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Synthesis of functionalized carbo- and heterocycles via gold-catalyzed cycloisomerization reactions of enynes

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ABSTRACT

The $PPh_3AuCl/AgSbF_6$ catalytic system promotes a tandem Friedel–Crafts' type addition of electron-rich aromatic and heteroaromatic derivatives to unactivated alkene followed by a C–C bond cyclization reaction. The efficiency of this system allowed room temperature reactions in a very short time. The scope and limitations of this reaction were investigated. The reaction conditions were compatible with various functional groups on the nucleophiles. Severe limitations were observed when the allylic position of the enyne is substituted by electron-withdrawing groups. The mechanism of the reaction was investigated via the synthesis of a deuterated aromatic ring: we showed that the source of proton involved in the protodemetallation step originates from the acidic activated C–H bond of the nucleophile.

1. Introduction

Over the past 10 years, significant efforts have been made to develop catalytic C–H bond activation reactions.[1] It indeed represent an ideal environmentally friendly and atom-economical concept as no by-products are produced during the whole process. Several metals have been recognized as excellent candidates for aromatic or heteroaromatic C–H bond activation.[2] In 1931, Kharash and Isbell were the first to show that Au(III) could activate aromatic compounds at room temperature.[3] In 1973, Braunstein described and characterized trihalogenoarylgold(III) complexes.[4] Since their seminal discovery, homogeneous gold catalysis was forsaken and it's only recently that gold was recognized as a fascinating metal, enable to promote a myriad of transformations and to surprise the organic chemist.[5] The use of gold for C–H activation followed by C–C bond formations was explored by Hashmi's group in 2000:[6] the addition of 2-methylfuran to methyl vinyl ketones was proven to be highly efficient. These findings opened the way to further studies: several groups then reported the addition of electron-rich arenes to various electrophiles such as alkynes, activated alkenes or allenes.[7] The groups of Nolan, Echavarren and Wang reported the hydroarylation of propargylic acetates, sulfides and dithiacetals leading to functionalized indenes or acyclic enol esters in good to excellent yields.[8] The addition of arenes to carbonyl derivatives (C=O and C=N), epoxides and *N*-protected aziridines has also been recently described.[9] As part of our ongoing program towards the development of catalytic cycloisomerization reactions,[10,11] we have been interested in the use of gold for hydroarylation reactions. In our preliminary communication, we have presented an efficient and atom-economical method for the synthesis of original and functionalized carbo- and heterocycles via a tandem Friedel–Crafts' type addition/cyclization process.[12,13] Here we report a detailed study based on our preliminary research with the emphasis on showing the scope and limitations of the above method.

2. Results and discussion

In order to test the feasibility of the reaction, enyne **1** as the substrate and 1,3-dimethoxybenzene as the nucleophile were reacted in the presence of different metal catalysts and solvents (Table 1). Disappointing results were obtained using $AuCl_3/AgSbF_6$ and $PtCl_2/AgSbF_6$ systems (Table 1, entries 1 and 2). No conversion was observed with $AgSbF_6$, $Cu(OTf)_2$, $In(OTf)_3$ or $Sc(OTf)_3$ (Table 1, entries 3–6). A moderate activity was found when AuCl was associated with silver salts (Table 1, entry 7). These results prompted us to further investigate a catalytic system based on gold. The use of cationic Au(III) and Au(I) in the presence of triphenylphosphane as an external ligand or in the gold precursor led to a total conversion (Table 1, entries 8 and 9). The best reproducible system was found to be 3 mol % of the commercially available PPh_3AuCl and 3 mol % of $AgSbF_6$, the functionalized alkene **2** being isolated in 73% yield (Table 1, entry 9). The desired cyclic derivative **2** was detected as a unique diastereoisomer, fully characterized by NMR spectroscopy and the stereochemistry of the reaction was unambiguously established by X-ray analysis of a related derivative.[12] A screening

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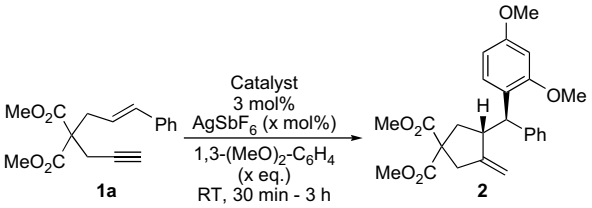
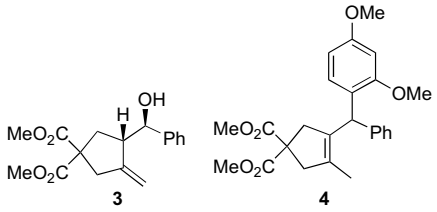
Table 1
Optimization of the catalytic system for the Friedel–Crafts' type addition/cyclization



Entry	Catalyst	$AgSbF_6$ (mol %)	Solvent	NuH (equiv)	Conv (yield) [%]
1	$AuCl_3$	9	Ether	3	—
2	$PtCl_2$	6	Ether	3	—
3	$AgSbF_6$	—	Ether	3	—
4	$Cu(OTf)_2$	—	Ether	3	—
5	$In(OTf)_3$	—	Ether	3	—
6	$Sc(OTf)_3$	—	Ether	3	—
7	AuCl	3	Ether	3	17
8[a]	$AuCl_3/PPh_3$	9	Ether	3	100
9	PPh_3AuCl	3	Ether	3	100 (73)
10	PPh_3AuCl	3	CH_3CN	3	<10
11	PPh_3AuCl	3	CH_2Cl_2	3	100[b]
12	PPh_3AuCl	3	Acetone	3	100[c]
13	PPh_3AuCl	3	Toluene	3	100[b]
14	PPh_3AuCl	3	Toluene	1.2	100[d]
15	PPh_3AuCl	3	Toluene	5	100[e]

[a] PPh_3 (3 mol %).
[b] Compound **4**: 10%.
[c] Compound **3**: 40%.
[d] Compound **4**: 30%.
[e] Compound **4**: 23%.



of different solvents such as CH_3CN, CH_2Cl_2, acetone and toluene was then performed leading generally to a total conversion of the enyne except in the case of acetonitrile (Table 1, entries 10–13).

Using acetone as the solvent, a mixture of alkene **2** and alcohol **3**, resulting from the competitive addition of water instead of the aromatic ring, was obtained in a 6/4 ratio. When the reaction was conducted in CH_2Cl_2 or toluene, the formation of side-product **4**, resulting from the internal isomerization of the alkene, was observed. In the case of toluene, the influence of the substrate to nucleophile ratio on the course of the reaction was investigated (Table 1, entries 14 and 15), the best result being observed in the presence of 3 equiv of 1,3-dimethoxybenzene. The compatibility of the system $PPh_3AuCl/AgSbF_6$ with various enyne substrates and its efficiency in the presence of other nucleophiles was then examined (Tables 2 and 3, Schemes 1 and 2).

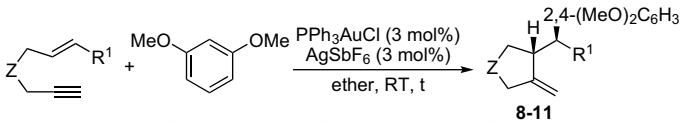
The addition of 1,3-dimethoxybenzene and 1,3,5-trimethoxybenzene to substrates containing carbon and heteroatom tethers, where $Z{=}C(CO_2R)_2$, $C(SO_2Ph)_2$, O or NTs, afforded the desired alkenes **8**–**19** in good to excellent isolated yields (Scheme 1 and Table 2, entries 1–8). The carbon tether could either be methyl, isopropyl or benzyl malonates (Table 2, entries 1–3), even though more hindered ester groups slowed down the reaction.

A prochiral enyne **1d** was prepared and reacted smoothly under the optimized conditions (Table 2, entry 4). The reaction led this time to a mixture of two diastereoisomers **15a**,**b** in 68% isolated yield.[12]

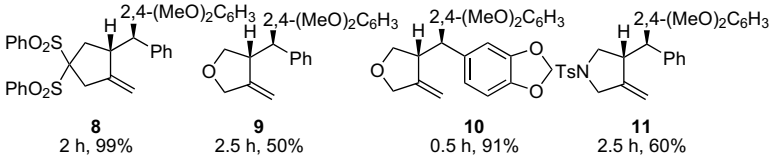
The generality of the addition/cyclization of carbon, oxygen and nitrogen tethered 1,6-enynes in the presence of electron-rich 1,3,5-trimethoxybenzene was fully demonstrated (Table 2, entries 5–8). Interestingly the addition of this latter was possible directly on a trisubstituted alkene **5b**, leading to disulfone **16** in 72% yield (Table 2, entry 5). The presence of halides may also be desirable for further organometallic couplings. We therefore examined the addition of 1-bromo-2,4-dimethoxybenzene as a nucleophile (Scheme 2). The reaction of both 1,6-enynes **5a** and **6b** proceeded smoothly and led to the corresponding brominated alkenes in 67% and 63% yield (Scheme 2, Eqs. 1 and 2).

Surprisingly, the addition of 1,2-benzodioxolane was unsuccessful as no conversion was observed in the case of standard enyne **1a** (Scheme 3, Eq. 3). The presence of a formyl group on the aromatic also inhibited the reaction. Other nucleophiles such as thiophene and ferrocene did not give better results. We also observed that the substitution of the alkenyl side chain turned to be a key parameter for the outcome of the reaction (Scheme 3, Eqs. 4 and 5). Indeed, the substitution by a methyl group at the internal or the external position of the alkenyl chain was detrimental to the tandem process, which was unexpected for us as the latter reacted particularly well in the presence of oxygen nucleophile such as water or methanol (Scheme 3, Eq. 4).[10c] In the same manner, no reaction was observed in the case of a 1,6-enyne bearing a geranyl side chain or a 1,7-enyne.[10c,14] We anticipated and verified that the substitution of the enyne by an electron-withdrawing group such as an ester group ($R^1{=}CO_2Me$ for the carbon-tethered enyne and propargylic ester as a substrate) completely inhibited any rearrangement (Scheme 3, Eqs. 4 and 5). Substituted alkynes (carbon or oxygen tethered) did not react under the standard conditions (Scheme 3, Eq. 5). More surprisingly nitrogen tethered enyne bearing a 3-methylbut-2-enyl side chain did not react at room temperature or at 40 °C (Scheme 3, Eq. 5). The only moderate activity was observed for enyne **1e**, which participated in the tandem reaction, leading to the substituted alkene **22** in 31% isolated yield (Scheme 3, Eq. 6).

Considering the occurrence of indolic skeleton in several pharmaceuticals, we also studied the introduction of electron-rich heteroaromatic derivatives (Table 3). Indoles have also been

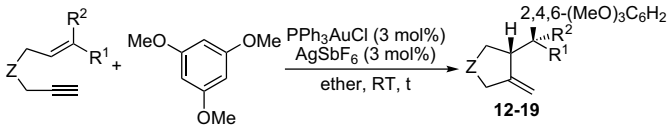


5a Z = $C(SO_2Ph)_2$, R^1 = Ph; **6a** Z = O, R^1 = Ph; **6b** Z = O, R^1 = 3,4-$(OCH_2O)C_6H_3$; **7** Z = NTs, R^1 = Ph

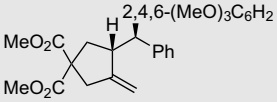
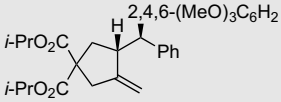
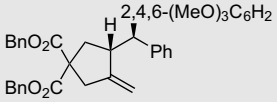
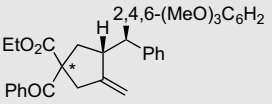
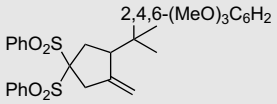
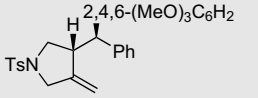
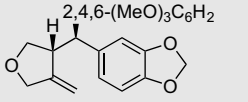
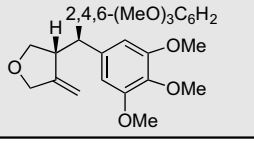


Scheme 1. Friedel–Crafts' type addition/cyclization in the presence of 1,3-dimethoxybenzene.

Table 2
Friedel–Crafts' type addition/cyclization in the presence of 1,3,5-trimethoxybenzene



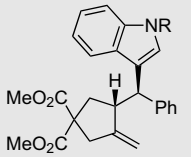
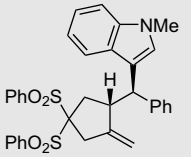
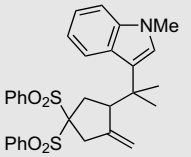
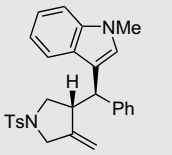
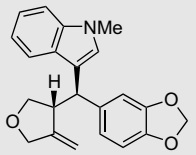
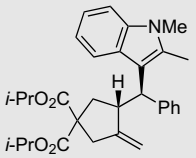
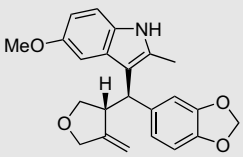
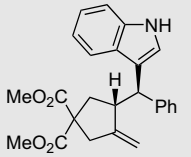
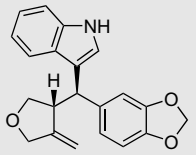
1a Z = $C(CO_2Me)_2$, R^1 = Ph, R^2 = H; **1b** Z = $C(CO_2i\text{-}Pr)_2$, R^1 = Ph, R^2 = H; **1c** Z = $C(CO_2Bn)_2$, R^1 = Ph, R^2= H; **1d** Z = $C(CO_2Et)(COPh)$, R^1 = Ph, R^2 = H; **5b** Z = $C(SO_2Ph)_2$, R^1 = Me, R^2 = Me; **6b** Z = O, R^1 = 3,4-$(OCH_2O)C_6H_3$, R^2 = H; **6c** Z = O, R^1 = 3,4,5-$(MeO)_3C_6H_2$, R^2 = H; **7** Z = NTs, R^1 = Ph, R^2 = H

Entry		*t* [h]	Product		Yield[a] [%]
1	**1a**	1		**12**	68
2[b]	**1b**	16		**13**	76
3[b]	**1c**	16		**14**	45
4[c]	**1d**	55		**15a,b**	68
5	**5b**	1		**16**	72
6	**7**	20		**17**	44
7	**6b**	3		**18**	60
8[b]	**6c**	16		**19**	67

[a] Isolated yield.
[b] AgOTf instead of $AgSbF_6$.
[c] Mixture (1/1) of 2 diastereomers.

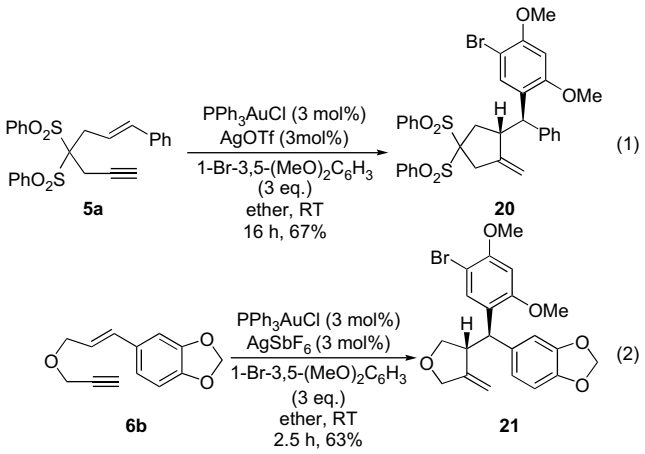
described as excellent nucleophilic partners in gold-catalyzed carbon–carbon bond forming reactions.[15] Methyl-, acetyl and benzyl substituted indoles were suitable nucleophiles for the Friedel–Crafts' type addition and carbocyclization tandem reaction of enyne **1a** (Table 3, entry 1). As the *N*-Me-indole derivative **23a** was isolated in a higher yield, we screened the reactivity of other enynes (Table 3, entries 2–5). The corresponding *N*-Me-indole heterocycles **24**–**27** were obtained in 47–99% isolated yields. Both hindered and free indoles were also introduced in moderate to excellent yields (Table 3, entries 6–9). Varying the enyne/nucleophilic indole combination, a total regioselectivity in C-3 position was observed, with only one exception. The addition of 4-methoxy-2-methylindole did not occur regioselectively in the case of enyne **5b** (Scheme 4) as two isomers **32** and **33** were isolated, respectively, in

Table 3
Gold-catalyzed diastereoselective tandem addition/carbocyclization of heteroaromatic derivatives[a]

Entry		*t* [h]	Product		Yield[b] [%]
1	**1a**	0.5		**23a**, **23b**, **23c**	R=Me, 81, R=Ac, 36, R=Bn, 78
2	**5a**	3.5		**24**	99
3	**5b**	2		**25**	82
4	**7**	6		**26**	47[c]
5	**6b**	0.75		**27**	77
6[d]	**1b**	17		**28**	72
7	**6b**	2.5		**29**	43
8	**1a**	2		**30**	68
9	**6b**	2.5		**31**	99

[a] General conditions: PPh_3AuCl (3 mol %), $AgSbF_6$ (3 mol %), ether, rt.
[b] Isolated yield.
[c] Catalyst (10 mol %), 40 °C.
[d] PPh_3AuNTf_2 (3 mol %).[16]

33% and 25% yield. Formation of alkene **33** could be explained via a Friedel–Crafts' type addition of the phenyl ring of the indole followed by the cyclization. The regioselectivity of the addition was

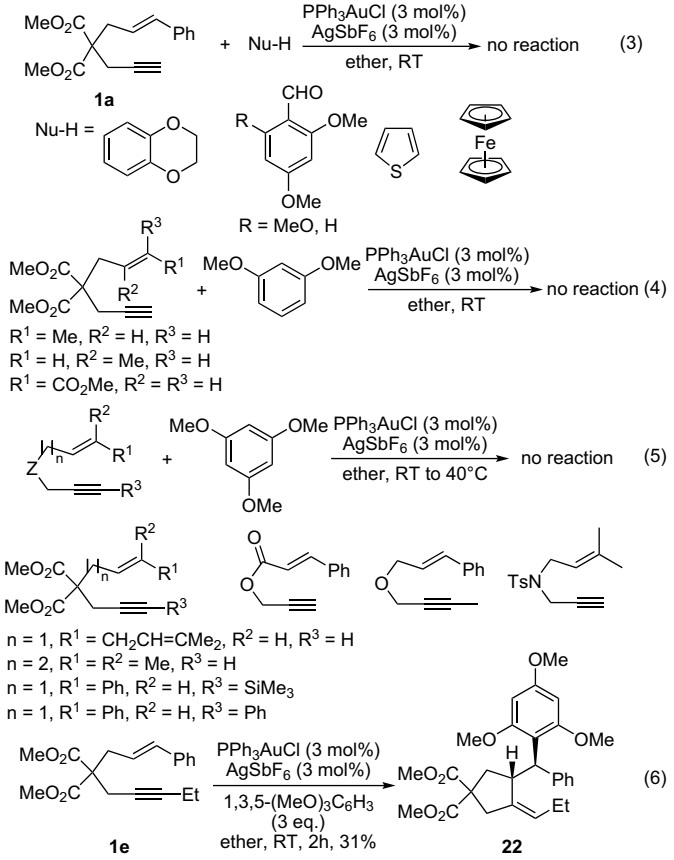


Scheme 2. Friedel–Crafts' type addition/cyclization in the presence of 1-bromo-2,4-dimethoxybenzene.

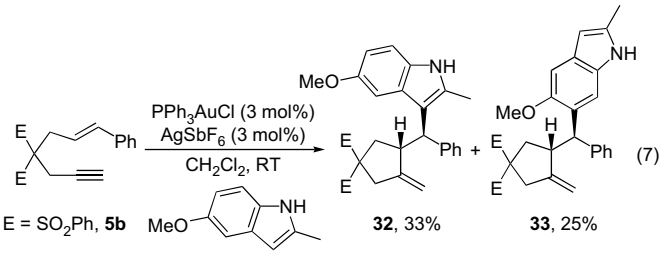
not total in the case of pyrrole for enynes **1a** and **5b** (Scheme 5, Eq. 8). As expected, the 2- and 3-substituted isomers **34a**,**b** and **35a**,**b** were obtained, the overall yield being, respectively, 58% and 90%.

The addition of a furanyl moiety was also investigated. As a mixture of unseparable isomers was obtained in the case of furane, we used 2,5-dimethylfurane as nucleophile (Scheme 5, Eq. 9). The tandem reaction proceeded smoothly with enynes **1a** and **5b** and afforded the corresponding heterocycles **36** and **37** in 39% and 67% yield.

The addition of *N*-Me-indole was evaluated varying the carbon tether on the enyne. We anticipated that the tandem process would



Scheme 3. Limitations in terms of nucleophiles and enynes for the Friedel–Crafts' type addition/cyclization.



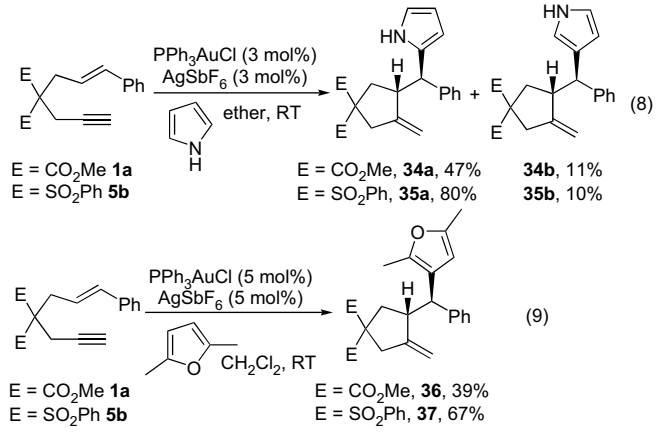
Scheme 4. Friedel–Crafts' type addition/cyclization in the presence of 4-methoxy-2-methylindole.

be highly dependent on the conformation of the enyne.[17] Indeed we observed a good reactivity of enyne **1f**, bearing two hindered *tert*-butylic esters, the functionalized alkene **38** was obtained in 80% yield. A contrario, the presence of a cyclic rigid diester completely inhibited the reaction (Scheme 6).

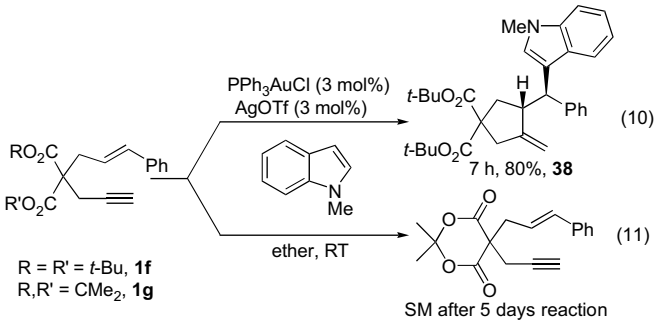
In the same manner as previously observed with 1,3-dimethoxybenzene and 1,3,5-trimethoxybenzene as the nucleophiles (Scheme 3), a strong influence of the electronic effects for substituted enynes has been observed. All the enynes bearing electron-withdrawing groups at the allylic position were unreactive. A peculiar example is described in Scheme 7. Propargylic ester **6d** did not react according the Friedel–Crafts' type addition/cyclization process, but a total conversion of the starting material was observed (Scheme 7, Eq. 12).

The formation of the isolated products **39** and **40** could be explained via a gold-catalyzed Michael-type 1,4-addition of the nucleophile to the activated alkyne (for **39**) and a second addition to the resulting α,β-unsaturated ester (for **40**). This reactivity was similar to the previously published work by several groups.[18,5] We also showed that another nucleophile such as 1,3,5-trimethoxybenzene reacted in the same manner, the mono- and di-hydroarylated products **41** and **42** being isolated in 15% and 22% yield, respectively (Scheme 7, Eq. 13).

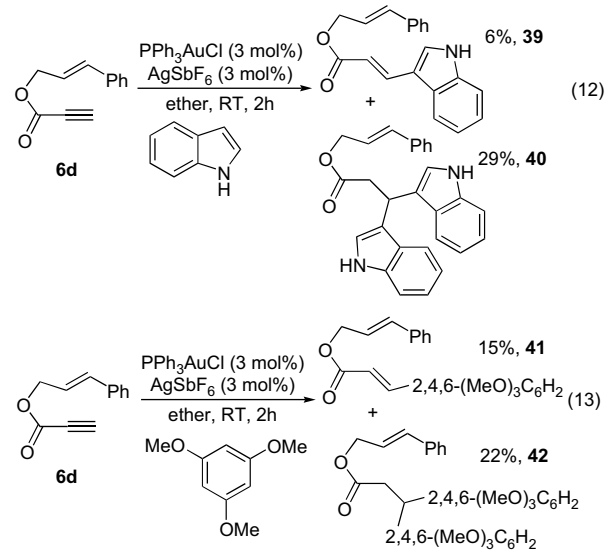
In consideration of the tandem Friedel–Crafts' addition/cyclization reaction mechanism, we and others had previously proposed the formation of a cationic gold catalyst in the presence of silver salts followed by the complexation of the Lewis acid cationic gold catalyst to the alkyne function leading to intermediate **A** (Scheme 8). The cyclization step may then occur directly via a concerted diastereoselective Friedel–Crafts' type addition/carbocyclization sequence leading to vinylaurate intermediate **B** or may proceed transiently by stereoselective attack of the nucleophile on a carbenic species, as advocated in several metal-catalyzed



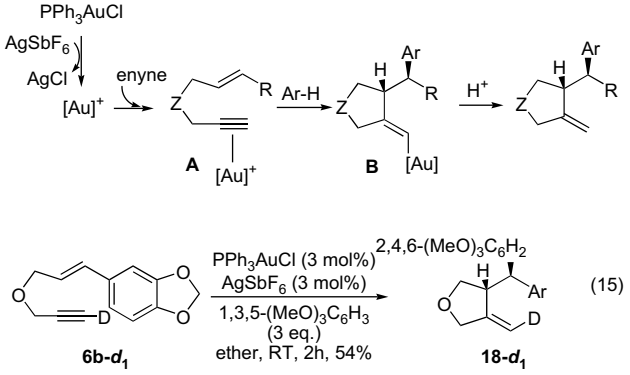
Scheme 5. Friedel–Crafts' type addition/cyclization in the presence of pyrrole or 1,4-dimethylfurane as nucleophiles.



Scheme 6. Friedel–Crafts' type addition/cyclization of enynes **1f** and **1g.**

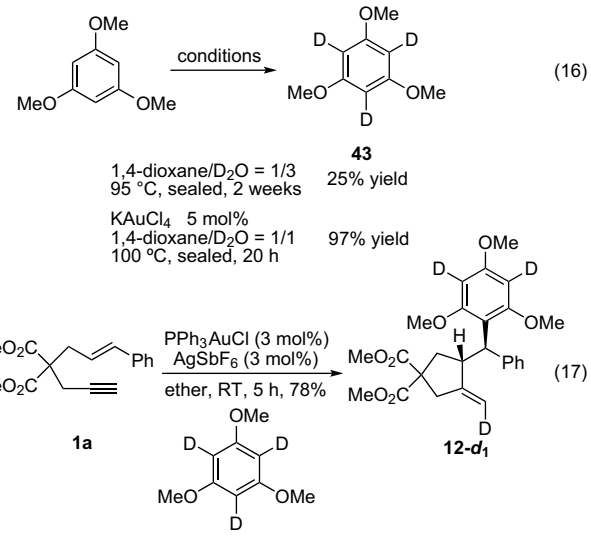


Scheme 7. Michael-type addition/cyclization of enynes **6d.**



Scheme 8. Mechanistic rationale.

cycloisomerization reactions.[5,11] The last step is the protodemetallation of the aurate intermediate. We previously showed that the process is completely stereoselective, since the deuterated enyne **6b**-d_1 (>95% D) underwent a clean tandem reaction in the presence of 3 mol % $PPh_3AuCl/AgSbF_6$ and 3 equiv of 1,3,5-trimethoxybenzene leading to the unique deuterated alkene **18**-d_1. The alkene (>95% D, ^1H NMR of crude product) was isolated in 54% yield (Scheme 8, Eq. 15).



Scheme 9. Deuteration experiments.

For further mechanistic study, we envisaged to demonstrate that the protodemetallation step occurred selectively in the presence of a deuterated nucleophile. We decided to prepare the deuterated compound **43** (Scheme 9, Eq. 16).

We used a published procedure based on an hydrogen/deuterium exchange in the absence of any acidic catalyst, however, most of the starting material left without reacting even though the reaction mixture was heated in a dioxane/D_2O (1/3) mixture over 2 weeks.[19] We decided to take advantage of the ability of Au(III) catalyst to activate an aromatic C–H bond and thus we accomplished the desired reaction in the presence of a catalytic amount of $KAuCl_4$ to obtain 97% deuterium exchanged product. The cycloisomerization reaction accomplished using this perdeuterio nucleophile furnished product **12**-d_1 in 78% yield (Scheme 9, Eq. 17); thus proving that the source of proton involved in the protodemetallation step originates from the acidic activated C–H bond of the nucleophile.

3. Conclusion

We have therefore showed that the gold-catalyzed cycloisomerization of 1,6-enynes in the presence of an external nucleophile such as an electron-rich aromatic ring lead to carbo- and heterocycles in good to excellent yields. A simple catalytic system based on the association of Au(I) and silver salts was found to be highly efficient. The scope and limitations have been studied and we observed that carbon, oxygen and nitrogen tethered 1,6-enynes reacted smoothly with methoxysubstituted benzene, indoles, pyrroles and furane nucleophilic partners. The reaction conditions were compatible with the presence of bromide on the aromatic nucleophile, allowing further potential functionalization. Nevertheless, some severe limitations come from the fact that several enynes are not reactive under the reaction conditions tested. For example, we proved that electron-withdrawing groups on 1,6-enynes or 1,7-enynes are not tolerated. The substitution of the alkene is also crucial, as a crotyl side chain does not react at all compared to a cinnamyl side chain. From a mechanistic point of view, we demonstrated that the tandem process implies a stereoselective protodemetallation, the transferred proton coming from the nucleophile. Further studies will be dedicated to the construction of elaborated structural units, whose skeleton could be integrated in pharmaceutically active compounds.

4. Experimental

4.1. General

PPh_3AuCl was purchased from Cortecnet. $AgSbF_6$ and AgOTf were purchased from Acros. All manipulations were carried out under argon. ^1H NMR and ^{13}C NMR were recorded on a Bruker AV 300 instrument. All signals for ^1H and ^{13}C NMR were expressed as parts per million downfield from Me_4Si used as an internal standard (δ). Coupling constants (J) are reported in hertz and refer to apparent peak multiplicities. Mass spectrometry analyses (direct introduction by chemical ionization with ammoniac or electrospray) were performed at the Ecole Nationale Supérieure de Chimie de Paris. High resolution mass spectra were performed on a Varian MAT311 instrument at the Ecole Normale Supérieure (Paris). Enynes **1a–c**, **5a**,**b**, **6a–d** and **7** were prepared according to the published procedures.[10,20] Enynes **1d** and **1e** were prepared in analogy with a published procedure.[10] ^1H, ^{13}C NMR and mass spectroscopy data for compounds **2**, **3**, **8–12**, **14–16**, **21**, **24–26**, **29–31**, **34**, **35**, **37** and **38** were described elsewhere.[10k,12]

4.2. Analytical and spectroscopic data of enynes

*4.2.1. (E) Ethyl 2-benzoyl-5-phenyl-2-(prop-2-ynyl)pent-4-enoate **1d***

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 1.04 (t, J=6.9 Hz, 3H), 1.99 (t, J=3.0 Hz, 1H), 2.91 (d, J=3.0 Hz, 2H), 2.99–3.15 (m, 2H), 4.10 (q, J=9 Hz, 2H), 5.82 (dt, J=15.6, 7.5 Hz, 1H), 6.35 (d, J=15.6 Hz, 1H), 7.09–7.20 (m, 5H), 7.33–7.38 (m, 2H), 7.44–7.50 (m, 1H), 7.77–7.81 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 13.9, 23.7, 36.4, 60.5, 61.9, 72.2, 78.9, 122.8, 126.3 (2C), 127.5, 128.5 (4C), 128.7 (2C), 133.0, 134.8, 135.6, 136.9, 171.6, 195.0. ES-MS: 369.4 $[M+Na]^+$.

*4.2.2. Dimethyl 2-[3-(E)-cinnamyl]-2-pent-2-ynyl malonate **1e***

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 1.02 (t, J=7.2 Hz, 3H), 2.07 (m, 2H), 2.71 (dd, J=4.5, 2.4 Hz, 2H), 2.85 (dd, J=7.5, 0.9 Hz, 2H), 3.64 (s, 6H), 5.94 (dt, J=15.6, 7.8 Hz, 1H), 6.40 (d, dt, J=15.9 Hz, 1H), 7.11–7.24 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 12.4, 14.2, 23.3, 36.0, 52.6 (2C), 57.7, 73.7, 85.2, 123.6, 126.3 (2C), 127.4, 128.5 (2C), 134.3, 137.1, 170.5 (2C). EIMS: 315 $(M+H)^+$.

4.3. General procedure for the Friedel–Crafts' type addition/cyclization

A mixture of PPh_3AuCl (3 mol %) and $AgSbF_6$ (3 mol %) in distilled ether (2.5 M) was stirred under argon atmosphere at room temperature for 3 min. The aromatic nucleophile (3 equiv) was then added and the mixture was stirred for 3 min. The enyne (1 equiv) was finally added and the mixture was stirred for 0.5–3.5 h (Tables 2 and 3, Schemes 1–8). After completion of the reaction, the mixture was filtered through a short pad of silica (cyclohexane/EtOAc, 50/50) and the solvents were evaporated under reduced pressure. The crude product was purified by silica gel flash chromatography if necessary.

4.4. Analytical and spectroscopic data of products

*4.4.1. Dimethyl-3-[1-(2,4-dimethoxyphenyl)phenylmethyl]-4-methyl-cyclopent-3-ene-1,1-dicarboxylate (**4**)*

^1H NMR (300 MHz, $CDCl_3$; δ ppm): 1.60 (s, 3H), 2.74 (q, J=9.0 Hz, 2H), 2.94 (q, J=6.0 Hz, 2H), 3.67 (s, 3H), 3.71 (s, 6H), 3.79 (s, 3H), 5.38 (s, 1H), 6.32–6.38 (m, 2H), 6.82 (d, J=8.4 Hz, 1H), 7.06–7.26 (m, 5H). ^{13}C NMR (75.5 MHz, $CDCl_3$; δ ppm): 13.6, 41.8, 42.9, 45.9, 52.7, 55.3, 55.5, 57.3, 98.5, 103.9, 123.8, 125.7, 128.0, 128.4, 130.1, 131.3, 133.0, 143.2, 158.2, 159.3, 172.8, 172.9. MS-CI (NH_3): m/z 425 (MH^+), 442 (MNH_4^+).

*4.4.2. Diisopropyl 3-methylene-4-(phenyl(2,4,6-trimethoxyphenyl)methyl)cyclopentane-1,1-dicarboxylate (**13**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 1.15–1.23 (m, 12H), 1.58 (s, 1H), 1.69 (dd, J=12.9, 2.1 Hz, 1H), 2.27 (dd, J=12.9, 5.1 Hz, 1H), 2.91–3.04 (m, 2H), 3.76 (d, J=7.2 Hz, 9H), 3.89–3.99 (m, 1H), 4.24 (d, J=1.5 Hz, 1H), 4.50 (d, J=10.8 Hz, 1H), 4.71 (d, J=1.5 Hz, 1H), 4.97 (quint, J=6.3 Hz, 1H), 5.06 (quint, J=6.3 Hz, 1H), 6.07 (s, 2H), 7.04–7.09 (m, 1H), 7.15–7.20 (m, 2H), 7.43 (d, J=7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 21.5, 39.6, 41.6, 42.7, 44.1, 55.2, 55.6, 57.7, 68.4, 68.6, 91.0, 107.8, 113.8, 125.3, 127.5, 128.7, 144.7, 151.8, 158.7, 159.4, 171.6. DCI/NH_3-MS: m/z 533.5 $[M+Na]^+$, 528.6 $[M+NH_4]^+$, 511.5 $[M+H]^+$. DCI/CH_4-HRMS calculated for $C_{30}H_{39}O_7$: 511.2696; found: 511.2682.

4.4.3. (1R,4R*,1′R*) and (1R*,4S*,1′S*) Ethyl-1-benzoyl-3-methylene-4-[phenyl-(2′,4′,6′-trimethoxyphenyl)phenylmethyl]-cyclopentanecarboxylates (**15a**,**b**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 0.98 (t, J=5.3 Hz, 3H), 1.99 (dd, J=9.9, 8.1 Hz, 1H), 2.30 (dd, J=9.9, 5.6 Hz, 1H), 3.11 (d, J=12.3 Hz, 1H), 3.19 (d, J=12.2 Hz, 1H), 3.74–3.79 (m, 9H), 4.06 (q, J=5.3 Hz, 2H), 4.11 (m, 1H), 4.34 (s, 1H), 4.53 (d, J=8.3 Hz, 1H), 4.72 (s, 1H), 6.04 (s, 2H), 7.05–7.81 (m, 10H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 13.8, 39.8, 42.0, 42.8, 43.6, 55.3 (2C), 55.7, 56.3, 61.4, 91.1, 92.0, 107.8, 113.8, 125.4, 127.7 (2C), 128.5 (2C), 128.7 (2C), 128.8 (2C), 132.8, 135.7, 144.7, 151.7, 159.5 (2C), 160.0, 174.3, 195.8. DCI/NH_3-MS: 532 $(M+NH_4)^+$, 515 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{32}H_{35}O_6$: 515.2434; observed: 515.2438.

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 0.93 (t, J=7.1 Hz, 3H), 1.78 (dd, J=12.7, 11.2 Hz, 1H), 2.48 (m, 1H), 3.23 (m, 2H), 3.75 (s, 9H), 3.94 (m, 1H), 3.98 (q, J=7.1 Hz, 2H), 4.29 (s, 1H), 4.56 (d, J=10.9 Hz, 1H), 4.71 (s, 1H), 6.05 (s, 2H), 7.06–7.86 (m, 10H). ^{13}C ($CDCl_3$, 75 MHz; δ ppm): 13.8, 39.8, 42.0, 42.8, 43.6, 55.3 (2C), 55.7, 56.3, 61.4, 91.1, 92.0, 107.8, 113.8, 125.4, 127.7 (2C), 128.5 (2C), 128.7 (2C), 128.8 (2C), 132.8, 135.7, 144.7, 151.7, 159.5 (2C), 160.0, 174.3, 195.8. DCI/NH_3-MS: 532 $(M+NH_4)^+$, 515 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{32}H_{35}O_6$: 515.2434; observed: 515.2438.

*4.4.4. 3-[1-(2′,4′,6′-Trimethoxyphenyl)phenylmethyl]-4-methylene-N-tosyl-pyrrolidine (**17**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 2.43 (s, 3H), 2.77 (dd, J=9.6, 8.1 Hz, 1H), 3.31 (dd, J=9.6, 7.5 Hz, 1H), 3.69 (s, 3H), 3.78 (s, 6H), 3.80 (d, J=10.2 Hz, 1H), 3.95 (d, J=13.8 Hz, 1H), 3.92–4.03 (m, 1H), 4.36 (br s, 1H), 4.47 (d, J=11.4 Hz, 1H), 4.70 (br s, 1H), 6.06 (s, 2H), 7.06–7.33 (m, 7H), 7.65 (d, J=8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 21.5, 41.9, 43.4, 53.0, 53.2, 55.2 (2C), 55.6, 91.1 (2C), 108.5, 112.4, 125.6, 127.7 (2C), 127.8 (2C), 128.5 (2C), 129.5 (2C), 133.4, 143.3, 143.4, 147.4, 158.6, 159.9 (2C). DCI/NH_3-MS: 494 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{28}H_{31}NO_5SNa^+$: 516.1815; observed: 516.1804.

*4.4.5. 3-[1-(3,4-Methylenedioxy)-(2′,4′,6′-trimethoxyphenyl)-phenylmethyl]-4-methylene-tetrahydrofuran (**18**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 3.38 (dd, J=8.5, 7.1 Hz, 1H), 3.77 (s, 3H), 3.80 (s, 6H), 3.82 (dd, J=8.4, 7.2 Hz, 1H), 3.95–4.10 (m, 1H), 4.38–4.48 (m, 4H), 4.76 (br s, 1H), 5.88 (s, 2H), 6.08 (s, 2H), 6.67 (d, J=8.0 Hz, 1H), 6.93 (dd, J=8.2, 1.7 Hz, 1H), 7.05 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 30.9, 42.2, 44.8, 55.2 (2C), 55.6, 72.3, 73.8, 90.9, 100.5, 105.2, 107.5, 109.2, 112.8, 121.8, 138.1, 145.3, 147.0, 151.4, 158.6, 159.6 (2C). DCI/NH_3-MS: 402 $(M+NH_4)^+$, 385 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{21}H_{25}O_6$: 385.1651; observed: 385.1646.

*4.4.6. 3-Methylene-4-((2,4,6-trimethoxyphenyl)(3,4,5-trimethoxyphenyl)methyl)tetrahydrofuran (**19**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 3.37 (dd, J=8.7, 1.5 Hz, 1H), 3.76 (s, 3H), 3.78 (s, 3H), 3.81 (s, 12H), 3.83 (s, 1H), 3.99–4.09 (m, 1H), 4.37 (s, 2H), 4.43 (s, 2H), 4.75 (d, J=2.1 Hz, 1H), 6.09 (s, 2H), 6.77 (s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 42.8, 44.6, 55.2, 55.6, 55.9, 60.8, 72.4, 73.8, 91.1, 105.2, 106.0, 112.7, 136.1, 139.8, 151.4, 152.4, 158.6, 159.7. DCI/

NH_3-MS: *m/z* 453.2 $[M+Na]^+$, 448.4 $[M+NH_4]^+$, 431.2 $[M+H]^+$. ESI-HRMS calculated for $C_{24}H_{31}O_7$: 431.2070; found: 431.2056.

*4.4.7. 1-Bromo-2,4-dimethoxy-5-(2-methylene-4,4-bis(phenylsulfonyl)cyclopentyl)(phenyl)methyl)benzene (**20**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 2.44 (d, *J*=9.6 Hz, 2H), 3.26–3.48 (m, 2H), 3.92 (s, 6H), 4.24 (d, *J*=2.1 Hz, 1H), 4.33 (d, *J*=11.4 Hz, 1H), 4.70 (d, *J*=1.8 Hz, 1H), 6.47 (s, 1H), 7.18–7.31 (m, 4H), 7.57–7.81 (m, 8H), 8.02–8.09 (m, 5H). ^{13}C ($CDCl_3$, 75 MHz; δ ppm): 36.7, 39.3, 45.2, 46.3, 55.9, 56.3, 90.2, 97.0, 102.2, 110.1, 126.0, 126.3, 127.9, 128.3, 128.6, 128.9, 131.2, 132.1, 134.5, 134.7, 136.0, 136.7, 142.8, 146.8, 155.1, 156.7. DCI/NH_3-MS: *m/z* 684.1 $[M+NH_4]^+$, 667.1 $[M+H]^+$. ESI-HRMS calculated for $C_{33}H_{32}^{79}BrO_6S_2$: 667.0824; found: 667.0813.

*4.4.8. Dimethyl-3-[1-(2′,4′,6′-trimethoxyphenyl)phenylmethyl]-4-propylidene-cyclopentane-1,1-dicarboxylate (**22**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 0.44 (t, *J*=7.5 Hz, 3H), 1.85 (dd, *J*=14.1, 3.3 Hz, 1H), 2.61 (m, 2H), 3.32 (d, *J*=15.9 Hz, 1H), 3.60 (s, 3H), 3.64 (s, 3H), 3.72 (s, 3H), 3.77 (s, 6H), 3.73–3.94 (m, 3H), 4.16 (d, *J*=11.7 Hz, 1H), 5.03 (m, 1H), 6.13 (s, 2H), 7.05–7.15 (m, 3H), 7.28–7.36 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 13.8, 21.4, 27.0, 38.6, 41.2, 43.0, 46.4, 52.4, 52.6, 55.2, 55.4, 58.1, 91.1 (2C), 112.4, 125.6, 126.2, 127.6 (2C), 129.3 (2C), 139.2, 145.0, 159.4 (2C), 159.5, 172.6, 172.8. DCI/NH_3-MS: 483 $(M+H)^+$, 500 $(M+NH_4)^+$. DCI/CH_4-HRMS calculated for $C_{28}H_{34}O_7Na^+$: 505.2197; observed: 505.2187.

*4.4.9. Dimethyl-3-[1-(1-acetyl-1H-indol-3-yl)phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (**23b**)*

^1H NMR (300 MHz, $CDCl_3$; δ ppm): 2.05 (dd, *J*=13.2, 5.1 Hz, 1H), 2.59 (s, 3H), 2.69 (ddd, *J*=13.8, 7.8, 1.5 Hz, 1H), 2.84 (d, *J*=15.9 Hz, 1H), 3.05 (d, *J*=15.9 Hz, 1H), 3.42 (q, *J*=9.9 Hz, 1H), 3.58 (s, 3H), 3.65 (s, 3H), 4.01–4.05 (m, 2H), 4.73 (s, 1H), 7.08–7.38 (m, 14H), 8.27 (d, *J*=8.1 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$; δ ppm): 24.2, 39.6, 41.6, 46.4, 47.6, 52.8, 58.4, 110.4, 116.5, 119.5, 122.0, 123.5, 124.6, 125.3, 126.7, 128.3, 128.5, 130.3, 135.9, 142.4, 148.3, 168.4, 172.0, 172.1. ESI-HRMS calculated for $C_{27}H_{27}O_5NNa$: 468.1781; observed: 468.1774.

*4.4.10. Dimethyl-3-[1-(1-acetyl-1H-indol-3-yl)phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (**23c**)*

^1H NMR (300 MHz, $CDCl_3$; δ ppm): 2.05 (dd, *J*=13.5, 8.1 Hz, 1H), 2.81 (dd, *J*=13.5, 7.8 Hz, 1H), 2.93 (d, *J*=15.9 Hz, 1H), 3.15 (d, *J*=16.2 Hz, 1H), 3.56 (q, *J*=9.3 Hz, 1H), 3.68 (s, 3H), 3.75 (s, 3H), 4.18 (s, 1H), 4.84 (s, 1H), 5.34 (s, 2H), 7.06–7.39 (m, 14H), 7.60 (d, *J*=8.1 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$; δ ppm): 39.8, 41.8, 46.9, 48.0, 50.0, 52.7, 52.8, 58.5, 109.7, 110.0, 117.8, 119.2, 119.6, 121.8, 125.7, 126.1, 126.6, 127.5, 128.0, 128.1, 128.5, 128.8, 136.6, 137.7, 144.4, 148.9, 172.1, 172.3. ESI-HRMS calculated for $C_{32}H_{31}O_4NNa$: 516.2145; observed: 516.2136.

*4.4.11. 3-[1-(1-Methyl-1H-indol-3-yl)-(3,4-methylenedioxy)-phenylmethyl]-4-methylenetetrahydrofuran (**27**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 3.43–3.47 (m, 1H), 3.77 (s, 3H), 3.85 (dd, *J*=8.9, 4.5 Hz, 1H), 3.99 (dd, *J*=8.9, 6.4 Hz, 1H), 4.18 (d, *J*=10.9 Hz, 1H), 4.38 (d, *J*=23.2 Hz, 1H), 4.43 (s, *J*=21.6 Hz, 1H), 4.84 (app s, 1H), 5.88 (d, *J*=8.4 Hz, 2H), 6.69–7.57 (m, 8H). ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 43.5, 45.5, 48.8, 71.8, 73.6, 100.8, 106.9, 107.8, 108.9, 109.2, 117.5, 119, 119.5, 121.7, 121.8, 125.6, 127.6, 137, 138.1, 145.7, 147.4, 149. DCI/NH_3-MS: 365 $(M+NH_4)^+$, 348 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{22}H_{22}O_3N$: 348.1600; observed: 348.1603.

*4.4.12. Diisopropyl 3-((1,2-dimethyl-1H-indol-3-yl)-(phenyl)methyl)-4-methylenecyclopentane-1,1-dicarboxylate (**28**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 1.10 (d, *J*=6.3 Hz, 3H), 1.15–1.20 (m, 9H), 1.83 (dd, *J*=13.5, 3.9 Hz, 2H), 2.43 (s, 3H), 3.02 (s, 2H), 3.60 (s, 3H), 3.86–3.93 (m, 1H), 4.09 (d, *J*=11.1 Hz, 1H), 4.27 (d, *J*=1.2 Hz, 1H), 4.81 (d, *J*=1.5 Hz, 1H), 4.94 (quint, *J*=6.3 Hz, 1H), 5.04 (quint, *J*=6.3 Hz, 1H), 7.02–7.23 (m, 6H), 7.41 (d, *J*=7.2 Hz, 2H), 7.76 (d, *J*=7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz; DEPT; δ ppm): 10.8, 21.4, 21.5, 29.5, 30.3, 39.6, 41.6, 45.1, 48.0, 58.0, 68.7, 68.8, 108.6, 109.0, 113.8, 119.0, 119.4, 120.2, 125.5, 125.7, 126.7, 128.1, 133.1, 135.8, 136.8, 145.0, 150.6, 171.4, 171.5. DCI/NH_3-MS: 510.4 $[M+Na]^+$, 505.4 $[M+NH_4]^+$, 488.4 $[M+H]^+$. DCI/CH_4-HRMS calculated for $C_{31}H_{38}NO_4$: 488.2801; found: 488.2784.

*4.4.13. 1,1-Bis(phenylsulfonyl)-3-[1-(2-methyl-5-methoxy-indol-3-yl)-phenylmethyl]-4-methylenecyclopentane (**32**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 1.67 (s, 1H), 2.36 (s, 3H), 2.39 (m, 2H), 3.35 (m, 2H), 3.85 (s, 3H), 4.09 (m, 2H), 4.45 (s, 1H), 4.77 (s, 1H), 6.79 (dd, *J*=11.1, 2.4 Hz, 1H), 7.11 (m, 3H), 7.23 (m, 1H), 7.36–7.50 (m, 6H), 7.61 (m, 3H), 7.84 (d, *J*=8.6 Hz, 2H), 7.90 (d, *J*=8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 12.4, 36.7, 39.0, 44.9, 46.1, 55.9, 90.4, 101.8, 109.9, 110.3, 111.1, 113.9, 127.9 (2C), 128.2 (2C), 128.6 (4C), 130.5, 131.2 (2C), 131.3 (2C), 132.2, 134.5 (2C), 135.7, 136.4, 143.4, 148.0, 153.9. DCI/NH_3-MS: 634.4 $(M+Na)^+$. DCI/CH_4-HRMS calculated for $C_{35}H_{33}NO_5S_2Na^+$: 634.1692; observed: 634.1682.

*4.4.14. 1,1-Bis(phenylsulfonyl)-3-[1-(2-methyl-5-methoxy-indol-6-yl)-phenylmethyl]-4-methylenecyclopentane (**33**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 1.61 (s, 1H), 2.38 (s, 3H), 2.47 (m, 2H), 3.18 (d, *J*=17.7 Hz, 1H), 3.38 (d, *J*=17.6 Hz, 1H), 3.71 (m, 1H), 3.88 (s, 3H), 4.22 (s, 1H), 4.45 (d, *J*=11.1 Hz, 1H), 4.63 (s, 1H), 6.09 (s, 1H), 6.93 (s, 1H), 7.04 (s, 1H), 7.09 (m, 1H), 7.19 (t, *J*=7.2 Hz, 2H), 7.28 (m, 1H), 7.48 (m, 4H), 7.65 (m, 3H), 7.90 (d, *J*=7.3 Hz, 2H), 8.01 (d, *J*=7.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 13.7, 37.0, 39.3, 46.2, 47.5, 56.1, 90.5, 100.0, 101.1, 109.8, 110.1, 125.9, 126.9, 127.8, 128.0 (2C), 128.3 (2C), 128.5 (2C), 128.6 (2C), 131.2 (2C), 131.3 (2C), 134.4, 134.5, 135.6, 136.2, 136.6, 144.1, 147.3 (2C), 151.5. DCI/NH_3-MS: 634.4 $(M+Na)^+$. DCI/CH_4-HRMS: Calculated for $C_{35}H_{33}NO_5S_2Na^+$: 634.1692; observed: 634.1682.

*4.4.15. Dimethyl-3-[1-(2,5-dimethylfuran-3-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (**36**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 2.18 (s, 6H), 2.88 (d, *J*=15 Hz, 1H), 3.08 (d, *J*=15 Hz, 1H), 3.28 (m, 1H), 3.58 (d, *J*=10.7 Hz, 1H), 3.69 (d, *J*=7.6 Hz, 1H), 3.71 (s, 3H), 3.73 (s, 3H), 3.75 (d, *J*=7.6 Hz, 1H), 4.12 (s, 1H), 4.75 (s, 1H), 5.95 (1H), 7.05–7.30 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 11.6, 13.6, 39.6, 41.8, 46.2, 47.0, 52.8, 58.1, 60.6, 105.7, 109.6, 121.8, 127.9 (2C), 128.1, 128.3 (2C), 144.2, 145.3, 149.1, 149.6, 172.2, 172.5. ESMS: 384 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{23}H_{26}O_5Na^+$: 405.1672; observed: 405.1671.

*4.4.16. (E,E)-3-Phenyl-allyl 3-(1H-indol-3-yl)acrylate (**39**)*

^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 4.89 (d, *J*=6.2 Hz, 2H), 6.41 (dt, *J*=16.0, 6.2 Hz, 1H), 6.51 (d, *J*=16.0 Hz, 1H), 6.73 (d, *J*=16.1 Hz, 1H), 7.17–7.50 (m, 10H), 7.97 (d, *J*=15.9 Hz, 1H), 8.49 (s, 1H). ^{13}C ($CDCl_3$, 75 MHz; δ ppm): 64.8, 111.1, 118.6, 119.3, 119.5, 121.7, 122.0, 123.3, 126.6 (2C), 126.7, 127.9, 128.5 (2C), 129.2, 129.3, 132.0, 133.6, 136.6, 172.3. DCI/NH_3-MS (*m/z*): 304 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{20}H_{17}NO_2Na^+$: 326.1151; observed: 326.1149.

*4.4.17. (E)-3-Phenyl-allyl 3,3-bis-(1H-indol-3-yl)propanoate (**40**)*

F=128 °C. ^1H NMR ($CDCl_3$, 300 MHz; δ ppm): 3.26 (d, *J*=7.7 Hz, 2H), 4.65 (d, *J*=5.8 Hz, 2H), 5.17 (t, *J*=7.5 Hz, 1H), 6.00–6.09 (m, 1H), 6.44 (d, *J*=15.7 Hz, 1H), 6.94 (s, 2H), 7.04–7.63 (m, 13H), 7.99 (s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 31.0, 41.2, 64.8, 111.2 (2C), 118.5 (2C), 119.3 (2C), 119.5 (2C), 121.8, 121.9 (2C), 123.3 (2C), 126.6, 127.9, 128.5 (2C), 133.6, 136.3 (2C), 136.6 (4C), 172.4. DCI/NH_3-MS (*m/z*): 438 $(M+NH_4)^+$. DCI/CH_4-HRMS calculated for $C_{28}H_{24}N_2O_2Na^+$: 443.1730; observed: 443.1723.

*4.4.18. (E,E)-3-Phenyl-allyl 3-(2,4,6-trimethoxyphenyl)acrylate (**41**)*

F=128 °C. ^{1}H NMR ($CDCl_3$, 300 MHz; δ ppm): 3.84 (s, 3H), 3.87 (s, 6H), 4.85 (d, *J*=6.3 Hz, 2H), 6.11 (s, 2H), 6.39 (dt, *J*=22.2, 6.3 Hz, 1H), 6.70 (d, *J*=16.0 Hz, 1H), 6.80 (d, *J*=16.2 Hz, 1H), 7.24–7.42 (m, 5H), 8.14 (d, *J*=16.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz; δ ppm): 55.3, 55.7 (2C), 64.6, 90.4 (2C), 105.9, 117.1, 124.1, 126.6 (2C), 127.8, 128.5 (2C), 133.6, 135.9, 136.6, 161.3 (2C), 162.8, 168.7. DCI/NH_3-MS: 355 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{21}H_{22}O_5Na^+$: 377.1359; observed: 377.1357.

*4.4.19. (E)-3-Phenyl-allyl 3,3-bis-(2,4,6-trimethoxy-phenyl)propanoate (**42**)*

F=92 °C. ^{1}H NMR ($CDCl_3$, 300 MHz; δ ppm): 3.13 (d, *J*=8.6 Hz, 2H), 3.66 (s, 12H), 3.74 (s, 6H), 4.68 (d, *J*=6.2 Hz, 2H), 5.23 (t, *J*=8.8 Hz, 1H), 6.05 (s, 4H), 6.16–6.21 (m, 1H), 6.51 (d, *J*=15.9 Hz, 1H), 7.23–7.33 (m, 5H). ^{13}C ($CDCl_3$, 75 MHz; δ ppm): 29.0, 37.9, 55.1 (2C), 55.7 (4C), 64.0, 91.1 (4C), 113.8 (2C), 124.2, 126.5 (2C), 127.8, 128.5 (2C), 133.0, 136.6, 158.8 (2C), 159.3 (4C), 173.3. DCI/NH_3-MS: 540 $(M+NH_4)^+$, 523 $(M+H)^+$. DCI/CH_4-HRMS calculated for $C_{30}H_{34}O_8Na^+$: 545.2146; observed: 545.2136.

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