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Gold(I) Catalyzes the Intermolecular Hydroamination of Alkynes with Imines and Produces α,α′,*N*-Triarylbisenamines: Studies on Their Use As Intermediates in Synthesis

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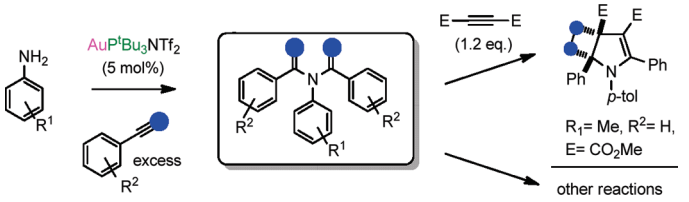

α,α′,*N*-Triarylbisenamines have been efficiently formed and isolated for the first time. The synthesis is based on an unprecedented gold(I)-catalyzed double intermolecular hydroamination between *N*-arylamines and aryl alkynes. This reaction constitutes a new example of the intriguing behavior of gold 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.

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]

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 toward the enamine by an electronic withdrawing (EW) effect, and scarce examples of molecules without this stabilizing effect can be found.[7] Consequently, the number of bisenamines reported to date is quite limited and there are no general methods reported 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]

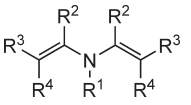

FIGURE 1. Structure of bisenamines.

Gold catalysis has emerged in the last years as a powerful tool in organic synthesis.[9] The particular Lewis acidity

(1) *Enamines: Synthesis, Structure and Reactions*; Cook, A. G., Ed.; Marcel Dekker Inc.: New York, 1988; p 717.
(2) (a) Beeson, T. D.; Mastracchio, A.; Hong, J.-B.; Ashton, K.; MacMillan, D. W. C. *Science* **2007**, *316*, 582. (b) Enders, D.; Hüttl, M. R. M.; Grondal, C.; Raabe, G. *Nature* **2006**, *441*, 861. For a review see: (c) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471.
(3) Lammertsma, K.; Prasad, B. V. *J. Am. Chem. Soc.* **1994**, *116*, 642.
(4) Thermal rearrangement of vinylaziridines (R^1 = H, R^2 = CO−, CN): (a) Gelas-Mialhe, Y.; Mabiala, G.; Vessière, R. *J. Org. Chem.* **1987**, *52*, 5395. (b) Gelas-Mialhe, Y.; Touraud, E.; Vessière, R. *Can. J. Chem.* **1982**, *60*, 2830.
(5) Reaction of thiazolidines with silver carbonate and DBU (R^1 = H, R^2 = CO_2Me or CO_2Et): Pinho e Melo, T. M. V. D.; Cabral, A. M. T. D. P. V.; Gonsalves, A. M. d. A. R.; Beja, A. M.; Paixao, J. A.; Silva, M. R.; Alte da Veiga, L.; Gilchrist, T. L. *J. Org. Chem.* **1999**, *64*, 7229.
(6) Reaction of methyl β-halo-α-aminopropionate hydrohalides with bases (R^1 = H, R^2 = CO_2Me): (a) Mitsuhashi, K. *Asahi Garasu Kogyo Gijutsu Shoreikai Kenkyu Hokoku* **1973**, *23*, 355. *Chem. Abstr.* **1975**, *82*, 86591. (b) Zaima, T.; Matsunaga, Y.; Mitsuhashi, K. *J. Heterocycl. Chem.* **1983**, *20*, 1.
(7) They have been described in some patents, where $R^1 = R^2$ = Me, as the methyl quaternary ammonium salt or R^1 = CO, R^2 = alkyl or alkyl/aryl: (a) *Jpn. Kokai Tokkyo Koho*, JP 59155366, 1984, p 14. (b) Martin, H.; Gysin, H.; Zaeslin, H.; Margot, A.; 1948, US 2447196. (c) Shr, K.-Y.; Wu, J.-J. Taiwan, TW 432092, 2001, p 2.
(8) We have found one example of phenyl groups as α-substituents in bisenamines, obtained as byproducts, see: Volckaerts, E.; Geise, H. J.; Daelemans, F.; Claereboudt, J. *Bull. Soc. Chim. Belg.* **1992**, *101*, 497.
(9) For reviews, see: (a) Ramón, R. S.; Gaillard, S.; Nolan, S. P. *Strem Chemiker* **2009**, *24*, 11. (b) Hutchings, G. J.; Brust, M.; Schmidbaur, H. *Chem. Soc. Rev.* **2008**, *9*, 1759. (c) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896.

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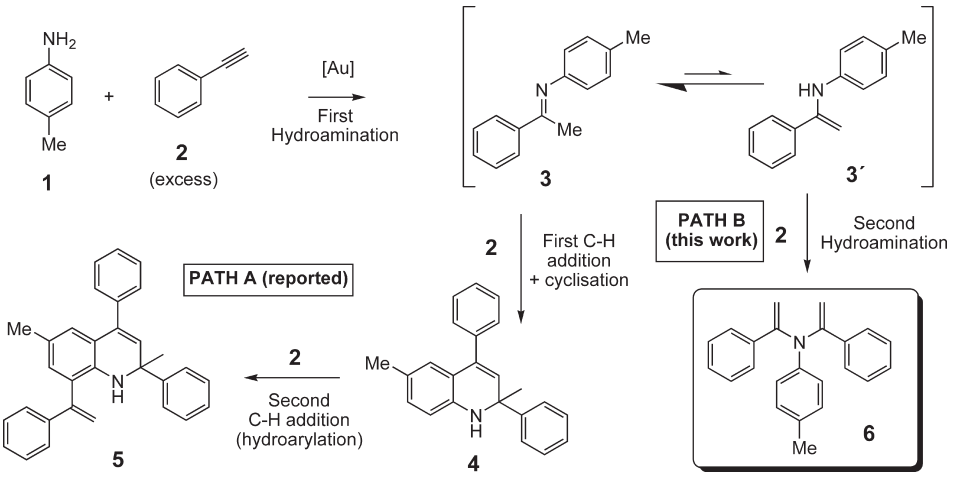
SCHEME 1. Mechanistic Pathways for the Gold(I)-Catalyzed Reaction of 1 with 2



of gold[10] makes this metal unique as a 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 the general formula $AuPR_3NTf_2$ (R = phenyl, ^{t}Bu, biphenyl-type, NTf_2 = triflimide)[14,15] have been shown to catalyze 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).

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 °C (pathway A). The reaction sequence involves a hydroamination to obtain **3**, addition of the alkyne to the imine, and later cyclization. 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 toward **3**. In fact, when using ^{13}C-marked phenylacetylene, ∼17% of enamine **3′** with 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 the SI). To our knowledge, this reaction has no precedent.

Li and co-workers[20] have reported a gold(III)-catalyzed 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 and 100 °C (Table 1, entries 2−4). The cyclized 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 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 noncoordinating counteranions also worked as catalysts (entries 10−13) as well as AuP^tBu_3OTf (entry 14).

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 and 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

(10) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395.
(11) Hashmi, A. S. K.; Kurpejovic, E.; Frey, W.; Bats, J. W. *Tetrahedron* **2007**, *63*, 5879.
(12) (a) Marion, N.; Ramón, R. S.; Nolan, S. P. *J. Am. Chem. Soc.* **2009**, *131*, 448. (b) Staben, S. T.; Kennedy-Smith, J. J.; Toste, F. D. *Angew. Chem., Int. Ed.* **2004**, *43*, 5350. (c) Zhang, X.; Llabres i Xamena, F. X.; Corma, A. *J. Catal.* **2009**, *265* (2), 155.
(13) (a) Grirrane, A.; Corma, A.; García, H. *Science* **2008**, *322*, 1661. (b) Zhang, X.; Corma, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 4358. (c) Corma, A.; Serna, P. *Science* **2006**, *313* (5785), 332.
(14) (a) Leyva, A.; Corma, A. *J. Org. Chem.* **2009**, *74*, 2067. (b) Leyva, A.; Corma, A. *Adv. Synth. Catal.* **2009**, *351*, 2876.
(15) Mezailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133.
(16) For a review on gold(I)-catalyzed hydroaminations, see: (a) Widenhoefer, R. A.; Han, X. *Eur. J. Org. Chem.* **2006**, 4555. For a review on hydroaminations, see: (b) Müller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795.
(17) Liu, X.-Y.; Ding, P.; Huang, J.-S.; Che, C.-M. *Org. Lett.* **2007**, *9*, 2645.
(18) Zeng, X.; Frey, G. D.; Kinjo, R.; Donnadieu, B.; Bertrand, G. *J. Am. Chem. Soc.* **2009**, *131*, 8690.
(19) For a silver-catalyzed reaction, see: (a) Luo, Y.; Li, Z.; Li, C.-J. *Org. Lett.* **2005**, *7*, 2675. For a ruthenium-catalyzed reaction, see: (b) Yi, C. S.; Yun, S. Y. *J. Am. Chem. Soc.* **2005**, *127*, 17000. (c) Yi, C. S.; Yun, S. Y.; Guzei, I. A. *J. Am. Chem. Soc.* **2005**, *127*, 5782.
(20) Zhang, Y.; Donahue, J. P.; Li, C.-L. *Org. Lett.* **2007**, *9*, 627.

TABLE 1. Formation of the Bisenamine 6 from *p*-Toluidine 1 and Phenylacetylene 2 under Different Conditions and Catalysts

entry	catalyst	**2** (equiv)	*T* (°C)	**1** (%, s.m.)[a]	**3** (%)[a]	**4** + **5** + others (%)[a]	**6** (%)[a]
1	**7a**	2	25	3	86	3	9
2	**7a**	4	50	8	10	5	76
3	**7a**	2	80	10	25		65
4	**7a**	3.5	100	3	3	11	83
5[b]	**7a**	3.5	100	10	8		82
6[c]	**7a**	3.5	100	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

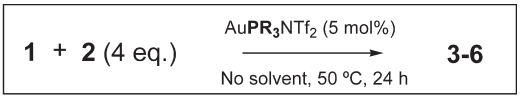
[a]See Scheme 1. For reaction conditions see Experimental Section. GC yield. [b]Reuse of entry 4. [c]Reuse of entry 5. [d]Isolated from AuSPhosCl and AgOTf. [e]Generated in situ from AuCl and $AgNTf_2$. [f]Generated in situ from chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) complex and $AgNTf_2$; see ref 17. [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**).

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 cyclized 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).

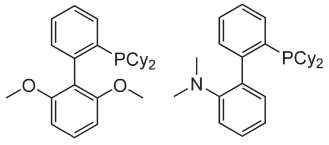
The influence of the electronic density of the aniline ring on the catalytic activity was also studied (Table S1, Supporting Information, SI). It was observed that electronically poor rings improve the formation of the corresponding bisenamines (entries 1 and 2) while electronically rich aniline rings hamper its formation (entry 4). The results are in agreement with those found by Tanaka and co-workers on gold(I)-catalyzed 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 and 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. Nonsymmetric 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 X-ray diffraction, XRD, for **13** in the 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 workup. The only product recovered from the decomposition of **25** was the corresponding aromatic imine, which comes from the tautomerization of the alkyl enamine functionality to the imine and subsequent hydrolysis. This degradation pathway confirms the results shown in the isotopic experiments (see Scheme S1 in the SI). 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 tautomerize to the imine form indeed occurs, the triarylbisenamines here prepared are stable enough and isolable.

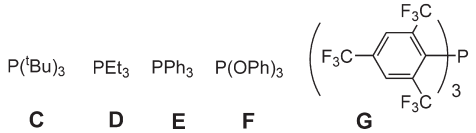
TABLE 2. Catalyst Screening for the Formation of Bisenamine 6



ligands:



SPhos **A** DavePhos **B**



C **D** **E** **F** **G**

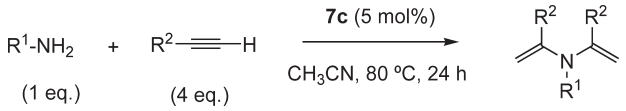
entry	catalyst	ligand	**1**[a]	**3**[a]	**4**[a]	**5**[a]	**6**[a]	others[a]
1	**7a**	A	8	10		5	76	
2	**7b**	B	7	5		4	84	
3	**7c**	**C**	**7**	**3**			**90**	
4	**7d**	D	8	35			52	6
5	**7d**[b]	D[b]	13	8			74	5
6	**7e**	E	10	60	11		19	
7	**7f**	F	12	48	15		26	
8	**7g**	G	7	57	19		16	

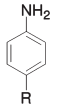
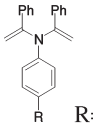
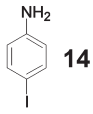
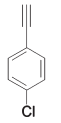
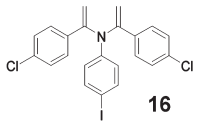
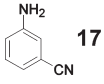
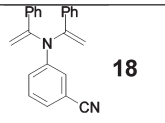
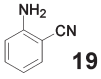
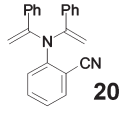
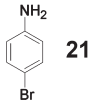
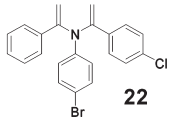
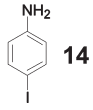
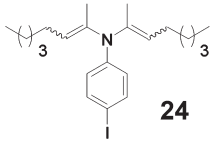
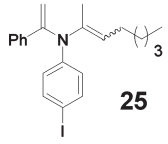
[a]GC yield, in percentage. [b]10 mol % of catalyst.

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. First, **6** was reduced with H_2 over Pt/C to form the corresponding racemic mixture of the diastereoisomers **26** and **27** (Scheme 2).

(21) Mizushima, E.; Hayashi, T.; Tanaka, M. *Org. Lett.* **2003**, *5*, 3349.
(22) However, the R_f values of the bisenamines could be calculated on silica TLC plates.

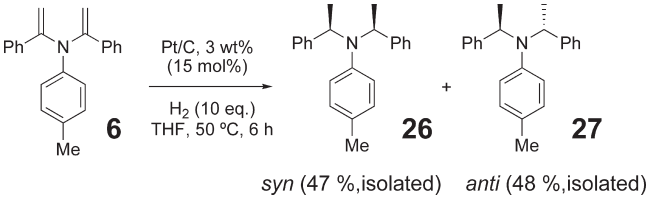
TABLE 3. Formation of Different Bisenamines Catalyzed by 7c



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 °C, solventless. [c]^{1}H NMR yield of the crude. [d]20 mol % catalyst, 8 equiv of alkyne, 48 h. [e]Room temperature for 24 h, then 80 °C for 24 h. [f]60 °C, solventless; **24** decomposes under chromatographic purification. [g]**7b** (1 mol %), 60 °C for 24 h, then **7b** (4 mol %), 60 °C for 24 h; **25** could be detected by GC-MS; the aromatic imine was the only product recovered after the workup.

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-catalyzed 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.

Second, the Pd-catalyzed Heck−Mizoroki coupling between the terminal bonds in **6** and PhI was attempted. To 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]

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]

According to the nucleophilic nature 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. XRD 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.

Given the inherent instability of bisenamines, a one-pot procedure to form the azabicycle 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.

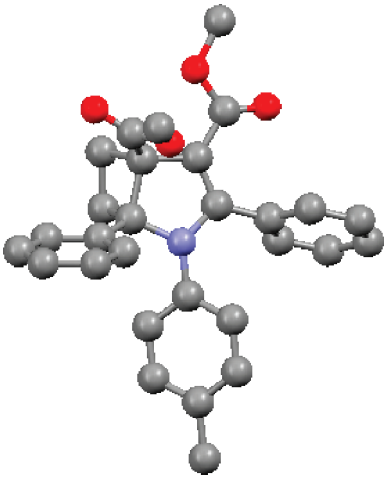
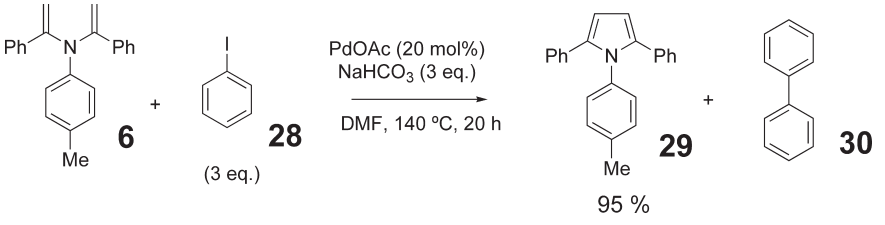


FIGURE 2. XRD structure of the azabicyclo **32** (N: purple, O: red, C: gray; hydrogens omitted for clarity).

This cyclobutapyrroline system is quite unusual[27] and may present pharmacological activity.[28] To shed light on the mechanism of this reaction, isotopic experiments were carried out. First, 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]

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 the 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

SCHEME 3. Pd-Catalyzed Intramolecular Oxidative Coupling of 6



SCHEME 4. Synthesis of the Azabicyclo 32 from Bisenamine 6 and DMAD (31)

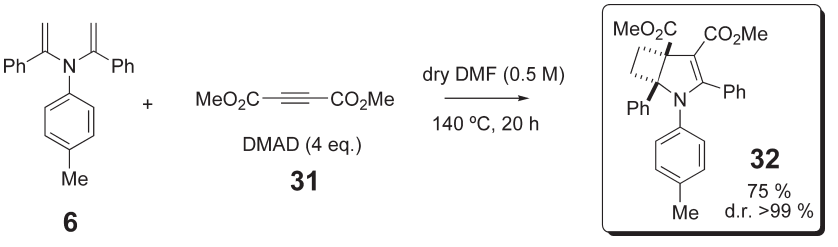
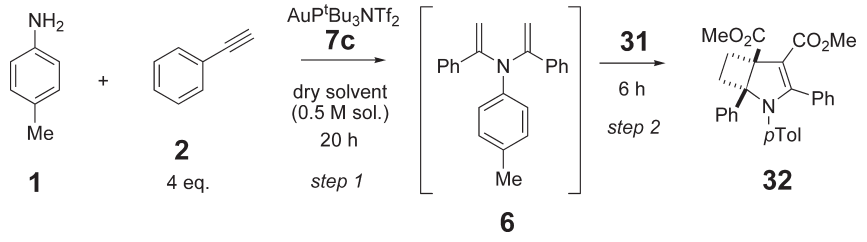


TABLE 4. One-Pot Formation of Azabicycle 32 from 1 and 2, Catalyzed by Gold(I) Complex 7c



entry	**7c** (mol %)	solvent[a] (step 1)	*T* (step 1, °C)	**31** (equiv)	*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.

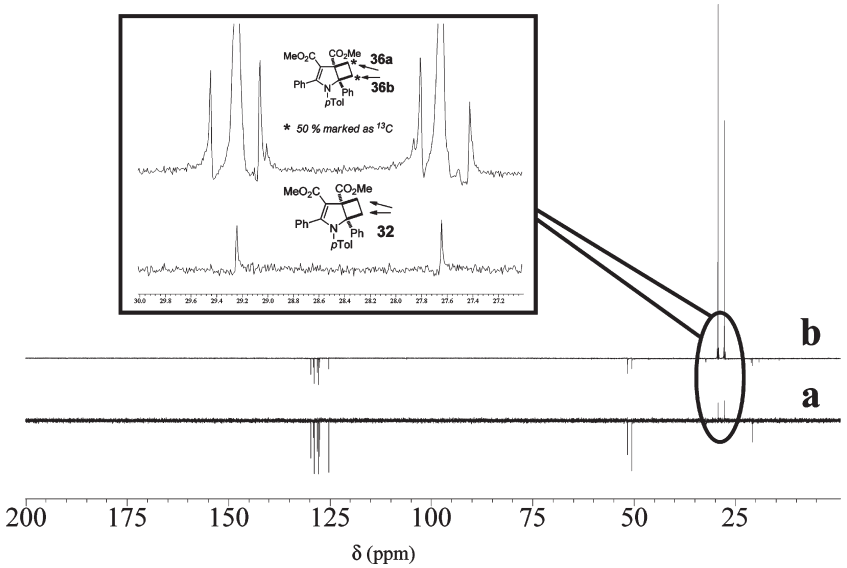
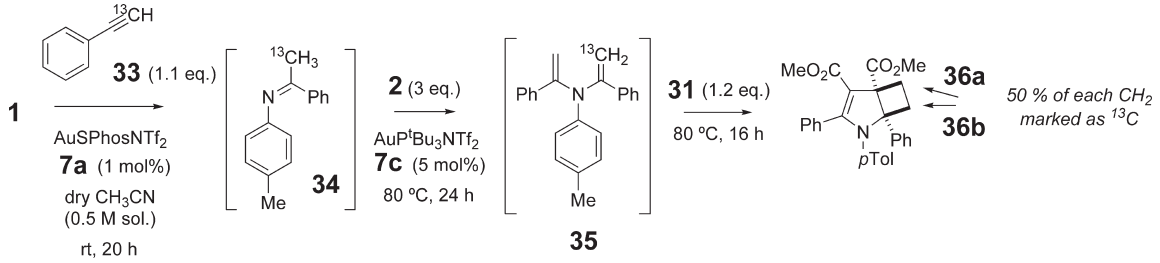


FIGURE 3. DEPT spectra of the azabicycles **32** (a) and **36a** + **b** (b); CH_2s upside.

SCHEME 5. Formation of the Azabicycles 36a and 36b, Marked with ^{13}C



singlets) and other lesser intense signals corresponding to the ^{12}C coupled with the neighboring ^{13}C (doublets, J = 29.1 Hz).

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

It was found that scrambling of the deuterium atom occurs in bisenamine **38**,[3] leading to the other three different

(23) (a) Mashima, K.; Kusano, K.; Sato, N.; Matsumura, Y.; Nozaki, K.; Kumobayashi, H.; Sayo, N.; Hori, Y.; Ishizaki, T.; Akutagawa, S.; Takaya, H. *J. Org. Chem.* **1994**, *59*, 3064. (b) Lee, N. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 5985.

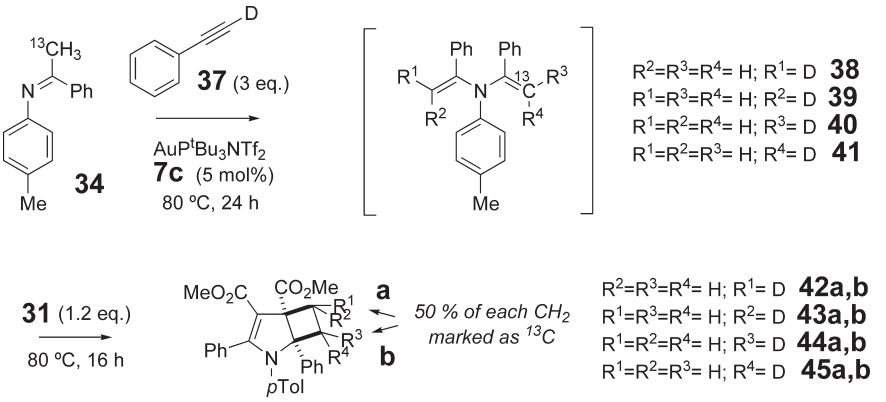
(24) For a review see: (a) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, *107*, 5318. For a related Pd-catalyzed intramolecular cyclization of enaminones to obtain carbazoles see: (b) Iida, H.; Yuasa, Y.; Kibayashi, C. *J. Org. Chem.* **1980**, *45*, 2938.

(25) Huerta, G.; Fomina, L.; Rumsh, L.; Zolotukhin, M. G. *Polym. Bull.* **2006**, *57*, 433.

(26) (a) Berchtold, G. A.; Uhlig, G. F. *J. Org. Chem.* **1963**, *28*, 1459. (b) Brannock, K. C.; Burpitt, R. D.; Goodlett, V. W.; Thweatt, J. G. *J. Org. Chem.* **1963**, *28*, 1464.

(27) Acheson, R. M.; Procter, G. *J. Chem. Soc., Perkin Trans. I* **1977**, 1924.

SCHEME 6. Formation of the Azabicycles 42−45a and 42−45b, Marked with ^{13}C and ^{2}H



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 the SI), since one $^{13}CH_2$ and one ^{13}CH signal are recorded in a similar ratio.

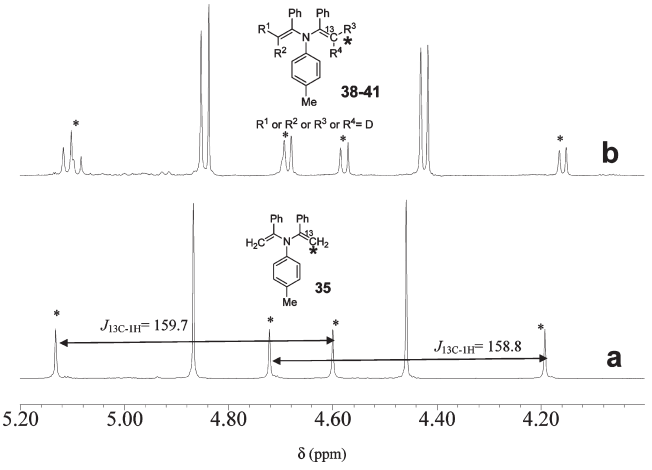


FIGURE 4. Vinylic region of the ^{1}H NMR spectra of the azabicycles **35** (a) and **38**−**41** (b).

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 the SI).

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.

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 forms **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 an 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 the 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 the cis position, conferring complete diastereoselectivity to the process. In fact, the trans diastereomer would be too unstable to form. 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

(28) For related structures see: (a) Attia, M. I.; Güclü, D.; Hertlein, B.; Julius, J.; Witt-Enderby, P. A.; Zlotos, D. P. *Org. Biomol. Chem.* **2007**, *5*, 2129. (b) Tang, P.; Lin, Z.; Yang, J.; Zhao, F.; Wang, Y.; Wang, Q. *China*, WO2008148279 (A1), 2008.

(29) Rearrangements are a cornerstone in organic synthesis since they give access to carbon skeletons otherwise difficult to achieve: (a) Corey, E. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1650. (b) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668. (c) Zimmerman, H. E.; Armesto, D. *Chem. Rev.* **1996**, *96*, 3065. (d) Cantín, A.; Leiva, S.; Jordá, J. L.; Valencia, S.; Rey, F.; Corma, A. *Stud. Surf. Sci. Catal.* **2007**, *170A*, 330. (e) Cantín, A.; Corma, A.; Leiva, S.; Rey, F.; Rius, J.; Valencia, S. *J. Am. Chem. Soc.* **2005**, *121*, 560. Polycyclic compounds, in particular those containing nitrogen, are ubiquitous in nature and different rearrangements are used in their synthetic route: (f) Perreault, S.; Rovis, T. *Chem. Soc. Rev.* **2009**, *38*, 3149. (g) Li, P.; Menche, D. *Angew. Chem., Int. Ed.* **2009**, *48* (28), 5078. (h) Singh, V.; Nedanthan, P.; Sahu, P. K. *Tetrahedron Lett.* **2002**, *43*, 519.

(30) Brannock, K. C.; Burpitt, R. D.; Goodlett, V. W.; Thweatt, J. G. *J. Org. Chem.* **1964**, *29*, 813–817.

(31) Brannock, K. C.; Bell, A.; Burpitt, R. D.; Kelly, C. A. *J. Org. Chem.* **1964**, *29*, 801.

(32) Brannock, K. C.; Bell, A.; Burpitt, R. D.; Kelly, C. A. *J. Org. Chem.* **1961**, *26*, 625.

(33) Smith, M. B.; March, J. In *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*. See [*2 + 2*] *cycloadditions*, pp 1077−1084; John Wiley and Sons: New York, 2001; p 2083.

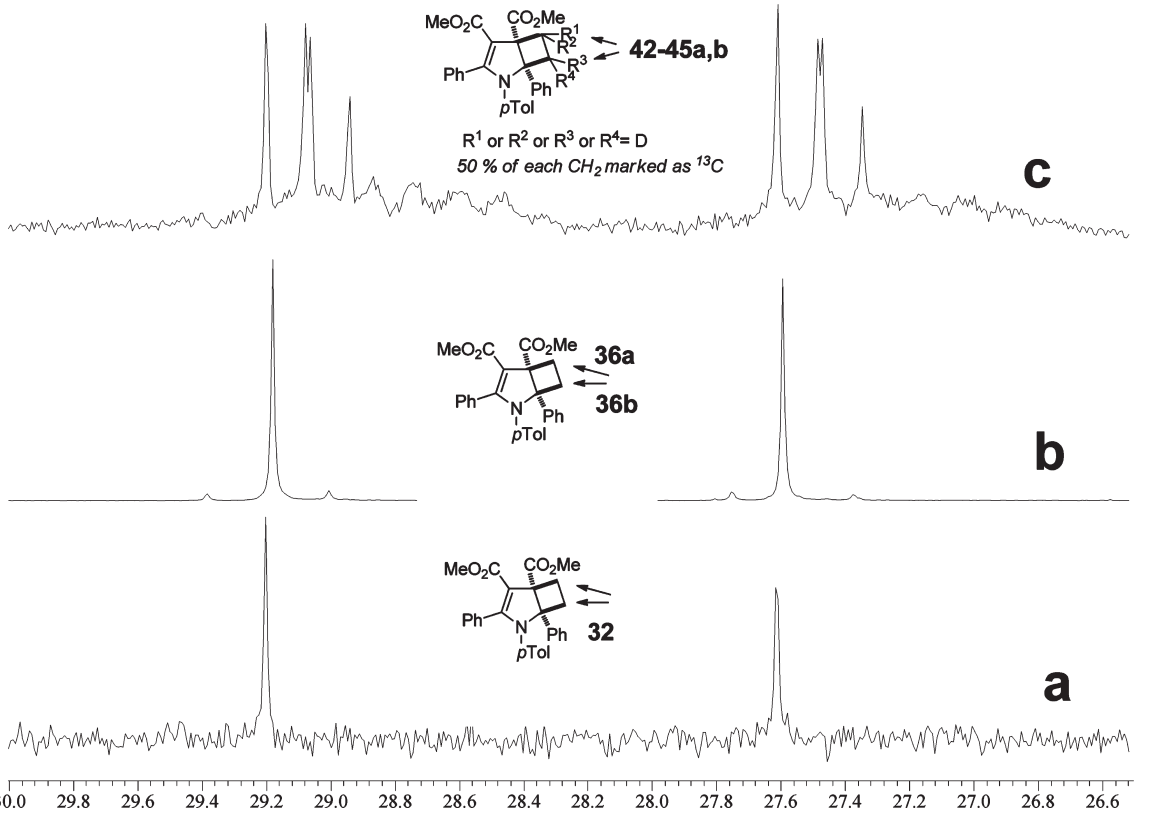
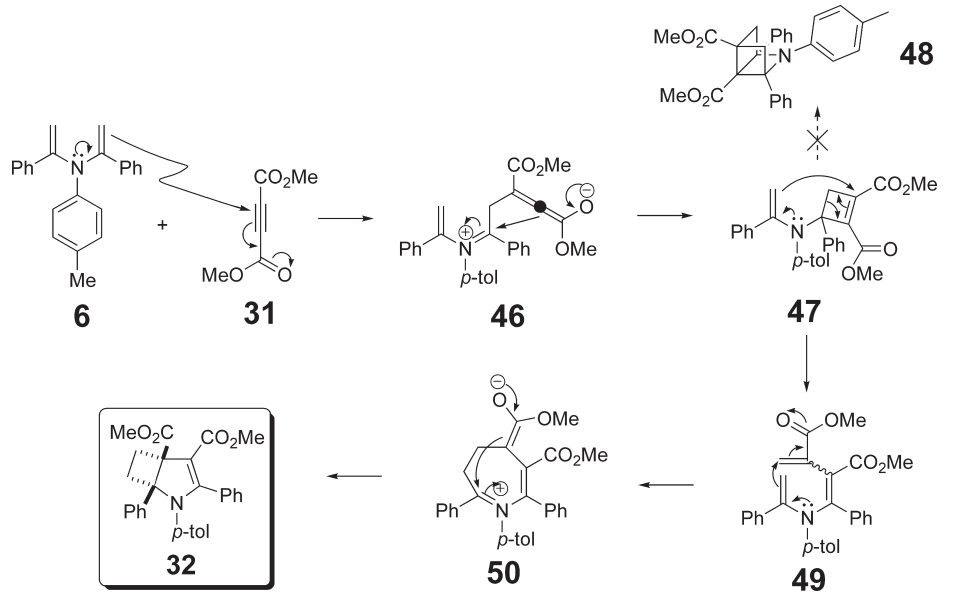


FIGURE 5. Part of the ^{13}C NMR spectra of the azabicycles **32** (a), **36a**,**b** (b), and **42**−**45a**,**b** (c).

SCHEME 7. Proposed Mechanism for the Addition of DMAD (31) to Bisenamine 6

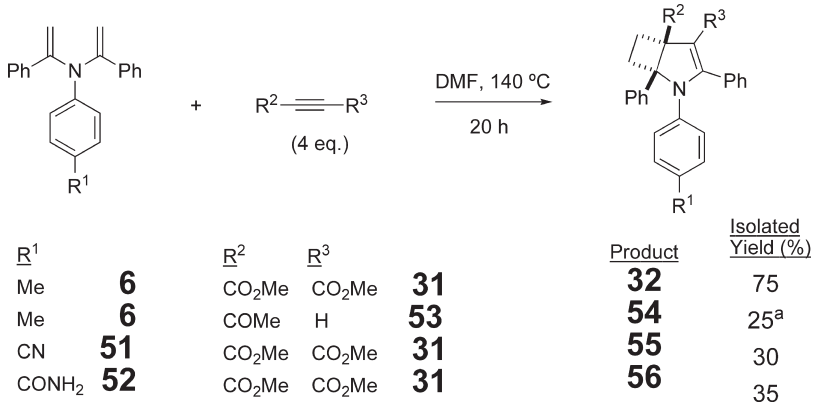


an important change in the reaction rate (Table 4, entries 4 and 5) and, in general, polar solvents are more suitable (see footnote in Table 4); (b) the nucleophilicity of the bisenamine and/or the electrophilicity of the Michael acceptor determines dramatically the reaction yield (Scheme 8 and Scheme S2 in the 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.

As can be seen, the better donor the aryl ring of the bisenamine (**6**) and the more electron acceptor the alkyne (**31**) are, 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.

Azabicycles as UV Sunscreeners. UV sunscreen organic chemicals are delocalized compounds such as *p*-octyl

SCHEME 8. Influence of the Electronic Nature of Both Bisenamine and Alkyne in the Reaction



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

[a]GC yield.

methoxycinnamate and bisoctrizole. The azobicycles here synthesized possess 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.

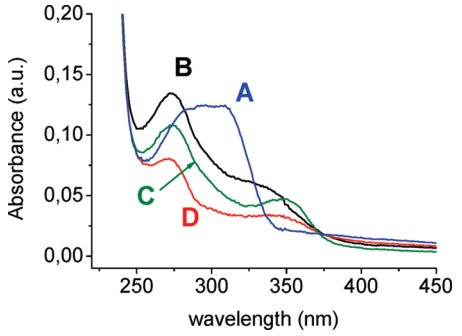


FIGURE 6. UV−vis spectra of *p*-octyl methoxycinnamate (A), compound **32** (B), compound **55** (C), and compound **56** (D), measured at 1 μM concentration in CH_2Cl_2.

As can be seen, azobicycles **32**, **55**, and **56** indeed absorb in the UVA and UVB ranges at similar concentrations as 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−enamines has 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 to other chemicals. As proof of reactivity, a catalytic hydrogenation, an intramolecular oxidative C−C coupling, and an addition to propiolates have been performed, giving access to useful intermediates. In particular, the latter allows the synthesis of UV absorber 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. Glassware was dried in an oven at 175 °C before use. Reagents and solvents were obtained from commercial sources and were used without further purification unless otherwise indicated. Gold(I) complexes **7a**,[14a] **7c**,[14a] and **7d**[15] were prepared as previously reported. All the products obtained were characterized by GC-MS, ^{1}H and ^{13}C NMR, and DEPT. Gas chromatographic analyses were performed in an instrument equipped with a 25 m capillary column of 5% phenylmethylsilicone. GC/MS analyses were performed on a spectrometer equipped with the same column as the GC and operated under the same conditions. HRMS were performed with the electrospray ionization technique. ^{1}H, ^{13}C, DEPT, and ^{31}P NMR were recorded in a 300 MHz instrument with $CDCl_3$ as solvent otherwise indicated, containing TMS as internal standard. IR spectra of the compounds were recorded on a spectrophotometer by impregnating the windows with a dichloromethane solution of the compound and leaving to evaporate before analysis. UV−visible measurements were recorded on a spectrophotometer with CH_2Cl_2 as solvent. Elemental analyses of the solids were determined by chemical combustion with a CHNSO analyzer.

Syntheses of Gold Catalysts. Synthesis of AuDavePhosCl. Tetrachloroauric acid trihydrate (394 mg, 1 mmol) was dissolved in distilled water (1 mL) under nitrogen and the solution was cooled in ice. Then, 2,2′-thiodiethanol was slowly added over 45 min until disappearance of the color (ca. 300 μL). After that, 2′-dicyclohexylphosphanylbiphenyl-2-yldimethylamine (DavePhos, 394 mg, 1 mmol) was added and then 3 mL of ethanol. The mixture was stirred at rt for 3 h. Then, a $NaHCO_3$ aqueous solution (ca. 20 mL) was added to the clear solution until at pH ∼7 a white solid starting precipitating. The solid was filtered off and redissolved in CH_2Cl_2, extracted with brine, dried over $MgSO_4$, and filtered. The solution was concentrated to dryness to obtain AuDavePhosCl as a white powder (500 mg, 0.80 mmol, 80%). IR (cm^{-1}): 2931, 2854, 1446, 1327, 1203, 1142, 1057, 741. ^{1}H NMR (δ, ppm; *J*, Hz): 7.60−7.40 (4H, mult), 7.36 (1H, ddd, *J* = 7.5, 4.1, 1.5), 7.06 (2H, mult), 6.97 (1H, dd, *J* = 7.4, 1.7), 2.46 (6H, s), 2.30 (1H, qt, *J* = 11.8, 2.8), 2.00 (3H, mult), 1.85 (1H, mult), 1.80−1.50 (8H, mult), 1.40−1.05 (9H, mult). ^{13}C NMR (δ, ppm; J_{C-P}, Hz): 151.1 (C), 148.5 (C, *J* = 12), 134.6 (C), 133.35 (CH, *J* = 8), 132.2 (CH, *J* = 4), 131.4 (CH), 130.8 (CH, *J* = 2), 129.3 (CH), 126.9 (CH, *J* = 7), 125.4 (C, *J* = 53), 121.9 (CH), 119.7 (CH), 43.7 ($2CH_3$), 37.7 (CH, *J* = 33), 35.6 (CH, *J* = 34), 30.7 (CH_2, *J* = 4), 30.2 (CH_2, *J* = 3), 29.9 (CH_2), 28.8 (CH_2), 26.9 (CH_2), 26.6 (CH_2, *J* = 3), 26.5 (CH_2, *J* = 5), 26.4 (CH_2), 25.6 (CH_2, *J* = 2), 25.5 (CH_2, *J* = 2). ^{31}P NMR (δ, ppm): 39.4. Elemental Anal. (calcd for $C_{26}H_{36}AuClNP$: C, 49.89; H, 5.80; N, 2.24) found: C 49.19, H 5.74, N 2.20. HRMS (ESI) [M^+; calcd for

$C_{26}H_{36}AuClNP$: 625.1939] found m/z 625.1936; [$(M - Cl)^+$, major peak ; calcd for $C_{26}H_{36}AuNP$: 590.2251] found m/z 590.2232.

Synthesis of AuDavePhosNTf$_2$ (7b). AuDavePhosCl (350 mg, 0.56 mmol) and $AgNTf_2$ (217 mg, 0.56 mmol) were placed in a round-bottomed flask. Air evacuation−nitrogen refilling cycles were carried out and a rubber septum was rapidly fitted after the last nitrogen refilling, a nitrogen balloon additionally coupled through a needle. Then, dry CH_2Cl_2 (15 mL) was added and the mixture was magnetically stirred at rt for 30 min. Then, the white solid formed (AgCl) was filtered off over Celite and the clear filtrates were concentrated to dryness to obtain AuDavePhosNTf$_2$ as a yellow-bright crystalline powder (490 mg, quantitative). Crystals can be obtained by dissolving the solid in the minimum amount of CH_2Cl_2 and adding hexane until blurring is observed, then leaving the mixture into a fridge at −14 °C overnight and filtering the crystal thus obtained. IR (cm^{-1}): 2931, 2854, 1342, 1196, 1142, 1057. ^{1}H NMR (δ, ppm; J, Hz): 7.64−7.38 (5H, mult), 7.11 (2H, t, J = 7.7), 6.99 (1H, d, J = 7.0), 2.46 (6H, s), 2.28−2.00 (4H, mult), 1.86−1.62 (8H, mult), 1.48−1.18 (10H, mult). ^{13}C NMR (δ, ppm; $J_{C-P,\text{otherwise indicated}}$, Hz): 151.2 (C), 148.1 (C), 133.4 (CH), 132.4 (CH), 131.6 (2 × CH), 129.3 (CH), 127.3 (CH), 124.0 (C), 123.3 (C,), 122.2 (CH), 119.4 (C, J_{C-F} = 323), 119.1 (CH), 43.4 (2 × CH_3), 37.4 (CH, J = 34), 36.3 (CH, J = 34), 31.0 (CH_2), 29.6 (CH_2), 26.6 (CH_2), 26.5 (2 × CH_2), 26.4 (CH_2), 26.3 (CH_2), 25.6 (CH_2), 25.5 (2 × CH_2). ^{31}P NMR (δ, ppm): 39.1. Elemental Anal. (calcd for $C_{28}H_{36}AuF_6N_2O_4PS_2$: C, 38,63; H, 4,17; N, 3,22; S, 7,37) found: C, 39,53; H, 4,32; N, 3,24; S, 7,43. HRMS (ESI) [$(M - Cl)^+$, major peak; calcd for $C_{26}H_{36}AuNP$: 590.2251] found m/z 590.2258.

Synthesis of Au(P^{t}Bu$_3$)NTf$_2$ (7c).[14a] Au(P^{t}Bu$_3$)Cl (435 mg, 1 mmol) and $AgNTf_2$ (388 mg, 1 mmol) were mixed in dry dichloromethane (25 mL). The mixture was stirred at rt under nitrogen for 30 min and filtered over Celite. The solution was concentrated to dryness to obtain Au(P^{t}Bu$_3$)NTf$_2$ as a white solid (675 mg, 0.99 mmol, quantitative). Crystals can be obtained by dissolving the solid in the minimum amount of CH_2Cl_2 and leaving to evaporate at room temperature. IR (cm^{-1}): 3437, 2951, 1398, 1205, 1134, 958. ^{1}H NMR (δ, ppm; J, Hz): 1.52 (27H, d, J = 14.3). ^{13}C NMR (δ, ppm; J, Hz): 119.3 (2C, q, J_{C-F} = 323.0), 39.8 (3C, d, J_{C-P} = 11.9), 32.1 (9C, d, J_{C-P} = 3.8). ^{31}P NMR (δ, ppm): 90.9. FAB$^+$ [M^+; calcd for $C_{14}H_{27}AuF_6NO_4PS_2$: 679] found m/z 399 ($M^+ - N(SO_2CF_3)_2$), 833 (P^{t}Bu$_3$AuClAuP^{t}Bu$_3$).

Synthesis of Au(PEt$_3$)NTf$_2$ (7d). The title compound was obtained by following the same procedure as for **7c** but with Au(PEt_3)Cl (200 mg, 0.57 mmol) as gold precursor (gray solid, 340 mg, quantitative). IR (cm^{-1}): 3511, 2928, 1342, 1200, 1140, 1057. ^{1}H NMR (δ, ppm; J, Hz): 1.90 (4H, dq, J_{H-P} = 10.6, J = 7.8), 1.21 (6H, dt, J_{H-P} = 19.7, J = 7.7). ^{13}C NMR (δ, ppm): 119.3 (2C, q, J_{C-F} = 322.7), 38.4 (3C, d, J_{C-P} = 38.4), 9.2 (3C, d, J_{C-P} = 1.7). ^{31}P NMR (δ, ppm): 32.6.

Synthesis of AuP(OPh)$_3$Cl. Tetrachloroauric acid trihydrate (394 mg, 1 mmol) was dissolved in distilled water (1 mL) under nitrogen and the solution was cooled in ice. Then, 2,2′-thiodiethanol was slowly added over 45 min until disappearance of the color (ca. 300 μL). After that, triphenylphosphite (236 μL, 1 mmol) was added and then 3 mL of ethanol. The mixture was stirred at rt for 3 h. The solid was filtered off and washed with methanol, redissolved in dry dichloromethane, and filtered again. The solution was concentrated to dryness to obtain $AuP(OPh)_3Cl$ as a white solid. ^{1}H NMR (δ, ppm; J, Hz): 7.32 (6H, t, J = 8.0), 7.17 (9H, mult). ^{13}C NMR (δ, ppm; J_{C-P}, Hz): 149.3 (3C, d, J = 4.9), 130.5 (6C, d, J = 1.7), 126.7 (3C, d, J = 1.6), 121.1 (6C, d, J = 5.6). ^{31}P NMR (δ, ppm): 109.7.

Synthesis of AuP(OPh)$_3$NTf$_2$ (7f). The title compound was obtained by following the same procedure as for **7c** but with $AuP(OPh)_3Cl$ (130 mg, 0.24 mmol) as gold precursor (white solid, 100 mg, 54% yield). IR (cm^{-1}): 3054, 2981, 1590, 1486, 1404, 1264, 1207, 1136, 952, 739. ^{1}H NMR (δ, ppm; J, Hz): 7.44 (6H, t, J = 7.7), 7.34 (3H, tq, J = 7.6, 1.3), 7.20 (6H, mult). ^{13}C NMR (δ, ppm; J_{C-P}, Hz): 148.8 (3C, d, J = 5.0), 130.6 (6C, d, J = 2.2), 127.1 (3C, d, J = 2.2), 121.1 (6C, d, J = 6.0). ^{31}P NMR (δ, ppm): 103.7.

Synthesis of AuP(trisCF$_3$-phenyl)$_3$NTf$_2$ (7g). The title compound was obtained by following the same procedure as for **7c** but with $AuP(trisCF_3\text{-phenyl})_3Cl$ complex (200 mg, 0.28 mmol) as gold precursor (slightly purple-white solid, 265 mg, 71%). IR (cm^{-1}): 1396, 1327, 1203, 1134, 1057, 956, 833, 710, 601. ^{1}H NMR (δ, ppm; J, Hz): 7.87 (3H, ddt, J = 8.1, 2.3, 0.6), 7.84 (3H, ddt, J = 13.4, 8.1, 0.6). ^{13}C NMR (δ, ppm; J_{C-P}, Hz): 134.6 (3C, d, J = 14.9), 126.9 (3C, dq, J = 12.4, 3.2), 135.9−112.9 (23C, mult). ^{31}P NMR (δ, ppm): 30.7. HRMS (ESI) [$M^+ + H^+$; calcd for $C_{29}H_7AuF_{33}NO_4PS_2$: 1351.8691] found m/z 1352.0453.

Reaction Procedures. 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 preheated oil bath at 80 °C for 24 h. After cooling, an aliquot was taken for GC analysis. The CH_3CN was removed in vacuo and CH_2Cl_2 (1 mL) was added to redissolve 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 analyzed 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 °C as yellow crystals, which were washed with *n*-hexane and dried.

Hydrogenation Procedure for Bisenamine 6 and Isolation of the Corresponding Tertiary Amines 26 and 27. Pt/C (3 wt%, 12 mg, Pt: 15 mol%) and bisenamine **6** (39 mg, 0.125 mmol) were placed into a 2 mL thin double-walled vial having a pressure controller and an H_2 inlet/outlet. Dry THF (1 mL) was added and the vial was sealed, purged three times with H_2 (8−10 atm), and finally loaded with H_2 (12 atm, 0.13 mmol, 5 equiv). The mixture was magnetically stirred in a preheated oil bath at 50 °C for 6 h. Progressive loss of the yellow color of the solution was observed. After cooling, the remaining H_2 was removed and the mixture was filtered. The resulting solution was analyzed by GC and GC-MS and the amines were quantitatively separated and purified by TLC on silica (2% AcOEt in hexane). After extraction from the silica with neat AcOEt and removal of the solvents, 18 mg of each amine was obtained as a white oil (>95% yield).

Pd-Catalyzed Intramolecular Oxidative Coupling of 6. Pd($OAc)_2$ (2.2 mg, 20 mol%), bisenamine **6** (15.6 mg, 0.05 mmol), and $NaHCO_3$ (12.6 mg, 3 equiv) were placed into a vial. Dry DMF (0.25 mL) and PhI (16.7 μL, 3 equiv) were added and the vial was sealed and magnetically stirred in a preheated oil bath at 140 °C for 20 h. After cooling, the resulting solution was analyzed by GC and GC-MS and the product was purified by TLC on silica (2% AcOEt in hexane). After extraction from the silica with neat AcOEt and removal of the solvents, 15 mg of pyrrole **29** was obtained (>95% yield). The spectroscopic data of **29** fit those previously reported.

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 equiv) were added and the vial was sealed and magnetically stirred in a preheated oil bath at 140 °C for 20 h. After cooling, the resulting solution was analyzed 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** was obtained (85% yield). Yellow crystals were obtained by redissolving in CH_2Cl_2 and slow evaporation. GC-MS (m/z): 453 ($M^{+\bullet}$, 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$^+$; calcd for $C_{29}H_{28}NO_4$: 454.2018] found m/z 454.1956.

Isotopic Experiments (Schemes 5 and 6). *p*-Toluidine (**1**) (21.4 mg, 0.2 mmol) and AuSPhosNTf$_2$ (**7a**) or AuP^{t}Bu$_3$NTf$_2$ (**7c**) (1 mol%) were placed into a vial equipped with a magnetic bar. Then, CD_3CN (0.4 mL, 0.5 M solution) and ^{13}C-marked phenylacetylene (**2**) (24 μL, 1.1 equiv) were sequentially added and the vial was sealed. The solution was magnetically stirred at room temperature for 24 h. Then, AuP^{t}Bu$_3$NTf$_2$ (**7c**) (17 mg, 5 mol %) and phenylacetylene (**2**) or d_1-phenylacetylene (**37**) (63 μL, 3 equiv) were added and the mixture was magnetically stirred in a preheated oil bath at 80 °C for 24 h. After this time, DMAD (**31**) (30 μL, 1.2 equiv) was added and the mixture was magnetically stirred at 80 °C for an additional 20 h. The resulting solution was analyzed by GC and GC-MS and the product was purified by TLC on silica (10−20% AcOEt in hexane). After extraction from the silica with neat AcOEt and removal of the solvents, 21 mg of **36a**,**b** (23%) or 30 mg of **42**−**45a**,**b** (35%) was obtained. All the intermediates were analyzed by in situ NMR and GC-MS.

UV Measurements. A 1 μM DCM solution of the compounds was prepared as follows: **32** (2.26 mg, 0.005 mmol) was diluted in 5 mL of DCM and then 25 μL of this solution was diluted in 25 mL of DCM. The same procedure was followed for **55** (2.32 mg, 0.005 mmol), **56** (2.40 mg, 0.005 mmol), and *p*-octylmethoxycinnamate (1.45 μL, 0.005 mmol).

Product Characterization. Compound 6. The yellow oil, after column chromatography, solidifies in a fridge at −14 °C as yellow crystals, which were washed with *n*-hexane and dried. R_f (10% AcOEt in hexane): 0.69. GC-MS (m/z): 311 (M$^{+\bullet}$, 100%), 283 (14%), 194 (100%). IR (cm^{-1}): 3034, 2924, 1611, 1505, 1321, 1258, 773, 702. ^{1}H NMR (δ, ppm; J, Hz): 7.49 (4H, mult), 7.11 (6H, mult), 6.89 (2H, d, J = 8), 6.82 (2H, d, J = 8), 4.91 (2H, s), 4.54 (2H, s), 2.08 (3H, s). ^{13}C NMR (δ, ppm): 151.7, 144.4 (2C), 138.9, 132.5 (2C), 129.3 (2C), 128.1 (2C), 127.9 (2C), 126.7 (4C), 125.2 (2C), 125.2 (2C), 106.1 (2C), 20.7. HRMS (ESI) [M$^+$; calcd for $C_{23}H_{21}N$: 311.1674] found m/z 311.1674.

Compound 9. The reaction was run at 1 mmol scale. The crude was purified by column chromatography on basic alumina (0−3% MeOH in AcOEt) to achieve 4-[bis(1-phenylvinyl)amino]benzamide (**9**) as a yellowish orange solid (190 mg, 56%). GC-MS (m/z): 340 (M$^{+\bullet}$, 100%), 312 (7%), 223 (100%). IR (cm^{-1}): 3353, 3207, 2921, 2855, 2304, 2200, 1806, 1708, 1494, 1371. ^{1}H NMR (δ, ppm; J, Hz): 7.48 (6H, mult), 7.20−7.17 (6H, mult), 6.97 (2H, dt, J = 8.7, 1.9), 5.80 (2H, br s), 5.12 (2H, s), 4.81 (2H, s). ^{13}C NMR (δ, ppm): 169.0, 151.0 (2C), 150.3, 138.0 (2C), 128.3 (4C), 128.2 (2C), 128.1 (2C), 126.7 (4C), 126.5, 123.6 (2C), 108.2 (2C). HRMS (ESI) [M + H$^+$; calcd for $C_{23}H_{21}N_2O$: 341.1654] found m/z 341.1665.

Compound 11. The reaction was run at 1 mmol scale. The crude was purified by column chromatography on basic alumina (1−5% AcOEt in hexane) to achieve 3-{4-[bis(1-phenylvinyl) amino]phenyl}acrylic acid ethyl ester (**11**) as a yellow oil (304 mg, 77%). R_f (5% AcOEt in hexane): 0.23. IR (cm^{-1}): 3057, 3032, 2977, 1706, 1624, 1600, 1505, 1315, 1265, 1171. ^{1}H NMR (δ, ppm; J, Hz): 7.61 (6H, mult), 7.29 (7H, mult), 7.06 (2H, dt, J = 8.6, 2.1), 6.28 (1H, d, J = 16.0), 5.20 (2H, s), 4.89 (2H, s), 4.26 (2H, q, J = 7.1), 1.33 (3H, t, J = 7.2). ^{13}C NMR (δ, ppm): 167.2, 151.0 (2C), 148.9, 144.2, 138.2 (2C), 128.6 (2C), 128.5, 128.3 (4C), 128.2 (2C), 126.7 (4C), 124.3 (2C), 116.1, 107.9 (2C), 60.2, 14.3. HRMS (ESI) [M$^+$; calcd for $C_{27}H_{26}NO_2$: 396.1964] found m/z 396.1955.

Compound 13. The reaction was run at 2 mmol scale. The crude was purified by column chromatography on basic alumina (0−10% AcOEt in hexane) to achieve 4-[bis(1-phenylvinyl)-amino]benzonitrile (**13**) as a yellow oil (152 mg, 47%). The product was dissolved in the minimum amount of hexane and kept overnight in a fridge at −14 °C to obtain yellow crystals, which were washed with cold *n*-hexane and dried. R_f (10% AcOEt in hexane): 0.61%. GC-MS (m/z): 322 (M$^{+\bullet}$, 86%), 294 (10%), 245 (12%), 205 (100%). IR (cm^{-1}): 3062, 3024, 2918, 2852, 2221, 1600, 1500, 1317, 1206. ^{1}H NMR (CD_3CN, δ, ppm; J, Hz): 7.61 (4H, mult), 7.43 (2H, dt, J = 9.0, 2.3), 7.31 (6H, mult), 7.09 (2H, dt, J = 8.8, 2.3), 5.28 (2H, d, J = 0.6), 4.95 (2H, d, J = 0.6). ^{13}C NMR (CD_3CN, δ, ppm): 151.8 (2C), 151.7, 138.6 (2C), 133.6 (2C), 129.5 (2C), 129.3 (4C), 127.8 (4C), 124.7 (2C), 119.8, 109.7 (2C), 105.1. HRMS (ESI) [M + H$^+$; calcd for $C_{23}H_{19}N_2$: 323.15548] found m/z 323.1555.

Compound 16. The reaction was run at 0.5 mmol scale (^{1}H NMR yield, 58%). The crude was purified by column chromatography on basic alumina (0−5% AcOEt in hexane) to achieve bis[1-(4-chlorophenyl)vinyl](4-iodophenyl)amine (**16**). R_f (5% AcOEt in hexane): 0.77. ^{1}H NMR (ppm; J, Hz): 7.37 (4H, mult), 7.19 (4H, mult), 7.17 (2H, dt, J = 8.8, 2.1), 6.71 (2H, dt, J = 8.2, 2.1), 5.01 (2H, d, J = 0.8), 4.64 (2H, d, J = 0.8). ^{13}C NMR (δ, ppm): 150.0 (2C), 146.2, 137.8 (2C), 136.6 (2C), 134.0 (2C), 128.6 (4C), 127.9 (4C), 126.8 (2C), 107.6 (2C), 86.8.

Compound 18. The reaction was run at 1 mmol scale. The crude was purified by column chromatography on basic alumina (0−15% AcOEt in hexane) to achieve 3-[bis(1-phenylvinyl)-amino]benzonitrile (**18**) as a yellow oil (306 mg, 95%). R_f (10% AcOEt in hexane): 0.52%. IR (cm^{-1}): 3059, 3033, 2954, 2925, 2229, 1686, 1602, 1485, 1437, 1318, 1276. ^{1}H NMR (δ, ppm; J, Hz): 7.47 (4H, mult), 7.24−7.14 (8H, mult), 7.09 (1H, td, J = 7.7, 0.5), 7.03 (1H, dt, J = 7.6, 1.4), 5.10 (2H, s), 4.98 (2H, s). ^{13}C NMR (δ, ppm): 150.8 (2C), 147.6, 137.6 (2C), 129.4, 128.7, 128.4 (4C), 128.3, 127.4 (2C), 126.7 (4C), 125.8, 118.7, 112.6, 108.1 (2C). HRMS (ESI) [M$^+$; calcd for $C_{23}H_{19}N_2$: 323.1548] found m/z 323.1553.

Compound 20. The reaction was run at 0.25 mmol scale for 48 h, using 20 mol % of **7c** (34 mg) as catalyst and 8 equiv of phenylacetylene **2** (220 μL). The crude was analyzed by GC, GC-MS, ^{1}H, ^{13}C NMR, and DEPT. GC-MS (m/z): 322 (M$^{+\bullet}$, 100%), 294 (5%), 245 (10%), 205 (68%).

Compound 24. The reaction was run at 1 mmol scale. After 24 h, hexane (10−20 mL) was added and precipitated solid was filtered off. After removal of the volatiles under vacuum, **24** was obtained as an orangish red oil (417 mg, 95%). GC-MS (m/z, three different peaks, major isomer shown here): 439 (M$^{+\bullet}$, 12%), 382 (40%), 368 (100%), 354 (33%), 298 (29%), 244 (79%). ^{1}H and ^{13}C NMR: see spectra.

Compound 25. The reaction was run at 1 mmol scale. The first imine with phenylacetylene (**2**) (121 μL, 1.1 equiv) was formed at 60 °C for 24 h, using **7b** (9 mg, 1 mol %) as catalyst. Then, additional catalyst (36 mg, 4 mol %) was added together with 1-octyne (444 μL, 3 equiv) and the mixture was reacted at 60 °C for 24 h, and analyzed by GC-MS. After the reaction was completed, volatiles were removed under vacuum and hexane (10−20 mL) was added to precipitate the catalyst. The solid was filtered off and, after removal of the solvents, an orange solid, corresponding to the aromatic imine, was recovered (225 mg, 70% yield). GC-MS of **25** (m/z, two peaks, major isomer shown here): 431 (M$^{+\bullet}$, 46%), 416 (48%), 374 (100%), 354 (13%), 298 (6%), 244 (31%).

Compound 32. R_f (20% AcOEt/hexane): 0.24. GC-MS (m/z): 453 (M$^{+\bullet}$, 3%), 425 (100%), 394 (39%), 194 (17%). ^{1}H NMR (δ, ppm; J, Hz): 7.46 (2H, dd, J = 8.5, 1.7), 7.40 (2H, mult), 7.31 (4H, mult), 7.22 (2H, mult), 6.67 (2H, dd, J = 8.6, 0.7), 6.37 (2H, dt, J = 8.5, 2.1), 3.52 (3H, s), 3.24 (3H, s), 3.21−2.96 (3H, mult), 2.45 (1H, mult), 2.07 (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) [$M + H^+$; calcd for $C_{29}H_{28}NO_4$: 454.2018] found m/z 454.1956.

Compound 55. R_f (25% AcOEt/hexane): 0.21. ^{1}H NMR (δ, ppm; J, Hz): 7.44−7.35 (2H, mult), 7.10 (2H, d, $J = 9$), 6.39 (2H, d, $J = 9$), 3.53 (3H, s), 3.24 (3H, s), 3.18 (2H, mult), 2.98 (1H, mult), 2.47 (1H, mult). ^{13}C NMR (δ, ppm): 170.5, 165.0, 159.0, 143.1, 135.8, 132.1 (2C), 130.9, 130.7, 129.7 (2C), 129.4, 128.5 (2C), 128.3 (2C), 128.2, 127.0 (2C), 123.5 (2C), 118.7, 109.5, 105.8, 62.2, 51.7, 50.8, 29.7, 27.3. HRMS (ESI) [$M + H^+$; calcd for $C_{29}H_{25}N_2O_4$: 465.1814] found m/z 465.1802.

Compound 56. R_f (75% AcOEt/hexane): 0.23. ^{1}H NMR (δ, ppm; J, Hz): 7.60−7.10 (12H, mult), 6.35 (2H, d, $J = 9$), 5.85−5.15 (2H, br s), 3.90−3.40 (3H, mult), 3.52 (3H, s), 3.24 (3H, s), 3.15 (1H, mult). ^{13}C NMR (δ, ppm): 171.1, 168.4, 165.2, 159.9, 142.5, 136.2, 131.2, 129.5, 129.4, 128.3 (2C), 128.1 (4C), 128.0, 127.6, 127.5 (2C), 127.2 (2C), 123.6 (2C), 108.3, 62.2, 51.7, 50.7, 29.7, 27.5. HRMS (ESI) [$M + H^+$; calcd for $C_{29}H_{27}N_2O_5$: 483.1920] found m/z 483.1879.

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Supporting Information Available: General methods, reaction procedures and compound characterization in detail, as well as additional schemes, tables, and figures, XRD 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.