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To be cited as: *Chem. Asian J.* 10.1002/asia.201700642

Link to VoR: http://dx.doi.org/10.1002/asia.201700642

A Journal of

ACES
Asian Chemical Editorial Society

A sister journal of Angewandte Chemie and Chemistry – A European Journal

WILEY-VCH

10.1002/asia.201700642

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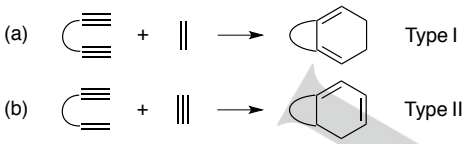
Ruthenium-Catalyzed [2 + 2 + 2] Cycloaddition of 1,6-Enynes and Unactivated Alkynes: Access to Ring-fused Cyclohexadienes

Rui Liu,[a] Laurent Giordano[a], Alphonse Tenaglia*,[a]

Abstract: The [2 + 2 + 2] *intermolecular* carbocyclization reactions between 1,6-enynes and alkynes catalyzed by Cp*Ru(cod)Cl are reported to provide bicyclohexa-1,3-dienes. The presented reaction conditions are compatible with internal and terminal alkynes and the chemo- and regioselectivity issues are controlled by the presence of substituents at the propargyl carbon center of the alkyne(s) partner(s).

Introduction

The development of synthetic strategies and methodologies based on transition-metal catalyzed transformations to construct complex molecular structures from readily available starting materials is an intensive area of research.[1] The generation of ring systems through cycloaddition reactions is representative of multiple bond- and/or stereocenters- forming synthetic methods preserving atom economy.[2] Thus, the [2 + 2 + 2] *intermolecular* carbocyclization reactions between two alkynes and one alkene conceptually represents a straightforward route to cyclohexa-1,3-dienes.[3] To this end, two main options have been devised to form Types I and II bicyclic cyclohexa-1,3-dienes from: (a) reactions between diynes and alkenes and (b) reactions between enynes and alkynes, respectively (Scheme 1). Early examples illustrating routes (a)[4] and (b)[5] were reported by Vollhardt and co-workers making use of stoichiometric cobalt-



Scheme 1. Substrate topology for cyclohexadiene synthesis through crossed intermolecular [2 + 2 + 2] carbocyclization

mediated processes. Rhodium-,[6] cobalt-[7] and ruthenium-based[8] complexes proved to be catalysts of choice among other transition-metal complexes[9] for reactions giving rise to Type I products. These reactions were however restricted to electron-deficient[6a,7b,8,9c-d] or strained[7a,7c] alkenes and, despite their use in large excess, substancial alkyne trimerization leading to aromatic compounds was observed when the alkyne functions are unsubstituted at the terminal position. This approach offered opportunities for the enantioselective construction of quaternary carbon stereocenters,[10] and DFT calculations,[11] kinetic studies as well as characterization of a rhoda(III)cyclopentadiene intermediate[12] supported similar reaction paths for the Co, Rh and Ru-catalyzed reactions.

The alternative strategy, consisting on the combination of 1,6-enynes and alkynes (Scheme 1, b), was scarcely investigated over the past decades and presented major challenges.[13] First, the competitive self-carbocyclization of enynes has long hampered the success of such an event.[6,14] To circumvent this issue, a large excess amounts of alkynes (up to 10 equiv) is often required. Second, specific structural requirements such as internal, terminal, electron-poor or unactivated alkynes and enynes featuring internal alkyne framework are often mandatory depending on the nature of the catalyst. To date, a general sketch of this simple assembly of reactants remains to establish. Recent developments accomplished by the groups of Shibata and Evans based on the use of cationic rhodium catalysts were dedicated to the enantioselective synthesis of chiral bicyclohexadienes containing one quaternary stereocenter generated at the ring-fused position.[15] Despite the ability of ruthenium complexes to catalyze a myriad of [2 + 2 + 2] cycloadditions of 1,6-diynes with alkynes[16] or electron-deficient carbon-heteroatom multiple bond compounds,[17] to the best of our knowledge, the *intermolecular* cross-carbocyclization of enynes with alkynes leading to Type II compounds has not yet been described. Herein, we have achieved the *intermolecular* carbocyclization of enynes with unactivated alkynes using a neutral ruthenium catalyst providing a ready access to cyclohexa-1,3-diene frameworks. Importantly, selectivities and regioselectivities issues can be controlled by a suitable choice of substituents at the propargyl carbon atom of one or both alkyne(s) partner(s).

Results and Discussion

We recently disclosed the ruthenium-catalyzed hydroalkynylative cyclizations of enynes.[18] These transformations generate five-membered cyclic compounds featuring a 1,5-enyne subunit through the formation of C(sp2)-H and C(sp3)-C(sp) bonds. During these studies, we observed few cases of self-coupling of enynes as a result of [2 + 2 + 2] cycloaddition, suggesting that the cross-cycloaddition between enynes and alkynes would be possible. Based on these observations, initial examination of the carbocyclization of enynes with alkynes was performed by using nitrogen tethered enynes **1a**/**1b** and but-2-yne-1,4-diyl diacetate (**2a**) in the presence of 5 mol% of Cp*Ru(cod)Cl in THF at 60°C. To our delight, the targeted bicyclodiene **3aa** was isolated from

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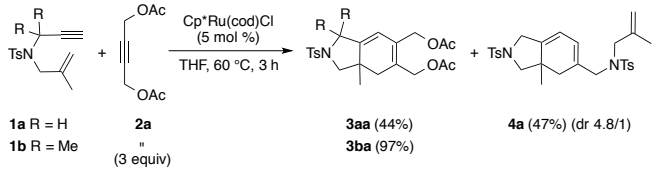
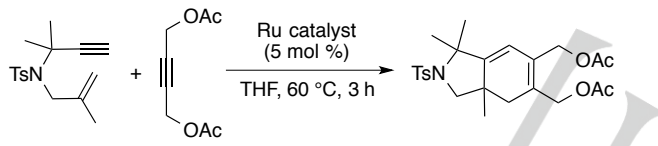
1a in 44% yield along with the cyclodimer **4a**[18] (47%) as a 4.8/1 mixture of regioisomers (the major isomer is depicted in Scheme 2). The reaction involving the enyne **1b** bearing methyl substituents at the propargyl carbon atom exclusively led to **3ba** in almost quantitative yield. At this stage, it seemed obvious that the competitive insertion of two different alkynes in the putative ruthenacyclopentene generated by the oxidative coupling of the enyne **1** could be oriented towards the cross-coupling product **3** by minimizing the non-bonded interactions between the metal ligands and the substituents at the propargyl position of alkynes.



Scheme 2. Initial studies

Having identified **1b** as the ideal enyne, the [2 + 2 + 2] cycloaddition involving **2a** was studied with a series of structurally close ruthenium complexes as catalysts. The screening results are summarized in Table 1.

Table 1. Screening of ruthenium catalysts[a]



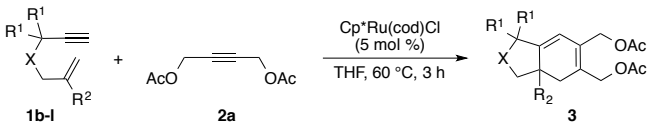
1b **2a** **3ba**

Entry	Ru catalyst	Yield [%][b]
1	$CpRu(PPh_3)_2Cl$	15[c]
2	$Cp^*Ru(PPh_3)_2Cl$	85
3	$CpRu(CH_3CN)_3]PF_6$	9[d]
4	$[Cp^*Ru(CH_3CN)_3]PF_6$	61
5	Cp*Ru(cod)Cl	97
6	Cp*Ru(cod)Cl[e]	89[f]
7	$[Cp^*Ru(CH_3CN)_3]PF_6/n-Bu_4NCl$[g]	91

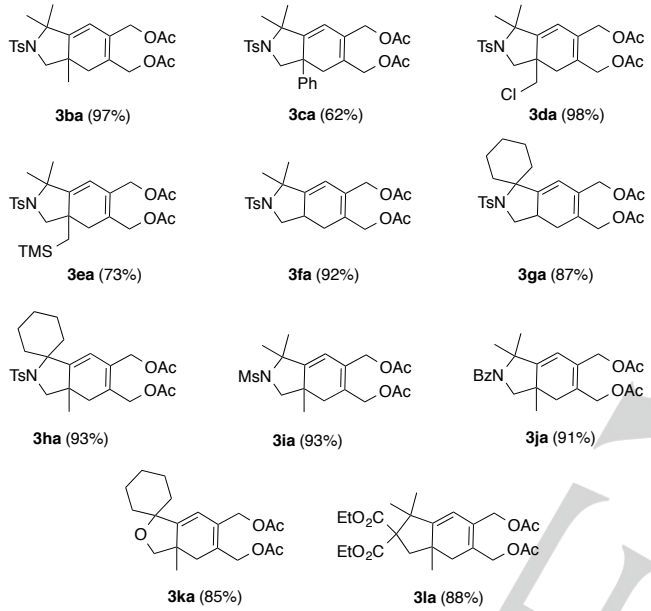
[a] Reaction conditions: [Ru] cat. (5 mol %), **1b** (1 equiv), **2a** (3 equiv), 60 °C, 3 h, c = 0.1 M. [b] Isolated yields. [c] 70% of **1b** was recovered. [d] 62% of **1b** was recovered. [e] 2.5 mol %. [f] reaction time: 24 h. [g] 10 mol % of $n-Bu_4NCl$.

These results showed that the [2 + 2 + 2] cycloaddition was best performed using electron-rich ruthenium complexes containing a pentamethylcyclopentadienyl (Cp*) ligand rather than the cyclopentadienyl (Cp) one (compare entries 1/2 and 3/4). The cationic complex such as $[Cp^*Ru(CH_3CN)_3]PF_6$ (entry 4) appeared less effective than the neutral ones (entries 2 and 5). This result was supported by the reaction carried out with a catalyst combining $[Cp^*Ru(CH_3CN)_3]PF_6$ with $n-Bu_4NCl$ to generate the neutral complex $Cp^*Ru(CH_3CN)_2Cl$[19] which restored the performance level at 91% yield (entry 7). Owing to the more labile bidentate cod ligand compared to the triphenylphosphine, Cp*Ru(cod)Cl gave the best result (entries 2 and 5). The Cp*Ru(cod)Cl catalyst loading can be lowered to 2.5 mol % to give 89% yield of **3ba**, however the reaction requires 24 h (instead of 3 h) for complete conversion (entry 6). The examination of the solvent effect of carbocyclization reaction using Cp*Ru(cod)Cl as the catalyst revealed that the polarity of solvent had no major influence on the catalyst efficiency. For instance, ethyl acetate (92%), acetone (90%), DCE (88%) or toluene (86%) can be used albeit slightly decreased yields of **3ba** were observed if compared to the reaction performed in THF (97%). However, when protic solvents such as MeOH were used, the yield of **3ba** dramatically dropped (61%). In these conditions, an *in situ* generated cationic ruthenium complex is likely to be formed and the yield of **3ba** matched with the one observed with a cationic catalyst (see entry 4). Interestingly, water as co-solvent along with THF (1/1 v/v) was not detrimental to the reaction since **3ba** was isolated in 95% yield. We found that **1b/2a** ratio of 1/3 was convenient to obtain **3ba** in high yields and to suppress the *homo*-hydroalkynylative cyclization of 1,6-enyne.[18] Indeed, carrying out the reaction with a 1/1 molar ratio **1b/2a** resulted in the formation of **3ba** with lower yield (52%). Most of the excess of **2a** is recovered unchanged and isolated by chromatography for recycling. Cyclotrimer was not detected in the crude reaction mixture by ^1H NMR.

Having the optimal conditions in hand, the scope of enyne substrates was then investigated. As shown in Scheme 3, a variety of bicyclodienes **3** was easily prepared in good to excellent yields with this simple protocol. Interestingly, the homodimerization of enynes (< 5%) was observed in few cases as judged by ^1H NMR analysis of the crude reaction mixture. First, variation of the substituent of double bond of enyne (R^2) showed that an electrophilic (**1d**) or nucleophilic (**1e**) functional group was well tolerated for the [2 + 2 + 2] cycloaddition providing the azabicycles **3da** (98%) and **3ea** (73%) respectively Interestingly the sterically demanding phenyl group, compared to the methyl group, can be introduced at the ring junction of the bicycle **3ca** although the yield dramatically dropped to 62%. Enynes **1f-g** lacking substituent R^1 were also good candidates, furnishing adducts such as **3fa** (92%) and **3ga** (87%). Variation of substitution at the propargyl carbon center of enyne (**3g-h**, **3k**) and groups in the nitrogen atom (**3h-i**) did not impact significantly the formation of the corresponding adducts. Oxygen and carbon containing tethered enynes could be employed as well thus providing oxabicycle **3ka** (85%) and bicylo[4.3.0]nonadiene **3la** (88%) respectively.

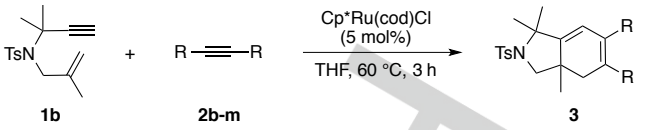


b X = NTs, R^1 = R^2 = Me
c X = NTs, R^1 = Me, R^2 = Ph
d X = NTs, R^1 = Me, R^2 = CH_2Cl
e X = NTs, R^1 = Me, R^2 = CH_2TMS
f X = NTs, R^1 = Me, R^2 = H
g X = NTs, R^1,R^1 = $(CH_2)_5$, R^2 = H
h X = NTs, R^1,R^1 = $(CH_2)_5$, R^2 = Me
i X = NMs, R^1 = R^2 = Me
j X = NBz, R^1 = R^2 = Me
k X = O, R^1,R^1 = $(CH_2)_5$, R^2 = Me
l X = $C(CO_2Et)_2$, R^1 = R^2 = Me



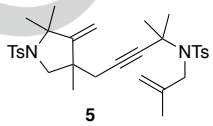
Scheme 3. Ruthenium-catalyzed [2 + 2 + 2] cycloaddition of 1,6-enynes **1b-l** and alkyne **2a**

To expand the scope of the intermolecular carbocyclization, the reaction of **1b** with various functionalized internal alkynes **2** was performed under the optimized conditions (Scheme 4). Bicyclic dienes **3bb-bk** were obtained in very good to excellent yields and protecting groups of hydroxyl group such as esters, mixed carbonates or ethers are well compatible with our conditions. Even functional groups such as free alcohol and chloride are satisfactory tolerated and unactivated alkyne such as hex-3-yne (**2k)** afforded **3bk** in an almost quantitative yield. Interestingly, diphenylacetylene **2l** allowed the formation of **3bl**, albeit in modest yield (21%), which contrasts with similar rhodium-catalyzed carbocyclization reactions.[13h] In this case, the major product (61%) was the alkynylative cyclized adduct **5**.[18] Similarly, bistrimethylsilylethyne **2m**, which is an excellent partner in cobalt-catalyzed cycloadditions,[20] did not provide the expected adduct, instead dienyne **5** was formed as the sole product in 86% yield instead.



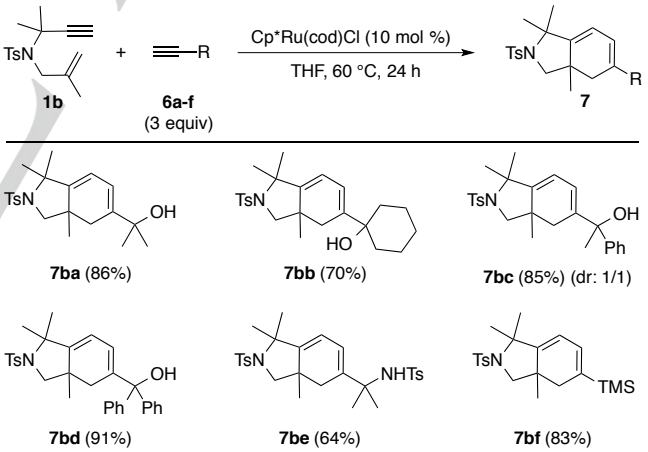
b R = CH_2OCO_2Me
c R = CH_2OMe
d R = CH_2OBn
e R = CH_2OBoc
f R = CH_2OCbz
g R = $CH_2OCOC_6H_4pNO_2$
h R = $CH_2OCOC_6H_4pOMe$
i R = CH_2OH
j R = CH_2Cl
k R = Et
l R = Ph
m R = TMS

3bb 95%
3bc 94%
3bd 92%
3be 89%
3bf 81%
3bg 83%
3bh 93%
3bi 86%
3bj 86%
3bk 98%
3bl 21%
3bm 0%



Scheme 4. Ruthenium-catalyzed [2 + 2 + 2] cycloaddition of **1b** and symmetrical alkynes **2b-m**

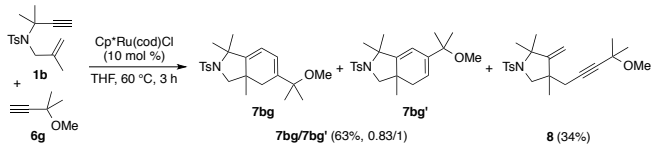
Interestingly, not only internal alkynes took part to the [2 + 2 + 2] co-cyclization reaction but also terminal alkynes participated as well under similar reaction conditions provided that a twofold catalyst charge (10 mol %) was used (Scheme 5).



Scheme 5. Regioselective ruthenium-catalyzed [2 + 2 + 2] cycloaddition of **1b** and terminal alkynes **6a-f**

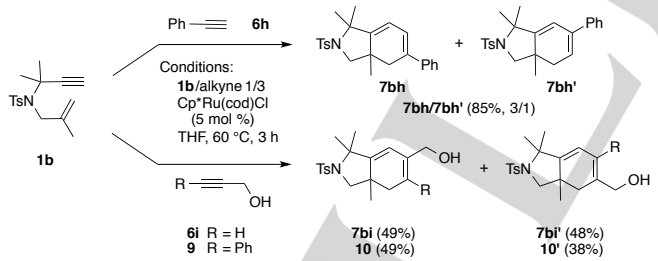
On the basis of our previous observations,[18] we thought that increasing the steric bulk at the propargyl carbon atom of **6** could impact the regioselectivity even though the selectivity of the reaction (self-coupling *vs* cross-coupling) might be eroded. Gratifyingly, tertiary propargyl alcohols **6a-d** afforded adducts **7ba-bd** as single regioisomers although the reactions required 24 hours for complete conversion. This trend was also observed with the tertiary propargyl sulfonamide **6e**[21] and alkyne **6f** featuring the bulky trimethylsilyl group which afforded **7be** (64%)

and dienylsilane **7bf**[18] (83%). We wondered on the regioselectivity observed in these reactions specially for cases involving tertiary propargyl alcohols insofar as the coordination of free hydroxyl group to ruthenium was invoked in a number of catalytic reactions involving this class of substrates.[22] Indeed, performing the reaction of 3-methoxy-3-methylbut-1-yne (**6g**)[23] with **1b** resulted in loss of both regio- and chemoselectivity thus leading to bicyclic dienes **7bg/7bg'** (63%, 0.83/1 ratio of regioisomers) and 1,5-enyne **8** (34%) arising from the alkynylative coupling reaction[18] (Scheme 6). The structure of regioisomer **7bg'** was confirmed by single crystal X-ray diffraction analysis.[24]

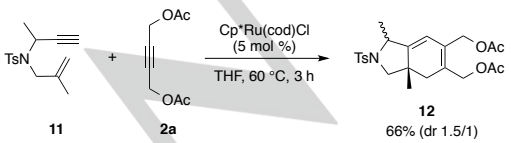


Scheme 6. Ru-catalyzed coupling of **1b** and **6g**

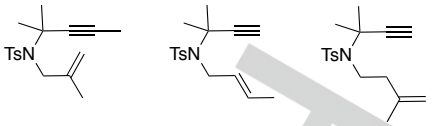
Further scope of the reaction was examined with variation of substitution either on the enyne or alkyne. Loss of regioselectivity was observed in coupling reactions involving phenylethyne **6h** and primary propargyl alcohols **6i** and **9** (Scheme 7). The pair of regioisomers **7bi/7bi'** and **10/10'** were separated by chromatography and fully characterized by spectroscopic means. Enyne **11**[25] with monosubstitution at propargyl carbon participate equally in the coupling reaction with **2a** and yielded bicyclohexadiene **12** with poor diastereoselectivity (Scheme 8). Examination of enynes featuring internal alkyne or 1,2-disubstituted alkene as well as 1,7-enyne failed to give cycloadducts with **2a**. Representative examples of such substrates are given in Scheme 9.



Scheme 7. Ruthenium-catalyzed [2 + 2 + 2] cycloaddition of **1b** with terminal arylalkyne **6h** or primary propargyl alcohols **6i** and **9**

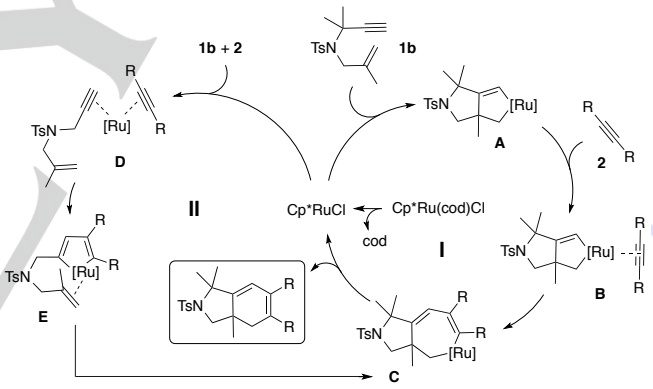


Scheme 8. Ruthenium-catalyzed [2 + 2 + 2] cycloaddition of **11** with **2a**



Scheme 9. Non-suitable enynes for ruthenium-catalyzed [2 + 2 + 2] cycloaddition

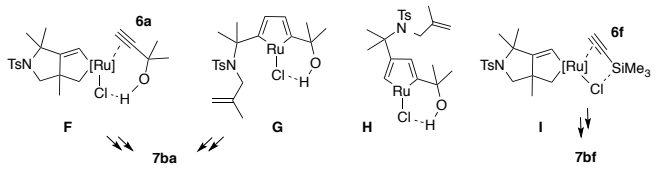
A mechanism rationale involving ruthenacycles as intermediates is depicted in Scheme 10. The catalytic cycle **I** starts with the dissociation of the weakly coordinated cod ligand from the ruthenium allowing intramolecular coordination of both triple and double bonds of enyne. Oxidative cyclization gave the bicyclic ruthenacyclopentene intermediate **A** which upon coordination of alkyne **2** to the ruthenium centre (**B**), followed by its insertion generated the ruthenacycloheptadiene **C**. Finally, reductive elimination released the bicyclic product and regenerated the active metal species. An alternative mechanism (**II**) leading to intermediate **C** might involve first intermolecular coordination of the alkyne reactants (**D**) to form ruthenacyclopentadiene **E** and subsequent insertion of the pendant olefin. At this point, it cannot be obvious to privilege one of the two pathways. However, on the basis of the hydroalkynylative cyclization of enyne **1b**,[18] achieved in the absence of **2a**, we are inclined to favor mechanism path **I**.



Scheme 10. Mechanism of the [2+2+2] intermolecular carbocyclization

The origin of the regioselectivity observed with tertiary propargylic alcohols (Scheme 5) can be ascribed to the notion of interligand interactions through hydrogen bonding of the hydroxyl proton to a chloride ligand of the RuCl fragment, recently introduced by Fürstner[26] (Scheme 11). This allowed to control the orientation of alkynol insertion within the ruthenacycle (**B** → **C**, Scheme 10). According to the mechanisms depicted in Scheme 10, intermediates **F**-**H** can be considered from the initial couplings of of enyne **1b** and **6a** but only **F** and **G** might lead to the formation of the cycloadduct **7ba** (Scheme 11). As the less congested ruthenacyclopentadiene **H**, compared to **G**, is catalytically inoperative, again we are inclined to favor the mechanism through ruthenacyclopentene. In analogy with intermediate **F**, the interaction between the chloride of [Ru]Cl

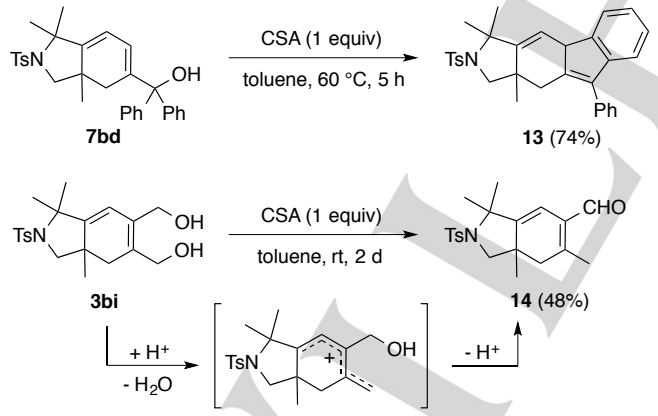
fragment with the TMS group of alkyne **6f**[26] might explain the formation of **7bf**.



Scheme 11. Possible intermediates for the regioselectivity control

To get insights on initial intermediates formed in the coupling reactions, we attempted the stoichiometric reaction of **1b** with **6b** and one molar equivalent of Cp*Ru(cod)Cl. Unfortunately, no metalacycle intermediate was detected and we observed the fast formation of **7bb** just after data aquisition by NMR.

Chemical transformations into more complex ring-fused polycycles were briefly examined (Scheme 12). Thus, the treatment of adduct **7bd** in toluene solution with camphorsulfonic acid (CSA) at 60 °C provided the tetracyclic structure **13** in 74% isolated yield through the dehydrative cyclization of a pentadienyl-like cation intermediate. Additionally, conversion of diol **3bi** to the conjugated aldehyde **14** (48%) occurred smoothly at room temperature in the presence of CSA. The location of the formyl group was ascertained by Noesy experiments. Interestingly, the formation of **14** as a single regioisomer could be rationalized on the basis of the preferred generation of a pentadienyl cation intermediate and subsequent release of a proton.



Scheme 12. Synthetic transformations of cycloadducts **3bi** and **7bd**

Conclusions

In summary, the crossed intermolecular ruthenium-catalyzed [2 + 2 + 2] carbocyclization reactions between 1,6-enynes with alkynes has been developed. This catalytic reaction provides a facile access to bicyclohexadienes containing a quaternary center at the ring junction and tolerates a wide range of functional groups. The chemo- and regioselectivity of the reaction is controlled by a suitable choice of substituents at the propargyl carbon(s) atom(s) of the reactants. The latent functions within these bicylic building blocks provide opportunities for chemical transformations into more complex and/or functionalized polycyclic molecules in a limited number of steps as illustrated with the generation of the tetracyclic structure **13** and aldehyde **14**.

Experimental Section

All reactions, unless otherwise stated, were carried out under argon atmosphere using oven-dried (120 °C) glassware. Reaction solvents were purified according to the standard procedures[27] and degased before use. All ruthenium complexes were purchased and used as received. ^{1}H NMR spectra were measured with 300 and 400 MHz spectrometers as solutions in deuterochloroform ($CDCl_3$), unless otherwise indicated. Chemicals shifts are given in parts per million (δ units) downfield from tetramethylsilane using the residual solvent signal ($CHCl_3$ 7.26) as internal standard. ^{1}H NMR information is given in the following format: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; sept, septet; m, multiplet), coupling constant(s) (*J*) in Hertz (Hz), number of protons. The prefix *app* is occasionally applied when the true signal multiplicity was unresolved and *br* indicates the signal in question broadened. ^{13}C NMR spectra are reported in ppm (δ) relative to residual $CHCl_3$ (77.4) unless otherwise noted. Ruthenium complexes and alkynes **2c**, **2i-m** were supplies from commercial sources. High-resolution mass spectra (HRMS) were performed at the "Spectropôle" of Aix-Marseille Université.

But-2-yne-1,4-diyl dimethyl bis(carbonate) (2b).[28] Methyl chloroformate (2.27 g, 24 mmol) was added dropwise to a solution of 2-butyne-1,4-diol (861 mg, 10 mmol), 4-dimethylaminopyridine (122 mg, 1 mmol) and triethylamine (4 g, 40 mmol) in dry dichloromethane (50 mL) at 0 °C. The mixture was stirred at room temperature overnight, then was washed with 10% HCl solution (50 mL), brine (30 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to afford 1.8 g (91%) of the title compound as a white semisolid. R_f (PE/Et_2O 4/6) 0.35. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77 (m, 4H), 3.81 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1 (C), 80.9 (C), 55.2 (CH_3), 55.1 (CH_2).

1,4-Bis(benzyloxy)but-2-yne (2d). [29] 2-Butyne-1,4-diol (861 mg, 10 mmol) was added dropwise to a suspension of NaH (880 mg, 22 mmol, 60 % dispersion in mineral oil) in dry THF (50 mL) at 0 °C. The mixture was stirred for 1 h, and then benzyl bromide (4.1 g, 24 mmol) was added dropwide. The mixture was warmed to rt and stirred until completion (TLC monitoring), diluted with a saturated aqueous NH_4Cl (30 mL), extracted with diethyl ether (3 x 15 mL). The combined extracts were washed with brine (30 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to afford 1.7 g (65%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/1) 0.45. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47–7.28 (m, 10H), 4.64 (s, 4H), 4.27 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6 (C), 128.6 (CH), 128.2 (CH), 128.0 (CH), 82.8 (C), 71.8 (CH_2), 57.6 (CH_2).

But-2-yne-1,4-diyl di-tert-butyl bis(carbonate) (2e). [30] A solution of di-*tert*-butyl dicarbonate (5.24 g, 24 mmol) in dichloromethane (25 mL) was added to a solution of 2-butyne-1,4-diol (861 mg, 10 mmol), 4-dimethylaminopyridine (122 mg, 1 mmol) and triethylamine (4 g, 40

mmol) in dichloromethane (50 mL). The mixture was stirred overnight, then washed with 10% HCl solution (50 mL), brine (30 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to afford 2.1 g (73%) of the title compound as a colorless oil. R_f (PE/Et_2O 1/1) 0.35. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (s, 4H), 1.47 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.9 (C), 83.0 (C), 81.1 (C), 54.6 (CH_2), 27.8 (CH_3).

Dibenzyl but-2-yne-1,4-diyl bis(carbonate) (2f). Benzyl chloroformate (4.09 g, 24 mmol) was added to a solution of 2-butyne-1,4-diol (861 mg, 10 mmol), 4-dimethylaminopyridine (122 mg, 1 mmol) and triethylamine (4 g, 40 mmol) in dichloromethane (50 mL) at 0 °C. The resulting mixture was stirred overnight at room temperature, washed with 10% HCl solution (50 mL), brine (30 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to afford 2.4 g (69%) of the title compound as a white solid, mp 74–75 °C. R_f (PE/Et_2O 3/2) 0.45. IR (neat) ν 3034, 2955, 1744, 1497, 1389, 1223, 1153, 932, 910, 751, 694, 576 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.31 (m, 10H), 5.19 (s, 4H), 4.78 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.8 (C), 135.2 (C), 128.9 (CH), 128.9 (CH), 128.6 (CH), 81.3 (C), 70.4 (CH_2), 55.7 (CH_2). HRMS (ESI-MS) calcd. for $C_{20}H_{22}NO_6^+$ ($[M+NH_4]^+$): 372.1442, found 372.1442.

General Procedure for Acylation of 2-butyne-1,4-diol (A). Acyl chloride (24 mmol) was added dropwise to a solution of 2-butyne-1,4-diol (861 mg, 10 mmol), 4-dimethylaminopyridine (122 mg, 1 mmol) and triethylamine (4 g, 40 mmol) in dry dichloromethane (50 mL) at 0 °C. The resulting mixture was stirred overnight at room temperature, washed with 10% HCl solution (50 mL), brine (30 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel.

But-2-yne-1,4-diyl bis(4-nitrobenzoate) (2g). The above procedure afforded 2.8 g (72%) of the title compound as a white solid, mp 148–149 °C. R_f (Et_2O) 0.40. IR (neat) ν 3113, 2913, 1729, 1522, 1344, 1262, 1094, 944, 878, 718 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.9 Hz, 4H), 8.25 (d, J = 9.0 Hz, 4H), 5.05 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2 (C), 151.1 (C), 135.0 (C), 131.3 (CH), 123.9 (CH), 81.3 (C), 53.6 (CH_2). HRMS (ESI-MS) calcd. for $C_{18}H_{16}N_3O_8^+$ ($[M+NH_4]^+$): 402.0932, found 402.0928.

But-2-yne-1,4-diyl bis(4-methoxybenzoate) (2h). The above procedure afforded 2.9 g (82%) of the title compound as a white solid, mp 117–118 °C. R_f (PE/AcOEt 4/1) 0.35. IR (neat) ν 2933, 2846, 1701, 1606, 1512, 1444, 1310, 1269, 1260, 1161, 1101, 842, 765, 693, 615 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 4H), 6.92 (d, J = 8.4 Hz, 4H), 4.96 (s, 4H), 3.86 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9 (C), 163.0 (C), 131.3 (CH), 121.2 (C), 113.1 (CH), 80.4 (C), 54.8 (CH_3), 51.7 (CH_2). HRMS (ESI-MS) calcd. for $C_{20}H_{19}O_6^+$ ($[M+H]^+$): 355.1176, found 355.1172.

General Procedure of the Ru(II)-catalyzed Coupling Reaction of Enynes and Alkynes (B). A solution of 1, 6-enyne (0.2 mmol) and alkyne (0.6 mmol) in THF (0.5 mL) was added to a solution of Cp*Ru(cod)Cl (3.80 mg, 0.01 mmol) in THF (0.5 mL). The mixture was stirred at 60 °C until completion of the reaction (TLC monitoring), cooled to room temperature, filtered over celite, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel.

(3a-methyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene)diacetate (3aa). General Procedure B afforded 38.1 mg (44%) of the title compound as colorless oil. R_f (PE/Et_2O 1/1) 0.30. IR (neat) ν 2960, 2862, 1734, 1376, 1221, 1161, 1092, 1021, 817, 711, 664, 601, 549 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 7.9 Hz, 2H), 5.70 (t, J = 2.1 Hz, 1H), 4.77 (d, J = 12.5 Hz, 1H), 4.70 (d, J = 12.4 Hz, 1H), 4.62 (d, J = 12.4 Hz, 1H), 4.54 (d, J = 12.5 Hz, 1H), 4.20 (dd, J = 15.6, 2.1 Hz, 1H), 3.75 (d, J = 15.6 Hz, 1H), 3.54 (d, J = 9.0 Hz, 1H), 2.78 (d, J = 9.0 Hz, 1H), 2.43 (s, 3H), 2.20 (s, 2H), 2.03 (s, 3H), 2.02 (s, 3H), 0.99 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1 (C), 144.1 (C), 144.0 (C), 133.2 (C), 130.1 (CH), 129.2 (C), 128.7 (C), 128.0 (CH), 116.9 (CH), 63.4 (CH_2), 62.1 (CH_2), 62.0 (CH_2), 50.2 (CH_2), 41.5 (C), 37.6 (CH_2), 21.9 (CH_3), 21.6 (CH_3), 21.2 (CH_3), 21.1 (CH_3). HRMS (ESI-MS) calcd. for $C_{22}H_{28}NO_6S^+$ ($[M+H]^+$): 434.1632, found 434.1627.

(1,1,3a-Trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) diacetate (3ba). General Procedure B afforded 89.5 mg (97%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/6) 0.35. IR (neat) ν 3055, 2979, 2254, 1733, 1353, 1264, 1091, 907, 727 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.9 Hz, 2H), 5.65 (s, 1H), 4.80 (d, J = 12.5 Hz, 1H), 4.74 (d, J = 12.4 Hz, 1H), 4.66 (d, J = 12.4 Hz, 1H), 4.57 (d, J = 12.5 Hz, 1H), 3.40 (d, J = 9.2 Hz, 1H), 3.01 (d, J = 9.2 Hz, 1H), 2.41 (s, 3H), 2.20–2.14 (m, 2H), 2.04 (s 3H), 2.03 (s, 3H), 1.69 (s, 3H), 1.46 (s, 3H), 0.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (C), 156.6 (C), 143.2 (C), 138.2 (C), 129.6 (CH), 129.4 (C), 128.7 (C), 127.7 (CH), 115.3 (CH), 67.3 (C), 63.3 (CH_2), 62.1 (CH_2), 60.8 (CH_2), 39.5 (C), 38.4 (CH_2), 31.1 (CH_3), 28.4 (CH_3), 21.9 (CH_3), 21.7 (CH_3), 21.1 (CH_3), 20.9 (CH_3). HRMS (ESI-MS) calcd. for $C_{24}H_{32}NO_6S^+$ ($[M+H]^+$): 462.1945, found 462.1947.

(1,1-Dimethyl-3a-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) diacetate (3ca). General Procedure B afforded 64.9 mg (62%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/6) 0.43. IR (neat) ν 2932, 2868, 2252, 1734, 1218, 1090, 1023, 728, 581 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.3 Hz, 2H), 7.19–7.11 (m, 5H), 6.99 (d, J = 8.0 Hz, 2H), 6.11 (s, 1H), 4.79 (d, J = 12.4 Hz, 1H), 4.69 (d, J = 12.4 Hz, 1H), 4.56 (d, J = 12.5 Hz, 1H), 4.31 (d, J = 12.5 Hz, 1H), 4.16 (d, J = 10.0 Hz, 1H), 3.49 (d, J = 10.0 Hz, 1H), 2.57 (d, J = 16.1 Hz, 1H), 2.52 (d, J = 16.1 Hz, 1H), 2.32 (s, 3H), 2.05 (s, 3H), 1.64 (s, 3H), 1.62 (s, 3H), 1.53 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (C), 170.5 (C), 152.7 (C), 142.8 (C), 140.7 (C), 138.6 (C), 130.6 (C), 129.3 (CH), 129.1 (C), 128.3 (CH), 127.1 (CH), 127.1 (CH), 127.0 (CH), 119.4 (CH), 66.8 (C), 62.6 (CH_2), 61.9 (CH_2), 61.4 (CH_2), 48.0 (C), 40.4 (CH_2), 29.1 (CH_3), 29.0 (CH_3), 21.6 (CH_3), 21.1 (CH_3), 20.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{29}H_{34}NO_6S^+$ ($[M+H]^+$): 524.2101, found 524.2101.

(3a-(Chloromethyl)-1,1-dimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) diacetate (3da). General Procedure B afforded 97.2 mg (98%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/6) 0.35. IR (neat) ν 2975, 2871, 1735, 1364, 1220, 1150, 1112, 1089, 991, 728, 576 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.81 (s, 1H), 4.83 (d, J = 12.7 Hz, 1H), 4.76 (dd, J = 12.5, 1.7 Hz, 1H), 4.67 (d, J = 12.5 Hz, 1H), 4.51 (d, J = 12.7 Hz, 1H), 3.91 (d, J = 10.2 Hz, 1H), 3.22 (dd, J = 10.9, 1.6 Hz, 1H), 3.17 (d, J = 10.9 Hz, 1H), 2.97 (dd, J = 10.2, 1.6 Hz, 1H), 2.78 (d, J = 17.0 Hz, 1H), 2.41 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.01 (br s, 1H), 1.61 (s, 3H), 1.49 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (C), 170.9 (C), 152.3 (C), 143.5 (C), 138.4 (C), 129.8 (CH), 129.6 (C), 129.5 (C), 127.4 (CH), 118.8 (CH), 66.9 (C), 62.6 (CH_2), 61.9 (CH_2), 56.0 (CH_2), 44.7 (C), 44.2 (CH_2), 32.4 (CH_2), 30.3 (CH_3), 28.9 (CH_3), 21.7 (CH_3), 21.2 (CH_3), 21.1 (CH_3). HRMS (ESI-MS) calcd. for $C24H_{31}ClNO6S^+$ ($[M+H]^+$): 496.1555, found 496.1553.

(1,1-Dimethyl-2-tosyl-3a-((trimethylsilyl)methyl)-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) diacetate (3ea). General Procedure B afforded 77.9 mg (73%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/6) 0.38. IR (neat) ν 2976, 2869, 2257, 1733, 1364, 1221, 1141, 1023, 959, 729 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.59 (s, 1H), 4.71–4.69 (m, 4H), 3.45 (d, J = 9.3 Hz, 1H), 2.94 (dd, J = 9.3, 2.0 Hz, 1H), 2.40 (s, 3H), 2.32

(d, *J* = 16.9 Hz, 1H), 2.20 (d, *J* = 16.9 Hz, 1H), 2.04 (s, 3H), 2.03 (s, 3H), 1.76 (s, 3H), 1.47 (s, 3H), 0.88 (dd, *J* = 14.9, 2.0 Hz, 1H), 0.72 (dd, *J* = 14.9, 1.3 Hz, 1H), -0.12 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (C), 171.0 (C), 158.5 (C), 143.4 (C), 138.1 (C), 130.1 (C), 129.7 (CH), 128.4 (C), 127.9 (CH), 114.3 (CH), 67.0 (C), 63.7 (CH_2), 62.3 (CH_2), 59.8 (CH_2), 41.9 (C), 38.1 (CH_2), 31.4 (CH_3), 28.7 (CH_3), 23.1 (CH_2), 21.7 (CH_3), 21.1 (CH_3). 0.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{27}H_{40}NO_6SSi^+$ ($[M+H]^+$): 534.2340, found 534.2339.

(1,1-Dimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) diacetate (3fa). General Procedure B afforded 82.3 mg (92%) of the title compound as a colorless oil. R_f (PE/Et_2O 2/3) 0.37. IR (neat) ν 2995, 2938, 1717, 1410, 1229, 1159, 1086, 723, 589 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 5.69 (d, *J* = 2.7 Hz, 1H), 4.79 (d, *J* = 12.6 Hz, 1H), 4.72 (dd, *J* = 12.4, 1.4 Hz, 1H), 4.65 (d, *J* = 12.4 Hz, 1H), 4.57 (d, *J* = 12.6 Hz, 1H), 3.82 (t, *J* = 7.8 Hz, 1H), 3.01–2.88 (m, 2H), 2.41 (s, 4H), 2.04 (s, 6H), 2.02 – 1.99 (m, 1H), 1.59 (s, 3H), 1.53 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (C), 171.0 (C), 151.8 (C), 143.3 (C), 138.3 (C), 130.4 (C), 129.7 (CH), 129.6 (C), 127.6 (CH), 115.8 (CH), 67.3 (C), 63.2 (CH_2), 62.2 (CH_2), 54.0 (CH_2), 36.0 (CH), 30.6 (CH_2), 30.5 (CH_3), 27.3 (CH_3), 21.7 (CH_3), 21.1 (CH_3). HRMS (ESI-MS) calcd. for $C_{23}H_{29}NO_6SNa^+$ ($[M+Na]^+$): 470.1608, found 470.1607.

(2'-Tosyl-2',3',3a',4'-tetrahydrospiro[cyclohexane-1,1'-isoindole]-5',6'-diyl)bis(methylene) diacetate (3ga). General Procedure B afforded 84.8 mg (87%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/6) 0.33. IR (neat) ν 2925, 2869, 1736, 1376, 1221, 1155, 1044, 663, 588 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.07 (s, 1H), 4.74–4.49 (m, 4H), 3.70 (t, *J* = 8.1 Hz, 1H), 2.95–2.77 (m, 2H), 2.55–2.45 (td, *J* = 12.5, 4.6 Hz, 2H), 2.34 (s, 3H), 2.30–2.25 (m, 1H), 1.98 (s, 3H), 1.97 (s, 3H), 1.80–1.75 (m, 1H), 1.67–1.41 (m, 7H), 1.35–1.19 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1 (C), 149.6 (C), 143.1 (C), 139.2 (C), 130.6 (C), 129.7 (CH), 129.5 (C), 127.5 (CH), 118.5 (CH), 70.9 (C), 63.2 (CH_2), 62.5 (CH_2), 53.8 (CH_2), 36.7 (CH), 36.1 (CH_2), 35.2 (CH_2), 30.7 (CH_2), 24.7 (CH_2), 22.9 (CH_2), 21.8 (CH_3), 21.2 (CH_3), 21.2 (CH_3). HRMS (ESI-MS) calcd. for $C_{26}H_{37}N_2O_6S^+$ ($[M+NH_4]^+$): 505.2367, found 505.2368.

(3a'-Methyl-2'-tosyl-2',3',3a',4'-tetrahydrospiro[cyclohexane-1,1'-isoindole]-5',6'-diyl)bis(methylene) diacetate (3ha). General Procedure B afforded 93.3 mg (93%) of the title compound as a colorless oil. R_f (PE/Et_2O 2/3) 0.33. IR (neat) ν 2931, 2872, 2255, 1733, 1225, 1154, 905, 724, 603 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 6.10 (s, 1H), 4.79 (d, *J* = 12.5 Hz, 1H), 4.74 (d, *J* = 12.4 Hz, 1H), 4.69 (d, *J* = 12.4 Hz, 1H), 4.56 (d, *J* = 12.5 Hz, 1H), 3.26 (d, *J* = 9.3 Hz, 1H), 3.10 (d, *J* = 9.3 Hz, 1H), 2.87–2.79 (m, 1H), 2.47–2.42 (m, 1H), 2.40 (s, 3H), 2.22 (d, *J* = 16.3 Hz, 1H), 2.10 (d, *J* = 16.3 Hz, 1H), 2.03 (s, 3H), 2.02 (s, 3H), 1.85 (d, *J* = 13.0 Hz, 1H), 1.74–1.59 (m, 6H), 1.42–1.33 (m, 1H), 0.86 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (C), 170.9 (C), 154.4 (C), 143.1 (C), 138.8 (C), 129.6 (C), 129.6 (CH), 128.6 (C), 127.5 (CH), 117.9 (CH), 70.8 (C), 63.2 (CH_2), 62.4 (CH_2), 60.3 (CH_2), 40.2 (C), 38.3 (CH_2), 36.3 (CH_2), 36.1 (CH_2), 24.5 (CH_2), 22.7 (CH_2), 22.2 (CH_2), 22.1 (CH_3), 21.7 (CH_3), 21.1 (CH_3), 20.9 (CH_3). HRMS (ESI-MS) calcd. for $C_{27}H_{36}NO_6S^+$ ($[M+H]^+$): 502.2258, found 502.2258.

(1,1,3a-Trimethyl-2-(methylsulfonyl)-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) diacetate (3ia). General Procedure B afforded 71.7 mg (93%) of the title compound as a colorless oil. R_f (PE/Et_2O 3/7) 0.35. IR (neat) ν 2998, 2819, 2254, 1761, 1395, 1210, 1159, 1034, 719, 537 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (s, 1H), 4.83 (d, *J* = 12.5 Hz, 1H), 4.78 (d, *J* = 12.4 Hz, 1H), 4.69 (d, *J* = 12.4 Hz, 1H), 4.60 (d, *J* = 12.5 Hz, 1H), 3.53 (d, *J* = 9.2 Hz, 1H), 3.10 (d, *J* = 9.2 Hz, 1H), 2.91 (s, 3H), 2.29 (d, *J* = 16.4 Hz, 1H), 2.24 (d, *J* = 16.4 Hz, 1H), 2.05 (s, 3H), 2.05 (s, 3H), 1.64 (s, 3H), 1.52 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (C), 156.2 (C), 129.4 (C), 128.8 (C), 115.7 (CH), 66.6 (C), 63.3 (CH_2), 62.1 (CH_2), 61.1 (CH_2), 40.3 (CH_3), 39.4 (C), 38.4 (CH_2), 30.9 (CH_3), 28.2 (CH_3), 22.2 (CH_3), 21.1 (CH_3), 21.0 (CH_3). HRMS (ESI-MS) calcd. for $C_{18}H_{31}N_2O_6S^+$ ($[M+NH_4]^+$): 403.1897, found 403.1897.

(2-Benzoyl-1,1,3a-trimethyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) diacetate (3ja). General Procedure B afforded 74.9 mg (91%) of the title compound as a colorless oil. R_f (PE/Et_2O 1/1) 0.36. IR (neat) ν 2974, 2891, 2252, 1734, 1628, 1445, 1225, 904, 723, 647 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 5H), 5.76 (s, 1H), 4.81 (d, *J* = 12.5 Hz, 1H), 4.78 (d, *J* = 12.4 Hz, 1H), 4.69 (d, *J* = 12.4 Hz, 1H), 4.58 (d *J* = 12.5 Hz, 1H), 3.49–3.44 (m, 1H), 3.20 (d, *J* = 10.7 Hz, 1H), 2.23 (d, *J* = 16.4 Hz, 1H), 2.13 (d, *J* = 16.4 Hz, 1H), 2.06 (s, 3H), 2.02 (s, 3H), 1.83 (s, 3H), 1.64 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (C), 170.9 (C), 170.2 (C), 157.1 (C), 138.9 (C), 129.4 (C), 129.3 (CH), 128.6 (CH), 128.2 (C), 126.3 (CH), 115.1 (CH), 64.6 (C), 63.3 (CH_2), 62.9 (CH_2) 62.1 (CH_2), 39.7 (C), 38.4 (CH_2), 29.2 (CH_3), 26.1 (CH_3), 22.1 (CH_3), 21.0 (CH_3), 20.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{24}H_{30}NO_5^+$ ($[M+H]^+$): 412.2118, found 412.2118.

(3a'-Methyl-3a',4'-dihydro-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-5',6'-diyl)bis(methylene) diacetate (3ka). General Procedure B afforded 59.2 mg (85%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/1) 0.45. IR (neat) ν 2932, 2855, 2255, 1734, 1375, 1221, 1021, 959, 727 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (s, 1H), 4.83 (d, *J* = 12.4 Hz, 1H), 4.79 (dd, *J* = 12.3, 1.3 Hz, 1H), 4.70 (d, *J* = 12.3 Hz, 1H), 4.61 (d, *J* = 12.4 Hz, 1H), 3.83 (d, *J* = 8.3 Hz, 1H), 3.51 (d, *J* = 8.3 Hz, 1H), 2.25 (d, *J* = 16.4 Hz, 1H), 2.16 (d, *J* = 16.4 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.80–1.51 (m, 8H), 1.30–1.21 (m, 2H), 1.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7 (C), 170.7 (C), 157.3 (C), 129.5 (C), 128.1 (C), 113.6 (CH), 82.3 (C), 77.8 (CH_2), 63.2 (CH_2), 62.0 (CH_2), 42.1 (C), 38.4 (CH_2), 37.1 (CH_2), 35.5 (CH_2), 25.2 (CH_2), 22.4 (CH_2), 22.1 (CH_2), 21.2 (CH_3), 20.8 (CH_3), 20.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{20}H_{32}NO_5^+$ ($[M+NH_4]^+$): 366.2275, found 366.2275.

Diethyl 5,6-bis(acetoxymethyl)-1,1,3a-trimethyl-1,3,3a,4-tetrahydro-2H-indene-2, 2-dicarboxylate (3la). General Procedure B afforded 79.3 mg (88%) of the title compound as a colorless oil. R_f (PE/Et_2O 3/1) 0.40. IR (neat) ν 2913, 2900, 1796, 1431, 1185,1025, 997, 835, 775, 564 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (s, 1H), 4.81 (d, *J* = 12.5 Hz, 1H), 4.75–4.68 (m, 2H), 4.50 (d, *J* = 12.5 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.10 (qd, *J* = 7.2, 1.5 Hz, 2H), 2.60–2.54 (m, 2H), 2.05 (s, 3H), 2.04 (s, 3H), 2.03 (d, *J* = 16.4 Hz, 1H), 1.98 (d, *J* = 16.4 Hz, 1H), 1.38 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.22–1.13 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8 (C), 171.19 (C), 171.15 (C), 170.7 (C), 158.5 (C), 129.8 (C), 129.6 (C), 114.8 (CH), 68.0 (C), 63.5 (CH_2), 62.4 (CH_2), 61.3 (CH_2), 61.2 (CH_2), 48.3 (C), 44.3 (CH_2), 41.6 (CH_2), 38.8 (C), 26.5 (CH_3), 25.9 (CH_3), 23.2 (CH_3), 21.3 (CH_3), 21.1 (CH_3), 14.4 (CH_3), 14.2 (CH_3). HRMS (ESI-MS) calcd. for $C_{24}H_{38}NO_8^+$ ($[M+NH_4]^+$): 468.2592, found 468.2593.

Dimethyl ((1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl) bis(methylene)) bis(carbonate) (3bb). General Procedure B afforded 93.8 mg (95%) of the title compound as a colorless oil. R_f (PE/Et_2O 1/1) 0.30. IR (neat) ν 2998, 2890, 1710, 1495, 1220, 1106, 895, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 5.69 (s, 1H), 4.88 (d, *J* = 12.5 Hz, 1H), 4.85 (d, *J* = 12.3 Hz, 1H), 4.73 (d, *J* = 12.3 Hz, 1H), 4.63 (d, *J* = 12.5 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.40 (d, *J* = 9.2 Hz, 1H), 3.00 (d, *J* = 9.2 Hz, 1H), 2.40 (s, 3H), 2.23 (s, 2H), 1.68 (s, 3H), 1.45 (s, 3H), 0.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2 (C), 155.9 (C), 155.8 (C), 143.3 (C), 138.2 (C), 129.7 (CH), 129.5 (C), 128.7 (C), 127.7 (CH), 115.0 (CH), 67.4 (C), 66.6 (CH_2), 65.4 (CH_2), 60.7 (CH_2), 55.2 (CH_3), 39.4 (C), 38.2 (CH_2), 31.0

(CH_3), 28.4 (CH_3), 21.9 (CH_3), 21.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{24}H_{32}NO_8S^+$ ($[M+H]^+$): 494.1843, found 494.1842.

5,6-Bis(methoxymethyl)-1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole (3bc). General Procedure B afforded 76.2 mg (94%) of the title compound as a colorless oil. R_f (PE/Et2O 4/6) 0.37. IR (neat) ν 3441, 2926, 2819, 1726, 1598, 1379, 1156, 1089, 663, 549 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.2 Hz, 2H), 5.71 (s, 1H), 4.05 (d, J = 12.0 Hz, 1H), 4.04 (dd, J = 11.6, 1.7 Hz, 1H), 3.98 (d, J = 11.6 Hz, 1H), 3.92 (d, J = 12.0 Hz, 1H), 3.40 (d, J = 9.1 Hz, 1H), 3.27 (s, 3H), 3.26 (s, 3H), 3.01 (d, J = 9.1 Hz, 1H), 2.41 (s, 3H), 2.27 (d, J = 16.4 Hz, 1H), 2.24 (d, J = 16.4 Hz, 1H), 1.70 (s, 3H), 1.46 (s, 3H), 1.00 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3 (C), 143.2 (C), 138.4 (C), 130.0 (C), 129.9 (C), 129.7 (CH), 127.7 (CH), 115.7 (CH), 71.1 (CH_2), 70.1 (CH_2), 67.5 (C), 61.1 (CH_2), 58.1 (CH_2), 39.5 (C), 38.3 (CH_2), 31.1 (CH_3), 28.6 (CH_3), 22.4 (CH_3), 21.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{22}H_{32}NO_4S^+$ ($[M+H]^+$): 406.2047, found 406.2047.

5,6-Bis((benzyloxy)methyl)-1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole (3bd). General Procedure B afforded 103 mg (92%) of the title compound as a colorless oil. R_f (PE/Et_2O 6/4) 0.45. IR (neat) ν 2919, 2893, 2230, 1317, 1153, 1094, 1039, 721, 544 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2H), 7.36 – 7.26 (m, 12H), 5.76 (s, 1H), 4.43 (dd, J = 11.8, 5.0 Hz, 2H), 4.37 (dd, J = 11.8, 2.7 Hz, 2H), 4.11 (d, J = 11.8 Hz, 1H), 4.09 (dd, J = 11.5, 1.5 Hz, 1H), 4.03 (d, J = 11.5 Hz, 1H), 3.98 (d, J = 11.8 Hz, 1H), 3.42 (d, J = 9.1 Hz, 1H), 3.03 (d, J = 9.1 Hz, 1H), 2.42 (s, 3H), 2.34 (d, J = 16.5 Hz, 1H), 2.20 (d, J = 16.5 Hz, 1H), 1.72 (s, 3H), 1.47 (s, 3H), 1.04 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3 (C), 143.2 (C), 138.6 (C), 138.4 (C), 138.4 (C), 130.2 (C), 130.0 (C), 129.7 (CH), 128.7 (CH), 128.7 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.7 (CH), 115.9 (CH), 72.2 (CH_2), 72.1 (CH_2), 68.7 (CH_2), 67.5 (CH_2), 67.5 (C), 61.1 (CH_2), 39.6 (C), 38.5 (CH_2), 31.2 (CH_3), 28.6 (CH_3), 22.5 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{34}H_{43}N_2O_4S^+$ ($[M+NH_4]^+$): 575.2938, found 575.2938.

Di-tert-butyl ((1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl) bis(methylene)) bis(carbonate) (3be). General Procedure B afforded 103 mg (89%) of the title compound as a colorless oil. R_f(PE/Et_2O 7/3) 0.48. IR (neat) ν 2980, 2259, 1737, 1270, 1149, 906, 725 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 5.68 (s, 1H), 4.81 (d, J = 12.5 Hz, 1H), 4.77 (d, J = 12.3 Hz, 1H), 4.65 (d, J = 12.3 Hz, 1H), 4.53 (d, J = 12.5 Hz, 1H), 3.38 (d, J = 9.2 Hz, 1H), 2.99 (d, J = 9.2 Hz, 1H), 2.41 (s, 3H), 2.24 (d, J = 16.7 Hz, 1H), 2.19 (d, J = 16.7 Hz, 1H), 1.68 (s, 3H), 1.46 (s, 9H), 1.44 (s, 12H), 0.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7 (C), 153.7 (C), 153.7 (C), 143.3 (C), 138.3 (C), 129.7 (CH), 129.5 (C), 128.8 (C), 127.7 (CH), 115.3 (CH), 82.6 (C), 82.5 (C), 67.5 (C), 65.7 (CH_2), 64.5 (CH_2), 60.8 (CH_2), 39.5 (C), 38.2 (CH_2), 31.1 (CH_3), 28.5 (CH_3), 28.1 (CH_3), 21.9 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{30}H_{47}N_2O_8S^+$ ($[M+NH_4]^+$): 595.3048, found 595.3052.

Dibenzyl ((1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis (methylene)) bis(carbonate) (3bf). General Procedure B afforded 112 mg (87%) of the title compound as a white waxy oil. R_f (PE/Et_2O 1/1) 0.53. IR (neat) ν 3086, 2916, 2230, 1711, 1236, 1244, 945, 726, 684 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 7.3 Hz, 2H), 7.45–7.26 (m, 12H), 5.69 (s, 1H), 5.15 (s, 4H), 4.91 (d, J = 12.4 Hz, 1H), 4.87 (d, J = 12.2 Hz, 1H), 4.77 (d, J = 12.2 Hz, 1H), 4.66 (d, J = 12.4 Hz, 1H), 3.40 (d, J = 8.7 Hz, 1H), 3.01 (d, J = 8.7 Hz, 1H), 2.44 (s, 3H), 2.22 (s, 2H), 1.68 (s, 3H), 1.46 (s, 3H), 0.92 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2 (C), 155.3 (C), 155.2 (C), 143.2 (C), 138.2 (C), 135.4 (C), 129.7 (CH), 129.5 (C), 128.9 (CH), 128.6 (C), 128.6 (CH), 127.7 (CH), 115.0 (CH), 70.0 (CH_2), 67.4 (C), 66.7 (CH_2), 65.5 (CH_2), 60.7 (CH_2), 39.4 (C), 38.1 (CH_2), 31.0 (CH_3), 28.4 (CH_3), 21.8 (CH_3), 21.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{36}H_{43}N_2O_8S^+$ ($[M+NH_4]^+$): 663.2735, found 663.2734.

(1,1,3a-Trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) bis(4-nitrobenzoate) (3bg). General Procedure B afforded 112 mg (83%) of the title compound as a white solid. Mp 156-158 °C, R_f(PE/Et_2O 4/6) 0.50. IR (neat) ν 3639, 3020, 2257, 1755, 1558, 1298, 1178, 1091, 862, 731, 647 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, J = 8.7 Hz, 4H), 8.14 (d, J = 8.7 Hz, 4H), 7.74 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 7.2 Hz, 2H), 5.78 (s, 1H), 5.22 (d, J = 12.5 Hz, 1H), 5.14 (d, J = 12.5 Hz, 1H), 5.07 (d, J = 12.5 Hz, 1H), 4.94 (d, J = 12.5 Hz, 1H), 3.42 (d, J = 9.2 Hz, 1H), 3.06 (d, J = 9.2 Hz, 1H), 2.41 (s, 3H), 2.35 (d, J = 6.4 Hz, 2H), 1.70 (s, 3H), 1.51 (s, 3H), 0.99 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8 (C), 164.7 (C), 157.9 (C), 151.0 (C), 151.0 (C), 143.5 (C), 138.2 (C), 135.5 (C), 135.5 (C), 131.0 (CH), 131.0 (CH), 129.98 (C), 129.8 (CH) 128.8 (C), 127.7 (CH), 124.0 (CH), 123.9 (CH), 115.2 (CH), 67.4 (C), 64.8 (CH_2), 63.6 (CH_2), 60.7 (CH_2), 39.7 (C), 38.6 (CH_2), 31.2 (CH_3), 28.5 (CH_3), 22.1 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{34}H_{34}N_3O_{10}S^+$ ($[M+H]^+$): 676.1959, found 676.1959.

(1,1,3a-Trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) bis(4-methoxybenzoate) (3bh). General Procedure B afforded 120 mg (93%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/6) 0.32. IR (neat) ν 2967, 2865, 1701, 1604, 1510, 1249, 1164, 1087, 815, 608, 549 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 9.0 Hz, 4H), 7.73 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 1.7 Hz, 2H), 6.86 (d, J = 1.7 Hz, 2H), 5.77 (s, 1H), 5.10 (d, J = 12.5 Hz, 1H), 5.03 (d, J = 12.4 Hz, 1H), 4.97 (d, J = 12.4 Hz, 1H), 4.85 (d J = 12.5 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.40 (d, J = 9.2 Hz, 1H), 3.03 (d, J = 9.2 Hz, 1H), 2.40 (s, 3H), 2.31 (s, 2H), 1.69 (s, 3H), 1.48 (s, 3H), 1.00 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3 (C2), 163.8 (C), 163.7 (C), 156.6 (C), 143.2 (C), 138.2 (C), 131.9 (CH), 131.9 (CH), 129.9 (C), 129.7 (CH), 129.2 (C), 127.7 (CH), 122.7 (C), 122.6 (C), 115.6 (CH), 114.0 (CH), 113.9 (CH), 67.4 (C), 63.7 (CH_2), 62.6 (CH_2), 60.8 (CH_2), 55.7 (CH_3), 39.6 (C), 38.6 (CH_2), 31.2 (CH_3), 28.5 (CH_3), 22.0 (CH_3), 21.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{36}H_{43}N_2O_8S^+$ ($[M+NH_4]^+$): 663.2735, found 663.2739.

(1,1,3a-Trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)dimethanol (3bi). General Procedure B afforded 64.9 mg (86%) of the title compound as a colorless oil. R_f (AcOEt) 0.36. IR (neat) ν 3516, 3086, 2965, 1680, 1236, 1185, 1055, 980, 796, 663, 544 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.69 (s, 1H), 4.26–4.08 (m, 4H), 3.38 (d, J = 9.1 Hz, 1H), 3.00 (d, J = 9.1 Hz, 1H), 2.41 (br s, 5H, CH_3 + 2OH), 2.26 (d, J = 16.6 Hz, 1H), 2.20 (d, J = 16.6 Hz, 1H), 1.68 (s, 3H), 1.45 (s, 3H), 0.98 (s, 3H). ^{13}C NMR (75 MHz $CDCl_3$) δ 155.6 (C), 143.4 (C), 138.3 (C), 131.8 (C), 129.8 (CH), 127.7 (CH), 116.3 (CH), 67.5 (C), 62.4 (CH_2), 61.3 (CH_2), 61.1 (CH_2), 39.6 (C), 39.1 (CH_2), 31.2 (CH_3), 28.6 (CH_3), 22.1 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{20}H_{27}NO_4SNa^+$ ($[M+Na]^+$): 400.1553, found 400.1553.

5,6-Bis(chloromethyl)-1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole (3bj). General Procedure B afforded 73.7 mg (89%) of the title compound as a colorless oil. R_f(PE/Et_2O 7/3) 0.38. IR (neat) ν 2931, 2878, 2255, 1733, 1375, 1225, 1154, 905, 724, 588 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 5.68 (s, 1H), 4.30 (d, J = 11.5 Hz, 1H), 4.19 (d, J = 11.6 Hz, 1H), 4.11 (d, J = 11.6 Hz, 1H), 4.06 (d, J = 11.5 Hz, 1H), 3.43 (d, J = 9.2 Hz, 1H), 3.04 (d, J = 9.2 Hz, 1H), 2.41 (s, 3H), 2.33 (d, J = 16.4 Hz, 1H), 2.23 (d, J = 16.4 Hz, 1H), 1.71 (s, 3H), 1.49 (s, 3H), 1.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8 (C), 143.4 (C), 138.2 (C), 130.8 (C), 129.7 (CH), 129.4 (C), 127.7 (CH), 115.3 (CH_2), 67.4 (C), 60.7 (CH_2), 43.9 (CH_2), 41.6 (CH_2), 39.8 (C), 38.9 (CH_2), 31.1 (CH_3), 28.5 (CH_3), 22.4 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{20}H_{26}NO_2SCl_2^+$ ($[M+H]^+$): 414.1056, found 414.1056.

5,6-Diethyl-1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole (3bk). General Procedure B afforded 73.2 mg (98%) of the title compound as a colorless oil. R_f (PE/Et_2O 8/2) 0.55. IR (neat) ν 2963, 2867, 1598, 1362, 1288 1148, 1014, 926, 799, 709, 548cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 7.2 Hz, 2H), 5.41 (s, 1H), 3.31 (d, J = 9.0 Hz, 1H), 2.91 (d, J = 9.0 Hz, 1H), 2.34 (s, 3H), 2.15 – 2.03 (m, 3H), 1.99 – 1.81 (m, 3H), 1.60 (s, 3H), 1.38 (s, 3H), 0.90 – 0.84 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.5 (C), 143.1 (C), 138.6 (C), 129.9 (C), 129.7 (C), 129.6 (CH), 127.8 (CH), 117.7 (CH), 67.5 (C), 61.3 (CH_2), 40.2 (CH_2), 39.9 (C), 31.4 (CH_3), 28.7 (CH_3), 25.9 (CH_2), 24.4 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 14.3 (CH_3), 13.0 (CH_3). HRMS (ESI-MS) calcd. for $C_{22}H_{32}NO_2S^+$ ([M+H]$^+$): 374.2148, found 374.2146.

1,1,3a-trimethyl-5,6-diphenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole (3bl). General Procedure B afforded 19.7 mg (21%) of the title compound as a colorless oil. R_f (PE/Et_2O 8/2) 0.45. IR (neat) ν 2965, 2918, 1612, 1497, 1381, 1153, 1036, 930, 723, 706, 528 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.16–7.08 (m, 6H), 7.01–6.96 (m, 4H), 5.88 (s, 1H), 3.49 (d, J = 9.1 Hz, 1H), 3.14 (d, J = 9.1 Hz, 1H), 2.76 (d, J = 16.1 Hz, 1H), 2.48 (d, J = 16.1 Hz, 1H), 2.43 (s, 3H), 1.76 (s, 3H), 1.56 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.0 (C), 143.3 (C), 142.5 (C), 141.2 (C), 138.4 (C), 132.9 (C), 131.2 (C), 129.8 (CH), 129.4 (CH), 129.1 (CH), 128.3 (CH), 128.3 (CH), 127.8 (CH), 126.8 (CH), 126.7 (CH), 119.1 (CH), 67.67 (C), 61.1 (CH_2), 43.2 (CH_2), 40.1 (CH_3), 31.4 (CH_3), 28.7 (CH_3), 22.1 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{30}H_{32}NO_2S^+$ ([M+H]$^+$): 470.2148, found 470.2146.

2-(1,1,3a-Trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindol-5-yl)propan-2-ol (7ba). General Procedure B using 10 mol % of Cp*Ru(cod)Cl afforded 64.6 mg (86%) of the title compound as a colorless oil. R_f (PE/Et_2O 1/1) 0.23. IR (neat) ν 3510, 3054, 2304, 1670, 1421, 1264, 1158, 730, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.95 (dd, J = 5.5, 2.9 Hz, 1H), 5.63 (d, J = 5.5 Hz, 1H), 3.41 (d, J = 9.1 Hz, 1H), 3.03 (d, J = 9.1 Hz, 1H), 2.41 (s, 3H), 2.19 (d, J = 16.1 Hz, 1H), 2.09 (dd, J = 16.1, 2.9 Hz, 1H), 1.67 (s, 3H), 1.45 (s, 3H), 1.37 (s, 1H), 1.33 (s, 3H), 1.31 (s, 3H), 0.98 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8 (C), 143.2 (C), 142.3 (C), 138.3 (C), 129.7 (CH), 127.7 (CH), 115.7 (CH), 113.8 (CH), 72.6 (C), 67.4 (C), 61.1 (CH_2), 40.0 (C), 35.8 (CH_2), 31.2 (CH_3), 28.6 (CH_3), 28.6 (CH_3), 28.4 (CH_3), 21.8 (CH_3), 21.6 (CH_3). HRMS (ESI-MS) calcd. for $C_{21}H_{30}NO_3S^+$ ([M+H]$^+$): 376.1941, found 376.1938.

1-(1,1,3a-Trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindol-5-yl)cyclohexan-1-ol (7bb). General Procedure B using 10 mol % of Cp*Ru(cod)Cl afforded 58.2 mg (70%) of the title compound as a white solid. Mp 71-73 °C. R_f (PE/Et_2O 1/1) 0.41. IR (neat) ν 2918, 2877, 2271, 1310, 1125, 1076, 959, 749, 544 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 5.96 (dd, J = 5.5, 2.9 Hz, 1H), 5.63 (d, J = 5.5 Hz, 1H), 3.41 (d, J = 9.1 Hz, 1H), 3.03 (d, J = 9.1 Hz, 1H), 2.41 (s, 3H), 2.24 (d, J = 16.0 Hz, 1H), 2.06 (dd, J = 16.0, 2.9 Hz, 1H), 1.67 (s, 3H), 1.65–1.51 (m, 9H), 1.45 (s, 3H), 1.26–1.13 (s, 2H), 0.98 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9 (C), 143.2 (C), 142.5 (C), 138.4 (C), 129.7 (CH), 127.8 (CH), 116.5 (CH), 113.9 (CH), 73.3 (C), 67.4 (C), 61.2 (CH_2), 40.0 (C), 35.7 (CH_2), 35.6 (CH_2), 35.5 (CH_2), 31.2 (CH_3), 28.6 (CH_3), 25.9 (CH_2), 22.2 (CH_2), 22.1 (CH_2), 21.8 (CH_3), 21.5 (CH_3). HRMS (ESI-MS) calcd. for $C_{24}H_{34}NO_3S^+$ ([M+H]$^+$): 416.2254, found 416.2254.

Phenyl-1-(1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindol-5-yl)ethan-1-ol (7bc). General Procedure B using 10 mol % of Cp*Ru(cod)Cl afforded 74.4 mg (85%) of the title compound as a white solid in a 1:1 mixture of diastereomers. Mp 75–76 °C. R_f (PE/Et_2O 1/1) 0.54. IR (neat) ν 2997, 2868, 2253, 1373, 1150, 1121, 904, 701, 593, 549 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.39–7.36 (m, 2H), 7.34–7.27 (m, 2H), 7.25–7.20 (m, 3H), 6.17 (dd, J = 5.5, 2.9 Hz, 0.5H), 6.11 (dd, J = 5.5, 2.9 Hz, 0.5H), 5.67 (dd, J = 5.4, 2.4 Hz, 1H), 3.28 (d, J = 9.0 Hz, 0.5H), 3.25 (d, J = 9.1 Hz, 0.5H), 2.91 (d, J = 9.2 Hz, 0.5H), 2.88 (d, J = 9.1 Hz, 0.5H), 2.39 (s, 3H), 1.97–1.80 (m, 2H), 1.78 (s, 0.5H), 1.76 (s, 0.5 H), 1.71–1.66 (m, 6H), 1.44 (s, 1.5H), 1.43 (s, 1.5H), 0.82 (s, 1.5H), 0.73 (s, 1.5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3 (C x 0.5), 154.1 (C x 0.5), 145.6 (C x 0.5), 145.4 (C x 0.5), 143.1 (C), 141.0 (C x 0.5), 140.8 (C x 0.5), 138.3 (C x 0.5), 138.2 (C x 0.5), 129.6 (CH x 2), 128.4 (CH x 2), 127.7 (CH x 2 x 0.5), 127.7 (CH x 2 x 0.5), 127.3 (CH x 0.5), 127.2 (CH x 0.5), 125.81(CH x 2 x 0.5), 125.7 (CH x 2 x 0.5), 117.5 (CH_2 x 0.5), 117.2 (CH_2 x 0.5), 113.6 (CH_2 x 0.5), 113.59 (CH_2 x 0.5), 76.6 (C x 0.5), 76.2 (C x 0.5), 67.3 (C), 61.0 (CH_2 x 0.5), 60.95 (CH_2 x 0.5), 40.0 (C x 0.5), 39.9 (C x 0.5), 35.8 (CH_2 x 0.5), 35.7 (CH_2 x 0.5), 31.4 (CH_3 x 0.5), 31.2 (CH_3 x 0.5), 28.6 (CH_3), 28.5 (CH_3 x 0.5), 28.1 (CH_3 x 0.5), 22.2 (CH_3 x 0.5), 21.8 (CH_3 x 0.5), 21.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{26}H_{32}NO_3S^+$ ([M+H]$^+$): 438.2097, found 438.2096.

Diphenyl(1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindol-5-yl)methanol (7bd). General Procedure B using 10 mol % of Cp*Ru(cod)Cl afforded 90.9 mg (91 %) of the title compound as a white solid. Mp 112-113 °C. R_f (PE/Et_2O 1/1) 0.60. IR (neat) ν 3018, 2947, 1610, 1508, 1485, 1112, 1023, 742, 712 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.3 Hz, 2H), 7.28–7.23 (m, 8H), 7.23–7.19 (m, 2H), 7.19–7.17 (m, 2H), 5.58 (dd, J = 5.5, 2.7 Hz, 1H), 5.52 (d, J = 5.5 Hz, 1H), 3.24 (d, J = 9.1 Hz, 1H), 2.86 (d, J = 9.1 Hz, 1H), 2.33 (s, 3H), 2.30 (s, 1H), 2.08 (d, J = 16.3 Hz, 1H), 1.98 (dd, J = 16.3, 2.7 Hz, 1H), 1.59 (s, 3H), 1.37 (s, 3H), 0.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.7 (C), 144.6 (C), 144.6 (C), 143.2 (C), 140.3 (C), 138.3 (C), 129.7 (CH), 128.3 (CH), 128.25 (CH), 128.0 (CH), 127.9 (CH), 127.7 (CH), 127.7 (CH), 122.2 (CH), 113.6 (CH), 82.6 (C), 67.3 (C), 61.1 (CH_2), 40.3 (C), 36.5 (CH_2), 31.3 (CH_3), 28.5 (CH_3), 22.5 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{31}H_{34}NO_3S^+$ ([M+H]$^+$): 500.2254, found 500.2256.

4-methyl-*N*-(2-(1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindol-5-yl)propan-2-yl)benzenesulfonamide (7be). General Procedure B afforded 67.6 mg (64%) of the title compound as a pale yellow solid, mp 58-59 °C. R_f (PE/Et_2O 4/6) 0.33. IR (neat) ν 3276, 2977, 1598, 1450, 1382, 1146, 1090, 909, 661, 548 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 5.88 (dd, J = 5.5, 2.8 Hz, 1H), 5.58 (d, J = 5.5 Hz, 1H), 4.43 (s, 1H), 3.38 (d, J = 9.1 Hz, 1H), 2.89 (d, J = 9.1 Hz, 1H), 2.42 (s, 3H), 2.37 (s, 3H), 2.07 (d, J = 16.1 Hz, 1H), 1.79 (dd, J = 16.1, 2.8 Hz, 1H), 1.66 (s, 3H), 1.42 (s, 3H), 1.36 (s, 3H), 1.28 (s, 3H), 0.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6 (C), 142.3 (C), 142.2 (C), 139.3 (C), 138.8 (C), 137.3 (C), 128.8 (CH), 128.7 (CH), 126.8 (CH), 126.4 (CH), 117.1 (CH), 112.6 (CH), 66.3 (C), 60.1 (CH_2), 58.1 (C), 39.1 (C), 34.4 (CH_2), 30.3 (CH_3), 27.5 (CH_3), 27.0 (CH_3), 25.3 (CH_3), 20.8 (CH_3), 20.7 (CH_3). HRMS (ESI-MS) calcd. for $C_{28}H_{37}N_2O_4S_2^+$ ([M+H]$^+$): 529.2189, found 529.2188.

5-(2-methoxypropan-2-yl)-1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole (7bg). General Procedure B afforded 22.3 mg (29%) of the title compound as a colorless oil. R_f (PE/Et_2O 3/1) 0.44. IR (neat) ν 3018, 2932, 1698, 1454, 1214, 1156, 1090, 940, 751, 667, 570 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 5.86 (dd, J = 5.5, 3.0 Hz, 1H), 5.62 (d, J = 5.5 Hz, 1H), 3.42 (d, J = 9.0 Hz, 1H), 3.05 (s, 3H), 3.02 (d, J = 9.0 Hz, 1H), 2.41 (s, 3H), 2.28 (d, J = 16.3 Hz, 1H), 1.95 (dd, J = 16.3, 2.9 Hz, 1H), 1.69 (s, 3H), 1.46 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H), 1.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5 (C), 143.2 (C), 139.9 (C), 138.3 (C), 129.7 (CH), 127.8 (CH), 119.2 (CH), 113.6 (CH), 76.8 (C), 67.4 (C), 61.3 (CH_2), 50.8 (CH_3), 40.1 (C), 35.0 (CH_2), 31.3 (CH_3), 28.6 (CH_3), 25.4 (CH_3), 25.1 (CH_3), 22.4 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{22}H_{32}NO_3S$ ([M+H]$^+$): 390.2097, found 390.2097.

6-(2-methoxypropan-2-yl)-1,1,3a-trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole (7bg'). General Procedure B afforded 26.8 mg (34%) of the title compound as a white solid. Slow evaporation technique from a petroleum ether solution of **7bg'** yielded good single crystals for X-ray analysis. Crystal data: $C_{22}H_{31}NO_3S$, FW = 389.54, monoclinic, *P* 1 21 1, a = 6.4533(5) Å, b = 8.1500(5) Å, c = 20.626(2) Å, β = 93.939(8)°, *V* = 1082.25(16) Å^3, *Z* = 2, D_{calcd} = 1.195 g cm^{-3}, *R* = 0.0684 (R_w = 0.1905) for 3537 reflections with $I > 2.00\sigma(I)$ and 251 variable parameters. CCDC 1535396 (**7bg'**) contains supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Mp 56–57 °C. R_f (PE/Et_2O 1/1) 0.60. IR (neat) ν 2975, 2821, 1599, 1451, 1271, 1223, 1074, 951, 903, 784, 598 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 5.82 (s, 1H), 5.50 (t, *J* = 4.5 Hz, 1H), 3.41 (d, *J* = 9.1 Hz, 1H), 3.01 (d, *J* = 9.1 Hz, 1H), 2.99 (s, 3H), 2.41 (s, 3H), 2.14 (d, *J* = 4.5 Hz, 2H), 1.70 (s, 3H), 1.48 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H), 1.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7 (C), 143.2 (C), 140.3 (C), 138.4 (C), 129.7 (CH), 127.8 (CH), 1178.0 (CH), 113.4 (CH), 76.1 (C), 67.6 (C), 61.2 (CH_2), 50.7 (CH_3), 39.3 (C), 35.6 (CH_2), 31.4 (CH_3), 28.7 (CH_3), 25.9 (CH_3), 25.5 (CH_3), 22.1 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{22}H_{32}NO_3S$ ([M+H]$^+$): 390.2097, found 390.2097.

(3,3,7a-Trimethyl-2-tosyl-2,3,7,7a-tetrahydro-1*H*-isoindol-5-yl)methanol (7bi). General Procedure B afforded 34.1 mg (49%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/6) 0.30. IR (neat) ν 3490, 2929, 2899, 1738, 1318, 1209, 953, 749, 559 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 5.57-5.54 (m, 1H), 5.66 (s, 1H), 4.14–4.07 (m, 2H), 3.37 (d, *J* = 9.1 Hz, 1H), 3.00 (d, *J* = 9.1 Hz, 1H), 2.41 (s, 3H), 2.14 (d, *J* = 4.4 Hz, 2H), 1.69 (s, 3H), 1.47 (s, 3H), 1.42 (br s, 1H), 1.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2 (C), 143.3 (C), 138.3 (C), 135.8 (C), 129.7 (CH), 127.8 (CH), 119.1 (CH), 113.9 (CH), 67.4 (C), 65.5 (CH_2), 61.1 (CH_2), 39.6 (C), 35.3 (CH_2), 31.2 (CH_3), 28.7 (CH_3), 22.3 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{19}H_{26}NO_3S^+$ ([M+H]$^+$): 348.1628, found 348.1630.

(1,1,3a-Trimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindol-5-yl)methanol (7bi'). General Procedure B afforded 33.4 mg (48%) of the title compound as a colorless oil. R_f (PE/Et_2O 4/6) 0.28. IR (neat) ν 3501, 2917, 2900, 1696, 1299, 1152, 949, 687, 660, 593 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 5.92–5.89 (m, 1H), 5.62 (d, *J* = 5.4 Hz, 1H), 4.13–4.05 (m, 2H), 3.39 (d, *J* = 9.1 Hz, 1H), 3.03 (d, *J* = 9.1 Hz, 1H), 2.41 (s, 3H), 2.19 – 2.11 (m, 1H), 2.06 (d, *J* = 16.4 Hz, 1H), 1.68 (s, 3H), 1.45 (s, 3H), 1.41 (br s, 1H), 1.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6 (C), 143.3 (C), 138.3 (C), 135.4 (C), 129.7 (CH), 127.8 (CH), 119.2 (CH), 113.5 (CH), 67.4 (C), 66.4 (CH_2), 61.0 (CH_2), 39.9 (C), 36.6 (CH_2), 31.2 (CH_3), 28.7 (CH_3), 22.2 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{19}H_{26}NO_3S^+$ ([M+H]$^+$): 348.1628, found 348.1631.

4-(4-methoxy-4-methylpent-2-yn-1-yl)-2,2,4-trimethyl-3-methylene-1-tosylpyrrolidine (8). General Procedure B afforded 26.5 mg (34%) of the title compound as a colorless oil. R_f (PE/Et_2O 7/3) 0.35. IR (neat) ν 3019, 2911, 1599, 1447, 1214, 1156, 1091, 930, 744, 667, 566, 550 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 4.89 (s, 1H), 4.87 (s, 1H), 3.37 (d, *J* = 9.7 Hz, 1H), 3.25 (s, 3H), 3.10 (d, *J* = 9.7 Hz, 1H), 2.41 (s, 3H), 2.30 (d, *J* = 16.7 Hz, 1H), 2.19 (d, *J* = 16.7 Hz, 1H), 1.55 (s, 3H), 1.53 (s, 3H), 1.35 (s, 6H), 1.17 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6 (C), 142.3 (C), 137.4 (C), 128.7 (CH), 126.8 (CH), 104.3 (CH_2), 83.5 (C), 80.4 (C), 69.8 (C), 67.7 (C), 56.3 (CH_2), 50.8 (CH_3), 43.1 (C), 29.1 (CH_2), 28.6 (CH_3), 28.5 (CH_3), 27.9 (CH_3), 27.8 (CH_3), 23.7 (CH_3), 20.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{22}H_{32}NO_3S$ ([M+H]$^+$): 390.2097, found 390.2097.

(3,3,7a-trimethyl-6-phenyl-2-tosyl-2,3,7,7a-tetrahydro-1*H*-isoindol-5-yl)methanol (10). General Procedure B afforded 41.5 mg (49%) of the title compound as a white solid, mp 61-62°C. R_f (PE/Et_2O 1/1) 0.42. IR (neat) ν 3520, 2974, 2929, 1598, 136, 1149, 1090, 1028, 703, 572, 549 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.36 – 7.26 (m, 5H), 7.15 (d, *J* = 7.2 Hz, 2H), 5.93 (s, 1H), 4.16 (d, *J* = 5.5 Hz, 2H), 3.43 (d, *J* = 9.2 Hz, 1H), 3.06 (d, *J* = 9.2 Hz, 1H), 2.60 (d, *J* = 16.2 Hz, 1H), 2.42 (s, 3H), 2.34 (d, *J* = 16.2 Hz, 1H), 1.75 (s, 3H), 1.54 (s, 3H), 1.24 (t, *J* = 5.4 Hz, 1H), 1.13 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1 (C), 143.2 (C), 141.3 (C), 138.3 (C), 132.8 (C), 130.6 (C), 129.7 (CH), 128.6 (CH), 128.2 (CH), 127.7 (CH), 127.5 (CH), 115.9 (CH), 67.6 (C), 62.0 (CH_2), 61.0 (CH_2), 42.8 (CH_2), 39.9 (C), 31.3 (CH_3), 28.7 (CH_3), 22.1 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{25}H_{29}NO_3SNa^+$ ([M+Na]$^+$): 446.1760, found 446.1759.

(1,1,3a-trimethyl-6-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindol-5-yl)methanol (10'). General Procedure B afforded 32.2 mg (38%) of the title compound as a white solid, mp 68-69 °C. R_f (PE/Et_2O 1/1) 0.40. IR (neat) ν 3515 2972, 2927, 1598, 1363, 1224, 1147, 973, 780, 701, 581 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.37 – 7.26 (m, 5H), 7.14 (d, *J* = 7.0 Hz, 2H), 5.72 (s, 1H), 4.19 (d, *J* = 11.7 Hz, 1H), 4.04 (d, *J* = 11.7 Hz, 1H), 3.47 (d, *J* = 9.2 Hz, 1H), 3.11 (d, *J* = 9.2 Hz, 1H), 2.44 (d, *J* = 16.3 Hz, 1H), 2.43 (s, 3H), 2.34 (d, *J* = 16.3 Hz, 1H), 1.70 (s, 3H), 1.50 (s, 3H), 1.22 (dt, *J* = 6.9, 4.3 Hz, 1H), 1.11 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3 (C), 143.3 (C), 140.1 (C), 138.4 (C), 134.1 (C), 129.8 (C), 129.7 (CH), 128.6 (CH), 128.5 (CH), 127.8 (CH), 127.5 (CH), 118.0 (CH), 67.6 (C), 63.2 (CH_2), 61.1 (CH_2), 39.7 (C), 38.0 (CH_2), 31.2 (CH_3), 28.7 (CH_3), 22.2 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{25}H_{29}NO_3SNa^+$ ([M+Na]$^+$): 446.1760, found 446.1757.

(1,3a-dimethyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindole-5,6-diyl)bis(methylene) diacetate (12); General Procedure B afforded 59.1 mg (66%, 15:1 md) of the title compound as a colorless oil. R_f (PE/Et_2O 6/4) 0.35. IR (neat) ν 2972, 2869, 1736, 1376, 1223, 1162, 1048, 915, 712, 549 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 0.8H), 7.69 (d, *J* = 8.1 Hz, 1.2H), 7.33 (d, *J* = 8.0 Hz, 1.2H), 7.30 (d, *J* = 8.0 Hz, 0.8H), 5.66 – 5.64 (m, 1H), 4.79 – 4.51 (m, 4H), 4.44 (q, *J* = 6.6 Hz, 0.4H), 3.89 (q, *J* = 6.6 Hz, 0.6H), 3.59 (d, *J* = 8.6 Hz, 0.6H), 3.56 (d, *J* = 10.8 Hz, 0.4H), 3.20 (d, *J* = 10.8 Hz, 0.4H), 2.65 (d, *J* = 8.6 Hz, 0.6H), 2.44 (s, 1.8H), 2.41 (s, 1.2H), 2.27 – 2.08 (m, 2H), 2.04– 2.02 (m, 6H), 1.60 (d, *J* = 6.6 Hz, 1.8H), 1.45 (d, *J* = 6.6 Hz, 1.2H), 1.15 (s, 1.8H), 0.51 (s, 1.2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (C), 150.9 (C), 150.7 (C), 144.1 (C), 143.7 (C), 136.8 (C), 132.6 (C), 130.0 (CH), 129.9 (CH), 129.2 (C), 129.1 (C), 128.9 (C), 128.8 (C), 128.4 (CH), 127.6 (CH), 116.7 (CH), 116.4 (CH), 63.4 (CH_2), 63.3 (CH_2), 62.2 (CH_2), 62.1 (CH_2), 61.0 (CH_2), 58.8 (CH), 57.4 (CH), 41.4 (C), 39.5 (C), 38.3 (CH_2), 38.1 (CH_2), 24.8 (CH_3), 22.6 (CH_3), 21.8 (CH_3), 21.7 (CH_3), 21.6 (CH_3), 21.2 (CH_3), 21.1(CH_3) , 21.0 (CH_3), 20.9 (CH_3). HRMS (ESI-MS) calcd. for $C_{23}H_{30}NO_6S^+$ ([M+H]$^+$): 448.1788, found 448.1786.

3,3,10a-Trimethyl-9-phenyl-2-tosyl-1,2,3,4a,10,10a-hexahydroindeno[1,2-f]isoindole (13). Camphorsulfonic acid (55.7 mg, 0.24 mmol) was added to a solution of dienol **7bd** (99.9 mg, 0.2 mmol) in toluene (10 mL). The mixture was stirred for 5 h at 60 °C, and then concentrated *in vacuo*. The crude residue was purified by flash chromatography on silica gel to give 69.4 mg (74%) of the title compound as a white solid. Mp 113–114 °C. R_f (PE/Et_2O 2/3) 0.28. IR (neat) ν 3025, 2930, 1598, 1363, 1156, 1038, 1015, 939, 702, 658, 546 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 7.0 Hz, 1H), 7.48–7.34 (m, 5H), 7.30–7.22 (m, 5H), 5.92 (d, *J* = 3.8 Hz, 1H), 4.07 (d, *J* = 3.8 Hz, 1H), 3.20 (d, *J* = 9.1 Hz, 1H), 3.07 (d, *J* = 9.1 Hz, 1H), 2.79 (d, *J* = 12.2 Hz, 1H), 2.47 (d, *J* = 12.2 Hz, 1H), 2.40 (s, 3H), 1.62 (s, 3H), 1.59 (s, 3H), 0.71 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1 (C), 145.1 (C), 144.6 (C), 143.9 (C), 143.2 (C), 139.1 (C), 138.4 (C), 134.8 (C), 129.7

(CH), 129.4 (CH), 128.9 (CH), 127.7 (CH), 127.2 (CH), 125.0 (CH), 123.0 (CH), 120.5 (CH), 115.9 (CH), 67.0 (C), 59.1 (CH_2), 50.9 (CH), 46.2 (C), 35.8 (CH_2), 30.7 (CH_3), 29.0 (CH_3), 26.7 (CH_3), 21.8 (CH_3). HRMS (ESI-MS) calcd. for $C_{31}H_{32}NO_2S^+$ ($[M+H]^+$): 482.2148, found 482.2148.

3,3,6,7a-tetramethyl-2-tosyl-2,3,7,7a-tetrahydro-1*H*-isoindole-5-carbaldehyde (14). Camphorsulfonic acid (46.4 mg, 0.2 mmol) was added to a solution of diol **3bi** (75.5 mg, 0.2 mmol) in toluene (10 mL). The mixture was stirred for 2 days at room temperature, and then concentrated *in vacuo*. The crude residue was purified by flash chromatography to give 34.5 mg (48 %) of the title compound as a yellow solid. Mp 144–145 °C, R_f (PE/Et_2O 1/1) 0.37. IR (neat) ν 3019, 2975, 2866, 1668, 1449, 1214, 1150, 1121, 1033, 747, 667, 540 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 7.75 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 6.18 (s, 1H), 3.42 (d, J = 9.2 Hz, 1H), 3.02 (d, J = 9.2 Hz, 1H), 2.43 (d, J = 17.3 Hz, 1H), 2.41 (s, 3H), 2.24 (d, J = 1.4 Hz, 3H), 2.14 (d, J = 17.3 Hz, 1H), 1.70 (s, 3H), 1.47 (s, 3H), 0.98 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.9 (CH), 154.3 (C), 152.3 (C), 143.3 (C), 138.2 (C), 130.9 (C), 129.7 (CH), 127.7 (CH), 109.8 (CH), 67.5 (C), 60.7 (CH_2), 44.8 (CH_2), 39.1 (C), 31.0 (CH_3), 28.5 (CH_3), 22.7 (CH_3), 21.8 (CH_3), 19.1 (CH_3). HRMS (ESI-MS) calcd. for $C_{20}H_{26}NO_3S^+$ ($[M+H]^+$): 360.1628, found 360.1628.

Acknowledgements

We thank the Cente National de la Recherche Scientifique (CNRS) and the Ministère de l'Enseignement Supérieur et de la Recherche (MESR) for financial support. R.L. is grateful for a Ph.D. fellowship from the China Scholarship Council (CSC). We thank Dr. I. DeRiggi (ECM) for help with the NMR spectra analysis, Dr. M. Giorgi (Aix-Marseille Université) for the X-ray structural analysis, Dr H. Clavier for help with the x-ray data and Dr V. Monnier (Aix-Marseille Université) for HRMS assistance.

Keywords: ruthenium • cycloaddition • enyne • alkyne • catalysis

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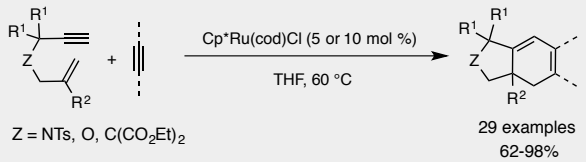

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Ruthenium-Catalyzed [2 + 2 + 2] Cycloaddition of 1,6-Enynes and Unactivated Alkynes: Access to Ring-fused Cyclohexadienes

The [2 + 2 + 2] *intermolecular* carbocyclization reactions between 1,6-enynes and alkynes catalyzed by Cp*Ru(cod)Cl are reported to provide bicyclohexa-1,3-dienes. The chemo- and regioselectivity issues are controlled by the presence of substituents at the propargyl carbon center of the alkyne(s) partner(s).