane). After extraction from the silica with neat AcOEt and removal of the solvents, 19 mg of **32** were obtained (85 % yield). Yellow crystals were obtained by re-dissolving in CH_2Cl_2 and slow evaporation. GC-MS (*m/z*): 453 ($M^{+\cdot}$, 3 %), 425 (100 %), 394 (39 %), 194 (17 %). ^{1}H NMR (δ, ppm; *J*, Hz): 7.44 (2H, dd,

J=8.5, 1.7), 7.38 (2H, mult), 7.29 (4H, mult), 7.20 (2H, mult), 6.65 (2H, dd, *J*=8.6, 0.7), 6.35 (2H, dt, *J*=8.5, 2.1), 3.50 (3H, s), 3.22 (3H, s), 3.19-2.94 (3H, mult), 2.43 (1H, mult), 2.05 (3H, s). ^{13}C NMR (δ, ppm): 171.3, 161.8, 137.0, 136.4, 136.3, 133.8, 131.7, 129.6, 129.0, 128.8 (2C), 128.6, 128.0 (2C), 127.8, 127.7 (2C), 127.4, 127.0, 125.2 (2C), 105.7, 77.6, 62.1, 51.5, 50.5, 29.2, 27.6, 20.7. HRMS (ESI) [M+H$^+$; calculated for $C_{29}H_{28}NO_4$: 454.2018] found *m/z* 454.1956.

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Supporting Information Available. General methods, reaction procedures, compound characterisation, additional schemes, tables and figures, DRX structure for compounds **6**, **7c**, **13** and **32** and copies of ^{1}H, ^{13}C, and DEPT spectra of compounds . This material is available free of charge via the Internet at http://pubs.acs.org.).

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