



**HAL**  
open science

# Copper(I)-Catalyzed Dearomative (3 + 2) Cycloaddition of 3-Nitroindoles with Propargylic Nucleophiles: An Access to Cyclopenta[ b ]indolines

Johanne Ling, David Mara, Baptiste Roure, Maxime Laugeois, Maxime R Vitale

► **To cite this version:**

Johanne Ling, David Mara, Baptiste Roure, Maxime Laugeois, Maxime R Vitale. Copper(I)-Catalyzed Dearomative (3 + 2) Cycloaddition of 3-Nitroindoles with Propargylic Nucleophiles: An Access to Cyclopenta[ b ]indolines. *Journal of Organic Chemistry*, 2020, 85 (5), pp.3838-3848. 10.1021/acs.joc.9b03459 . hal-02997831

**HAL Id: hal-02997831**

**<https://hal.science/hal-02997831>**

Submitted on 10 Nov 2020

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Copper(I)-Catalyzed Dearomative (3+2) Cycloaddition of 3-Nitroindoles with Propargylic nucleophiles: an Access to Cyclopenta[*b*]indolines

Johanne Ling, David Mara, Baptiste Roure, Maxime Laugeois and Maxime R. Vitale\*

Institute of Chemistry for Life and Health Sciences, PSL Université Paris, CNRS, Chimie ParisTech.  
11 rue Pierre et Marie Curie, 75005 Paris, France.

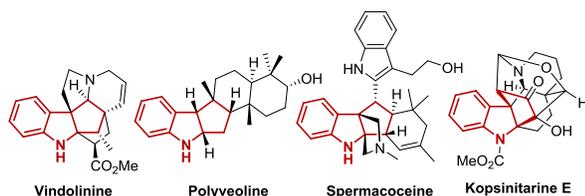
[maxime.vitale@chimieparistech.psl.eu](mailto:maxime.vitale@chimieparistech.psl.eu)

*Cyclopenta[*b*]indolines, dearomatization, (3+2) cycloaddition, 3-nitroindoles, copper(I)-catalysis.*

**ABSTRACT:** The copper(I)-catalyzed dearomatization of 3-nitroindoles with propargylic nucleophiles is described. In mild reaction conditions, this original dearomative (3+2) cycloaddition process gives access to a wide variety of cyclopenta[*b*]indolines in good to excellent yields, with high functional group tolerance. The proof of concept that an enantioselective version of this reaction is accessible by employing chiral phosphorous ligands was obtained. A mechanism proposal is given, based on kinetic studies.

## INTRODUCTION

Indolines constitute an important family of naturally occurring molecules,<sup>1</sup> within which several biologically active compounds, such as Vindolinine, Polyveoline, Spermacoceine and Kopsinitarine E, display a 2,3-fused cyclopentane ring (Figure 1).<sup>2</sup>

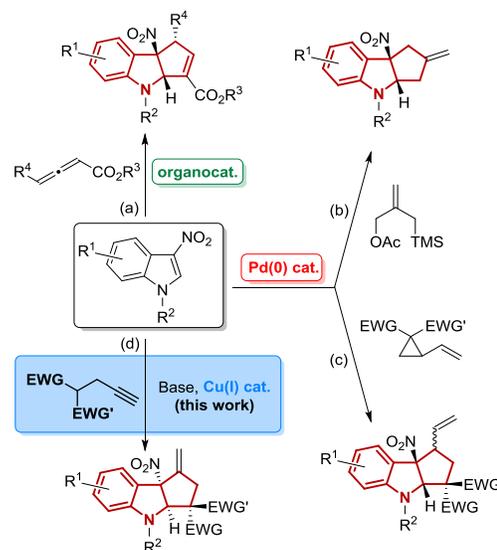


**Figure 1.** Relevant natural products containing a cyclopenta[*b*]indoline core.

For this reason, the cyclopenta[*b*]indoline core has attracted a lot of attention and many efforts have been dedicated to the preparation of this particular scaffold.<sup>3</sup> Among all possible methods, the direct introduction of the cyclopentane ring by means of a formal (3+2) cycloaddition process between an all-carbon 1,3-dipole and an indole partner remains undeniably the most straightforward.<sup>3</sup> Such a dearomative annulation strategy, which has long depended on the use of electron-rich indoles, based upon the seminal work of Kerr *et al.*,<sup>4</sup> has recently witnessed a change in paradigm, wherein electron-deficient indoles could be employed instead.<sup>5-7</sup>

More specifically, in direct connection with the seminal works from the groups of Chataigner and Gribble that showcased the unconventionally high reactivity of some nitroaromatics towards nitrogen-based 1,3-dipoles,<sup>8</sup> others and we demonstrated that cyclopenta[*b*]indolines could be straightforwardly obtained when 3-nitroindoles were engaged with all-carbon 1,3-dipoles.<sup>5-7</sup> In this field, in addition to recent achievements based on the use of allenates (or surrogates) via nucleophilic organocatalysis (Scheme 1, (a)),<sup>5</sup> metal catalysis revealed itself a privileged approach.<sup>6-7</sup> In particular, Trost *et al.* reported the dearomative (3+2) cycloaddition reaction of 3-nitroindoles via transiently generated palladium trimethylenemethane complexes (Scheme 1, (b)),<sup>6</sup> a metal-

catalyzed strategy which our group and that of Hyland later adopted by capitalizing on the palladium(0)-catalyzed ring opening of vinylcyclopropanes (Scheme 1, (c)).<sup>7,9</sup>



**Scheme 1.** Dearomative (3+2) cycloaddition reaction of 3-nitroindoles with *in situ* generated all-carbon 1,3-dipoles.

In continuation of our interest for such dearomative processes,<sup>7a,10</sup> we wish to report here that, by merging the use of a base with that of a catalytic copper(I) complex, cyclopenta[*b*]indolines can alternatively be obtained via the formal (3+2) cycloaddition of 3-nitroindole with simple and easily accessible propargylic nucleophiles (Scheme 1, (d)).<sup>11</sup>

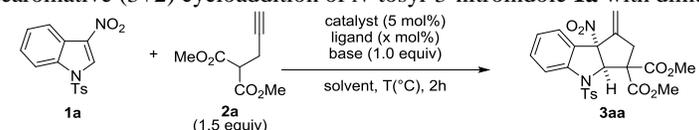
## RESULTS AND DISCUSSION

At the onset of our study, inspired by the work of Dulcère *et al.* regarding the base-catalyzed annulation of nitrostyrene with propargylic nucleophiles,<sup>12</sup> we wondered if 3-nitroindoles could behave likewise and would afford cyclopenta[*b*]indolines. To this aim, we studied the formal (3+2) cycloaddition of *N*-tosyl-3-nitroindole **1a** with dimethyl propargylmalonate **2a** (1.5 equiv) (Table 1). However, in the

reaction conditions previously reported by Dulcère *et al.*,<sup>12</sup> in the presence of Triton B (benzyltrimethylammonium hydroxide) at 50°C in dichloromethane, only traces of the desired cycloaddition product **3aa** could be observed (Table 1, Entry 1). For this reason, based on our previous interest for the metal-catalyzed carbocyclizations of formyl alkynes and other literature precedents, including Balme's and Dixon's seminal works,<sup>13,14</sup> we decided to evaluate if, using cesium carbonate as base (1 equiv), the use of a  $\pi$ -Lewis acid metal catalyst (5 mol%) could favour the desired dearomative process. Among the various metal sources which were tested, Pd(OAc)<sub>2</sub>, PPh<sub>3</sub>AuNTf<sub>2</sub> and FeCl<sub>3</sub> could not promote the expected reaction (Table 1, Entries 2-4). Nevertheless, we were pleased to witness that several silver salts, including silver nitrate or its bis(triflimide) analogue,

permitted the desired dearomatization reaction to take place with good yields of 72% and 84%, respectively (Table 1, Entries 5-6). Encouraged by these results, we turned ourselves toward less expensive metal sources such as copper. In the presence of triphenylphosphine, copper(I) bromide, copper(I) iodide and copper(II) triflate, all allowed to obtain the cycloaddition product **3aa** in good yields, comparable to that obtained with AgNO<sub>3</sub> (Table 1, entries 7-9). Worthy of note, in absence of triphenylphosphine, copper(II) triflate showed poorly capable of activating **2a** (Table 1, entry 10). In accord with previous observations,<sup>14e,f</sup> we concluded that Cu(OTf)<sub>2</sub> is actually a precatalyst and that, in such case, triphenylphosphine serves both as ligand and as reductant to promote the *in situ* generation of the more catalytically competent copper(I) trifluoromethanesulfonate complex. In order to reach milder reaction conditions, the cycloaddition reaction was then surveyed at room temperature. While, even after prolonged reaction times, silver salts exhibited a poorer reactivity in these new

**Table 1.** Optimization of the dearomative (3+2) cycloaddition of *N*-tosyl-3-nitroindole **1a** with dimethyl propargylmalonate **2a**.



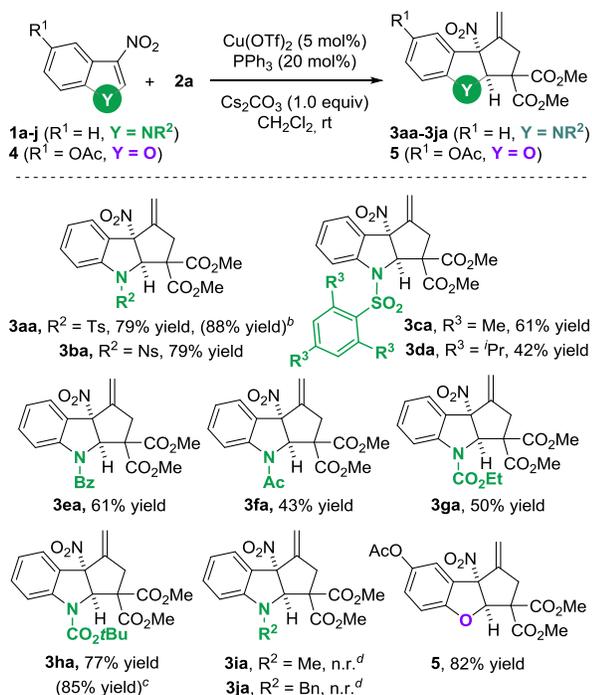
Entry	Catalyst	Ligand (x mol%)	Base	Solvent	Temperature (°C)	Yield (%) <sup>b</sup>
1	-	-	Triton B	CH <sub>2</sub> Cl <sub>2</sub>	50°C	1
2	Pd(OAc) <sub>2</sub>	-	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	- <sup>c</sup>
3	PPh <sub>3</sub> AuNTf <sub>2</sub>	-	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	- <sup>c</sup>
4	FeCl <sub>3</sub>	-	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	- <sup>c</sup>
5	AgNO <sub>3</sub>	-	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	72
6	AgNTf <sub>2</sub>	-	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	84
7	CuBr	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	69
8	CuI	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	66
9	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	72
10	Cu(OTf) <sub>2</sub>	-	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	50°C	16
11 <sup>d</sup>	AgNTf <sub>2</sub>	-	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	rt	55
12 <sup>d</sup>	AgNO <sub>3</sub>	-	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	rt	63
13	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	rt	86
14	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	K <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	rt	18
15	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Li <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	rt	- <sup>c</sup>
16	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	toluene	rt	81
17	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	MeOH	rt	30
18	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	1,2-DCE	rt	71
19	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	THF	rt	71
20	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	DMF	rt	64
21 <sup>f</sup>	Cu(OTf) <sub>2</sub>	PPh <sub>3</sub> (20)	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	rt	91 (79) <sup>e</sup>

<sup>a</sup> Reaction conditions: **1a** (0.4 mmol), **2a** (0.6 mmol), catalyst (5 mol%), ligand (x mol%), base (0.4 mmol) in 2 mL of solvent (0.2M) for 2 hours. <sup>b</sup> <sup>1</sup>H NMR yields determined using propylene carbonate as internal standard. <sup>c</sup> No reaction occurred. <sup>d</sup> Reaction run overnight. <sup>e</sup> Isolated yield. <sup>f</sup> Reaction run with 1.1 equiv **2a**.

reaction conditions (Table 1, Entry 11-12), we were pleased to witness that the Cu(OTf)<sub>2</sub>/PPh<sub>3</sub> system allowed to obtain **3aa** in 86% <sup>1</sup>H NMR yield after only two hours. The screening of a larger variety of bases and solvents led to no significant improvements (Table 1, Entries 14-20), but the desired dearoma-

tive cycloaddition worked as efficiently when only 1.1 equiv of propargylic derivative **1a** was used. In the later reaction conditions, which we used for the rest of our studies, the cyclopenta[*b*]indoline **3aa** was obtained in good 79% isolated yield (Table 1, entry 21).

With these optimized reaction conditions in hands, we then investigated the scope of this original dearomatization reaction, starting by evaluating the influence of the indole *N*-substitution pattern (Scheme 2).



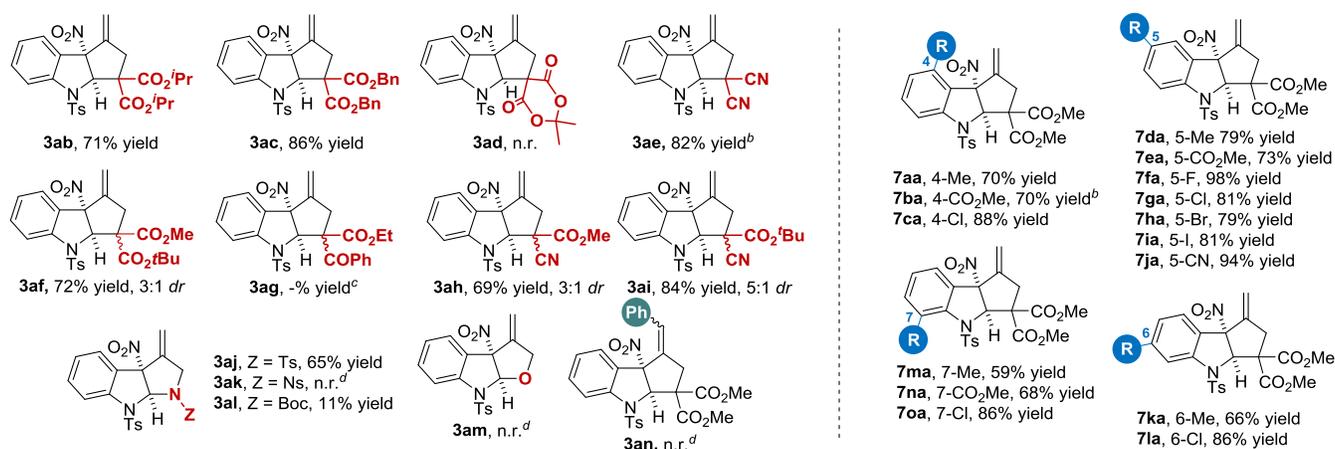
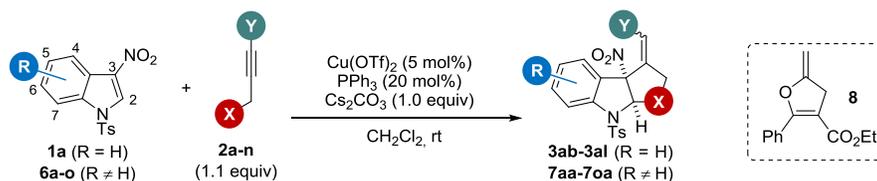
<sup>a</sup> Reaction conditions: **1a-j** or **4** (0.40 mmol), **2a** (0.44 mmol, 1.1 equiv), Cu(OTf)<sub>2</sub> (5 mol%), PPh<sub>3</sub> (20 mol%), Cs<sub>2</sub>CO<sub>3</sub> (0.40 mmol) in 2 mL of CH<sub>2</sub>Cl<sub>2</sub> (0.2M) at rt. <sup>b</sup> Starting from **1a** (2.50 mmol), 1.08 g of **3aa** was obtained. <sup>c</sup> With **1h** (2 equiv.). <sup>d</sup> No reaction occurred.

**Scheme 2.** Scope of the reaction – Influence of the nitrogen substitution pattern of the nitroindole partner – Extension to a 3-nitrobenzofuran.<sup>a</sup>

The model reaction of **1a** with **2a** could be scaled up to the gram scale preparation of **3aa** with good 88% yield and replacing the tosyl protecting group by a nosyl moiety had no detrimental effect (**3ba**, 79% yield). On the other hand, increasing the steric demand on the sulfonyl aromatic group tended to hamper the cyclization process. Indeed, the 3-nitroindole **1c** possessing a 2,4,6-trimethylbenzene sulfonyl moiety and its 2,4,6-triisopropyl analogue **1d** led to the corresponding dearomatized products **3ca** and **3da** in lower 61% and 42% yields, respectively. The reaction proved also compatible with carbonyl-based protected indoles such as **1e** (benzoyl), **1f** (acetyl), **1g** (ethoxycarbonyl) and **1h** (*tert*-butoxycarbonyl), although competitive *N*-deprotection could also be observed, especially for **1e** and **1g**. In the case of the Boc-substituted substrate **1h**, the inherent steric hindrance of this protecting group limited this side process, which allowed to obtain the cyclopenta[*b*]indoline **3ha** in good 77% yield in the standard reaction conditions, and up to 85% yield when **1h** was used in excess. Reminiscent of previous studies,<sup>7</sup> the *N*-methyl and *N*-benzyl substrates **1i** and **1j**, in which a push-pull effect is supposed to happen, remained completely unreactive. Additionally, such a dearomatization strategy could be successfully applied to the efficient preparation of the cyclopenta[*b*]benzofuran **5** in 82% yield (starting from the 3-nitrobenzofuran **4**), suggesting that this dearomatization process is compatible with a wider range of nitroaromatics.

We next explored the scope of propargylic nucleophiles compatible with this annulative process. For this purpose, nitroindole **1a** was engaged with **2b-m** (Scheme 3, left). Employing other malonate derivatives, such as the diisopropyl propargylmalonate **2b** or its dibenzyl analogue **2c**, allowed to obtain the corresponding cyclopenta[*b*]indoles **3ab** and **3ac** in 71% and 86% yield, respectively. However, in the case of the Meldrum's acid propargyl derivative **2d**, no (3+2) cycloaddition product could be detected. We assume that in this case, the deprotonated form of **2d**, in line with the low p*K*<sub>a</sub> of such compounds (Meldrum's acid p*K*<sub>a</sub> ≈ 5), possesses a nucleophilicity so weak that the initial Michael addition step would become inoperative. Nevertheless, the less acidic propargyl malonitrile **2e** could be employed to generate **3ae** in satisfactory 82% yield. A slow cyclization rate was observed, which could be easily overcome by using 10 mol% of Cu(OTf)<sub>2</sub> and 40 mol% PPh<sub>3</sub>. We next envisioned using unsymmetrical activated methylene derivatives (**2f-i**) to probe the diastereoselectivity of this cycloaddition reaction. Starting from the *tert*-butyl methyl propargyl malonate **2f**, the corresponding cycloadduct **3af** was isolated as a 3:1 mixture of diastereomers. On the other hand, the phenylketone derivative **2g** did not afford the expected product **3ag** and provided the intramolecular cyclization product **8** in 87% yield instead.<sup>15</sup> Better results were obtained with the propargylic cyanoacetates **2h** and **2i**, with which up to 5:1 *dr* and 84% yield were reached in the latter case, probably due to a better steric discrimination between the *tert*-butoxycarbonyl and the cyano groups. Heteroatom-based propargylic nucleophiles were tested next. While the *N*-Ts protected **2j** allowed to successfully obtain the corresponding desired pyrroloindoline **3aj** in 65% yield, the *N*-Ns equivalent **2k** remained completely unreactive and the *N*-Boc propargylamine **2l** only afforded very little of **3al** (11% yield). On the other hand, neither the propargyl alcohol **2m** nor the non-terminal phenyl-substituted propargylic malonate allowed the preparation of the corresponding cycloadducts **3am** and **3an**.

With regard to the influence of the indole aromatic substitution, we assessed it by engaging a variety of diversely substituted *N*-tosyl 3-nitroindoles **6a-o** with dimethyl propargyl malonate **1a** (Scheme 3, right).

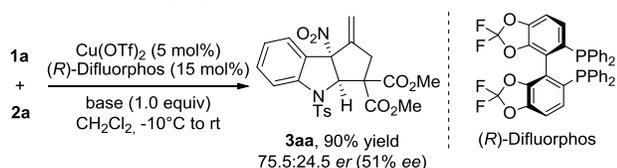


<sup>a</sup> Reaction conditions: **1a** or **6a-o** (0.40 mmol), **2a-1** (0.44 mmol, 1.1 equiv), Cu(OTf)<sub>2</sub> (5 mol%), PPh<sub>3</sub> (20 mol%), Cs<sub>2</sub>CO<sub>3</sub> (0.40 mmol) in 2 mL of CH<sub>2</sub>Cl<sub>2</sub> (0.2M) at rt. <sup>b</sup> 10 mol% Cu(OTf)<sub>2</sub>, 40 mol% PPh<sub>3</sub> were used. <sup>c</sup> **8** was isolated in 87% yield. <sup>d</sup> No reaction occurred.

### Scheme 3. Scope of the reaction – Influence of both the propargylic nucleophile and the nitroindole aromatic substitution.<sup>a</sup>

In either position 4, 5, 6 or 7, we were pleased to observe little influence of the substitution pattern of the starting nitroarene onto the efficiency of this new dearomatization process. Indeed, in all the cases studied, the desired cyclopenta[*b*]indolines **7aa-7la** (15 examples) were obtained in good yields ranging from 66% to 98%. Various electron-donating (Me) as well as electron-withdrawing (halogens, CN, CO<sub>2</sub>Me) groups were well tolerated.

In order to test the feasibility of developing an enantioselective version of this reaction, a screening of few chiral diphosphine ligands was performed. To our delight, after a quick optimization study,<sup>16</sup> we could demonstrate that the readily available atropisomeric diphosphine (*R*)-Difluorpos<sup>17</sup> allowed to induce a significant level of enantioselectivity in the model reaction of nitroindole **1a** with dimethyl propargylmalonate **2a**. Indeed, when starting the reaction at -10°C and slowly warming up the reaction mixture to room temperature, the cyclopenta[*b*]indoline **3aa** was obtained in encouraging 51% enantiomeric excess (Scheme 4).



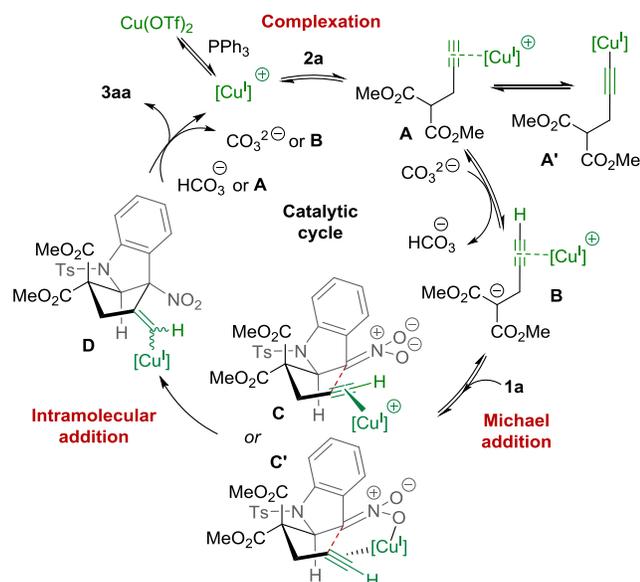
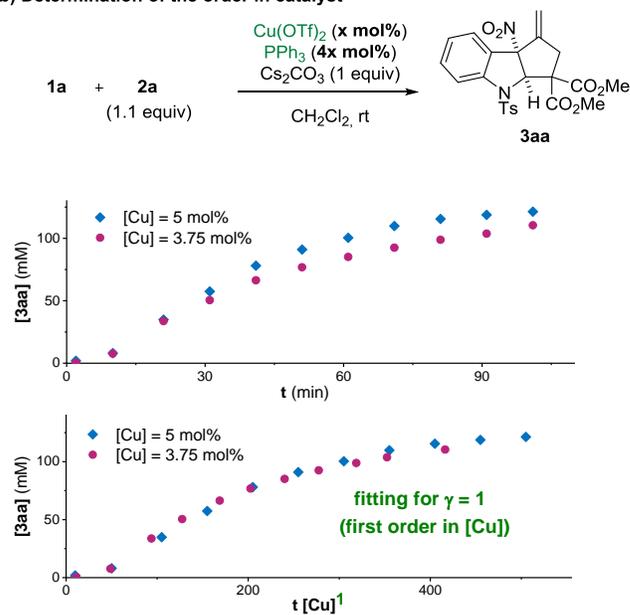
### Scheme 4. Proof of concept for an enantioselective version of this dearomatization process.

This result represents the proof of concept that the development of an enantioselective version of this dearomatization

process is reachable, even if higher stereocontrol would require an in-depth chiral ligand screening.

From a mechanistic perspective (Scheme 5, (a)), in line with previous works,<sup>13,14</sup> we propose that the copper(I) complex resulting from the reduction of copper(II) triflate with triphenylphosphine may form the  $\pi$ -alkyne copper intermediate **A** in the presence of a propargylic nucleophile. While in basic reaction conditions **A** may likely exist in equilibrium with the corresponding alkynylcopper(I) derivative **A'**, the former would be prone to deprotonation in the presence of cesium carbonate and should thereby generate the pseudo anion **B**. Upon Michael addition onto the 3-nitroindole, the resulting nitronate would then cyclize according to a chair like transition state through either an *anti*-carbocupration (**C**) or a *syn*-carbocupration (**C'**) pathway to afford the vinylcopper(I) intermediate **D**.<sup>18</sup> After protodecupration, either mediated by hydrogenocarbonate, **2a** or **A**, the dearomatization product would be released, together with the regeneration of the catalytically competent copper(I) complex.

To support this mechanistic picture further, we decided to perform some kinetic analyses. More specifically, we aimed to determine the order in catalyst so as to rule out a mechanistic scenario in which alkyne activation would entail the formation of a  $\pi$ -coordinated copper(I)acetylide copper(I) complex (second order in copper(I)). Indeed, the involvement of such binuclear copper intermediates, uncovered by Fokin in the context of the copper(I)-catalyzed alkyne/azide cycloaddition,<sup>19</sup> could have explained why the non-terminal propargylic derivative **2n** did not allow to obtain the corresponding dearomatization product **3an**.

**(a) Mechanistic proposal****(b) Determination of the order in catalyst****Scheme 5.** Mechanistic proposal and kinetic analyses

For this purpose, considering the dearomatization reaction of **1a** with **2a**, we applied the Variable Time Normalization Analysis (VTNA) method developed by Burés.<sup>20</sup> The concentration of cycloadduct **3aa** was monitored over time by <sup>1</sup>H NMR while employing two different initial catalyst loadings (Scheme 5, (b)).<sup>21</sup> By plotting product concentration against  $t[\text{Cu}]^\gamma$  for several values of  $\gamma$  (0.5, 1, 2), the best overlay was obtained when  $\gamma=1$ ,<sup>16</sup> which allowed to confirm a first order in catalyst, in line with our mechanistic proposal, and to affirm the occurrence of binuclear copper intermediates.

In conclusion, we have developed a straightforward access to cyclopenta[*b*]indolines. This new method, which is based on a copper(I)-catalyzed dearomative (3+2) cycloaddition reaction between 3-nitroindoles and propargylic nucleophiles, occurs with remarkably mild reaction conditions and is compatible with a large substrate scope. Chiral phosphorus ligands can be used and induce relevant levels of enantioselectivity, thereby, finally, a plausible mechanistic proposal is given, supported by kinetic analyses.

**EXPERIMENTAL SECTION**

**General Methods.** All reactions were run under argon atmosphere unless specified. Reaction vessels were oven-dried, cooled under vacuum and flushed with argon before use. Cyclohexane and ethyl acetate were distilled under reduced pressure prior silica gel chromatography. 1,2-dichloroethane was distilled over calcium hydride. Methanol was distilled over sodium. THF, CH<sub>2</sub>Cl<sub>2</sub>, DMF and toluene were dried over alumina columns. Reagent grade diisopropyl ether and hexane were purchased and used without further purification. Every reagent was either purified following the methods described in the literature or used without further purification. Starting materials **1a-j**, **4**, **2a-n** and **6a-o** were prepared according to known protocols.<sup>7,9,22</sup>

Proton nuclear magnetic resonance (<sup>1</sup>H NMR) spectra were recorded at 400 MHz. Chemical shifts are reported in delta ( $\delta$ ) units part per million (ppm) relative to the residual protiated

solvent. Coupling constants are reported in Hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, sept = septuplet, m = multiplet, brs = broad singlet. Carbon-13 nuclear magnetic resonance (<sup>13</sup>C NMR) spectra were recorded at 101 MHz. Chemical shifts are reported in delta ( $\delta$ ) units part per million (ppm) relative to the centre line of the triplet at 77.16 ppm for deuteriochloroform. <sup>13</sup>C NMR experiments were routinely run with <sup>1</sup>H broadband decoupling. Fluorine-19 nuclear magnetic resonance (<sup>19</sup>F NMR) spectra were recorded at 376 MHz.

HRMS analyses were performed at Sorbonne Université by ESI-orbitrap (electrospray ionization – ion trapping). Melting point values were recorded on a Kofler bench. Enantiomeric excesses (*ees*) were determined by high-performance liquid chromatography using a chiral stationary phase (Chiralpak IA). Optical rotation value was measured with instruments operating at  $\lambda = 589$  nm, corresponding to the sodium D line at the temperatures indicated.

**5-iodo-3-nitro-1-tosyl-1H-indole (6i).** Obtained according to the procedure described by Hyland *et al.*,<sup>9</sup> starting from 5-iodo-*N*-tosylindole (1.27 g, 3.2 mmol), as a pale yellow solid (461 mg, 35% yield) after trituration in methanol. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.60 (s, 1H), 8.50 (s, 1H), 7.90 – 7.80 (m, 2H), 7.75 (dd,  $J = 1.8, 1.2$  Hz, 2H), 7.40 – 7.29 (m, 2H), 2.41 (s, 3H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  147.0, 135.7, 133.7, 132.9, 132.1, 130.8 (2C), 130.2, 128.4, 127.6 (2C), 123.7, 115.4, 90.7, 21.9 ppm; IR (film):  $\nu$  3145, 2360, 2338, 1738, 1535, 1386, 1220 cm<sup>-1</sup>; mp (°C) = 206–208; HRMS (ESI) [M+H<sup>+</sup>] calculated for (C<sub>15</sub>H<sub>12</sub>IN<sub>2</sub>O<sub>4</sub>S)<sup>+</sup>: 442.9557, found 442.9557.

**General protocol for the (3+2) cycloaddition reaction.** In a screw-capped vial under argon atmosphere, cesium carbonate (130.4 mg, 0.40 mmol), nitroindole (0.40 mmol) and dichloromethane (800  $\mu$ L) were successively added. To the resulting mixture was added the propargylated derivative (0.44 mmol) and the mixture was stirred at room temperature for 5

minutes. A solution of Cu(OTf)<sub>2</sub> (7.2 mg, 0.02 mmol) and PPh<sub>3</sub> (21.0 mg, 0.08 mmol) in dichloromethane (800  $\mu$ L), previously stirred at room temperature for 30 minutes, was then transferred via cannula. The cannula was washed with additional dichloromethane (400  $\mu$ L) (total volume of solvent = 2.0 mL) and the mixture was stirred at room temperature until TLC indicated full conversion of the starting nitroindole. The mixture was diluted with dichloromethane (10 mL), loaded onto a small silica plug, eluted with dichloromethane (40 mL) and evaporated under reduced pressure. The resulting crude mixture was purified by flash column chromatography or trituration to afford the desired cycloadduct.

Analytical data for the major isomer of compounds **3af**, **3ah** and **3ai** are described below. Selected <sup>1</sup>H NMR peaks for minor isomers of compounds **3af**, **3ah** and **3ai** are also reported.

**(±)-Dimethyl 1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (3aa)**. Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **1a** (127 mg, 0.40 mmol), as a white solid (158 mg, 81% yield) after flash column chromatography (petroleum ether/methyl tert-butyl ether 9:1 to 8:2). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.72 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.53 – 7.40 (m, 4H), 7.23 (td, *J* = 7.6, 1.0 Hz, 1H), 7.17 – 7.07 (m, 2H), 6.50 (s, 1H), 5.29 – 5.22 (m, 1H), 5.21 – 5.14 (m, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.07 (dt, *J* = 16.1, 2.5 Hz, 1H), 2.94 (dt, *J* = 16.1, 1.1 Hz, 1H), 2.33 (s, 3H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  169.6, 167.3, 145.2, 144.0, 143.2, 132.9, 132.3, 129.9 (2C), 127.7 (2C), 127.3, 127.2, 126.3, 118.3, 110.5, 100.1, 73.3, 63.9, 53.8, 53.5, 40.5, 21.7 ppm; IR (film):  $\nu$  2950, 2161, 2020, 1732, 1547, 1292, 1169 cm<sup>-1</sup>; mp (°C) = 147–149; HRMS (ESI) [M+NH<sub>4</sub><sup>+</sup>] calculated for (C<sub>23</sub>H<sub>22</sub>N<sub>2</sub>O<sub>8</sub>SNH<sub>4</sub>)<sup>+</sup>: 504.1435, found 504.1433.

**(-)-Dimethyl 1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate ((-)-3aa)**. Obtained following the general procedure starting from **1a** (127 mg, 0.40 mmol), **2a** (75 mg, 0.44 mmol), Cu(OTf)<sub>2</sub> (8.6 mg, 0.024 mmol) and (*R*)-Difluorophos (41 mg, 0.06 mmol). The reaction was started at -10°C and slowly warmed up to room temperature. **3aa** was obtained as a white solid (175 mg, 90% yield). The enantiomeric excess (51%) was determined by HPLC (Daicel Chiralpak IA, T = 20 °C, 254 nm, 2-propanol:dichloromethane = 85:15, flow rate = 0.4 mL.min<sup>-1</sup>): t<sub>R</sub> (minor) = 16.69 min, t<sub>R</sub> (major) = 19.95 min. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -2.4 (c 0.01, dichloromethane).

**(±)-Dimethyl 1-methylene-8b-nitro-4-((2-nitrophenyl)sulfonyl)-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (3ba)**. Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **1b** (139 mg, 0.40 mmol), as a pale yellow solid (164 mg, 79% yield) after trituration in diisopropyl ether. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.85 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.70 (td, *J* = 7.8, 1.4 Hz, 1H), 7.67 – 7.60 (m, 1H), 7.62 – 7.51 (m, 3H), 7.55 – 7.46 (m, 1H), 7.30 (td, *J* = 7.6, 1.1 Hz, 1H), 6.62 (d, *J* = 0.6 Hz, 1H), 5.52 – 5.41 (m, 1H), 5.34 – 5.25 (m, 1H), 3.90 (s, 3H), 3.72 (s, 3H), 3.22 – 3.06 (m, 1H), 3.05 – 2.94 (m, 1H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  169.5, 167.3, 148.5, 143.0, 142.7, 135.1, 132.5, 131.7, 131.2, 129.8, 127.0, 126.8, 126.6, 124.5, 117.9, 111.9, 99.8, 72.9, 63.2, 53.9, 53.5, 40.9 ppm; IR (film):  $\nu$  3103, 2957, 2360, 2173, 1978, 1732,

1546 cm<sup>-1</sup>; mp (°C) = 201–203; HRMS (ESI) [M+NH<sub>4</sub><sup>+</sup>] calculated for (C<sub>22</sub>H<sub>19</sub>N<sub>3</sub>O<sub>10</sub>SNH<sub>4</sub>)<sup>+</sup>: 535.1129, found 535.1130.

**(±)-Dimethyl 4-(mesitylsulfonyl)-1-methylene-8b-nitro-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (3ca)**. Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **1c** (138 mg, 0.40 mmol), as a brownish solid (126 mg, 61% yield) after trituration in diisopropyl ether. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.57 – 7.51 (m, 2H), 7.46 – 7.40 (m, 1H), 7.28 (dd, *J* = 7.6, 1.1 Hz, 1H), 6.98 – 6.85 (m, 2H), 6.22 (s, 1H), 5.32 – 5.23 (m, 1H), 5.23 – 5.14 (m, 1H), 3.78 (s, 3H), 3.69 (s, 3H), 3.09 – 2.86 (m, 2H), 2.45 (s, 6H), 2.29 (s, 3H) ppm;

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  169.6, 167.2, 144.4, 144.2, 144.0, 141.2, 132.6 (3C), 131.8, 131.1, 127.4 (2C), 126.3, 119.9, 110.4, 100.4, 72.5, 63.4, 53.7, 53.4, 40.8, 23.5 (2C), 21.2 ppm; IR (film):  $\nu$  2950, 2360, 2338, 1737, 1550, 1355, 1166 cm<sup>-1</sup>; mp (°C) = 158–160; HRMS (ESI) [M+NH<sub>4</sub><sup>+</sup>] calculated for (C<sub>25</sub>H<sub>26</sub>N<sub>2</sub>O<sub>8</sub>SNH<sub>4</sub>)<sup>+</sup>: 532.1748, found 532.1748.

**(±)-Dimethyl 1-methylene-8b-nitro-4-((2,4,6-triisopropylphenyl)sulfonyl)-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (3da)**. Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **1d** (171 mg, 0.40 mmol), as a white solid (100 mg, 42% yield) after flash column chromatography (petroleum ether/ethyl acetate 98:2 to 8:2). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.58 – 7.48 (m, 2H), 7.44 (td, *J* = 7.6, 1.4 Hz, 1H), 7.25 (td, *J* = 7.6, 1.1 Hz, 1H), 7.12 (s, 2H), 6.30 (s, 1H), 5.33 – 5.24 (m, 1H), 5.22 – 5.12 (m, 1H), 3.95 (hept, *J* = 6.7 Hz, 2H), 3.79 (s, 3H), 3.71 (s, 3H), 3.03 (dt, *J* = 16.0, 2.3 Hz, 1H), 2.98 – 2.79 (m, 2H), 1.25 (d, *J* = 5.4 Hz, 6H), 1.23 (d, *J* = 5.4 Hz, 6H), 0.89 (s, 6H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  169.5, 167.3, 154.2, 152.0 (2C), 144.2, 143.9, 131.7, 130.1, 127.9, 127.4, 126.4, 124.6 (2C), 120.0, 110.3, 99.8, 72.0, 63.4, 53.6, 53.3, 40.7, 34.3, 30.9 (2C), 24.9 (2C), 24.8 (2C), 23.61, 23.57 ppm; IR (film):  $\nu$  2955, 2359, 1735, 1600, 1551, 1172 cm<sup>-1</sup>; mp (°C) = 197–199; HRMS (ESI) [M+H<sup>+</sup>] calculated for (C<sub>31</sub>H<sub>38</sub>N<sub>2</sub>O<sub>8</sub>SH)<sup>+</sup>: 599.2422, found 599.2423.

**(±)-Dimethyl 4-benzoyl-1-methylene-8b-nitro-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (3ea)**. Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (150 mg, 0.88 mmol), starting from **1e** (213 mg, 0.80 mmol), as a yellow oil (223 mg, 61% yield) after flash column chromatography (petroleum ether/ethyl acetate 8:2 to 6:4). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.67 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.57 (s, 1H), 7.55 (p, *J* = 2.0 Hz, 2H), 7.52 (t, *J* = 1.5 Hz, 1H), 7.48 (dd, *J* = 7.9, 6.6 Hz, 2H), 7.26 – 7.18 (m, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.78 (s, 1H), 5.77 (q, *J* = 1.9 Hz, 1H), 5.39 (q, *J* = 1.9 Hz, 1H), 3.65 (s, 3H), 3.48 (s, 3H), 3.27 (dt, *J* = 16.3, 2.0 Hz, 1H), 3.04 (d (broad), *J* = 16.3 Hz, 1H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  169.3, 169.1, 167.4, 142.9, 142.7, 135.3, 131.6, 131.1, 128.7 (2C), 127.6 (2C), 126.5, 126.0, 124.7, 116.2, 112.7, 98.3, 73.3, 61.4, 53.5, 53.1, 41.4 ppm; IR (film):  $\nu$  3008, 2953, 2360, 1732, 1660, 1550, 1378 cm<sup>-1</sup>; HRMS (ESI) [M+H<sup>+</sup>] calculated for (C<sub>23</sub>H<sub>20</sub>N<sub>2</sub>O<sub>7</sub>H): 437.1343<sup>+</sup>, found 437.1344.

**(±)-Dimethyl 4-acetyl-1-methylene-8b-nitro-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (3fa)**. Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (150 mg, 0.88 mmol), starting

from **1f** (163 mg, 0.80 mmol), as a pale brown solid (128 mg, 43% yield) after flash column chromatography (petroleum ether/ ethyl acetate 9:1 to 8:2).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (brs, 1H), 7.60 (d,  $J = 7.7$  Hz, 1H), 7.42 (td,  $J = 7.7$ , 1.4 Hz, 1H), 7.20 (td,  $J = 7.6$ , 1.0 Hz, 1H), 6.66 (s, 1H), 5.58 (dt,  $J = 2.5$ , 1.3 Hz, 1H), 5.33 (dt,  $J = 2.5$ , 1.3 Hz, 1H), 3.85 (s, 3H), 3.57 (s, 3H), 3.30 (d,  $J = 16.6$  Hz, 1H), 3.02 (d,  $J = 16.6$  Hz, 1H), 2.41 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.2, 169.5, 167.4, 143.3, 142.2, 132.2, 126.5, 125.5, 125.1, 118.1, 111.5, 99.9, 72.1, 62.7, 53.9, 53.4, 40.7, 23.9 ppm; IR (film):  $\nu$  3008, 2957, 2360, 1756, 1732, 1677, 1543  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 118–120; HRMS (ESI)  $[\text{M}+\text{H}^+]$  calculated for  $(\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_7\text{H})^+$ : 375.1187, found 375.1186.

( $\pm$ )-4-ethyl 3,3-dimethyl 1-methylene-8b-nitro-1,2,3a,8b-tetrahydrocyclopenta[b]indole-3,3,4-tricarboxylate (**3ga**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **1g** (94 mg, 0.40 mmol), as a yellow oil (81 mg, 50% yield) after flash column chromatography (petroleum ether/ ethyl acetate 9:1 to 8:2).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.81 (brs, 1H), 7.65 (dd,  $J = 7.6$ , 1.3 Hz, 1H), 7.48 – 7.35 (m, 1H), 7.13 (td,  $J = 7.6$ , 1.1 Hz, 1H), 6.56 (s, 1H), 5.69 (dt,  $J = 3.3$ , 1.6 Hz, 1H), 5.36 (dt,  $J = 2.9$ , 1.5 Hz, 1H), 4.37 – 4.13 (m, 2H), 3.86 (s, 3H), 3.49 (s, 3H), 3.23 (dt,  $J = 15.9$ , 1.9 Hz, 1H), 3.10 (dt,  $J = 15.9$ , 2.2 Hz, 1H), 1.35 (t,  $J = 7.2$  Hz, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.7, 167.8, 152.3, 144.0, 142.7, 132.1, 126.5, 124.7, 123.9, 115.6, 112.4, 99.3, 72.4, 62.6, 62.1, 53.5, 53.1, 41.9, 14.4 ppm; IR (film):  $\nu$  2955, 2359, 1731, 1551, 1273, 1067  $\text{cm}^{-1}$ ; HRMS (ESI)  $[\text{M}+\text{H}^+]$  calculated for  $(\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_8\text{H})^+$ : 405.1292, found 405.1292.

( $\pm$ )-4-(*tert*-butyl) 3,3-dimethyl 1-methylene-8b-nitro-1,2,3a,8b-tetrahydrocyclopenta[b]indole-3,3,4-tricarboxylate (**3ha**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **1h** (105 mg, 0.40 mmol), as a yellow solid (133 mg, 77% yield) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 9:1 to 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.74 (brs, 1H), 7.62 (dd,  $J = 7.6$ , 1.1 Hz, 1H), 7.45 – 7.34 (m, 1H), 7.11 (td,  $J = 7.6$ , 1.1 Hz, 1H), 6.56 (s, 1H), 5.72 – 5.51 (m, 1H), 5.40 – 5.23 (m, 1H), 3.86 (s, 3H), 3.56 (s, 3H), 3.29 – 3.01 (m, 2H), 1.56 (s, 9H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.8, 168.0, 151.4, 144.3, 143.1, 132.1, 126.6, 124.8, 123.6, 115.8, 111.5, 99.4, 83.0, 72.3, 62.5, 53.6, 53.2, 41.8, 28.3 (3C) ppm; IR (film):  $\nu$  2996, 2968, 2360, 2342, 1734, 1716, 1548  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 123–125; HRMS (ESI)  $[\text{M}+\text{Na}^+]$  calculated for  $(\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_8\text{Na})^+$ : 455.1425, found 455.1424.

( $\pm$ )-Dimethyl 7-acetoxy-1-methylene-8b-nitro-1,2,3a,8b-tetrahydro-3H-cyclopenta[b]benzofuran-3,3-dicarboxylate (**5**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **4** (89 mg, 0.40 mmol), as a pale yellow solid (129 mg, 82% yield) after flash column chromatography (petroleum ether/ ethyl acetate 9:1 to 8:2).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 (d,  $J = 2.4$  Hz, 1H), 7.06 (dd,  $J = 8.8$ , 2.4 Hz, 1H), 6.82 (d,  $J = 8.8$  Hz, 1H), 6.57 (d,  $J = 1.2$  Hz, 1H), 5.69 – 5.54 (m, 1H), 5.36 – 5.23 (m, 1H), 3.83 (s, 3H), 3.75 (s, 3H), 3.27 – 3.10 (m, 1H), 3.10 – 2.96 (m, 1H), 2.28 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.6, 168.9, 166.7, 157.3, 145.5, 143.8, 126.0, 123.3, 119.1, 111.9, 111.1, 101.1, 92.1, 63.3, 53.7, 53.3, 39.3, 21.1 ppm; IR (film):  $\nu$  3019, 2955, 2359, 1738, 1556, 1481, 1216  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 136–138; HRMS

(ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{18}\text{H}_{17}\text{NO}_9\text{NH}_4)^+$ : 409.1242, found 409.1242.

( $\pm$ )-Dimethyl 8-methyl-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (**7aa**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6a** (132 mg, 0.40 mmol), as a pale brown solid (140 mg, 70% yield) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 9:1 to 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.59 (d,  $J = 7.9$  Hz, 1H), 7.48 – 7.40 (m, 2H), 7.36 (t,  $J = 7.9$  Hz, 1H), 7.16 – 7.08 (m, 2H), 6.98 (d,  $J = 7.9$  Hz, 1H), 6.38 (d,  $J = 1.0$  Hz, 1H), 5.41 – 5.31 (m, 1H), 5.07 – 4.96 (m, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.06 (dt,  $J = 15.5$ , 2.6 Hz, 1H), 2.89 (dd,  $J = 15.5$ , 0.9 Hz, 1H), 2.35 (s, 3H), 2.24 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.6, 167.1, 145.2, 144.1, 141.8, 139.4, 133.1, 132.3, 129.9 (2C), 129.3, 127.7 (2C), 124.5, 116.4, 113.6, 101.6, 74.0, 63.5, 53.9, 53.6, 40.9, 21.7, 18.6 ppm; IR (film):  $\nu$  3004, 2955, 2360, 2342, 1732, 1552, 1171  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 176–178; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_8\text{SNH}_4)^+$ : 518.1592, found 518.1590.

( $\pm$ )-Trimethyl 1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3,8(2H)-tricarboxylate (**7ba**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6b** (151 mg, 0.40 mmol), as a pale pink solid (153 mg, 70% yield) after trituration in diisopropyl ether.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 (dd,  $J = 8.3$ , 1.1 Hz, 1H), 7.75 (dd,  $J = 7.7$ , 1.1 Hz, 1H), 7.58 – 7.47 (m, 3H), 7.23 – 7.14 (m, 2H), 5.92 (s, 1H), 5.37 – 5.31 (m, 2H), 3.87 (s, 3H), 3.87 (s, 3H), 3.74 (s, 3H), 2.93 (d,  $J = 1.6$  Hz, 2H), 2.35 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.1, 165.0, 145.6, 145.6, 139.7, 132.9, 132.0, 130.1 (2C), 128.27, 128.25, 128.0, 127.9 (2C), 122.1, 117.4, 97.8, 76.6, 63.4, 53.8, 53.6, 52.4, 41.5, 21.8 ppm; IR (film):  $\nu$  3004, 2955, 2359, 2340, 1731, 1559, 1365  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 163–165; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{25}\text{H}_{24}\text{N}_2\text{O}_{10}\text{SNH}_4)^+$ : 562.1490, found 562.1486.

( $\pm$ )-Dimethyl 8-chloro-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (**7ca**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6c** (140 mg, 0.40 mmol), as a white solid (182 mg, 88% yield) after flash column chromatography (petroleum ether/methyl *tert*-butyl ether 8:2 to 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (dd,  $J = 8.3$ , 0.9 Hz, 1H), 7.48 – 7.34 (m, 3H), 7.20 – 7.11 (m, 3H), 6.24 (d,  $J = 1.1$  Hz, 1H), 5.45 (dt,  $J = 2.6$ , 1.0 Hz, 1H), 5.19 (dt,  $J = 2.7$ , 0.7 Hz, 1H), 3.88 (s, 3H), 3.88 (s, 3H), 3.07 (dt,  $J = 15.7$ , 2.6 Hz, 1H), 2.96 (dd,  $J = 15.7$ , 1.1 Hz, 1H), 2.36 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.0, 145.7, 145.6, 139.6, 134.0, 133.2, 132.6, 130.1 (2C), 128.1, 127.5 (2C), 124.1, 117.0, 116.3, 100.4, 75.0, 63.5, 53.9, 53.6, 40.8, 21.7 ppm; IR (film):  $\nu$  3020, 2957, 2358, 2338, 1731, 1552, 1365  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 147–149; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{23}\text{H}_{21}\text{ClN}_2\text{O}_8\text{SNH}_4)^+$ : 538.1045, found 538.1045.

( $\pm$ )-Dimethyl 7-methyl-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (**7da**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6d** (132 mg, 0.40 mmol), as a yellow solid (158 mg, 79% yield) after trituration in diisopropyl

ether.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57 (d,  $J = 8.3$  Hz, 1H), 7.48 – 7.40 (m, 2H), 7.28 – 7.21 (m, 1H), 7.21 – 7.15 (m, 1H), 7.10 (d,  $J = 8.1$  Hz, 2H), 6.47 (d,  $J = 0.9$  Hz, 1H), 5.24 – 5.18 (m, 1H), 5.18 – 5.05 (m, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.05 (dt,  $J = 16.1, 2.5$  Hz, 1H), 2.91 (dq,  $J = 16.1, 1.1$  Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.6, 167.2, 145.0, 144.0, 140.8, 136.3, 133.2, 132.8, 129.8 (2C), 127.7 (2C), 127.4, 127.1, 118.0, 110.3, 100.1, 73.4, 63.8, 53.7, 53.4, 40.3, 21.6, 21.2 ppm; IR (film):  $\nu$  3002, 2957, 2359, 1735, 1561, 1170  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 176-178; HRMS (ESI)  $[\text{M}+\text{NH}_4]^+$  calculated for  $(\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_8\text{SNH}_4)^+$ : 518.1592, found 518.1591.

**(±)-Trimethyl 1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3,7(2H)-tricarboxylate (7ea).** Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6e** (151 mg, 0.40 mmol), as a pale brown solid (160 mg, 73% yield) after trituration in diisopropyl ether.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.28 – 8.03 (m, 2H), 7.74 (dd,  $J = 8.6, 0.6$  Hz, 1H), 7.56 – 7.39 (m, 2H), 7.21 – 7.02 (m, 2H), 6.54 (d,  $J = 1.0$  Hz, 1H), 5.44 – 5.29 (m, 1H), 5.29 – 5.14 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.82 (s, 3H), 3.08 (dt,  $J = 16.2, 2.4$  Hz, 1H), 2.97 (dq,  $J = 16.2, 1.2$  Hz, 1H), 2.31 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.15, 165.7, 146.6, 145.6, 143.1, 133.9, 132.8, 130.0 (2C), 129.0, 128.2, 127.5 (2C), 127.3, 117.3, 111.5, 99.3, 73.8, 63.8, 53.8, 53.5, 52.4, 40.6, 21.7 ppm; IR (film):  $\nu$  3012, 2955, 2360, 2342, 1737, 1718, 1558  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 181-183; HRMS (ESI)  $[\text{M}+\text{NH}_4]^+$  calculated for  $(\text{C}_{25}\text{H}_{24}\text{N}_2\text{O}_{10}\text{SNH}_4)^+$ : 562.1490, found 562.1486.

**(±)-Dimethyl 7-fluoro-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (7fa).** Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6f** (135 mg, 0.40 mmol), as a white solid (197 mg, 98% yield) after flash column chromatography (petroleum ether/methyl *tert*-butyl ether 8:2).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (dd,  $J = 8.9, 4.4$  Hz, 1H), 7.48 – 7.38 (m, 2H), 7.21 – 7.08 (m, 4H), 6.48 (d,  $J = 1.0$  Hz, 1H), 5.20 (ddt,  $J = 7.9, 2.6, 1.3$  Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.07 (dt,  $J = 16.2, 2.6$  Hz, 1H), 2.95 (dq,  $J = 16.2, 1.2$  Hz, 1H), 2.35 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.1, 160.8 (d,  $J_{\text{C-F}} = 246.6$  Hz), 145.5, 143.8, 139.3, 132.4, 130.0 (2C), 129.0 (d,  $J_{\text{C-F}} = 8.9$  Hz), 127.7 (2C), 119.79 (d,  $J_{\text{C-F}} = 8.5$  Hz), 119.77 (d,  $J_{\text{C-F}} = 23.8$  Hz), 114.2 (d,  $J_{\text{C-F}} = 25.0$  Hz), 110.9, 99.6, 73.7, 63.9, 53.9, 53.6, 40.3, 21.7 ppm;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -114.77 (m) ppm; IR (film):  $\nu$  3008, 2955, 2360, 2338, 1732, 1547, 1483, 1167  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 150-152; HRMS (ESI)  $[\text{M}+\text{NH}_4]^+$  calculated for  $\text{C}_{23}\text{H}_{21}\text{FN}_2\text{O}_8\text{SNH}_4$ : 522.1341, found 522.13437.

**(±)-Dimethyl 7-chloro-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (7ga).** Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6g** (140 mg, 0.40 mmol), as a white solid (168 mg, 81% yield) after flash column chromatography (petroleum ether/methyl *tert*-butyl ether 8:2 to 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.65 (dd,  $J = 8.6, 0.6$  Hz, 1H), 7.50 – 7.42 (m, 2H), 7.46 – 7.36 (m, 2H), 7.21 – 7.11 (m, 2H), 6.48 (s, 1H), 5.24 (dt,  $J = 2.5, 1.2$  Hz, 1H), 5.20 (dt,  $J = 2.6, 1.2$  Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.08 (dt,  $J = 16.2, 2.6$  Hz, 1H), 2.95 (dq,  $J = 16.2, 1.1$  Hz, 1H), 2.35 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.1, 145.5, 143.5, 141.8,

132.5, 132.5, 131.7, 130.0 (2C), 128.7, 127.6 (2C), 127.4, 119.3, 111.1, 99.5, 73.6, 63.8, 53.8, 53.5, 40.4, 21.7 ppm; IR (film):  $\nu$  3103, 2998, 2359, 1736, 1563, 1171  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 156-158; HRMS (ESI)  $[\text{M}+\text{NH}_4]^+$  calculated for  $(\text{C}_{23}\text{H}_{21}\text{ClN}_2\text{O}_8\text{SNH}_4)^+$ : 538.1045, found 538.1046.

**(±)-Dimethyl 7-bromo-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (7ha).** Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6h** (159 mg, 0.40 mmol), as a yellow solid (165 mg, 79% yield) after trituration in diisopropyl ether.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.63 – 7.53 (m, 3H), 7.49 – 7.44 (m, 2H), 7.19 – 7.14 (m, 2H), 6.48 (d,  $J = 0.9$  Hz, 1H), 5.25 (dt,  $J = 2.6, 1.2$  Hz, 1H), 5.21 (dt,  $J = 2.6, 1.3$  Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.08 (dt,  $J = 16.2, 2.5$  Hz, 1H), 2.96 (dq,  $J = 16.1, 1.1$  Hz, 1H), 2.36 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.2, 145.6, 143.5, 142.3, 135.4, 132.6, 130.4, 130.1 (C2), 129.0, 127.7 (2C), 119.7, 119.1, 111.2, 99.5, 73.5, 63.9, 53.9, 53.6, 40.5, 21.8 ppm; IR (film):  $\nu$  2998, 2955, 2360, 2342, 2024, 1736, 1171  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 164-166; HRMS (ESI)  $[\text{M}+\text{NH}_4]^+$  calculated for  $(\text{C}_{23}\text{H}_{21}\text{BrN}_2\text{O}_8\text{SNH}_4)^+$ : 582.0540, found 582.0543.

**(±)-Dimethyl 7-iodo-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (7ia).** Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6i** (177 mg, 0.40 mmol), as a brown solid (199 mg, 81% yield) after trituration in diisopropyl ether.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.80 – 7.66 (m, 2H), 7.53 – 7.43 (m, 3H), 7.21 – 7.10 (m, 2H), 6.46 (d,  $J = 0.9$  Hz, 1H), 5.27 – 5.22 (m, 1H), 5.22 – 5.16 (m, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.08 (dt,  $J = 16.2, 2.6$  Hz, 1H), 2.95 (dq,  $J = 16.2, 1.1$  Hz, 1H), 2.36 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.1, 145.5, 143.4, 143.0, 141.2, 136.2, 132.6, 130.1 (2C), 129.2, 127.6 (2C), 119.9, 111.2, 99.4, 89.4, 73.3, 63.9, 53.9, 53.6, 40.5, 21.7 ppm; IR (film):  $\nu$  2953, 2360, 2342, 1736, 1562, 1173  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 173-175; HRMS (ESI)  $[\text{M}+\text{NH}_4]^+$  calculated for  $(\text{C}_{23}\text{H}_{21}\text{IN}_2\text{O}_8\text{SNH}_4)^+$ : 630.0402, found 630.0403.

**(±)-Dimethyl 7-cyano-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (7ja).** Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6j** (137 mg, 0.40 mmol), as a white solid (192 mg, 94% yield) after flash column chromatography (petroleum ether/methyl *tert*-butyl ether 8:2 to 6:4).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.80 (dd,  $J = 8.4, 0.7$  Hz, 1H), 7.77 – 7.68 (m, 2H), 7.54 – 7.46 (m, 2H), 7.21 – 7.14 (m, 2H), 6.53 (d,  $J = 0.9$  Hz, 1H), 5.33 (dt,  $J = 2.7, 1.5$  Hz, 1H), 5.30 – 5.24 (m, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 3.08 (dt,  $J = 16.4, 2.4$  Hz, 1H), 3.01 (dq,  $J = 16.4, 1.3$  Hz, 1H), 2.34 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.2, 167.1, 146.4, 146.0, 142.9, 136.1, 132.6, 131.7, 130.2 (2C), 127.9, 127.4 (2C), 118.2, 117.8, 111.9, 109.7, 99.0, 73.6, 63.7, 53.9, 53.6, 40.6, 21.7 ppm; IR (film):  $\nu$  3000, 2959, 2359, 2234, 1737, 1566, 1171  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 130-140; HRMS (ESI)  $[\text{M}+\text{NH}_4]^+$  calculated for  $(\text{C}_{24}\text{H}_{21}\text{N}_3\text{O}_8\text{SNH}_4)^+$ : 529.1388, found 529.13874.

**(±)-Dimethyl 6-methyl-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (7ka).** Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg,

0.44 mmol), starting from **6k** (132 mg, 0.40 mmol), as a pale brown solid (132 mg, 66% yield) after trituration in diisopropyl ether.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 – 7.50 (m, 1H), 7.51 – 7.43 (m, 2H), 7.29 (d,  $J = 8.0$  Hz, 1H), 7.16 – 7.08 (m, 2H), 7.03 (dq,  $J = 8.0, 0.7$  Hz, 1H), 6.47 (d,  $J = 0.9$  Hz, 1H), 5.20 (dt,  $J = 2.4, 1.1$  Hz, 1H), 5.14 (dt,  $J = 2.5, 1.2$  Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.07 (dt,  $J = 16.0, 2.6$  Hz, 1H), 2.92 (dq,  $J = 16.0, 1.1$  Hz, 1H), 2.42 (t,  $J = 0.7$  Hz, 3H), 2.33 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.5, 167.2, 145.0, 144.0, 143.2, 143.1, 132.8, 129.8 (2C), 127.5 (2C), 127.3, 126.7, 124.3, 118.5, 110.0, 99.9, 73.4, 63.7, 53.7, 53.4, 40.3, 21.9, 21.6 ppm; IR (film):  $\nu$  2957, 2359, 2023, 1749, 1724, 1550, 1172  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 177-179; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_8\text{SNH}_4)^+$ : 518.1592, found 518.1583.

( $\pm$ )-Dimethyl 6-chloro-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (**7la**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6l** (140 mg, 0.40 mmol), as a white solid (178 mg, 86% yield) after flash column chromatography (petroleum ether/methyl *tert*-butyl ether 8:2 to 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.72 (d,  $J = 1.8$  Hz, 1H), 7.57 – 7.44 (m, 2H), 7.35 (d,  $J = 8.3$  Hz, 1H), 7.22 – 7.13 (m, 3H), 6.49 (d,  $J = 0.9$  Hz, 1H), 5.27 – 5.21 (m, 1H), 5.21 – 5.18 (m, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.09 (dt,  $J = 16.2, 2.5$  Hz, 1H), 2.96 (dq,  $J = 16.2, 1.1$  Hz, 1H), 2.35 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.2, 145.6, 144.2, 143.6, 138.6, 132.7, 130.1 (2C), 128.2, 127.7 (2C), 126.7, 125.6, 118.3, 110.9, 99.5, 73.7, 63.8, 53.9, 53.6, 40.5, 21.7 ppm; IR (film):  $\nu$  3026, 2959, 2359, 2338, 1748, 1727, 1551  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 190-192; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{23}\text{H}_{21}\text{ClN}_2\text{O}_8\text{SNH}_4)^+$ : 538.1045, found 538.1046.

( $\pm$ )-Dimethyl 5-methyl-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (**7ma**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6m** (132 mg, 0.40 mmol), as a white solid (118 mg, 59% yield) after trituration in diisopropyl ether.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 – 7.30 (m, 1H), 7.31 – 7.24 (m, 1H), 7.28 – 7.21 (m, 3H), 7.15 – 7.07 (m, 2H), 6.42 (s, 1H), 5.04 – 4.96 (m, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 2.83 – 2.70 (m, 2H), 2.55 (s, 3H), 2.38 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.5, 167.2, 145.7, 145.5, 142.4, 134.6, 132.6, 131.9, 130.3, 129.9 (2C), 128.4 (2C), 127.8, 125.4, 109.2, 99.5, 73.4, 64.0, 53.8, 53.5, 39.6, 21.8, 20.2 ppm; IR (film):  $\nu$  3034, 2955, 2359, 2340, 1730, 1544, 1163  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 174-176; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_8\text{SNH}_4)^+$ : 518.1592, found 518.1584.

( $\pm$ )-Trimethyl 1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3,5(2H)-tricarboxylate (**7na**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6n** (151 mg, 0.40 mmol), as a yellow solid (148 mg, 68% yield) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 8:2 to 6:4).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90 (dd,  $J = 7.7, 1.4$  Hz, 1H), 7.59 (dd,  $J = 7.7, 1.4$  Hz, 1H), 7.39 (t,  $J = 7.7$  Hz, 1H), 7.26 (d,  $J = 8.1$  Hz, 2H), 7.11 (d,  $J = 8.1$  Hz, 2H), 6.35 (s, 1H), 5.13 – 5.06 (m, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 3.85 (s, 3H), 2.99 (dt,  $J = 16.3, 2.6$  Hz, 1H), 2.92 – 2.86 (m, 1H), 2.37 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.1, 166.6, 145.8, 144.9,

141.4, 133.7, 131.8, 130.7, 130.0 (2C), 129.9, 128.2 (2C), 127.2, 125.8, 110.1, 99.6, 73.6, 63.9, 53.8, 53.5, 52.5, 39.8, 21.8 ppm; IR (film):  $\nu$  3094, 3026, 2955, 2357, 1734, 1555, 1433  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 164-166; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{25}\text{H}_{24}\text{N}_2\text{O}_{10}\text{SNH}_4)^+$ : 562.1490, found 562.14825.

( $\pm$ )-Dimethyl 5-chloro-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (**7oa**). Obtained following the general procedure with dimethyl 2-(prop-2-yn-1-yl)malonate **2a** (75 mg, 0.44 mmol), starting from **6o** (140 mg, 0.40 mmol), as a white solid (179 mg, 86% yield) after flash column chromatography (petroleum ether/ ethyl acetate 8:2 to 6:4).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.62 – 7.54 (m, 2H), 7.49 (dd,  $J = 7.8, 1.2$  Hz, 1H), 7.39 (dd,  $J = 7.8, 1.2$  Hz, 1H), 7.27 (t,  $J = 7.8$  Hz, 1H), 7.23 – 7.17 (m, 2H), 6.59 (s, 1H), 5.14 (ddt,  $J = 7.2, 2.9, 1.5$  Hz, 2H), 3.81 (s, 3H), 3.67 (s, 3H), 2.95 – 2.82 (m, 2H), 2.40 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.4, 167.0, 145.5, 144.8, 141.0, 133.6, 133.2, 132.3, 129.8 (2C), 128.7, 128.5 (2C), 127.1, 126.3, 110.6, 99.8, 74.4, 63.4, 53.8, 53.5, 39.6, 21.8 ppm; IR (film):  $\nu$  3020, 2953, 2360, 2342, 1729, 1546, 1432  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 163-165; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{23}\text{H}_{21}\text{ClN}_2\text{O}_8\text{SNH}_4)^+$ : 538.1045, found 538.1044.

( $\pm$ )-Diisopropyl 1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (**3ab**). Obtained following the general procedure with **2b** (100 mg, 0.44 mmol), starting from **1a** (127 mg, 0.40 mmol), as a white solid (155 mg, 71% yield) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 9:1 to 8:2).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.73 (dd,  $J = 8.2, 0.8$  Hz, 1H), 7.51 – 7.39 (m, 4H), 7.23 (td,  $J = 7.6, 1.0$  Hz, 1H), 7.09 (dd,  $J = 8.0, 0.7$  Hz, 2H), 6.49 (s, 1H), 5.28 – 5.14 (m, 2H), 5.18 – 5.11 (m, 1H), 5.07 (hept,  $J = 6.3$  Hz, 1H), 3.16 – 2.99 (m, 1H), 2.99 – 2.76 (m, 1H), 2.32 (s, 3H), 1.42 (d,  $J = 6.3$  Hz, 3H), 1.34 (d,  $J = 6.3$  Hz, 3H), 1.30 (d,  $J = 6.3$  Hz, 3H), 1.29 (d,  $J = 6.3$  Hz, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.6, 166.5, 145.1, 144.6, 143.4, 133.0, 132.2, 129.8, 127.7, 127.5, 127.4, 126.3, 118.6, 110.1, 100.4, 73.2, 71.1, 70.4, 63.8, 40.9, 21.8, 21.7 (3C), 21.6 ppm; IR (film):  $\nu$  3447, 2981, 2933, 2360, 2025, 1724, 1551, 1167  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 132-134; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{27}\text{H}_{30}\text{N}_2\text{O}_8\text{SNH}_4)^+$ : 560.2061, found 560.2061.

( $\pm$ )-Dibenzyl 1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (**3ac**). Obtained following the general procedure with **2c** (142 mg, 0.44 mmol), starting from **1a** (127 mg, 0.40 mmol), as a white solid (219 mg, 86% yield) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 85:15 to 8:2).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (dd,  $J = 8.6, 1.0$  Hz, 1H), 7.47 – 7.36 (m, 4H), 7.30 (m, 8H), 7.26 – 7.15 (m, 3H), 7.10 – 7.01 (m, 2H), 6.51 (s, 1H), 5.34 (d,  $J = 12.2$  Hz, 1H), 5.24 – 5.18 (m, 1H), 5.18 (d,  $J = 5.6$  Hz, 2H), 5.13 (d,  $J = 12.2$  Hz, 1H), 5.12 – 5.05 (m, 1H), 3.04 (dt,  $J = 16.0, 2.5$  Hz, 1H), 2.93 (dq,  $J = 16.0, 1.2$  Hz, 1H), 2.29 (s, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.8, 166.6, 145.2, 144.0, 143.2, 135.2, 134.9, 132.8, 132.3, 129.9 (2C), 128.7 (2C), 128.63 (2C), 128.62, 128.57 (2C), 128.55 (2C), 128.4, 127.7 (2C), 127.2, 127.1, 126.2, 118.3, 110.6, 100.1, 73.3, 68.6, 68.5, 64.1, 40.6, 21.7 ppm; IR (film):  $\nu$  3018, 2360, 1722, 1595, 1552, 1162  $\text{cm}^{-1}$ ; mp ( $^\circ\text{C}$ ) = 135-137; HRMS (ESI)  $[\text{M}+\text{NH}_4^+]$  calculated for  $(\text{C}_{35}\text{H}_{30}\text{N}_2\text{O}_8\text{SNH}_4)^+$ : 656.2061, found 656.2063.

**(±)-1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarbonitrile (3ae).** Obtained following the general procedure with **2e** (46 mg, 0.44 mmol), starting from **1a** (127 mg, 0.40 mmol), as a brown solid (138 mg, 82% yield) after trituration in a mixture diisopropyl ether/hexane (1:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.87 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.60 – 7.53 (m, 3H), 7.30 (td, *J* = 7.7, 1.0 Hz, 1H), 7.19 (dd, *J* = 8.0, 0.6 Hz, 2H), 5.91 (dq, *J* = 2.4, 1.3 Hz, 1H), 5.85 (s, 1H), 5.67 – 5.62 (m, 1H), 3.39 (dt, *J* = 15.6, 2.4 Hz, 1H), 3.22 (dt, *J* = 15.6, 1.4 Hz, 1H), 2.36 (s, 3H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>) δ 146.1, 142.2, 139.5, 133.3, 132.5, 130.3 (2C), 127.6 (2C), 126.7, 126.6, 125.2, 118.9, 117.6, 113.1, 111.4, 97.4, 75.8, 43.6, 41.1, 21.8 ppm; IR (film): ν 3008, 2360, 2338, 2022, 1743, 1557, 1370 cm<sup>-1</sup>; mp (°C) = 178–180; HRMS (ESI) [M+NH<sub>4</sub><sup>+</sup>] calculated for (C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>4</sub>SNH<sub>4</sub>)<sup>+</sup>: 438.1231, found 438.1230.

**(±)-3-(tert-butyl) 3-methyl 1-methylene-8b-nitro-4-tosyl-1,3a,4,8b-tetrahydrocyclopenta[b]indole-3,3(2H)-dicarboxylate (3af).** Obtained following the general procedure with **2f** (93 mg, 0.44 mmol), starting from **1a** (127 mg, 0.40 mmol), as an orange oil (159 mg, 72% yield, *dr* 3:1) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 85:15 to 8:2). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ **maj** : 7.76 – 7.69 (m, 1H), 7.50 – 7.42 (m, 2H), 7.46 – 7.38 (m, 2H), 7.27 – 7.18 (m, 1H), 7.12 – 7.04 (m, 2H), 6.47 (s, 1H), 5.20 – 5.16 (m, 1H), 5.16 – 5.12 (m, 1H), 3.86 (s, 3H), 3.03 (dt, *J* = 16.3, 2.5 Hz, 1H), 2.90 – 2.80 (m, 1H), 2.31 (s, 3H), 1.51 (s, 9H) ppm; **min** (selected signals) : 6.43 (s, 1H), 5.21 (dt, *J* = 2.2, 1.0 Hz, 1H), 3.81 (s, 3H), 3.00 – 2.90 (m, 2H), 1.51 (s, 9H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>) δ **maj** : 170.1, 165.4, 145.1, 144.5, 143.4, 132.9, 132.2, 129.8 (2C), 127.6 (2C), 127.5, 127.4, 126.3, 118.6, 110.3, 100.4, 83.8, 73.2, 64.2, 53.4, 40.5, 27.7, 21.6 ppm; **min** : 170.1, 167.6, 145.1, 144.4, 143.1, 132.8, 132.2, 129.8(2C), 127.6 (2C), 127.4, 127.2, 126.2, 118.3, 109.7, 100.0, 83.5, 73.0, 64.5, 53.2, 40.5, 27.7, 21.6 ppm; IR (film): ν 2978, 2359, 1729, 1551, 1367, 1170 cm<sup>-1</sup>; HRMS (ESI) [M+NH<sub>4</sub><sup>+</sup>] calculated for (C<sub>26</sub>H<sub>28</sub>N<sub>2</sub>O<sub>8</sub>SNH<sub>4</sub>)<sup>+</sup>: 546.1905, found 546.1904.

**(±)-Methyl-3-cyano-1-methylene-8b-nitro-4-tosyl-1,2,3,3a,4,8b-hexahydrocyclopenta[b]indole-3-carboxylate (3ah).** Obtained following the general procedure with **2h** (60 mg, 0.44 mmol), starting from **1a** (127 mg, 0.40 mmol), as a yellow oil (125 mg, 69% yield, *dr* 3:1) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 8:2 to 7:3). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ **maj** : 7.86 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.69 (ddd, *J* = 7.9, 1.3, 0.6 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.56 – 7.48 (m, 1H), 7.30 – 7.22 (m, 1H), 7.22 – 7.15 (m, 2H), 5.91 (ddd, *J* = 2.9, 1.6, 1.0 Hz, 1H), 5.88 (s, 1H), 5.60 – 5.54 (m, 1H), 4.03 (s, 3H), 3.36 (dt, *J* = 15.6, 2.8 Hz, 1H), 3.06 (dd, *J* = 15.6, 0.8 Hz, 1H), 2.35 (s, 3H) ppm; **min** (selected signals) : 7.49 – 7.46 (m, 1H), 7.17 – 7.13 (m, 2H), 5.94 (s, 1H), 5.61 (m, 1H), 5.41 (m, 1H), 3.85 (s, 3H), 3.13 – 3.09 (m, 2H), 2.33 (s, 3H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>) δ **maj** : 167.1, 145.6, 142.3, 141.6, 132.8, 132.5, 130.1 (2C), 127.3 (2C), 126.9, 126.3, 125.8, 118.1, 117.1, 116.8, 98.0, 75.9, 54.8, 54.5, 43.1, 21.7 ppm; **min** : 164.7, 145.1, 142.6, 142.4, 133.0, 132.4, 130.1 (2C), 127.5 (2C), 127.3, 126.4, 126.3, 117.6, 115.0, 113.6, 99.1, 76.017, 54.3, 52.1, 41.7, 21.7 ppm; IR (film): ν 3022, 2055, 2360, 2340, 1748, 1555, 1170 cm<sup>-1</sup>; HRMS (ESI) [M+NH<sub>4</sub><sup>+</sup>] calculated for (C<sub>22</sub>H<sub>19</sub>N<sub>3</sub>O<sub>6</sub>SNH<sub>4</sub>)<sup>+</sup>: 471.1333, found 471.1332.

**(±)-Tert-butyl-3-cyano-1-methylene-8b-nitro-4-tosyl-1,2,3,3a,4,8b-hexahydrocyclopenta[b]indole-3-carboxylate (3ai).** Obtained following the general procedure with **2i** (79 mg, 0.44 mmol), starting from **1a** (127 mg, 0.40 mmol), as a brown oil (167 mg, 84% yield, *dr* 5:1) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 9:1 to 7:3). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ **maj** : 7.84 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.66 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.55 – 7.52 (m, 2H), 7.52 – 7.47 (m, 1H), 7.23 (m, 1.1 Hz, 1H), 7.16 (m, 2H), 5.92 (s, 1H), 5.86 – 5.79 (m, 1H), 5.54 – 5.48 (m, 1H), 3.26 (dt, *J* = 15.5, 2.8 Hz, 1H), 3.08 – 2.99 (m, 1H), 2.32 (d, *J* = 2.0 Hz, 3H), 1.64 (s, 9H) ppm; **min** (selected signals) : 7.74 – 7.69 (m, 1H), 7.63 – 7.59 (m, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 5.90 (s, 1H), 5.62 (q, *J* = 1.9 Hz, 1H), 5.39 (q, *J* = 1.9 Hz, 1H), 3.21 – 3.10 (m, 2H), 2.31 (s, 3H), 1.42 (s, 9H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>) δ **maj** : 165.0, 145.4, 142.4, 141.9, 132.9, 132.6, 130.0 (2C), 127.3 (2C), 126.3, 125.9, 125.7, 117.4, 117.0, 115.3, 98.3, 86.1, 75.3, 55.2, 43.5, 27.8, 21.6 ppm; **min** : 163.1, 145.6, 143.2, 142.8, 132.4, 132.2, 130.0 (2C), 127.4 (2C), 126.7, 126.7, 126.1, 118.1, 117.0, 113.7, 99.4, 85.9, 76.3, 52.7, 42.1, 27.5, 21.6 ppm; IR (film): ν 2979, 2931, 1737, 1555, 1369, 1171, 1151 cm<sup>-1</sup>; HRMS (ESI) [M+NH<sub>4</sub><sup>+</sup>] calculated for (C<sub>25</sub>H<sub>25</sub>N<sub>3</sub>O<sub>6</sub>SNH<sub>4</sub>)<sup>+</sup>: 513.1802, found 513.1802.

**(±)-3-methylene-3a-nitro-1,8-ditosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (3aj).** Obtained following the general procedure with **2j** (184 mg, 0.88 mmol), starting from **1a** (253 mg, 0.80 mmol), as an orange oil (275 mg, 65% yield) after flash column chromatography (petroleum ether/ ethyl acetate 8:2 to 6:4). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.04 – 7.91 (m, 2H), 7.62 – 7.52 (m, 3H), 7.48 – 7.38 (m, 2H), 7.38 – 7.30 (m, 2H), 7.19 (td, *J* = 7.6, 1.1 Hz, 1H), 7.17 – 7.11 (m, 2H), 6.94 (s, 1H), 5.41 (q, *J* = 1.7 Hz, 1H), 5.18 (q, *J* = 1.8 Hz, 1H), 4.38 (dt, *J* = 14.6, 1.5 Hz, 1H), 3.74 (dt, *J* = 14.7, 2.3 Hz, 1H), 2.43 (s, 3H), 2.33 (s, 3H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>) δ 145.1, 144.3, 141.8, 141.1, 135.5, 133.4, 132.3, 129.8 (2C), 129.7 (2C), 128.0 (2C), 127.5 (2C), 126.8, 126.1, 125.2, 117.8, 110.1, 99.0, 84.2, 52.5, 21.5, 21.5 ppm; IR (film): ν 2917, 2359, 2340, 1748, 1597, 1553, 1160 cm<sup>-1</sup>; HRMS (ESI) [M+NH<sub>4</sub><sup>+</sup>] calculated for (C<sub>25</sub>H<sub>23</sub>N<sub>3</sub>O<sub>6</sub>S<sub>2</sub>NH<sub>4</sub>)<sup>+</sup>: 543.1367, found 543.1364.

**(±)-tert-butyl-3-methylene-3a-nitro-8-tosyl-3,3a,8,8a-tetrahydropyrrolo[2,3-*b*]indole-1(2H)-carboxylate (3al).** Obtained following the general procedure with **2l** (137 mg, 0.88 mmol), starting from **1a** (253 mg, 0.80 mmol), as a yellow oil (42 mg, 11% yield) after flash column chromatography (petroleum ether/ methyl *tert*-butyl ether 9:1 to 8:2). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.72 (d, *J* = 8.2 Hz, 1H), 7.63 (s, 1H), 7.53 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.48 – 7.39 (m, 1H), 7.36 – 7.27 (m, 1H), 7.22 – 7.09 (m, 3H), 5.42 (dd, *J* = 2.7, 1.5 Hz, 1H), 5.25 (q, *J* = 1.8 Hz, 1H), 4.52 (dt, *J* = 15.2, 1.6 Hz, 1H), 3.76 (d, *J* = 15.3 Hz, 1H), 2.34 (s, 3H), 1.58 (s, 9H) ppm; <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>) δ 153.2, 144.9, 143.0, 142.0, 133.9, 132.1, 129.9 (2C), 128.6, 127.7 (2C), 126.6, 125.6, 117.5, 110.3, 98.7, 83.4, 82.5, 51.0, 28.5, 21.7 ppm; IR (film): ν 2974, 2927, 2871, 2359, 2340, 1704, 1553 cm<sup>-1</sup>; HRMS (ESI) [M+Na<sup>+</sup>] calculated for (C<sub>23</sub>H<sub>25</sub>N<sub>3</sub>O<sub>6</sub>SNa)<sup>+</sup>: 494.1356, found 494.1354.

**Ethyl 5-methylene-2-phenyltetrahydrofuran-3-carboxylate (8).** Obtained following the general procedure starting from **2g** (101 mg, 0.44 mmol), as a colourless oil (88 mg, 87% yield) after flash column chromatography (pure petroleum ether to petroleum ether/ methyl *tert*-butyl ether

95:5). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.94–7.80 (m, 2H), 7.50–7.34 (m, 3H), 4.72 (q, *J* = 2.9 Hz, 1H), 4.33 (q, *J* = 2.9 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.82 (t, *J* = 2.9 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H) ppm. Spectral data of the product were in accordance with those reported in the literature.<sup>14</sup>

## ASSOCIATED CONTENT

**Supporting Information.** Copies of <sup>1</sup>H and <sup>13</sup>C NMR Spectra for all new compounds and more details concerning the screening of chiral ligands for the enantioselective version and the kinetic studies.

## AUTHOR INFORMATION

### Corresponding Author

[maxime.vitale@chimieparitech.psl.eu](mailto:maxime.vitale@chimieparitech.psl.eu)

## ACKNOWLEDGMENT

J. Ling and M. Laugeois warmly thank the Ministère National de l'Enseignement Supérieur et de la Recherche for their PhD research grants. CNRS and ChimieParisTech are also acknowledged for their financial support. Charlène Féraud is gratefully acknowledged for her previous involvement in the preparation of some starting 3-nitroindoles. Dr Laurence Grimaud is acknowledge for the fruitful discussions about Burés' VTNA method and, together with Dr Olivia Bistri, for their thorough proofreading of this manuscript.

## REFERENCES

(1) (a) *Medicinal Natural Products : A Biosynthetic Approach*; Dewick P. M., Ed.; Wiley-VCH: New York, 2002. (b) *Modern Alkaloids: Structure, Isolation, Synthesis, and Biology*; Fattorusso E., Taglietela-Scafati O., Eds.; Wiley-VCH: Weinheim, 2007.

(2) For selected examples of natural products and biologically active molecules containing a cyclopenta[b]indoline skeleton, see: (a) Craven, B. M. The Crystal Structure and Absolute Configuration of the *N(b)*-Methiodide of (–)-Kopsanone. *Acta Crystallogr. Sec. B* **1969**, *25*, 2131–2139. (b) Magnus, P.; Gallagher, T.; Brown, P.; Huffman, J. C. Synthesis of (±)-10,22-Dioxokopsane and (±)-Kopsanone, Heptacyclic Indole Alkaloids. *Synthetic and Mechanistic Studies. J. Am. Chem. Soc.* **1984**, *106*, 2105–2114. (c) Baldé, A. M.; Pieters, L. A.; Gergely, A.; Wray, V.; Claeys, M.; Vlietinck, A. J. Spermaceoine, a Bis-Indole Alkaloid from *Borreria Verticillata*. *Phytochemistry* **1991**, *30*, 997–1000. (d) Lim, S.-H.; Sim, K.-M.; Abdullah, Z.; Hiraku, O.; Hayashi, M.; Komiyama, K.; Kam, T.-S. Leuconoxine, Kopsintarine, Kopsijasmine, and Kopsinone Derivatives from *Kopsia*. *J. Nat. Prod.* **2007**, *70*, 1380–1383. (e) Ngantchou, I.; Nyasse, B.; Denier, C.; Blonski, C.; Hannaert, V.; Schneider, B. Antitrypanosomal Alkaloids from *Polyalthia Suaveolens* (Annonaceae): Their Effects on Three Selected Glycolytic Enzymes of *Trypanosoma Brucei*. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3495–3498. (f) Lu, Y.; Khoo, T. J.; Wiart, C. The Genus *Melodinus* (Apocynaceae): Chemical and Pharmacological Perspectives. *Pharmacology & Pharmacy*, **2014**, *5*, 540–550. (g) Aynilian, G. H.; Weiss, S. G.; Cordell, G. A.; Abraham, D. J.; Crane, F. A.; Farnsworth, N. R. Catharanthus Alkaloids XXIX: Isolation and Structure Elucidation of Vincoline. *J. Pharm. Sci.* **1974**, *63*, 536–538.

(3) For recent reviews, see: (a) Haak, E. Modern Annulation Strategies for the Synthesis of Cyclo[b]Fused Indoles. *Synlett* **2019**, *30*, 245–251. (b) Huang, G.; Yin, B. Recent Developments in Transition Metal-Catalyzed Dearomative Cyclizations of Indoles as Dipolarophiles for the Construction of Indolines. *Adv. Synth. Catal.* **2019**, *361*, 405–425. (c) Vivekanand, T.; Satpathi, B.; Bankar, S. K.; Ramasastry, S. S. V. Recent Metal-Catalysed Approaches for the Synthesis of Cyclopenta[b]Indoles. *RSC Adv.* **2018**, *8* (33), 18576–18588.

(4) (a) Kerr, M. A.; Keddy, R. G. The Annulation of 3-Alkylindoles with 1,1-Cyclopropanediester. *Tetrahedron Lett.* **1999**,

*40*, 5671–5675. (b) England, D. B.; Kuss, T. D. O.; Keddy, R. G.; Kerr, M. A. Cyclopentannulation of 3-Alkylindoles: A Synthesis of a Tetracyclic Subunit of the Kopsane Alkaloids. *J. Org. Chem.* **2001**, *66*, 4704–4709.

(5) (a) Birbaum, L.; Gillard, L.; Gérard, H.; Oulyadi, H.; Vincent, G.; Moreau, X.; De Paolis, M.; Chataigner, I. Dearomatization of 3-Nitroindoles with Highly  $\gamma$ -Functionalized Allenates in Formal (3+2) Cycloadditions. *Chem. - A Eur. J.* **2019**, *25* (60), 13688–13693. (b) Cerveri, A.; Faza, O. N.; López, C. S.; Grilli, S.; Monari, M.; Bandini, M. Phosphine-Catalyzed Stereoselective Dearomatization of 3-NO<sub>2</sub>-Indoles with Allenates. *J. Org. Chem.* **2019**, *84* (10), 6347–6355. (c) Li, K.; Gonçalves, T. P.; Huang, K. W.; Lu, Y. Dearomatization of 3-Nitroindoles by a Phosphine-Catalyzed Enantioselective [3+2] Annulation Reaction. *Angew. Chem. Int. Ed.* **2019**, *58* (16), 5427–5431. (d) Wang, H.; Zhang, J.; Tu, Y.; Zhang, J. Phosphine-Catalyzed Enantioselective Dearomative [3+2]-Cycloaddition of 3-Nitroindoles and 2-Nitrobenzofurans. *Angew. Chem. Int. Ed.* **2019**, *58* (16), 5422–5426. (e) Liu, K.; Wang, G.; Cheng, S. J.; Jiang, W. F.; He, C.; Ye, Z. S. Phosphine-Catalyzed Dearomative [3+2] Annulation of 3-Nitroindoles and Allenates. *Tetrahedron Lett.* **2019**, *60* (29), 1885–1890. (f) Jin, L. W.; Jiang, F.; Chen, K. W.; Du, B. X.; Mei, G. J.; Shi, F. Phosphine-Catalyzed Regiospecific (3 + 2) Cyclization of 3-Nitroindoles with Allene Esters. *Org. Biomol. Chem.* **2019**, *17* (16), 3894–3901.

(6) Trost, B. M.; Ehmke, V.; Michael O'Keefe, B.; Bringley, D. A. Palladium-Catalyzed Dearomative Trimethylenemethane Cycloaddition Reactions. *J. Am. Chem. Soc.* **2014**, *136* (23), 8213–8216.

(7) (a) Laugeois, M.; Ling, J.; Féraud, C.; Michelet, V.; Ratovelomanana-Vidal, V.; Vitale, M. R. Palladium(0)-Catalyzed Dearomative [3 + 2] Cycloaddition of 3-Nitroindoles with Vinylcyclopropanes: An Entry to Stereodefined 2,3-Fused Cyclopentannulated Indoline Derivatives. *Org. Lett.* **2017**, *19* (9), 2266–2269. (b) Gee, Y. S.; Rivinoja, D. J.; Wales, S. M.; Gardiner, M. G.; Ryan, J. H.; Hyland, C. J. T. Pd-Catalyzed Dearomative [3 + 2] Cycloaddition of 3-Nitroindoles with 2-Vinylcyclopropane-1,1-Dicarboxylates. *J. Org. Chem.* **2017**, *82* (24), 13517–13529. For enantioselective versions, see: (c) Sun, M.; Zhu, Z. Q.; Gu, L.; Wan, X.; Mei, G. J.; Shi, F. Catalytic Asymmetric Dearomative [3 + 2] Cycloaddition of Electron-Deficient Indoles with All-Carbon 1,3-Dipoles. *J. Org. Chem.* **2018**, *83* (4), 2341–2348. (d) Zhang, J. Q.; Tong, F.; Sun, B. B.; Fan, W. T.; Chen, J. B.; Hu, D.; Wang, X. W. Pd-Catalyzed Asymmetric Dearomative Cycloaddition for Construction of Optically Active Pyrroloindoline and Cyclopentaindoline Derivatives: Access to 3a-Aminopyrroloindolines. *J. Org. Chem.* **2018**, *83* (5), 2882–2891.

(8) (a) Pelkey, E. T.; Gribble, G. W. Synthesis and Reactions of N-Protected 3-Nitroindoles. *Synthesis* **1999**, 1117–1122. (b) Roy, S.; Kishbaugh, T. L. S.; Jasinski, J. P.; Gribble, G. W. 1,3-Dipolar Cycloaddition of 2- and 3-Nitroindoles with Azomethine Ylides. A New Approach to Pyrrolo[3,4-b]Indoles. *Tetrahedron Lett.* **2007**, *48* (8), 1313–1316. (c) Lee, S.; Chataigner, I.; Pietre, S. R. Facile Dearomatization of Nitrobenzene Derivatives and Other Nitroarenes with *N*-Benzyl Azomethine Ylide. *Angew. Chem. Int. Ed.* **2011**, *50* (2), 472–476. (d) Lee, S.; Diab, S.; Queval, P.; Sebban, M.; Chataigner, I.; Pietre, S. R. Aromatic C=C Bonds as Dipolarophiles: Facile Reactions of Uncomplexed Electron-Deficient Benzene Derivatives and Other Aromatic Rings with a Non-Stabilized Azomethine Ylide. *Chem. - A Eur. J.* **2013**, *19* (22), 7181–7192.

(9) The palladium-catalyzed dearomatization of 3-nitroindoles with vinylaziridines was reported shortly before, see: Rivinoja, D. J.; Gee, Y. S.; Gardiner, M. G.; Ryan, J. H.; Hyland, C. J. T. The Diastereoselective Synthesis of Pyrroloindolines by Pd-Catalyzed Dearomative Cycloaddition of 1-Tosyl-2-Vinylaziridine to 3-Nitroindoles. *ACS Catal.* **2017**, *7* (2), 1053–1056.

(10) Ling, J.; Laugeois, M.; Michelet, V.; Ratovelomanana-Vidal, V.; Vitale, M. R. Palladium(0)-Catalyzed Dearomatization of 2-Nitrobenzofurans through Formal (3+2) Cycloadditions with Vinylcyclopropanes: A Straightforward Access to Cyclopenta[b]Benzofurans. *Synlett* **2018**, *29* (7), 928–932.

(11) An initial version of this work was deposited in ChemRxiv on 26.th December 2019. Ling, J.; Mara, D.; Roure, B.; Laugeois, M.; Vitale, M. Copper(I)-Catalyzed Dearomative (3+2) Cycloaddition of 3-Nitroindoles with Propargylic Nucleophiles: a Straightforward Entry for The Preparation of Cyclopenta[b]indolines, *ChemRxiv* **2019**, doi: 10.26434/chemrxiv.11462085.

(12) Guillaume, M.; Dumez, E.; Rodriguez, J.; Dulcère, J. P. One-Pot Michael Addition/Intramolecular Carbocyclization of Dimethyl Propargylmalonate with Nitroalkenes: A New Stereoselective [3+2] Annulation to 1-Nitro 2-Methylenecyclopentanes. *Synlett* **2002**, No. 11, 1883–1885.

(13) (a) Montaignac, B.; Vitale, M. R.; Ratovelomanana-Vidal, V.; Michelet, V. Cooperative Copper(I) and Primary Amine Catalyzed Room-Temperature Carbocyclization of Formyl Alkynes. *European J. Org. Chem.* **2011**, No. 20–21, 3723–3727. (b) Montaignac, B.; Östlund, V.; Vitale, M. R.; Ratovelomanana-Vidal, V.; Michelet, V. Copper(I)-Amine Metallo-Organocatalyzed Synthesis of Carbo- and Heterocyclic Systems. *Org. Biomol. Chem.* **2012**, *10* (11), 2300–2306. (c) Montaignac, B.; Praveen, C.; Vitale, M. R.; Michelet, V.; Ratovelomanana-Vidal, V. Enantioselective Metallo-Organocatalyzed Preparation of Cyclopentanes Bearing an All-Carbon Quaternary Stereocenter. *Chem. Commun.* **2012**, *48* (52), 6559–6561. (d) Praveen, C.; Montaignac, B.; Vitale, M. R.; Ratovelomanana-Vidal, V.; Michelet, V. Enantioselective Merger of Aminocatalysis with  $\pi$ -Lewis Acid Metal Catalysis: Asymmetric Preparation of Carbo- and Heterocycles. *ChemCatChem* **2013**, *5* (8), 2395–2404.

(14) (a) Bouyssi, D.; Monteiro, N.; Balme, G. Intramolecular Carbocupration Reaction of Unactivated Alkynes Bearing a Stabilized Nucleophile: Application to the Synthesis of Iridoid Monoterpenes. *Tetrahedron Lett.* **1999**, *40* (7), 1297–1300. (b) Clique, B.; Monteiro, N.; Balme, G. A One Pot Synthesis of Various Pyrrolidines via a Tandem Michael Addition-Transition Metal-Catalyzed Cyclisation Reaction. *Tetrahedron Lett.* **1999**, *40* (7), 1301–1304. (c) Coia, N.; Bouyssi, D.; Balme, G. Efficient, Transition Metal Mediated, Sequential, Two- and Three-Component Coupling Reactions for the Synthesis of Highly Substituted Five-Membered Ring Carbocycles. *European J. Org. Chem.* **2007**, *2007* (19), 3158–3165. (d) Yang, T.; Ferrali, A.; Sladojevich, F.; Campbell, L.; Dixon, D. J. Brønsted Base/Lewis Acid Cooperative Catalysis in the Enantioselective Conia-Ene Reaction. *J. Am. Chem. Soc.* **2009**, *131* (26), 9140–9141. (e) Yang, T.; Ferrali, A.; Campbell, L.; Dixon, D. J. Combination Iminium, Enamine and Copper(I) Cascade Catalysis: A Carboannulation for the Synthesis of Cyclopentenes. *Chem. Commun.* **2008**, 2923–2925. (f) Wang, H.-F.; Yang, T.; Xu, P.-F.; Dixon, D. J. Base and Copper(I) Catalyzed Mannich, Alkyne Hydroamination Cascades for the Direct Synthesis of 2-Methylenepyrrolidines. *Chem. Commun.* **2009**, 3916. (g) Yuan, Z.; Liu, L.; Pan, R.; Yao, H.; Lin, A. Silver-Catalyzed Cascade 1,6-Addition/Cyclization of Para-Quinone Methides with Propargyl Malonates: An Approach to Spiro[4.5]Deca-6,9-Dien-8-Ones. *J. Org. Chem.* **2017**, *82* (16), 8743–8751.

(15) Tiecco, M.; Testaferri, L.; Tingoli, M.; Marini, F. Elimination Reactions of Terminal  $\beta$ -Oxy Selenoxides. Synthesis of Aryl and Vinyl Enol Ethers and of Furans, Oxazoles, and Thiazoles. *J. Org. Chem.* **1993**, *58* (6), 1349–1354.

(16) See Supporting Information for more details

(17) Genet, J.-P.; Ayad, T.; Ratovelomanana-Vidal, V. Electron-Deficient Diphosphines: The Impact of DIFLUORPHOS in Asymmetric Catalysis. *Chem. Rev.* **2014**, *114* (5), 2824–2880.

(18) Both reaction mechanisms have been proposed depending on the nature of the nucleophile. See references 12 and 13. See also:

Sladojevich, F.; Fuentes de Arriba, Á. L.; Ortín, I.; Yang, T.; Ferrali, A.; Paton, R. S.; Dixon, D. J. Mechanistic Investigations into the Enantioselective Conia-Ene Reaction Catalyzed by Cinchona-Derived Amino Urea Pre-Catalysts and Cu(I). *Chem. - A Eur. J.* **2013**, *19* (42), 14286–14295.

(19) (a) Worrell, B. T.; Malik, J. A.; Fokin, V. V. Direct Evidence of a Dinuclear Copper Intermediate in Cu(I)-Catalyzed Azide-Alkyne Cycloadditions. *Science* **2013**, *340*, 457–460. (b) Ahlquist, M.; Fokin, V. V. Enhanced Reactivity of Dinuclear Copper(I) Acetylides in Dipolar Cycloadditions. *Organometallics* **2007**, *26* (18), 4389–4391. (c) Iacobucci, C.; Reale, S.; Gal, J.-F.; De Angelis, F. Dinuclear Copper Intermediates in Copper(I)-Catalyzed Azide-Alkyne Cycloaddition Directly Observed by Electrospray Ionization Mass Spectrometry. *Angew. Chem. Int. Ed.* **2015**, *54* (10), 3065–3068. (d) Jin, L.; Tolentino, D. R.; Melaimi, M.; Bertrand, G. Isolation of Bis(Copper) Key Intermediates in Cu-Catalyzed Azide-Alkyne “Click Reaction.” *Science Advances* **2015**, *1* (5), e1500304.

(20) (a) Burés, J. Variable Time Normalization Analysis: General Graphical Elucidation of Reaction Orders from Concentration Profiles. *Angew. Chem. Int. Ed.* **2016**, *55* (52), 16084–16087. (b) Burés, J. A Simple Graphical Method to Determine the Order in Catalyst. *Angew. Chem. Int. Ed.* **2016**, *128* (6), 2028–2031. (c) Nielsen, C. D. T.; Burés, J. Visual Kinetic Analysis. *Chem. Sci.* **2019**, *10*, 348–353

(21) During these kinetic studies, a small induction period was observed as a result of the difficulty to homogenize the reaction mixture in the NMR tube. Indeed, cesium carbonate is poorly soluble in dichloromethane and which tended to slow down the heterogeneous deprotonation of **2a**. In between two NMR measurements the NMR tube was shaken manually.

(22) (a) Dötz, K. H.; Popall, M. Carbene Ligands as Anthracyclinone-Synthons-ii<sup>o</sup>: Chromium mediated cycloaddition of alkynes, carbenes and carbon monoxide: application to ring b synthesis in anthracyclinones. *Tetrahedron* **1985**, *41*, 5797–5802. (b) Czekelius, C.; Hafer, J.; Tonzetich, Z. J.; Schrock, R. R.; Christensen, R. L.; Müller, P. Synthesis of Oligoenes That Contain up to 15 Double Bonds from 1,6-Heptadiynes. *J. Am. Chem. Soc.* **2006**, *128*, 16664–16675. (c) Kourra, C.; Klotter, F.; Sladojevich, F.; Dixon, D. J. Alkali Base-Initiated Michael Addition/Alkyne Carbocyclization Cascades. *Org. Lett.* **2012**, *14*, 1016–1019. (d) Tian, Y.; Wang, Y.; Shang, H.; Xu, X.; Tang, Y. Rhodium(II)-Catalyzed Intramolecular Formal [4 + 3] Cycloadditions of Dienyltriazoles: Rapid Access to Fused 2,5-Dihydroazepines. *Org. Biomol. Chem.* **2015**, *13*, 612–619. (e) Demir, A. S.; Emrullahoğlu, M.; Buran, K. Gold(I)/Zn(II) Catalyzed Tandem Hydroamination/Annulation Reaction of 4-Yne-Nitriles. *Chem. Commun.* **2010**, *46*, 8032. (f) Chang, M.-Y.; Cheng, Y.-C.; Lu, Y.-J. Bi(OTf)<sub>3</sub>-Mediated Cycloisomerization of  $\gamma$ -Alkynyl Arylketones: Application to the Synthesis of Substituted Furans. *Org. Lett.* **2015**, *17* (5), 1264–1267. (g) Biletskyi, B.; Tenaglia, A.; Clavier, H. Cobalt-Catalyzed versus Uncatalyzed Intramolecular Diels-Alder Cycloadditions. *Tetrahedron Lett.* **2018**, *59*, 103–107. (h) Wang, Z.; Lin, X.; Luck, R. L.; Gibbons, G.; Fang, S. Synthesis of Cyclic Allyl Vinyl Ethers Using Pt(II)-Catalyzed Isomerization of Oxo-Alkynes. *Tetrahedron* **2009**, *65*, 2643–2648. (i) Chachignon, H.; Scalacci, N.; Petricci, E.; Castagnolo, D. Synthesis of 1,2,3-Substituted Pyrroles from Propargylamines via a One-Pot Tandem Enyne Cross Metathesis–Cyclization Reaction. *J. Org. Chem.* **2015**, *80*, 5287–5295. (j) Gasperini, D.; Maggi, L.; Dupuy, S.; Veenboer, R. M. P.; Cordes, D. B.; Slawin, A. M. Z.; Nolan, S. P. Gold(I)-Catalyzed Cyclisation of Alkynoic Acids: Towards an Efficient and Eco-Friendly Synthesis of  $\gamma$ -,  $\delta$ - and  $\epsilon$ -Lactones. *Adv. Synth. Catal.* **2016**, *358*, 3857–3862.

