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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/jo401075n • Publication Date (Web): 01 Jul 2013

Just Accepted

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Gold(I) Catalyzed Benzo[c]azepin-4-ol Synthesis by Intermolecular [5 + 2] Cycloaddition

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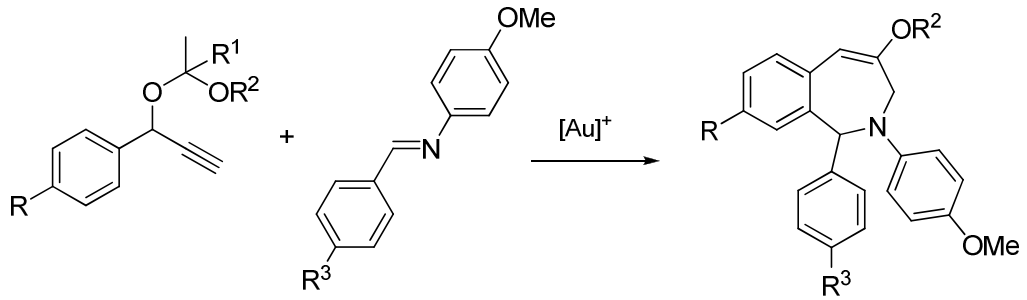


Abstract

A gold(I) catalyzed intermolecular formal [2+5] cycloaddition for the preparation of benzofused *N*-heterocyclic azepine products is presented. A number of benzo[c]azepin-4-ol products were readily prepared in one step from easily accessible phenylpropargyl acetals and benzaldimine substrates in the presence of a gold(I) catalyst. A direct one-pot procedure from the propargyl and the respective aldehyde and amine substrates was successful, as well. The reaction to access the benzofused azepines could be rationalized by a cascade reaction, including a nucleophilic benzaldimine *N*-attack at a highly reactive phenylpropargyl-gold(I) carbenoid complex, generated from propargyl acetal. A subsequent deauration step promotes ring closure by 1,7-electrocyclization through an intramolecular Pictet-Spengler type reaction with the aldiminium moiety.

Introduction

The seven-membered ring-fused benzazepine heterocycles contain a framework that is often observed among bioactive natural products and pharmaceuticals.[1] Due to their chemotherapeutic properties, exhibiting biological activity toward various targets, such as enzymes, ion channels, and different receptors, these benzannulated compounds represent a particularly interesting class of aza-heterocycles.[2] Compounds containing the benzo[a, b or c]azepine skeleton, mainly at the tetrahydro level, display important physiological properties and are known to exhibit strong neuroleptic and neurotropic activities.[3] Other representatives have been found to display anti-HIV activity[4], to promote healing of skin wounds[5] and to treat cardiovascular diseases, especially glaucoma and hypertension.[6] Benzazepine derivatives are also used as antiarrythmic,[7] CNS agents,[8] as inhibitors of PNMT,[9] recommended for the treatment of stomach disorders[10] and could be used in the treatment of Alzheimer disease.[11] Several substances that include the specific benzo[c]azepine moiety possess useful biological properties.[12] The commercially available benzazepine Capsazepine **A**[13] (Figure 1) is a competitive agonist for the vanilloid receptor (VR1), used in treatment of neuropathic pain, while compound **B** is a Gram-positive antibacterial agent[14] and compound **C** is a potent histamine H3 receptor antagonist.[15]

Since several powerful drugs have been obtained from benzazepine compounds, considerable efforts have been made to establish new methods for the synthesis of these heterocycles.[2b,c,16,17] Different strategies, including the Heck[16a] coupling, intramolecular Claisen-Schmidt cyclization,[16c] Dieckmann cyclization,[16d] $SnCl_2$ mediated reduction and cyclization[16e] and Michael type addition[16g] have been applied for benzazepine synthesis, while ring closing metathesis (RCM)[16a,b,f,i,] and a multistep tandem reaction[16h] have been used for the preparation of unsaturated benzo[c]azepines. Most of these methods are complex and require several steps. Benzo[c]azepin-4-ones with the general structure **D** have been identified as selective muscarine antagonists. They

were synthesized by reductive amination[17c] or by Mitsunobu conditions[17d] for heterocyclic cyclization by the formation of the C1-N bond. Benzo[c]azepin-4-ones derivatives have been prepared by ester condensation[18] and ring closure with formaldehyde.[17e] Alternatively, intramolecular acylation has afforded functionalized benzo[c]azepin-4-ones by cyclization through C4-C5 bond formation.[19] Benzo[c]azepin-3-ones, potentially good candidates for new drug therapies to treat skin wounds, were prepared via an intramolecular Friedel−Crafts reaction.1

Compounds based on the general 4-oxo structure **E** (2,3-dihydro-1H-benzo[c]azepin-4(5H)-one) or the corresponding enol form **E'** have been studied, due to their structure similarities with bioactive natural alkaloids and, thus, potential biological activity. The 4-oxo group would also offer opportunities for further functionalization of the benzazepine skeleton.

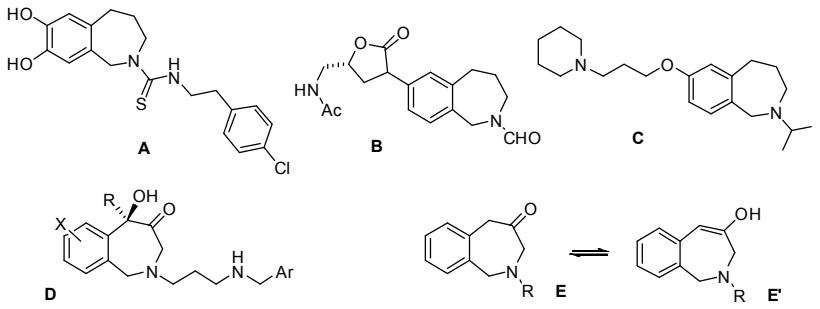
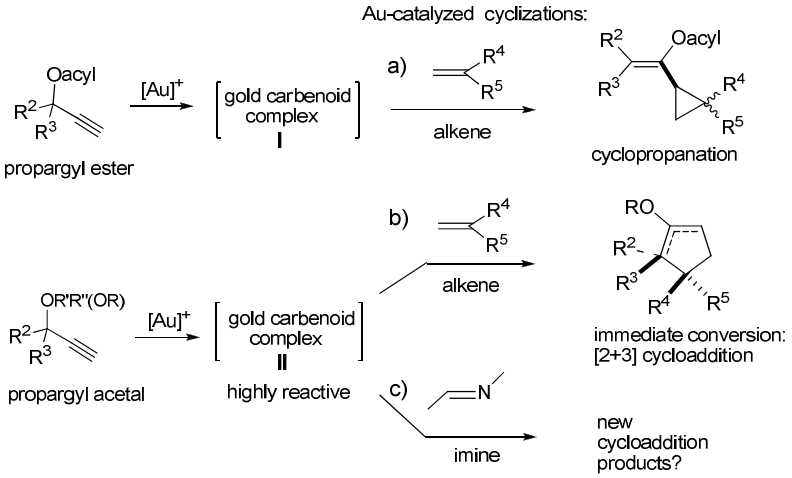


Fig 1: Benzo[c]azepine-containing compounds

Propargyl esters are known to undergo a number of gold catalyzed [2+3], [2+4] and [3+4] cycloaddition reactions.[20] We have recently performed a comparative study on reactivity and chemoselective gold(I) catalyzed alkenes cycloadditions of propargyl esters and acetals, respectively.[21] Such propargyl derivatives are known to give gold carbenoid intermediates (**I**, **II**, Scheme 1) which can be trapped with different reagents, typically alkenes. By changing from propargylic esters to acetals, the reaction pathway switches from a) cyclopropanation to b) [2+3] cycloaddition. The propargyl acetals gave immediate conversion and were significantly more

reactive than the corresponding esters. Hence, the highly reactive propargyl acetals would be promising substrates for potential cycloaddition reactions with other alternatives to alkenes, e.g. heteroatom compounds with a C=X double bond. Thus, we wanted to investigate the potential of c) imines to undergo cycloaddition reactions via the highly reactive propargyl acetal gold(I) carbenoid complexes **II** (Scheme 1). Gold catalysis has been applied for azepine synthesis by intramolecular hydroamination[16i] and [3+4] cycloadditions.[20e,f] However, to the best of knowledge, neither cycloaddition, nor gold(I) catalysis have been applied in benzazepine synthesis. We herein report the results from our study of gold(I) catalyzed cyclization reactions of propargyl acetals with imines.

Scheme 1. Gold(I) promoted reactions of propargyl substrates.



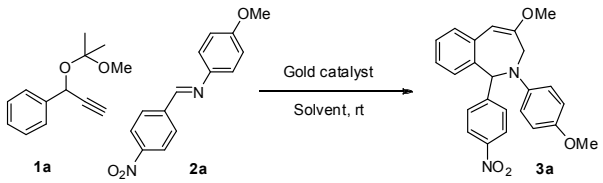
Results and Discussion

Aiming at trapping the highly reactive propargyl acetal gold(I) carbenoid complex **II** (Scheme 1) with imines, cyclization reactions with *N*-arylbenzaldimines, readily available from aniline and benzaldehyde derivatives, were studied, focusing on phenylpropargyl acetals. Rapid and full conversion of the substrates into benzo[c]azepin-4-ol products, analogous to the enolic structure **E'** above (Fig. 1) was observed. The reaction of phenylpropargyl acetal **1a** with *N*-benzylideneaniline

2a in DCM at room temperature in the presence of commercially available Au[P(*t*-Bu)$_2$(*o*-biphenyl)CH_3CN]SbF_6 gave full conversion into benzazepine product **3a** within one hour (entry 1, Table 1). The outcome of the reaction indicated that a new formal [2+5] cycloaddition of propargyl acetal with aldimine through a gold carbenoid intermediate **II** took place.

Optimization. In order to optimize reaction conditions, an introductory study on the cycloaddition of propargyl acetal **1a** and diarylimine **2a** was performed by using different gold(I/III) catalysts and solvents (Table 1). The *in situ* generation of the active gold(I) catalyst by chloride counterion exchange with NTf_2^- or SbF_6^- afforded more active catalytic systems, since full conversion was obtained in 15 minutes, both in DCM and DCE (entries 3, 4, 11). Triphenyl phosphine liganded gold catalysts ($Au(PPh_3)Cl$ + $AgSbF_6$, entry 8) gave low conversion (24%) as compared to the biphenylphosphine complex above. No reaction took place without chloride counterion exchange (entries 2, 7). The cycloaddition reaction was not catalyzed by silver salts (entries 5, 6) and gold (III) catalysts were also found inactive for the reaction (entries 9, 10). Reduced efficiency of the biphenylphosphine gold(I) catalyst (30-64% conversion) was observed in other solvents, such as THF, acetonitrile, nitromethane or toluene (entries 12-15). Since DCE would allow higher reaction temperatures, if required, this solvent was used in the further studies on [2+5] cycloaddition of propargyl acetals and imines in the presence of the Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl + $AgSbF_6$ catalytic system (entry 11).

Table 1 Reaction optimization of [5+2] cycloaddition reaction of propargyl acetal with imine.



entry	Gold catalyst	Time / solvent	Conversion[a]
1	Au[P(*t*-Bu)$_2$(*o*-biphenyl)]CH_3CN]SbF_6	1h / DCM	99%
2	Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl	24h / DCM	nc[b]
3	Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl + $AgSbF_6$	15min / DCM	99%
4	Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl + $AgNTf_2$	15min / DCM	99%
5	$AgSbF_6$	24h / DCM	nc[b]
6	$AgNTf_2$	24h / DCM	nc[b]
7	Au(PPh_3)Cl	24h / DCM	nc[b]
8	Au(PPh_3)Cl+ $AgSbF_6$	24h / DCM	24%
9	$AuCl_3$(III)	24h / DCM	nc[b]
10	Pic$AuCl_2$(III)	24h / DCM	nc[b]
11	**Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl + $AgSbF_6$**	**15min / DCE**	**99%**
12	Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl + $AgSbF_6$	15min / THF	54%
13	Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl + $AgSbF_6$	15min / CH_3CN	64%
14	Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl + $AgSbF_6$	15min / CH_3NO_2	45%
15	Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl + $AgSbF_6$	15min / Toluene	30%

[a] conversion by GC, [b] no conversion

Scope and limitations. By varying the electronic and steric properties of a series of substituted *N*-aryl-benzaldimine **2a-f**, the scope and limitations of the new [2+5] cycloaddition reaction was studied (Table 2). A number of *O*-alkylated benzo[c]azepin-4-ol structures **3a-j** were readily formed by cyclization of propargyl methyl acetal **1a** (entries 1-5) and ethyl acetal **1b** (entries 7-10) with *N*-benzylideneaniline derivatives **2a-e** in high yields (62-80%). The double activation of imine **2a** by an electron-donating *p*-methoxy aniline substituent and an additional *p*-nitro EWG substitution at the benzylidene moiety would afford a push-pull activating effect, as shown by the fast reaction of imine **2a** with acetals **1a** and **1b** (15-30 min, rt, entries 1 and 6). The imines **2b-e**, being only partly activated, reacted significantly slower as the push-pull effect was

reduced. Hence, the reaction rates decreased and higher temperature was required to obtain comparable yields (1-24h, reflux, entries 2-5 and 7-10) as the electron-withdrawing effect of the benzylidene *p*-substituent was reduced by replacement of more ERG substituents, such as H, Cl, OMe, *t*-Bu. Correspondingly, substitution of the aniline part also affected the reactivity, as the non-methoxy *N*-benzylideneaniline **2f** was significantly less reactive, affording 52% yield of benzazepine **3k** (entry 11), relative to the corresponding methoxy substrate **2a** (entry 1, 80%). Moreover, it was observed that *p*-substitution of the phenylpropargyl acetal may influence the activity of the propargyl substrates (see *Selectivity and reactivity* and Scheme 2 below). The effects were shown by the higher yields obtained of the benzo[c]azepine products **3l-n**, as the electrophilicity of the propargyl substrate was increased (**1c**/OMe, 63%; **1d**/Cl, 78%; **1e**/NO_2, 84%; entries 12-14). The ability of the benzaldimines to undergo hydrolysis was shown by the formation of the corresponding benzaldehyde by-products (NMR).

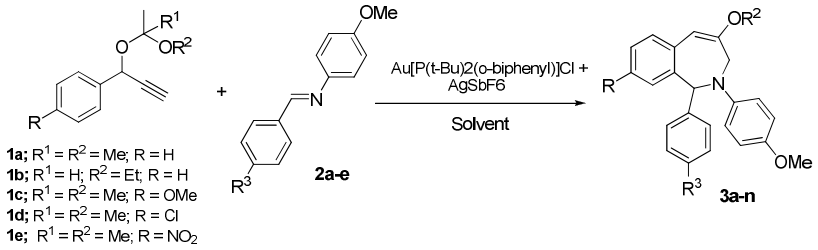
The significance of the *C*- or *N*-arylaldimine groups was studied. It was shown that the *N*-aryl moiety was not an essential requirement for cyclization, as the aliphatic *N*-benzylidenethanamine (**2g**) did undergo gold catalyzed [5+2] cycloaddition with propargyl acetal (**1a**). The reaction afforded 2-ethylbenzo[c]azepine **3o** (entry 15), albeit slower than the aniline analogues **2f** (entry 11) and in moderate yield (45%, reflux, 16h, DCE). The *C*-arylaldimine moiety was, however, crucial for the cyclization to take place, as C-alkylaldimines **2h** and **2h'** (entry 16) failed to afford benzazepine products. The cyclization of the bulky *o*-(di)nitrobenzaldimine analogues **2i,j** with propargyl acetal **1a** was unsuccessful, as well (entry 17).

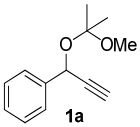
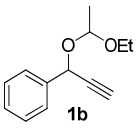
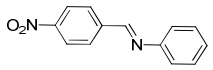
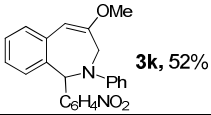
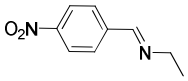
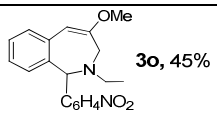
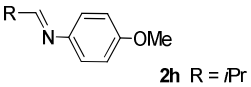
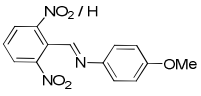
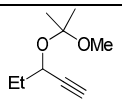
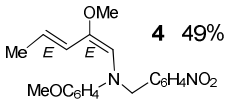
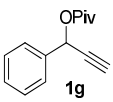
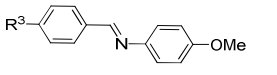
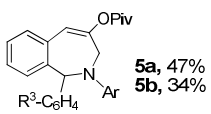
To further investigate the potential and reactivity of propargyl acetals with aldimines in the presence of gold(I), we wanted to study whether alternative reactions would take place by replacing phenylpropargyl substrates with alkylpropargyl acetals. In fact, a new non-cyclic

coupling product **4** (49%, entry 18) was formed when ethylpropargyl acetal (**1f**) was subjected to gold catalysis with aldimine **2a**. The reaction pathway for the formation of *N*-benzyl-*N*-(penta-1,3-dienyl)aniline **4** may be explained by a related mechanism as suggested for the benzazepines **3** (see *Selectivity and reactivity* and Scheme 2 below).

In order to study whether the significantly less reactive propargyl esters would undergo gold(I) catalyzed [2+5] cycloaddition in a similar way, reactions of propargyl ester **1g** with imines **2a**,**b** were performed. The reactions afforded considerably lower yields of the corresponding benzazepine esters **5a**,**b** (34-47%, entry 19) and full conversion could not be obtained, even within several days of reflux.

Table 2 Gold(I) catalyzed propargyl [2+5] cycloaddition with aldimines.



entry	Acetals:		Imine; R^3		Condition	Product, yield
1			**2a**	NO_2	DCE, rt,15min	**3a**, 80%[a]
2			**2b**	H	DCE, reflux, 1h	**3b**, 74%[b]
3			**2c**	Cl	DCE, reflux, 3h	**3c**, 68%
4			**2d**	OMe	DCE, reflux, 5h	**3d**, 61%
5			**2e**	*tert*-Bu	DCE, reflux, 6h	**3e**, 75%
6			**2a**	NO_2	DCE, reflux, 30min	**3f**, 69%
7			**2b**	H	DCE, reflux, 1h	**3g**, 71%
8			**2c**	Cl	DCE, reflux, 5h	**3h**, 62%
9			**2d**	OMe	DCE, reflux, 24h	**3i**, 64%
10			**2e**	tert-Bu	DCE, reflux, 16h	**3j**, 70%
11	**1a**	R = H	 **2f**		DCE, rt, 30 min	 **3k,** 52%
12	**1c**	R = OMe	**2a**	NO_2	DCM, rt, 30min	**3l,** 63%
13	**1d**	R = Cl	**2a**	NO_2	DCM, rt, 15min	**3m**, 78%
14	**1e**	R = NO_2	**2a**	NO_2	DCM, rt, 15min	**3n**, 84%[c]
15			 **2g**		DCE, reflux, 16h	 **3o,** 45%
16			 **2h** R = *i*Pr **2h'** R = Me		DCE, reflux, 72h	nc[d]
17			 **2i,j**		DCE, reflux, 72h	nc[d]
18[e]			**2a**		DCE, rt, 15, min	 **4** 49%
19	**Ester:** 		 **2a,** R^3= NO_2 **2b,** R^3= H		DCE, reflux 24h DCE, reflux 72h	 **5a,** 47% **5b,** 34%

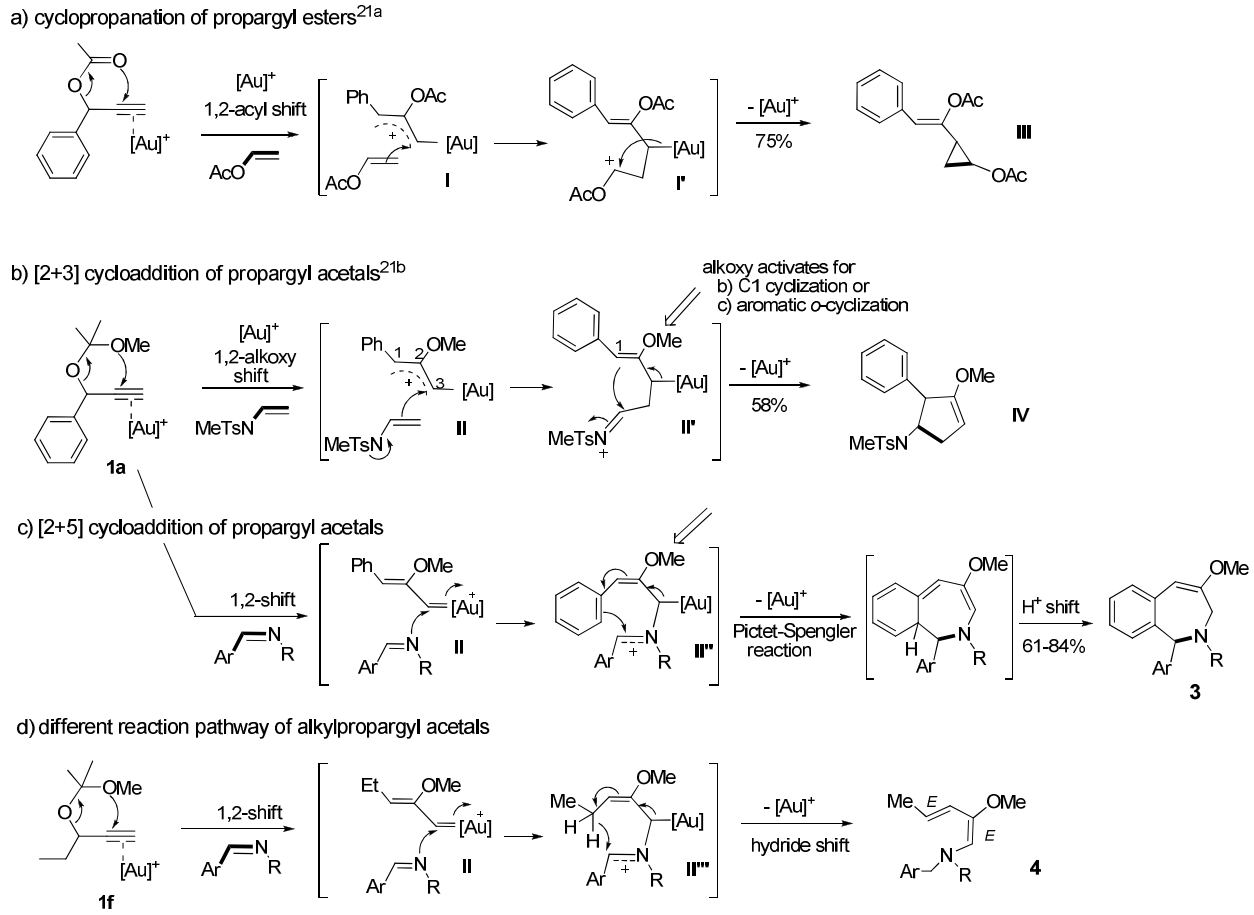
[a] a one-pot procedure from 4-nitrobenzaldehyde, 4-methoxyaniline and propargyl acetal **1a** afforded 52% yield of product **3a**; [b] a one-pot procedure from benzaldehyde, 4-methoxyaniline and propargyl acetal **1a** afforded 48% yield of product **3b**; [c] a one-pot procedure from 4-nitrobenzaldehyde, 4-methoxyaniline and propargyl acetal **1e** afforded 60% yield of product **3n**; [d] no conversion; [e] the reaction afforded the non-cyclic product **4**.

Having studied the potential and limitations of the intermolecular [2+5] cycloaddition reaction of propargyl acetals and benzaldimines, the potential for a one-pot procedure, including both the preceding benzaldimine condensation step and the subsequent [2+5] cycloaddition reaction, was examined. In fact, a multi-step cascade reaction of 4-nitrobenzaldehyde, 4-methoxyaniline and propargyl acetal **1a** provided the benzazepine product **3a** (46%) in the presence of the gold catalyst. The reaction was slow and 24h reflux was required. However, a one-pot sequential synthesis allowed milder reaction conditions and was slightly more efficient, as overnight stirring of the benzaldehyde and aniline precursors prior to the addition of propargyl acetal **1a** and the gold catalyst afforded the desired product **3a** in 4h reflux (52% yield, entry 1, Table 2). Thus, this direct procedure represents a convenient alternative preparation method, as the respective two-step protocol afforded 68% over-all yield of **3a** (85% imine condensation product **2a**; 80% benzazepine product **3a**). Similarly, the one-pot sequential protocol afforded products **3b** and **3n** in 48% and 60% yields (entries 2, 14) from the respective benzaldehyde, aniline and propargyl substrates.

Selectivity and reactivity. Our previous studies on gold(I) catalyzed alkenes cycloadditions of propargyl esters[21a] and acetals[21b] have shown that the reaction pathway, going via gold carbenoid intermediates (**I**, **II**, Scheme 2a,b), formed by gold catalyzed 1,2-acyloxy and -alkoxy migration, switches from cyclopropanation to [2+3] cycloaddition by changing from propargylic esters to acetals. The reactions might proceed through the intermediate adducts (**I', II'**), formed by initial nucleophilic attack of e.g. vinyl acetate and vinylamide at the allylic C3-position of gold complexes **I, II**, to afford vinylpropane **III** and cyclopentenyl products **IV**, respectively. The outcome of the chemoselective reactions of propargyl esters and acetals may be rationalized by the deactivating and the corresponding activating effects of the C2-acyloxy and -alkoxy groups of

adducts **I'**/**II'**. Thus, the "C3-C1" reaction sequence, favoured for acetal substrates, may be caused by the specific vinylalkoxy activation of the C1 position of adduct **II'**. The regioselectivity of such [2+3] cycloadditions may be controlled by the electronic nature of the propargyl substrate, as the opposite "C1-C3" reaction order has been reported for non-terminal propargyl acetals, connected to C3-EWG, with aldehydes.[22] Our investigations indicated that a direct [2+3] cycloaddition pathway, involving intermediate **II'** is more likely than a subsequent ring-expansion of cyclopropane **III**, being discussed by others.[20a,b,23]

Scheme 2 Proposed mechanisms of gold(I) catalysed propargyl cycloadditions



The new formal [2+5] cycloaddition (Scheme 2c) of phenylpropargyl acetals with benzaldimines may go through the highly reactive propargyl carbenoid gold(I) complex **II**, as well. A subsequent *N*-nucleophilic imine attack would give the activated vinyl ether adduct **II"**. The deauration step

promotes a kind of 1,7-electrocyclization of the conjugated diene-azomethine ylide-gold(I) complex **II"** by a Pictet-Spengler process, including ring closure of the *ortho* phenyl position and the electrophilic benzaldiminium carbon to give azepine products. A final [1,5]-sigmatropic hydrogen shift takes place to give the benzo[c]azepine structure **3** by re-aromatization.

The expected effects on reactivity by modifying of the electronic properties of the aldimine reactants were discussed above for benzylideneanilines **2a-f** (Table 2, entries 1-11). The limitation of the cycloaddition reaction with bulky substrates is demonstrated by the unsuccessful cyclization of the sterically hindered but electronically activated *o*-(di)nitro-benzaldimine analogue **2i,j** (entry 17). *p*-ERG-phenylpropargyl substrates (e.g. *p*-OMe) would hamper the reaction by giving a less electrophilic[24] propargyl substrate **1** and gold complex **II**, but might also activate for the final aromatic 1,7-cyclization step. Actually, the reactivity dropped as the electron releasing character of the *p*-substituent increased (entries 14/13/12, 84-63%), showing that the electronic nature of the propargyl acetal mostly affects the reactivity of the propargyl-gold complex intermediate **II** and plays a less important role for the final cyclization.

Even if slow, the fact that a similar reaction took place with propargyl ester **1c** (Table 2, entry 19), demonstrated that the [2+5] cyclization pathway is not controlled by the different nature of the gold(I) carbenoid complexes **I** and **II**. Thus, the fact that the cyclization pathway switches into the formal [2+5] cycloaddition reaction with imines, indicates that the essential feature of complex **II"** to selectively afford the new reaction seems to be the presence of the activated electrophilic iminium group (Scheme 2c). Hence, the deauration step of the 1,3-dipole gold complex **II"** activates the vinyl-aromatic system to favour a Pictet-Spengler type reaction with the benzaldiminium moiety and gives a 1,7-mode of cyclization by aminoalkylation. The Pictet-Spengler reaction of electron-rich aromatic rings with imines represents a useful and important

cyclization method in heterocyclic chemistry. The general challenge of the reaction appears, however, to be the low reactivity of the imine substrate and such reactions are mostly promoted by strong acids to generate the activated aldiminium group. In the present reaction, the important iminium activation is performed by mild gold(I) catalysis through the gold-propargyl-iminium adduct **II'**. The proposed reaction pathway is in line with a suggested mechanism[25] for benzazepine synthesis, based on a non-catalyzed related 1,7-mode of ring closure from 3-phenylpropenylbenzamide and PCl_5 via imidoyl chloride and diene-nitrile ylide. The mechanism is also in accordance with previously reported gold(III) catalyzed [3+4] cycloadditions of propargyl esters with a,b-unsaturated imine substrates[20e] or vinyl imine intermediates, generated from alkyl azides.[20f] Being applied in azepine synthesis, the final ring closure of the generated iminium gold complex included an intramolecular conjugated addition to the a,b-unsaturated iminium electrophile. Propargyl esters and azomethine imines are reported to undergo [3+3] cycloaddition to give biazabicycles based on a similar reaction pathway.[20g] Other gold catalyzed [2+3], [2+4] and [3+4] cycloaddition reactions with vinyl ethers, nitrosobenzene, cyclopentadiene as well as enones with propargyl esters have lately been studied by others and are reported to be based on related reaction principles of propargyl substrates.[20a-e] Gold catalyzed Pictet-Spengler cyclizations have also been used for the preparation of benzofused pyrido-*N*-heterocycles[26]. Gold(I)[27]and gold(III)[28] catalyzed alkyne reactions have been combined with conventional Mannich-type reactions to give cascade or sequential one-pot cyclizations for the preparation of heterocycles.[27,28] Two different catalytic systems may be applied,[27a-c] as the Mannich-type enantioselective organocatalyzed reactions of benzaldimines and enols have been combined with gold(I) catalyzed alkyne hydroamination to give *N*-heterocycles. Gold catalyzed carbon-heteroatom formation has been reviewed,[29a] including hydroamination of alkynes with imines and enamines.[29b]

The benzylic activation seems to be crucial, as all benzaldimine substrates (**2a-g**) readily afforded cycloaddition, while the corresponding *C*-alkylimine substrates **2h** and **2h'** (entry 16, Table 2) failed to undergo [2+5] cycloaddition, in accordance with non-successful acid catalyzed Pictet-Spengler benzazepine cyclization of aliphatic aldimines.[30] The application of *N*-Et benzaldimine **2g** (entry 15) in the new benzazepine synthesis; demonstrates the versatility of the new cyclization reaction.

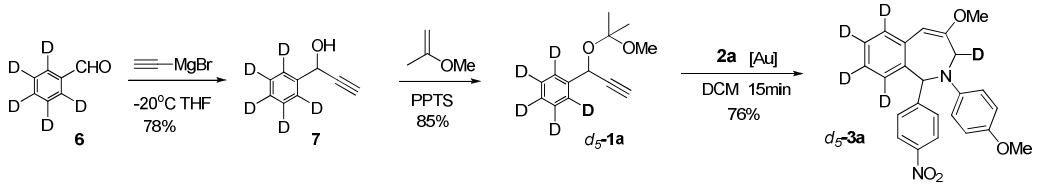
Aliphatic propargyl acetals gave a different outcome by the gold(I) catalysed reaction with benzaldimine **2a**. A new open-chained coupling product **4** was isolated (49%, entry 18) when ethyl-propargyl substrate **1f** was subjected to analogous reaction conditions as above. The formation of the non-cyclic compound may be rationalized by a related reaction mechanism as for benzazepines and is proposed to go through an analogous intermediate adduct **II"'** (Scheme 2d) to adduct **II"**, discussed above (Scheme 2c). The subsequent deauration step of intermediate **II"'** would take place in a somewhat different manner in the absence of an aromatic group and promotes a hydride shift to give the *N*-benzyl moiety of the *N*-(penta-1,3-dienyl)aniline product **4**. NOESY NMR data indicated *1E,3E*-stereochemistry.

In order to study whether the benzo[c]azepine products would be formed by some kind of ring-expansion of a cyclopropyl **III** or cyclopentenyl **IV** intermediate, attempt to identify possible intermediates during the reaction were made. However, GC and NMR monitoring of the reaction of acetal **1a** with imine **2a**, indicated no other intermediates, as only product **3a** could be observed. Thus, a direct [2+5] cycloaddition pathway, involving intermediate **II"** seems likely, in accordance with our previous investigations on [2+3] cycloaddition reaction[21]. Investigations on similar systems have also focussed on whether direct cycloaddition pathways or ring-expansion

mechanisms take place. The evidences are often consistent with a direct cycloaddition mechanism rather than a stepwise cyclopropanation/ring-expansion pathway.[20a,b]

A deuterated benzo[c]azepine d_5-**3a** (76%) was prepared from deuterated phenylpropargyl acetal d_5-**1a** and *N*-benzylideneaniline **2a** (Scheme 3). The deuterium labeling experiments showed specific and complete incorporation of one deuterium in the 3-position (-CHD-). This is in accordance with a 1,7-electrocyclization through a Pictet-Spengler type reaction and a final re-aromatization by an *o*-phenyl proton shift, as shown in the proposed reaction mechanism (Scheme 2c).

Scheme 3. Deuterium labeling [2+5] cycloaddition experiment



In conclusion, as part of our investigations on the chemistry and the potential of the highly reactive propargyl acetals, we have developed a synthetic approach to access benzo[c]azepine derivatives by a gold(I) catalysed formal [2+5] cycloaddition reaction. The benzo[c]azepine products **3a-o,** were readily prepared in 45-84% yield in one step from easily accessible phenylpropargyl acetals **1a-e** and benzaldimine substrates **2a-g** in the presence of a gold(I) catalyst. A one-pot synthesis from propargyl acetal and the benzaldehyde and aniline precursors could be applied, as well. To the best of our knowledge, our reported [2+5] cycloaddition represents a new concept for the preparation of *N*-heterocycles by an entirely gold(I) catalysed reaction.

The favoured [2+5] cycloaddition pathway of phenylpropargyl acetals and benzaldimines could be rationalized by a cascade reaction. An initial intermolecular nucleophilic aldimine *N*-attack at

propargyl-gold(I) carbenoid complex (**II**) would afford an activated iminium-propargyl-gold adduct **II"**. The following deauration of complex **II"** provides an electron-rich vinyl-aromatic group and activates for a 1,7-electrocyclization. The ring closure thus takes place by an intramolecular Pictet-Spengler type reaction with the activated electrophilic benzaldiminium moiety of gold(I) adduct **II"**. The strong activating effect provided through deauration is also shown by the coupling reaction of a corresponding alkyl substrate, ethylpropargyl acetal **1f**, affording the open-chained *N*-benzyl-*N*-((*1E,3E*)-penta-1,3-dienyl)aniline product **4** by a related mechanism through a hydride shift.

Experimental

General methods. All reactions were performed under argon atmosphere. Commercial grade reagents were used as received. Dry solvents were collected from a solvent purification system (SPS-800, filter column MB-KOL-A-C). All reactions were monitored by GC and thin-layer chromatography (TLC) using silica gel 60 F254 (0.25-mm thickness). Flash chromatography was carried out using silica gel 60 (0.040-0.063 mm). High Throughput Flash Purification (HPFP) was performed on pre-packed cartridges. ^{1}H and ^{13}C NMR spectra were recorded using a 400 MHz spectrometer. Chemical shifts are reported in ppm (δ) downfield from tetramethylsilane (TMS) as internal standard. Coupling constants (*J*) are reported in Hertz (Hz). The attributions of the chemical shifts were determined by means of COSY, HMQC, HMBC and NOESY NMR experiments. Melting points (mp) were determined using a Stuart apparatus and are uncorrected. Accurate mass determination (HRMS) was performed using EI or ESI. Direct injection was performed for the EI analyses at a magnetic-electric sector (double focusing) instrument. For ESI analyses, samples were injected into a TOF MS instrument using HPLC. IR spectra were obtained

using a Smart Endurance reflexion cell. Imines[31] and propargyl acetals (**1a-f**)[22] were prepared according to a literature procedures.

Typical Procedure for the Gold-Catalyzed Cyclization reaction.

The gold catalyst (Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl and $AgSbF_6$) was dissolved in approximately one third of the total amount of solvent ([*c* = 100 mM] of propargyl acetal) and filtered through a small pad of Celite to remove AgCl. A solution of the propargyl acetal and the imine derivative was subsequently added. The reaction mixture was stirred/refluxed and the reaction was monitored by TLC and GC. After full conversion the reaction mixture was either used for product isolation by flash chromatography or filtered through a small pad of Celite for subsequent ^{1}H NMR analysis of the crude reaction mixture after evaporation of the solvent.

One-pot procedures i) - ii):

i) In a *one-pot synthesis,* the gold catalyst (Au[P(*t*-Bu)$_2$(*o*-biphenyl)Cl and $AgSbF_6$) was dissolved in DCM and then a solution of 4-nitrobenzaldehyde, 4-methoxyaniline and propargyl acetal **1a** in DCM was added. The mixture was refluxed for 24h. ii) In a *one-pot sequential synthesis,* a solution of 4-nitrobenzaldehyde and 4-methoxyaniline in DCM was stirred overnight (r.t) before a solution of propargyl acetal **1a** and gold catalyst (Au[P(*t*-Bu)$_2$(*o*-biphenyl)Cl and $AgSbF_6$) in DCM was added The reaction mixture was refluxed for 4h.

In both cases, the reaction was monitored by TLC and GC. The reaction mixture was filtered through a small pad of Celite and the crude product was purified by flash chromatography to afford product **3a** in i) 46% and ii) 52% yield, respectively.

4-Methoxy-2-(4-methoxyphenyl)-1-(4-nitrophenyl)-2,3-dihydro-1H-benzo[c]azepine 3a. According to the typical procedure from **1a** (60 mg, 0.29 mmol), imine **2a** (111.3 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for 15 min. Flash chromatography (*n*-pentane/EtOAc 20:1) yielded **3a** (94 mg, 80 %) as a viscous yellow oil; R_f = 0.48 (*n*-pentane/EtOAc 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.09 (d, J = 4.8 Hz, 2 H_{arom}), 7.28 (d, J = 8.8 Hz, 2 H_{arom}), 7.11-7.24 (m, 4 H_{arom}), 6.85 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.75 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 5.91 (s, 1 H, CH=C), 5.50 (s, 1 H, CHN), 3.80 (d, J = 16.4 Hz, 1 H, CH_2), 3.71(d, J = 16.4 Hz, 1 H, CH_2), 3.70 (s, 3 H, (OCH_3), 3.51 (s, 3 H, ($ArOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.3 (1 C, C=*C*OCH_3), 152.9 (1 C, C_{arom}), 150.0 (1 C, C_{arom}), 146.8 (1 C, C_{arom}), 143.5 (1 C, C_{arom}), 136.4 (1 C, C_{arom}), 135.0 (1 C, C_{arom}), 130.7 (1 C, CH_{arom}), 130.6 (1 C, CH_{arom}), 128.8 (2 C, CH_{arom}), 128.0 (1 C, CH_{arom}), 125.4 (1 C, CH_{arom}), 123.3 (2 C, CH_{arom}), 116.6 (2 C, CH_{arom}), 114.4 (2 C, CH_{arom}), 102.0 (1 C, C=*C*H), 68.9 (1 C, CHN), 55.4 (1 C, Ar*O*CH_3), 54.8 (1 C, OCH_3), 49.1 (1 C, CH_2); IR (neat, cm^{-1}) 2989, 1286, 1062. HRMS (EI) calcd for $C_{24}H_{22}O_4N_2$, 402.1574, obsd 402.1575.

4-Methoxy-2-(4-methoxyphenyl)-1-phenyl-2,3-dihydro-1H-benzo[c]azepine 3b. According to the typical procedure from **1a** (60 mg, 0.29 mmol), imine **2b** (92.8 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for 1h reflux. Flash chromatography (*n*-pentane/DCM 3:1) yielded **3b** (77.7 mg, 74%) as a yellow oil; R_f = 0.58 (*n*-pentane/DCM 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.21-7.28 (m, 3 H_{arom}), 7.02-7.18 (m, 6 H_{arom}), 6.88 (d, J = 8.8 Hz, 2 H_{arom}), 6.72 (d, J = 9.2 Hz, 2 H_{arom}), 6.01 (s, 1 H, CH=C), 5.54 (s, 1 H, CHN), 3.90 (d, J = 17.6 Hz, 1 H, CH_2), 3.77(d, J = 18.0 Hz, 1 H, CH_2), 3.67 (s, 3 H, OCH_3), 3.55 (s, 3 H, $ArOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.0 (1 C, C=*C*OCH_3), 152.3 (1 C, C_{arom}), 143.3 (1 C, C_{arom}), 141.6 (1 C, C_{arom}), 137.5 (1 C, C_{arom}), 134.4(1 C, C_{arom}), 130.8 (1 C, CH_{arom}), 130.5 (1 C, CH_{arom}), 128.7 (2 C, CH_{arom}), 128.3 (2 C, CH_{arom}), 127.2 (1 C, CH_{arom}), 127.1 (1 C, CH_{arom}), 124.8 (1 C, CH_{arom}), 116.4 (2 C, CH_{arom}), 114.3 (2 C, CH_{arom}),

102.4 (1 C, C=*C*H), 68.0 (1 C, CHN), 55.4 (1 C, ArO*C*H_3), 54.6 (1 C, OCH_3), 48.4 (1 C, CH_2); IR (neat, cm^{-1}) 2899, 1316, 1112. HRMS (EI) calcd for $C_{24}H_{23}NO_2$ 357.1723, obsd 357.1720.

1-(4-Chlorophenyl)-4-methoxy-2-(4-methoxyphenyl)-2,3-dihydro-1H-benzo[c]azepine 3c. According to the typical procedure from **1a** (60 mg, 0.29 mmol), imine **2c** (107.8 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 µmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 µmol, 0.05 equiv) in DCE for 3h reflux. Flash chromatography (*n*-pentane/DCM 3:1) yielded **3c** (78.2 mg, 68%) as a yellow oil; R_f = 0.61 (*n*-pentane/DCM 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.22 (d, J = 8.8 Hz, 2 H_{arom}), 7.04-7.15 (m, 4 H_{arom}), 7.02 (d, J = 8.0 Hz, 2 H_{arom}), 6.85 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.72 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 5.91 (s, 1 H, CH=C), 5.52 (s, 1 H, CHN), 3.88 (d, J = 17.6Hz, 1 H, CH_2), 3.73(d, J = 17.6 Hz, 1 H, CH_2), 3.66 (s, 3 H, OCH_3), 3.54 (s, 3 H, $ArOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.8 (1 C, C=*C*OCH_3), 152.5 (1 C, C_{arom}), 143.2 (1 C, C_{arom}), 140.2 (1 C, C_{arom}), 137.1 (1 C, C_{arom}), 134.4 (1 C, C_{arom}), 132.8 (1 C, C_{arom}), 130.8 (1 C, CH_{arom}), 130.5 (1 C, CH_{arom}), 129.9 (2 C, CH_{arom}), 128.4 (2 C, CH_{arom}), 127.5 (1 C, CH_{arom}), 125.0 (1 C, CH_{arom}), 116.3 (2 C, CH_{arom}), 114.4 (2 C, CH_{arom}), 102.3 (1 C, C=*C*H), 67.8 (1 C, CHN), 55.4 (1 C, ArO*C*H_3), 54.6 (1 C, OCH_3), 48.6 (1 C, CH_2); IR (neat, cm^{-1}) 2969, 1277, 1088. HRMS (EI) calcd for $C_{24}H_{22}O_2NCl$ 391.1334, obsd 391.1335.

4-Methoxy-1,2-bis(4-methoxyphenyl)-2,3-dihydro-1H-benzo[c]azepine 3d. According to the typical procedure from **1a** (60 mg, 0.29 mmol), imine **2d** (106.0 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 µmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 µmol, 0.05 equiv) in DCE for 5h reflux. Flash chromatography (*n*-pentane/DCM 3:1) yielded **3d** (69.4 mg, 61%) as a yellow oil; R_f = 0.51 (*n*-pentane/DCM 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.03-7.17 (m, 4 H_{arom}), 6.99 (dt, J = 8.8 Hz, J = 3.6 Hz, 2 H_{arom}), 6.88 (dt, J = 9.2 Hz, J = 4.0 Hz, 2 H_{arom}), 6.80 (dt, J = 8.8 Hz, J = 2.4 Hz, 2 H_{arom}), 6.72 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 5.97 (s, 1 H, CH=C), 5.55 (s, 1 H, CHN), 3.90 (d, J = 18.0Hz, 1 H, CH_2), 3.83 (d, J = 19.2 Hz, 1 H, CH_2), 3.75 (s, 3 H,

$ArOCH_3$), 3.67 (s, 3 H, OCH_3), 3.58 (s, 3 H, $ArOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.2 (1 C, C=*C*OCH_3), 158.6 (1 C, C_{arom}), 152.2 (1 C, C_{arom}), 143.2 (1 C, C_{arom}), 137.8 (1 C, C_{arom}), 134.2 (1 C, C_{arom}), 133.6 (1 C, C_{arom}), 130.9 (1 C, CH_{arom}), 130.4 (1 C, CH_{arom}), 129.9 (2 C, CH_{arom}), 127.1 (1 C, CH_{arom}), 124.8 (1 C, CH_{arom}), 116.1 (2 C, CH_{arom}), 114.4 (2 C, CH_{arom}), 113.7 (2 C, CH_{arom}), 102.5 (1 C, C=*C*H), 67.3 (1 C, CHN), 55.4 (1 C, ArO*C*H_3), 55.1 (1 C, ArO*C*H_3), 54.6 (1 C, OCH_3), 48.3 (1 C, CH_2); IR (neat, cm^{-1}) 2913, 1316, 1032. HRMS (EI) calcd for $C_{25}H_{25}O_3N$ 387.1829, obsd 387.1832.

1-(4-(tert-Butyl)phenyl)-4-methoxy-2-(4-methoxyphenyl)-2,3-dihydro-1H-benzo[c]azepine 3e. According to the typical procedure from **1a** (60 mg, 0.29 mmol), imine **2e** (117.0 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for 6h reflux. Flash chromatography (*n*-pentane/DCM 3:1) yielded **3e** (91.1 mg, 75%) as a white solid; R_f = 0.65 (*n*-pentane/DCM 1:1), m.p 56-60°C; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.29 (d, J = 8.4 Hz, 2 H_{arom}), 7.03-7.18 (m, 4 H_{arom}), 7.00 (d, J = 8.4 Hz, 2 H_{arom}), 6.88 (d, J = 8.4 Hz, 2 H_{arom}), 6.73 (d, J = 9.2 Hz, 2 H_{arom}), 6.00 (s, 1 H, CH=C), 5.55 (s, 1 H, CHN), 3.91 (d, J = 18.0 Hz, 1 H, CH_2), 3.80 (d, J = 18.0 Hz, 1 H, CH_2), 3.69 (s, 3 H, OCH_3), 3.59 (s, 3 H, $ArOCH_3$), 1.29 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm) 159.1 (1 C, C=*C*OCH_3), 152.2 (1 C, C_{arom}), 150.0 (1 C, C_{arom}), 143.2 (1 C, C_{arom}), 138.6 (1 C, C_{arom}), 137.7 (1 C, C_{arom}), 134.2 (1 C, C_{arom}), 130.9 (1 C, CH_{arom}), 130.6 (1 C, CH_{arom}), 128.5 (2 C, CH_{arom}), 127.1 (1 C, CH_{arom}), 125.3 (2 C, CH_{arom}), 124.8 (1 C, CH_{arom}), 116.1 (2 C, CH_{arom}), 114.4 (2 C, CH_{arom}), 102.5 (1 C, C=*C*H), 67.5 (1 C, CHN), 55.5 (1 C, ArO*C*H_3), 54.6 (1 C, OCH_3), 48.3 (1 C, CH_2) 34.4 (1 C, *C*$(CH_3)_3$), 31.3 (3 C, C(*C*$H_3)_3$); IR (neat, cm^{-1}) 2972, 1196, 1042. HRMS (EI) calcd for $C_{28}H_{31}O_2N$ 413.2349, obsd 413.2347.

4-Ethoxy-2-(4-methoxyphenyl)-1-(4-nitrophenyl)-2,3-dihydro-1H-benzo[c]azepine 3f. According to the typical procedure from **1b** (60.0 mg, 0.29 mmol), imine **2a** (112.6 mg, 0.43

mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for 30min reflux. Flash chromatography (*n*-pentane/DCM 2:1) yielded **3f** (84 mg, 69%) as a yellow viscous oil; R_f = 0.48 (*n*-pentane/DCM 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.10 (d, J = 8.8 Hz, 2 H_{arom}), 7.30 (d, J = 8.8 Hz, 2 H_{arom}), 7.09-7.27 (m, 4 H_{arom}), 6.84 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.76 (dt, J = 9.2 Hz, J = 3.2 Hz, 2 H_{arom}), 5.89 (s, 1 H, CH=C), 5.47 (s, 1 H, CHN), 3.83 (d, J = 16.4 Hz, 1 H, CH_2), 3.78 (d, J = 16.4 Hz, 1 H, CH_2), 3.72 (s, 3 H, $ArOCH_3$), 3.54 (dq, J = 7.2 Hz, J = 6.8 Hz, 2 H, OCH_2CH_3), 1.27 (t, J = 6.8 Hz, 3 H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.6 (1 C, C=*C*OC_2H_5), 152.9 (1 C, C_{arom}), 150.3 (1 C, C_{arom}), 146.9 (1 C, C_{arom}), 143.6 (1 C, C_{arom}), 136.5 (1 C, C_{arom}), 135.3 (1 C, C_{arom}), 130.7 (1 C, CH_{arom}), 130.5 (1 C, CH_{arom}), 128.8 (2 C, CH_{arom}), 128.0 (1 C, CH_{arom}), 125.3 (1 C, CH_{arom}), 123.3 (2 C, CH_{arom}), 116.6 (2 C, CH_{arom}), 114.5 (2 C, CH_{arom}), 102.4 (1 C, C=*C*H), 69.1 (1 C, CHN), 63.0 (1 C, O*C*H_2CH_3), 55.5 (1 C, $ArOCH_3$), 49.3 (1 C, CH_2) 14.4 (1 C, OCH_2CH_3); IR (neat, cm^{-1}) 2992, 1199, 1152. HRMS (EI) calcd for $C_{25}H_{24}N_2O_4$ 416.1731, obsd 416.1736.

4-Ethoxy-2-(4-methoxyphenyl)-1-phenyl-2,3-dihydro-1H-benzo[c]azepine 3g. According to the typical procedure from **1b** (60 mg, 0.29 mmol), imine **2b** (92.5 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for 1h reflux. Flash chromatography (*n*-pentane/DCM 2:1) yielded **3g** (77mg, 71%) as a yellow viscous oil; R_f = 0.45 (*n*-pentane/DCM 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.04-7.29 (m, 9 H_{arom}), 6.88 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.74 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.00 (s, 1 H, CH=C), 5.53 (s, 1 H, CHN), 3.89 (d, J = 17.6 Hz, 1 H, CH_2), 3.89 (d, J = 18.0 Hz, 1 H, CH_2), 3.72 (dq, J = 6.8 Hz, J = 6.2 Hz, 2 H, OCH_2CH_3), 3.70 (s, 3 H, $ArOCH_3$), 1.27 (t, J = 7.2 Hz, 3 H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.4 (1 C, C=*C*OC_2H_5), 152.3 (1 C, C_{arom}), 143.4 (1 C, C_{arom}), 141.8 (1 C, C_{arom}), 137.5 (1 C, C_{arom}), 134.7 (1 C, C_{arom}), 130.7 (1 C, CH_{arom}), 130.6 (1 C, CH_{arom}), 128.7 (2 C, CH_{arom}), 128.3 (2 C, CH_{arom}), 127.2 (1 C, CH_{arom}), 127.0 (1 C, CH_{arom}), 124.7 (1 C, CH_{arom}), 116.1 (2 C, CH_{arom}), 114.4 (2 C, CH_{arom}), 102.9 (1 C, C=*C*H),

68.1 (1 C, CHN), 62.8 (1 C, O*C*H_2CH$_3$), 55.5 (1 C, ArOCH_3), 48.7 (1 C, CH_2) 14.5 (1 C, OCH$_2$*C*H$_3$); IR (neat, cm^{-1}) 2984, 1311, 992. HRMS (EI) calcd for $C_{25}H_{25}O_2N$ 371.1886, obsd 371.1880.

1-(4-Chlorophenyl)-4-ethoxy-2-(4-methoxyphenyl)-2,3-dihydro-1H-benzo[c]azepine 3h. According to the typical procedure from **1b** (60 mg, 0.29 mmol), imine **2c** (107.0 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 µmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 µmol, 0.05 equiv) in DCE for 5h reflux. Flash chromatography (*n*-pentane/DCM 2:1) yielded **3h** (73 mg, 62%) as a yellow viscous oil; R_f = 0.49 (*n*-pentane/DCM 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.24 (d, J = 8.8 Hz, 2 H$_{arom}$), 7.05-7.18 (m, 4 H$_{arom}$), 7.03 (d, J = 8.4 Hz, 2 H$_{arom}$), 6.86 (dt, J = 9.2 Hz, J = 4.0 Hz, 2 H$_{arom}$), 6.73 (dt, J = 8.8 Hz, J = 4.0 Hz, 2 H$_{arom}$), 5.91 (s, 1 H, CH=C), 5.52 (s, 1 H, CHN), 3.89 (d, J = 17.2 Hz, 1 H, CH_2), 3.73 (d, J = 16.4 Hz, 1 H, CH_2), 3.70 (s, 3 H, ArOCH_3), 3.62-3.83 (m, 2 H, OCH$_2$CH$_3$), 1.28 (t, J = 7.2 Hz, 3 H, OCH$_2$CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.2 (1 C, C=*C*OC$_2$H$_5$), 152.5 (1 C, C$_{arom}$), 143.4 (1 C, C$_{arom}$), 140.4 (1 C, C$_{arom}$), 137.1 (1 C, C$_{arom}$), 134.8 (1 C, C$_{arom}$), 132.8 (1 C, C$_{arom}$), 130.7 (1 C, CH$_{arom}$), 130.5 (1 C, CH$_{arom}$), 129.9 (2 C, CH$_{arom}$), 128.4 (2 C, CH$_{arom}$), 127.5 (1 C, CH$_{arom}$), 124.9 (1 C, CH$_{arom}$), 116.3 (2 C, CH$_{arom}$), 114.4 (2 C, CH$_{arom}$), 102.7 (1 C, C=*C*H), 67.9 (1 C, CHN), 62.8 (1 C, O*C*H$_2$CH$_3$), 55.5 (1 C, ArOCH_3), 48.8 (1 C, CH_2) 14.4 (1 C, OCH$_2$*C*H$_3$); IR (neat, cm^{-1}) 2949, 1276, 1082. HRMS (EI) calcd for $C_{25}H_{24}O_2NCl$ 405.1496, obsd 405.1489.

4-Ethoxy-1,2-bis(4-methoxyphenyl)-2,3-dihydro-1H-benzo[c]azepine 3i. According to the typical procedure from **1b** (60 mg, 0.29 mmol), imine **2d** (106.0 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 µmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 µmol, 0.05 equiv) in DCE for 5h reflux. Flash chromatography (*n*-pentane/EtOAc 30:1) yielded **3i** (75mg, 64%) as a yellow oil; R_f = 0.43 (*n*-pentane/EtOAc 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.03-7.17 (m, 4 H$_{arom}$), 7.00 (d, J = 8.4 Hz, 2 H$_{arom}$), 6.88 (d, J = 9.2 Hz, 2 H$_{arom}$), 6.81 (d, J = 8.8 Hz, 2 H$_{arom}$),

6.73 (d, J = 9.2 Hz, 2 H_{arom}), 5.96 (s, 1 H, CH=C), 5.54 (s, 1 H, CHN), 3.90 (d, J = 18.0 Hz, 1 H, CH_2), 3.71-3.88 (m, 2 H, OCH_2CH_3), 3.75 (d, J = 18.0 Hz, 1 H, CH_2), 3.77 (s, 3 H, $ArOCH_3$), 3.69 (s, 3 H, $ArOCH_3$), 1.29 (t, J = 6.8 Hz, 3 H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.6 (1 C, C=*C*OC_2H_5), 158.5 (1 C, C_{arom}), 152.2 (1 C, C_{arom}), 143.2 (1 C, C_{arom}), 137.8 (1 C, C_{arom}), 134.5 (1 C, C_{arom}), 133.7 (1 C, C_{arom}), 130.8 (1 C, CH_{arom}), 130.4 (1 C, CH_{arom}), 129.9 (2 C, CH_{arom}), 127.1 (1 C, CH_{arom}), 124.7 (1 C, CH_{arom}), 116.1 (2 C, CH_{arom}), 114.3 (2 C, CH_{arom}), 113.7 (2 C, CH_{arom}), 103.0 (1 C, C=*C*H), 67.3 (1 C, CHN), 62.7 (1 C, O*C*H_2CH_3), 55.5 (1 C, $ArOCH_3$), 55.2 (1 C, $ArOCH_3$), 48.3 (1 C, CH_2) 14.5 (1 C, OCH_2*C*H_3); IR (neat, cm^{-1}) 2989, 1271, 1112. HRMS (EI) calcd for $C_{26}H_{27}O_3N$ 401.1985, obsd 401.1984.

1-(4-(tert-Butyl)phenyl)-4-ethoxy-2-(4-methoxyphenyl)-2,3-dihydro-1H-benzo[c]azepine 3j. According to the typical procedure from **1b** (60 mg, 0.29 mmol), imine **2e** (117.0 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for overnight reflux. Flash chromatography (*n*-pentane/DCM 2:1) yielded **3j** (76mg, 70%) as a yellow oil; R_f = 0.53 (*n*-pentane/DCM 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.29 (d, J = 8.4 Hz, 2 H_{arom}),7.02-7.18 (m, 4 H_{arom}), 7.00 (d, J = 8.4 Hz, 2 H_{arom}), 6.89 (dt, J = 9.2 Hz, J = 4.0 Hz, 2 H_{arom}), 6.73 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.00 (s, 1 H, CH=C), 5.54 (s, 1 H, CHN), 3.90 (d, J = 18.0 Hz, 1 H, CH_2), 3.80 (d, J = 17.6 Hz, 1 H, CH_2), 3.77 (dm, 2 H, OCH_2CH_3), 3.70 (s, 3 H, $ArOCH_3$), 1.29 (t, J = 5.2 Hz, 3 H, OCH_2CH_3), 1.29 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.4 (1 C, C=*C*OC_2H_5), 152.1 (1 C, C_{arom}), 149.9 (1 C, C_{arom}), 143.3 (1 C, C_{arom}), 138.7 (1 C, C_{arom}), 137.7 (1 C, C_{arom}), 134.5 (1 C, C_{arom}), 130.8 (1 C, CH_{arom}), 130.6 (1 C, CH_{arom}), 128.4 (2 C, CH_{arom}), 127.1 (1 C, CH_{arom}), 125.2 (2 C, CH_{arom}), 124.6 (1 C, CH_{arom}), 116.0 (2 C, CH_{arom}), 114.4 (2 C, CH_{arom}), 103.1 (1 C, C=*C*H), 67.5 (1 C, CHN), 62.7 (1 C, O*C*H_2CH_3), 55.5 (1 C, $ArOCH_3$), 48.5 (1 C, CH_2), 34.4, (1C, *C*$(CH_3)_3$), 31.3, (3C, C(*C*$H_3)_3$), 14.5 (1 C, OCH_2*C*H_3); IR (neat, cm^{-1}) 2939, 1266, 1092. HRMS (EI) calcd for $C_{29}H_{33}O_2N$ 427.2511, obsd 427.2512.

4-Methoxy-1-(4-nitrophenyl)-2-phenyl-2,3-dihydro-1H-benzo[c]azepine 3k. According to the general procedure from **1a** (127.0 mg, 0.62 mmol), imine **2f** (211.0 mg, 0.93 mmol, 1.5 equiv), the gold chloride (13.0 mg, 24.5 µmol 0.05 equiv) and $AgSbF_6$ (8,4 mg, 24,5 µmol 0.05 equiv) in DCE for 30 min. Flash chromatography (*n*-pentane:DCM, 1:1) yielded **3k** (144 mg, 84 %) as a yellow oil; R_f = 0.49 (*n*-pentane:DCM, 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8.10 (m, 2 H_{arom}), 7.12-7.30 (m, 7 H_{arom}), 6.87 (d, J = 8.1 Hz, 2 H_{arom}), 6.79 (d, J = 7.2 Hz, 2 H_{arom}), 6.01 (s, 1 H, CH=C), 5.47 (s, 1 H, CHN), 3.92 (d, J = 16.2 Hz, 1 H, CH_2), 3.79 (d, J = 15.9 Hz, 1 H, CH_2), 3.50 (s, 3 H, (OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$ δ ppm 158.1 (1 C, C=*C*OCH_3), 150.2 (1 C, C_{arom}), 149.1 (1 C, C_{arom}), 147.0 (1 C, C_{arom}), 136.1 (1 C, C_{arom}), 135.2 (1 C, C_{arom}), 130.9 (1 C, CH_{arom}), 130.7 (1 C, CH_{arom}), 129.3 (2 C, CH_{arom}), 128.8 (2 C, CH_{arom}), 128.2 (1 C, CH_{arom}), 125.6 (1 C, CH_{arom}), 123.4 (2 C, CH_{arom}), 118.9 (1 C, CH_{arom}), 114.6 (2 C, CH_{arom}), 102.1 (1 C, C=*C*H), 68.2 (1 C, CHN), 55.0 (1 C, OCH_3), 48.3 (1 C, CH_2); IR (neat, cm^{-1}) 2931, 1251, 1089. HRMS (EI) calcd for $C_{23}H_{20}O_3N_2$ 372.1466, obsd 372.1466.

4,8-Dimethoxy-2-(4-methoxyphenyl)-1-(4-nitrophenyl)-2,3-dihydro-1H-benzo[c]azepine 3l. According to the general procedure from **1c** (68.7 mg, 0.29 mmol), imine **2a** (112.6 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 µmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 µmol, 0.05 equiv) in DCE for 30 min. Flash chromatography (DCM) yielded **3l** (79 mg, 63 %) as a yellow oil; R_f = 0.45 (DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.11 (d, J = 8.8 Hz, 2 H_{arom}), 7.31 (d, J = 8.8 Hz, 2 H_{arom}), 7.09 (d, J = 8.4 Hz, 1 H_{arom}), 6.73-6.87 (m, 6 H_{arom}), 5.85 (s, 1 H, CH=C), 5.44 (s, 1 H, CHN), 3.83 (d, J = 15.2 Hz, 1 H, CH_2), 3.78 (s, 3 H, (OCH_3), 3.73 (s, 3 H, ($ArOCH_3$), 3.68 (d, J = 16.4 Hz, 1 H, CH_2), 3.49 (s, 3 H, ($ArOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.3 (1 C, C=*C*OCH_3), 156.6 (1 C, C_{arom}), 152.9 (1 C, C_{arom}), 149.8 (1 C, C_{arom}), 146.9 (1 C, C_{arom}), 143.5 (1 C, C_{arom}), 137.9 (1 C, C_{arom}), 131.9 (1 C, C_{arom}), 130.4 (1 C, CH_{arom}), 129.0 (2 C, CH_{arom}), 124.2 (1 C, CH_{arom}), 123.4 (2 C, CH_{arom}), 122.6 (1 C, CH_{arom}), 116.7 (2 C, CH_{arom}), 114.5 (2 C, CH_{arom}), 101.5 (1 C, C=*C*H), 69.0 (1 C, CHN), 55.5 (1 C, Ar*O*CH_3), 55.2 (1 C, Ar*O*CH_3),

54.7 (1 C, OCH_3), 49.1 (1 C, CH_2); IR (neat, cm^{-1}) 2957, 1276, 1091. HRMS (EI) calcd for $C_{25}H_{24}O_5N_2$ 432.1680, obsd 432.1677.

8-Chloro-4-methoxy-2-(4-methoxyphenyl)-1-(4-nitrophenyl)-2,3-dihydro-1H-benzo[c]azepine 3m. According to the general procedure from **1d** (70.0 mg, 0.29 mmol), imine **2a** (112.6 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for 15 min. Flash chromatography (DCM) yielded **3m** (100 mg, 78 %) as a yellow oil; R_f = 0.38 (DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.12 (d, J = 8.8 Hz, 2 H_{arom}), 7.29 (d, J = 8.4 Hz, 2 H_{arom}), 7.08-7-19 (m, 3 H_{arom}), 6.85 (d, J = 9.2 Hz, 2 H_{arom}), 6.77 (d, J = 8.8 Hz, 2 H_{arom}), 5.87 (s, 1 H, CH=C), 5.47 (s, 1 H, CHN), 3.85 (d, J = 16.8 Hz, 1 H, CH_2), 3.72 (s, 3 H, (OCH_3), 3.67 (d, J = 16.8 Hz, 1 H, CH_2), 3.52 (s, 3 H, ($ArOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.0 (1 C, C=*C*OCH_3), 153.2 (1 C, C_{arom}), 148.9 (1 C, C_{arom}), 147.1(1 C, C_{arom}), 143.1 (1 C, C_{arom}), 138.1 (1 C, C_{arom}), 133.5 (1 C, C_{arom}), 131.9 (1 C, C_{arom}), 130.7 (1 C, CH_{arom}), 130.1 (1 C, CH_{arom}), 129.0 (2 C, CH_{arom}), 128.1 (1 C, CH_{arom}), 123.5 (2 C, CH_{arom}), 116.9 (2 C, CH_{arom}), 114.5 (2 C, CH_{arom}), 101.2 (1 C, C=*C*H), 68.4 (1 C, CHN), 55.4 (1 C, Ar*O*CH_3), 54.9 (1 C, OCH_3), 49.2 (1 C, CH_2); IR (neat, cm^{-1}) 2969, 1286, 1110. HRMS (EI) calcd for $C_{24}H_{21}ClN_2O_4$ 436.1184, obsd 436.1184.

4-Methoxy-2-(4-methoxyphenyl)-8-nitro-1-(4-nitrophenyl)-2,3-dihydro-1H-benzo[c]azepine 3n. According to the general procedure from **1e** (36.6 mg, 0.14 mmol), imine **2a** (56.3 mg, 0.21 mmol, 1.5 equiv), the gold chloride (3.9 mg, 7.0 μmol, 0.05 equiv) and $AgSbF_6$ (2.4 mg, 7.0 μmol, 0.05 equiv) in DCE for 15 min. Flash chromatography (DCM) yielded **3n** (55 mg, 84 %) as a yellow oil; R_f = 0.46 (DCM)**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.17 (d, J = 8.8 Hz, 2 H_{arom}), 8.05-8.08 (m, 2 H_{arom}), 7.27-7.30 (m, 3 H_{arom}), 6.87 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.77 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.10 (s, 1 H, CH=C), 5.65 (s, 1 H, CHN), 3.96 (d, J = 17.6 Hz, 1 H, CH_2), 3.72 (s, 3 H, (OCH_3), 3.73 (d, J = 18.0 Hz, 1 H, CH_2), 3.63 (s, 3 H, ($ArOCH_3$); ^{13}C

NMR (100 MHz, $CDCl_3$) δ ppm 163.4 (1 C, C=*C*OCH_3), 153.5 (1 C, C_{arom}), 147.4 (1 C, C_{arom}), 147.4 (1 C, C_{arom}), 144.5 (1 C, C_{arom}), 142.3 (1 C, C_{arom}), 141.9 (1 C, C_{arom}), 137.3 (1 C, C_{arom}), 131.4 (1 C, CH_{arom}), 129.2 (2 C, CH_{arom}), 125.5 (1 C, CH_{arom}), 123.8 (2 C, CH_{arom}), 123.2 (1 C, CH_{arom}), 117.2 (2 C, CH_{arom}), 114.6 (2 C, CH_{arom}), 101.4 (1 C, C=*C*H), 68.2 (1 C, CHN), 55.4 (1 C, Ar*O*CH_3), 55.2 (1 C, OCH_3), 49.5 (1 C, CH_2); IR (neat, cm^{-1}) 2971, 1281, 1087. HRMS (EI) calcd for $C_{24}H_{21}O_6N_3$ 447.1425, obsd 447.1422.

2-Ethyl-4-methoxy-1-phenyl-2,3-dihydro-1H-benzo[c]azepine 3o. According to the typical procedure from **1a** (60 mg, 0.29 mmol), imine **2g** (58.3 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for overnight reflux. Flash chromatography (DCM) yielded **3o** (37mg, 45%) as a yellow oil; R_f = 0.39 (DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.21-7.28 (m, 5 H_{arom}), 7.13 (d, J = 7.6 Hz, 2 H_{arom}), 7.02-7.06 (m, 1 H_{arom}), 6.99 (d, J = 7.6 Hz, 1 H_{arom}), 5.69 (s, 1 H, CH=C), 5.09 (s, 1 H, CHN), 3.60 (s, 3 H, OCH_3), 3.37 (d, J = 17.6 Hz, 1 H, CH_2), 3.63 (dq, J = 7.2 Hz, J = 1.6 Hz, 2 H, NCH_2CH_3), 3.25 (d, J = 17.6 Hz, 1 H, CH_2), 1.14 (t, J = 7.2 Hz, 3 H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.1 (1 C, C=*C*OC_2H_5), 142.1 (1 C, C_{arom}), 137.4 (1 C, C_{arom}), 135.4 (1 C, C_{arom}), 130.6 (1 C, CH_{arom}), 129.7 (1 C, CH_{arom}), 128.8 (2 C, CH_{arom}), 128.1 (2 C, CH_{arom}), 127.0 (1 C, CH_{arom}), 126.8 (1 C, CH_{arom}), 124.8 (1 C, CH_{arom}), 101.9 (1 C, C=*C*H), 69.6 (1 C, CHN), 54.4 (1 C, OCH_3), 51.2 (1 C, N*C*H_2CH_3), 46.6 (1 C, CH_2), 13.4 (1 C, NCH_2CH_3); IR (neat, cm^{-1}) 2987, 1266, 1082. HRMS (EI) calcd for $C_{19}H_{21}ON$ 279.1618, obsd 279.1613.

4-Methoxy-*N*-((*1E,3E*)-2-methoxypenta-1,3-dienyl)-*N*-(4-nitrobenzyl)aniline 4. According to the general procedure from **1f** (45.8 mg, 0.29 mmol), imine **2a** (112.6 mg, 0.44 mmol, 1.5 equiv),gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCM for 15min. Flash chromatography (20:1, *n*-pentane:EtOAc) yielded **4** (50 mg, 49 %) as a yellow oil; R_f = 0.56 (10:1,*n*-pentane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.16 (d, J = 8.4

Hz, 2 H_{arom}), 7.41 (d, J = 8.8 Hz, 2 H_{arom}), 6.77 (dt, J = 9.2 Hz, J = 3.2 Hz, 2 H_{arom}), 6.69 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.16 (s, 1 H, CH_3CH=C*H*), 6.09-6.20 (m, 2 H, CH_3C*H*=C*H*), 5.54 (s, 1 H, CH=$COCH_3$), 4.71 (s, 2 H, CH_2N), 3.74 (s, 3 H, (OCH_3), 3.68 (s, 3 H, ($ArOCH_3$), 1.74 (d, J = 6.0 Hz, 3 H, (CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 154.1 (1 C, C=*C*OCH_3), 152.5 (1 C, C_{arom}), 147.0 (1 C, C_{arom}), 142.6 (1 C, C_{arom}), 128.1 (1 C, CH_3*C*H=CH), 127.6 (2 C, CH_{arom}), 123.7 (2 C, CH_{arom}), 122.0 (1 C, CH_3CH=*C*H), 115.1 (2 C, CH_{arom}), 114.6 (2 C, CH_{arom}), 110.2 (1C, C=*C*OCH_3), 57.2 (1 C, CH_2N), 55.7 (1 C, $ArOCH_3$), 55.6 (1 C, OCH_3), 18.3 (1 C, CH_3); IR (neat, cm^{-1}) 3013, 1253, 1089. HRMS (EI) calcd for $C_{20}H_{22}O_4N_2$ 354.1574, obsd 354.1573.

2-(4-Methoxyphenyl)-1-(4-nitrophenyl)-2,3-dihydro-1H-benzo[c]azepin-4-yl pivalate 5a. According to the general procedure from **1g** (63.5 mg, 0.29 mmol), imine **2a** (112 mg, 0.44 mmol, 1.5 equiv), gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for 24h. Flash chromatography (DCM:*n*-pentane (4:1)) yielded **5a** (65 mg, 47 %) as a yellow oil; R_f = 0.43 (DCM)**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.16 (d, J = 8.8 Hz, 2 H_{arom}), 7.32 (d, J = 8.4 Hz, 2 H_{arom}), 7.13-7-25 (m, 4 H_{arom}), 7.04 (dt, J = 8.8 Hz, J = 4.0 Hz,2 H_{arom}), 6.76 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.22 (d, J = 2.0 Hz,1 H, CH=C), 6.08 (s, 1 H, CHN), 3.97 (d, J = 19.2 Hz, 1 H, CH_2), 3.75 (d, J = 19.8 Hz, 1 H, CH_2), 3.69 (s, 3 H, ($ArOCH_3$), 1.23 (s, 9 H, ((CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 177.1 (1 C, C=O), 153.4 (1 C, C=*C*OCH_3), 150.8 (1 C, C_{arom}), 147.6 (1 C, C_{arom}), 147.2 (1 C, C_{arom}), 142.8 (1 C, C_{arom}), 138.3 (1 C, C_{arom}), 132.2 (1 C, C_{arom}), 132.0 (1 C, CH_{arom}), 130.4 (1 C, CH_{arom}), 129.7 (1 C, CH_{arom}), 128.0 (2 C, CH_{arom}), 127.3 (1 C, CH_{arom}), 123.7 (2 C, CH_{arom}), 121.0 (1 C, C=*C*H), 118.2 (2 C, CH_{arom}), 114.4 (2 C, CH_{arom}), 68.7 (1 C, CHN), 55.4 (1 C, $ArOCH_3$), 48.5 (1 C, CH_2), 38.8 (1 C, *C*(CH_3)$_3$), 27.0 (1 C, C(*C*H_3)$_3$); IR (neat, cm^{-1}) 2991, 1271, 1081. HRMS (EI) calcd for $C_{28}H_{28}O_5N_2$ 472.1993, obsd 472.1994.

2-(4-Methoxyphenyl)-1-phenyl-2,3-dihydro-1H-benzo[c]azepin-4-yl pivalate 5b. According to the general procedure from **1f** (63.5 mg, 0.29 mmol), imine **2a** (92.5 mg, 0.44 mmol, 1.5 equiv), gold chloride (7.8 mg, 14.0 µmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 µmol, 0.05 equiv) in DCE for 72h. Flash chromatography (DCM) yielded **5b** (42 mg, 34 %) as a yellow oil; R_f = 0.39 (DCM)**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.27-7.34 (m, 3 H_{arom}), 7.12-7.19 (m, 6 H_{arom}), 7.04 (dt, J = 8.8 Hz, J = 4.0 Hz, 2 H_{arom}), 6.75 (dt, J = 9.2 Hz, J = 3.6 Hz, 2 H_{arom}), 6.19 (d, J = 1.6 Hz,1 H, CH=C), 6.10 (s, 1 H, CHN), 3.93 (d, J = 18.8 Hz, 1 H, CH_2), 3.84 (d, J = 20.0 Hz, 1 H, CH_2), 3.69 (s, 3 H, ($ArOCH_3$), 1.24 (s, 9 H, (($CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 177.1 (1 C, C=O),152.7 (1 C, C=*C*OCH_3), 151.1 (1 C, C_{arom}), 143.0 (1 C, C_{arom}), 140.4 (1 C, C_{arom}), 139.8 (1 C, C_{arom}), 132.1 (1 C, C_{arom}), 132.0 (1 C, CH_{arom}), 130.5 (1 C, CH_{arom}), 128.9 (2 C, CH_{arom}), 128.5 (2 C, CH_{arom}), 127.5 (1 C, CH_{arom}), 127.3 (1 C, CH_{arom}), 126.9 (1 C, CH_{arom}), 120.9 (1 C, C=*C*H), 117.5 (2 C, CH_{arom}), 114.3 (2 C, CH_{arom}), 68.5 (1 C, CHN), 55.4 (1 C, $ArOCH_3$), 47.8 (1 C, CH_2), 38.5 (1 C, *C*$(CH_3)_3$), 27.0 (1 C, C(*C*$H_3)_3$); IR (neat, cm^{-1}) 2993, 1271, 1109. HRMS (EI) calcd for $C_{28}H_{29}O_3N$ 427.2142, obsd 427.2146.

(1-(2,3,4,5,6-*d*$_5$-Phenyl)prop-2-yn-1-ol-*d*$_5$ 7. According to the reported procedure[22] from 2,3,4,5,6-*d*$_5$-benzaldehyde **6** (666 mg, 6 mmol) in 10ml THF, ethynylmagnesium bromide (18 ml, 9 mmol, 0.5 M in THF). Flash chromatography (*n*-pentane/EtOAc 5:1) yielded **7** (641 mg, 78%) as a colorless oil; R_f = 0.41 (*n*-pentane/EtOAc 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 5.47 (d, J = 3.6 Hz,1 H, CH(OH)C≡C), 2.67 (d, J = 2.4 Hz,1 H, C≡CH), 2.65 (bs, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 139.8 (1 C, C_{arom}), 127.8-128.4 (m, 3 C, CD_{arom}), 126.2 (t, $J_{C\text{-}D}$ = 24.2, 2 C, CD_{arom}), 83.4 (1 C, *C*≡CH), 74.8 (1 C, C≡*C*H), 64.4 (1 C, *C*H(OH)C≡C); IR (neat, cm^{-1}) 3410, 2969, 1296, 1092. HRMS (EI) calcd for $C_9H_3D_5O$ 137.0884, obsd 137.0885.

2,3,4,5,6-*d*$_5$-(1-((2-Methoxypropan-2-yl)oxy)prop-2-yn-1-yl)benzene *d*$_5$-1a. According to the reported procedure[22] from **7** (500 mg, 3.6 mmol), 2-methoxypropene (4 ml, solvent) and PPTS (a

few crystals). Flash chromatography (*n*-pentane/EtOAc 50:1) yielded ***d*$_5$-1a** (650 mg, 85%) as a colorless viscous oil; R_f = 0.48 (*n*-pentane/EtOAc 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 5.42 (d, J = 2.4 Hz,1 H, CHC≡C), 3.18 (s, 3 H, OCH_3), 2.53 (d, J = 2.0 Hz, 1 H, C≡CH), 1.54 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 140.0 (1 C, C_{arom}), 127.2-128.2 (m, 3 C, CD_{arom}), 126.4 (t, J_{C-D} = 24.2, 2 C, CD_{arom}), 101.8 (1 C, $C(CH_3)_2$), 84.4 (1 C, *C*≡CH), 73.6 (1 C, C≡*C*H), 62.5 (1 C, OCH_3), 49.4 (1 C, *C*HC≡C), 25.3 (1 C, C(CH_3)$_2$), 24.9 (1 C, C(CH_3)$_2$); IR (neat, cm^{-1}) 2969, 1284, 1093. HRMS (EI) calcd for $C_{12}H_7D_5O$ [M-MeOH]$^+$ 177.1197, obsd 177.1195.

3,6,7,8,9-*d*$_5$-4-Methoxy-2-(4-methoxyphenyl)-1-(4-nitrophenyl)-2,3-dihydro-1H-benzo[c]azepine *d*$_5$-3a. According to the general procedure from ***d*$_5$-1a** (61.4 mg, 0.29 mmol), imine **2a** (112.6 mg, 0.43 mmol, 1.5 equiv), the gold chloride (7.8 mg, 14.0 μmol, 0.05 equiv) and $AgSbF_6$ (4.8 mg, 14.0 μmol, 0.05 equiv) in DCE for 15 min. Flash chromatography (*n*-pentane/EtOAc 20:1) yielded ***d*$_5$-3a** (90 mg, 76 %) as a viscous yellow oil; R_f = 0.55 (*n*-pentane/EtOAc 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.10 (d, J = 8.8 Hz, 2 H_{arom}), 7.29 (d, J = 8.4 Hz, 2 H_{arom}), 6.85 (d, J = 9.2 Hz, 2 H_{arom}), 6.76 (d, J = 9.2 Hz, 2 H_{arom}), 5.91 (s, 1 H, CH=C), 5.50 (s, 1 H, CHN), 3.71 (s, 3 H, OCH_3), 3.69 (s, 1 H, CHD), 3.52 (s, 3 H, $ArOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.3 (1 C, C=*C*OCH_3), 152.9 (1 C, C_{arom}), 150.0 (1 C, C_{arom}), 146.9 (1 C, C_{arom}), 143.5 (1 C, C_{arom}), 136.3 (1 C, C_{arom}), 134.9 (1 C, C_{arom}), 130.4 (1 C, CD_{arom}), 130.3 (t, J_{C-D} = 23.1, 1 C, CD_{arom}), 128.9 (2 C, CH_{arom}), 127.5 (t, J_{C-D} = 24.3, 1 C, CD_{arom}), 124.9 (t, J_{C-D} = 22.9, 1 C, CD_{arom}), 123.4 (2 C, CH_{arom}), 116.6 (2 C, CH_{arom}), 114.5 (2 C, CH_{arom}), 102.0 (1 C, C=*C*H), 68.8 (1 C, CHN), 55.5 (1 C, $ArOCH_3$), 54.8 (1 C, OCH_3), 48.9 (t, J_{C-D} = 21.0, 1 C, CHD); IR (neat, cm^{-1}) 2981, 1298, 1087. HRMS (EI) calcd for $C_{24}H_{17}D_5O_4N_2$ 407.1888, obsd 407.1885.

Acknowledgement We thank the Research Council of Norway for financial support.

Supporting Information: Copies of ^{1}H and ^{13}C NMR spectra are available free of charge at http://pubs.acs.org.

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