Gold(I)-Catalyzed Rautenstrauch/Hetero-Diels–Alder/Retro-aza-Michael Cascade Reaction for the Synthesis of α-Hydrazineyl-2-

Gold(I)-catalyzed Rautenstrauch/Hetero-Diels-Alder/retro-aza-Michael Cascade Reaction for the Synthesis of α-Hydrazineyl-2-Cyclopentenones

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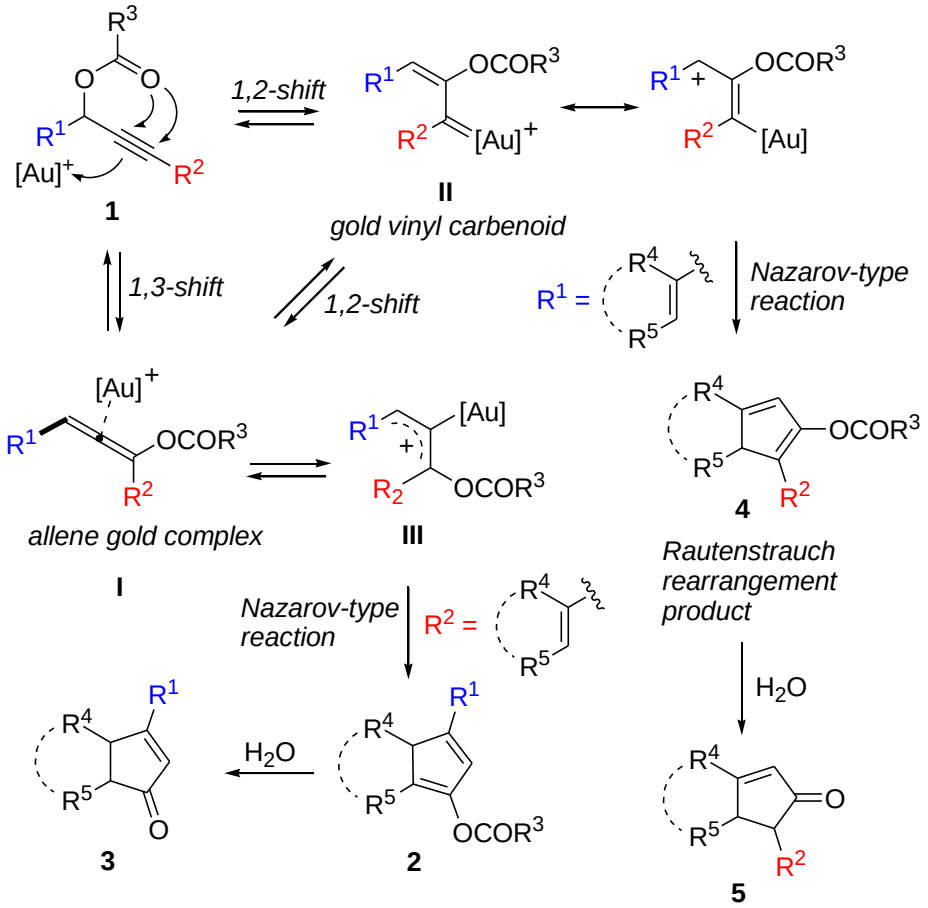
Abstract. A one-pot synthesis of ring-fused, α-hydrazineyl-2-cyclopentenone derivatives is achieved by a gold(I)-catalyzed Rautenstrauch/hetero Diels-Alder/ring opening tandem reaction of suitable propargyl esters. By mixing the latter with a dialkylazodicarboxylate in the presence of a gold(I) catalyst, the 1,2-acyloxy migration/cyclization process (Rautenstrauch reaction) leads to cyclopentadienyl ester intermediates which are trapped by the heterodienophile present in situ. This provides strained intermediates which spontaneously undergo highly regioselective ring opening by a retro aza-Michael reaction promoted by the gold(I) catalyst, eventually yielding the target compounds. Six- and seven-membered ring-fused cyclopentenones bearing a pendant α-hydrazineyl moiety can be obtained in moderate to excellent yield (50-98%) by this approach, with a minimal erosion of the initial optical purity when using enantioenriched substrates.

Introduction

Propargylic esters **1** (Scheme 1) have been widely investigated as substrates for gold(I)-catalyzed reactions in which 1,3- and 1,2-acyloxy migration generate gold allene complexes **I** and gold vinyl carbenoids **II**, respectively.[1] Based on DFT calculation, it has been suggested that these intermediates interconvert easily through sequential 1,2-acyloxy shifts in what has been called a "golden carousel".[2] These activated intermediates, depending on the nature of the tethered R^1 and R^2 groups, can undergo further transformations leading to an array of structurally diverse products.[1,3] In particular, if R^2 is a vinyl moiety, the

Nazarov-type cyclization of cationic Au(I) σ-complex **III**,[4] in equilibrium with **I**, forms 2-acyloxy-1,3-cyclopentadienes **2** which, in the presence of water, undergo hydrolysis to give the corresponding cyclopentenones **3**.[5,6] On the other hand, if R^1 is a vinyl moiety, the carbocationic resonance structure of **II** has the right 4π electronic arrangement for a Nazarov-type reaction leading to 2-acyloxy-1,3-cyclopentadienes **4**.[7] Overall, the latter process is called the Rautenstrauch reaction,[8] initially reported to occur under palladium catalysis,[8a] and, as the former, eventually generates 2-cyclopentenones **5** upon hydrolysis. The latter are valuable compounds as building blocks for many synthetic targets, including several natural and bioactive products.[9]

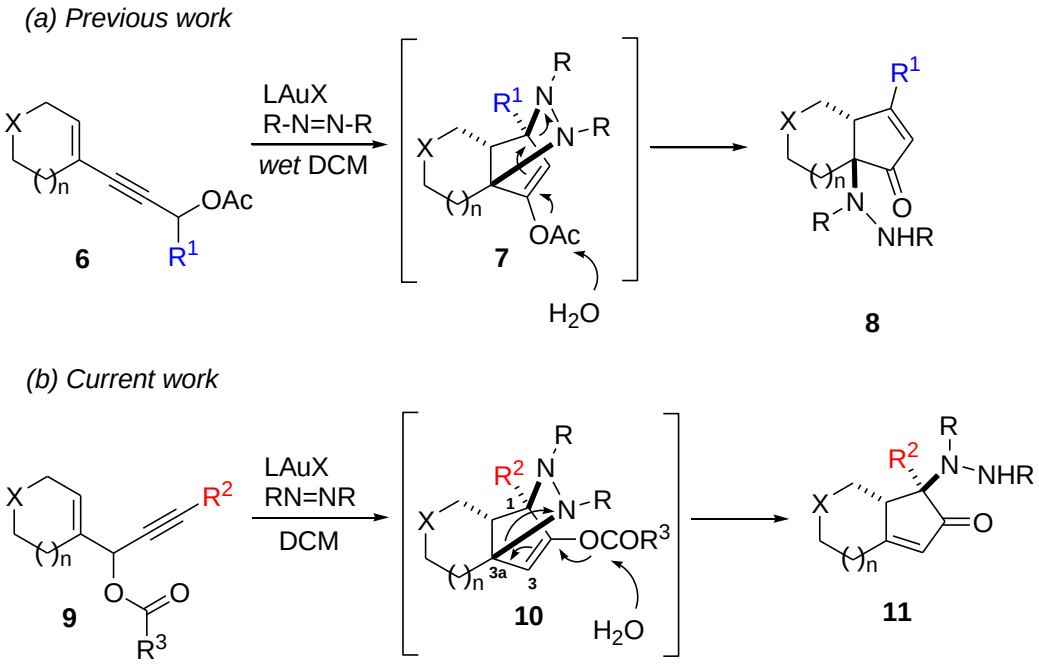
Scheme 1. 1,2- and 1,3-Acyloxy Shifts in Propargyl Esters



2-Acyloxy-1,3-dienes **2** derived from the initial 1,3-shift in 5-acyloxy-1-en-3-ynes have been exploited as platforms for further elaborations,[5c-g] including cycloaddition processes carried out by trapping **2** (in situ or

after its isolation) with (hetero)dienophiles to form a variety of more complex, polysubstituted products.[4a,10] We recently contributed to this field (Scheme 2, a) by establishing a cascade process which entailed, after the 1,3-shift, a hetero-Diels-Alder reaction with dialkylazodicarboxylates and a ring opening of cycloadduct **7** by a water-promoted retro aza-Michael reaction, ultimately forming 2-cyclopentenone derivatives **8** with a protected α-hydrazine moiety at the bridgehead quaternary center.[11] On the other hand, 2-acyloxy-1,3-dienes **4** deriving from the gold-catalyzed Rautenstrauch reaction have never been employed as dienes in hetero Diels-Alder reactions.[3f] Therefore, on the grounds of our recent results with propargyl esters **6**,[11] and because of our recent interest in gold-catalyzed cascade processes,[12] we decided to study the gold-catalyzed reaction of propargyl esters **9** (3-acyloxy-1-en-4-ynes), (Scheme 2, b) suitable to give the Rautenstrauch rearrangement, in the presence of dialkylazodicarboxylates.

Scheme 2. Previous (a) and Current Studies (b) on Cycloisomerization/HDA/Ring-Opening Tandem Reactions of Propargyl Esters



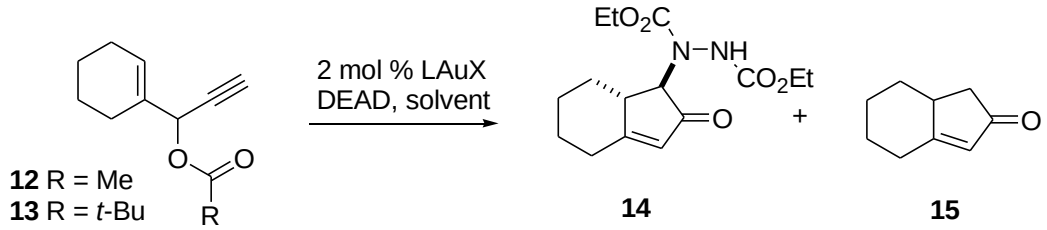
We hoped that after trapping the diene intermediate with the heterodienophile, cycloadduct **10** would undergo the same fate as **7** in the presence of water to form unprecedented cyclopentenones **11** bearing an α-hydrazine moiety.[13] As synthetically useful intermediates, which can readily be converted into products

such as amines and 1,2-amino alcohols, α-hydrazineyl cycloalkanones have received much attention recently and various methods for their preparation have been developed.[14] With our approach, the construction of the carbocycle bearing the carbonyl functionality and the installation of the α-hydrazineyl moiety would occurs all in one-pot from simple precursors, hopefully with complete control of both the regio- and stereochemistry of the products.

Results and discussion

We started our investigation (Table 1) with substrates **12** and **13**,[7a] bearing a terminal alkyne moiety and with the vinyl moiety embedded in a six-membered ring.

Table 1. Survey of the Conditions for the Tandem Reaction Leading to 14.[a]



entry	catalyst	R	solvent	Time (min)[b]	**14** (%)[c]	**15** (%)[c]
1	*t*-$Bu_3PAuNTf_2$	CH_3	"wet" CH_2Cl_2[d]	25	61	19
2	*t*-$Bu_3PAuNTf_2$	CH_3	CH_2Cl_2[e]	22	76	-[f]
3	*t*-$Bu_3PAuNTf_2$	$(CH_3)_3C$	CH_2Cl_2[e]	30	82	-[f]
4	*t*-$Bu_3PAuNTf_2$	$(CH_3)_3C$	CH_2Cl_2[g]	30	38	-[f]
5	*t*-$Bu_3PAuNTf_2$	$(CH_3)_3C$	CH_3CN[e]	420	53	-[f]
6	*t*-$Bu_3PAuNTf_2$	$(CH_3)_3C$	THF[e]	300	0[h]	-[f]
7	*t*-$Bu_3PAuNTf_2$	$(CH_3)_3C$	"wet" Toluene[d]	360	17	36
8	*t*-$Bu_3PAuCl/AgNTf_2$	$(CH_3)_3C$	CH_2Cl_2[e]	30	73	-[f]
9	$Ph_3PAuCl/AgNTf_2$	CH_3	CH_2Cl_2[e]	30	62	-[f]
10	*t*-$Bu_3PAuCl/AgSbF_6$	$(CH_3)_3C$	CH_2Cl_2[e]	30	66	-[f]
11	*t*-$Bu_3PAuCl/AgOTf$	$(CH_3)_3C$	CH_2Cl_2[e]	18	0	50
12	*t*-$Bu_3PAuCl/AgOTf$	CH_3	CH_2Cl_2[e]	25	18	33
13	$Ph_3PAuCl/AgNTf_2$	$(CH_3)_3C$	CH_2Cl_2[e]	30	59	-[f]
14	$Ph_3PAuCl/AgOTf$	$(CH_3)_3C$	CH_2Cl_2[e]	30	0	48
15	$(2,4\text{-di-}^tBuC_6H_3O)_3PAuCl/AgNTf_2$	$(CH_3)_3C$	CH_2Cl_2[e]	30	63	-[f]

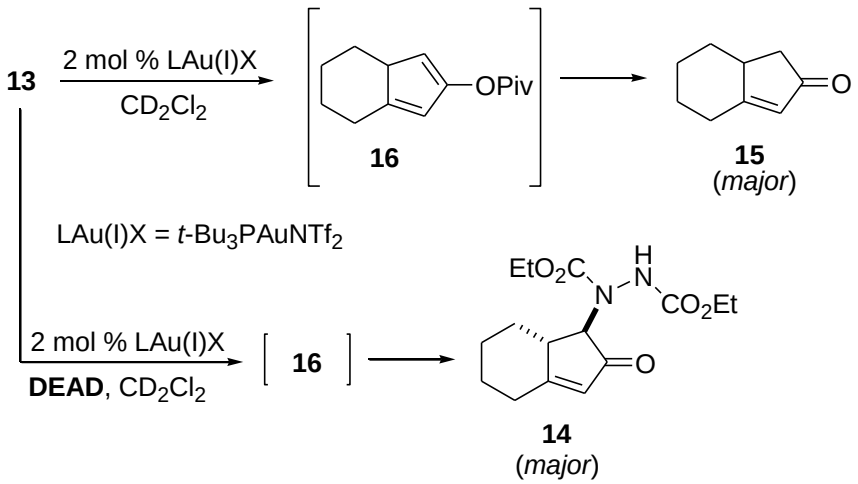
[a]Reactions carried out by adding a 0.1 M solution of the substrate (0.2 mmol) and DEAD (1 equiv) in CH_2Cl_2 to a 0.1 M solution of the catalyst in the same solvent; [b]Reaction stopped after complete disappearance of the starting material by TLC; [c]Yield after chromatography; [d]Prepared by adding water (0.3% v/v) to the solution of the catalyst in the undistilled solvent; [e]Undistilled solvent (declared water content of the lot of CH_2Cl_2: 0.01%); [f]Not isolated (present in the crude reaction mixture in a ratio lower than 1:10 with **14** as determined by ^1H NMR analysis); [g]Distilled over CaH_2 prior use; [h]Mixture of decomposition products.

From the analysis of the ^{1}H NMR of the crude reaction mixtures, in most cases we observed the formation of **14** as the major product with variable amounts of α,β-unsaturated ketone **15** derived from hydrolysis of the 2-acyloxydiene intermediate of type **4** [R_2 = H, R_4-R_5 = -$(CH_2)_4$-] occurring before the cycloaddition. In a few cases **15** was instead the major product and only then chromatography was performed to evaluate its yield. The first experiment (entry 1) was carried out by adding a solution of a 1:1 mixture of **12** and DEAD (diethylazodicarboxylate) to a solution of the catalyst (*t*-$Bu_3PAuNTf_2$) in "wet" CH_2Cl_2, according to the best conditions we had found in our previous work,[11] to favor the retro-aza-Michael step determining the final ring opening. The reaction occurred readily to provide target product **14** (61%),[15] although in a 3:1 mixture with **15** (19%). The reaction carried out in undistilled dichloromethane (i.e., without the addition of 0.3 % of water) (entry 2) provided **14** in a much higher yield (76% after chromatography), and even better results were obtained with pivalate ester **13** (entry 3) under the same conditions (82% yield). Instead in anhydrous solvent (entry 4) the isolated yield of **14** was very low (38%), as much degradation occurred. Results were worse in other solvents used in previous studies on the Rautenstrauch reaction[7] (entries 5-7), either because of longer reaction times (CH_3CN),[7a] formation of higher amount of **15** ("wet" toluene), or complete degradation of the starting material (THF). With the latter solvent, Toste had reported very long reaction times (14 h) and low yields with his model substrate.[7a] Further experiments were carried out by generating the catalyst with some silver salts. With $AgNTf_2$ (entries 8-9) and $AgSbF_6$ (entry 10) the results were just slightly worse than with the preformed catalyst (yield of **14** from 62 to 73%). Very interestingly, when we used AgOTf (entries 11 and 12) with both substrates only or mainly the Rautenstrauch product (**15**) was obtained (in 33-50% yield after chromatography). The same result (48% yield of **15**) was obtained by premixing Ph_3PAuCl and AgOTf to generate the catalyst (entry 14) suggesting that with TfO^- as the counterion hydrolysis of the 2-acyloxydiene intermediate must be much faster than the cycloaddition process.[16] With the same ligand (entry 13), and with a phosphite ligand (entry 15) as well, the yield of **14** did not ameliorate when using $AgNTf_2$ (cfr. entry 8) as the source of the counterion. Thus *t*-Bu_3P seems the best ligand out of the three tested in this work and Tf_2N^- the best counterion.

Comparing the above results to those reported in our previous work,[11] the hydrolysis of the 2-acyloxy-1,3-diene intermediate of type **4**, generated by the gold-catalyzed 1,2-acyloxy shift, seems to be faster than that of the acyloxydiene of type **2** obtained by the 1,3-shift, as with compounds **6** (Scheme 2) we never observed hydrolysis of **2** to the corresponding cyclopentenone during the reaction in the presence of DEAD, even in "wet" solvent.[11] Under such conditions, with current substrates **12** and **13** we instead observe the formation of a relatively high amount of Rautenstrauch product **15**, so that the reaction is better carried out in commercial dichloromethane (declared water content: 0.01%) without addition of further water.

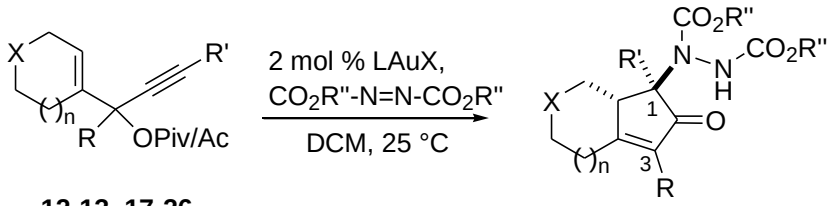
The observation that hydrolysis of the 2-acyloxydiene intermediate occurs very quickly to form **15**, unless trapped by the heterodienophile, was confirmed by monitoring by ^{1}H NMR the reaction of **13** in CD_2Cl_2 in an NMR tube (see Supporting Information). In a first experiment (Scheme 3) we added the substrate to the solution of the catalyst and, by recording the first spectrum just after 1 min, we observed the immediate formation of ketone **15**, in a roughly 1:1 ratio with both the unreacted starting material (**13**) and the 2-acyloxydiene intermediate (**16**), in mixture with some unidentified byproducts. After 7 min, **13** was almost completely converted into **15**, with smaller relative amounts of **16** still remaining in solution. A second experiment was carried by adding a solution of **13** and DEAD to the catalyst and, after 1 min, only the signals of the starting material and target product **14** were present in a 1:1.8 ratio until, after 10 min, only α-hydrazineyl ketone **14** was present in the NMR tube with traces of unreacted starting material **13**. This last experiment proves, besides the intermediacy of 2-acyloxydiene **16**, that hydrolysis of the latter to **15** is largely avoided (in the commercial solvent) if immediately trapped by DEAD.

Scheme 3. Experiments on 13 in CD_2Cl_2 for Direct Monitoring by ^{1}H NMR



The scope of the reaction (Table 2) was evaluated with substrates (either pivalate or acetate esters) bearing different rings, both terminal and internal acetylenic moieties, and unsubstituted and substituted carbinolic C atom, to obtain in many cases densely functionalized cyclopentenone products. Also, two more azodicarboxylates were evaluated, i.e., DIAD and DBAD, with pivalate **13** providing compounds **27** and **28** in 53[17] and 84% yield, respectively. With internal alkyne **17** (R' = Ph) the reaction provided **29** in 50% yield as a 14:1 mixture with a minor isomer probably deriving from the $LAu(I)^+/H^+$-assisted heterolytic cleavage of the other C-N bond (C1-N) that would generate a benzylic positive charge.[18] Instead, when the reaction was carried with *n*-butyl substituted alkyne **18** only the desired product **30** deriving from the retro aza-Michael pathway was obtained, and in excellent yield (98%). The reaction occurred uneventfully with substrate **19** bearing a functionalized side chain, too, providing cyclopentenone **31** in 90% yield, whereas with *N*-heterocyclic substrate **22** the rearrangement step was slow, and the reaction was left overnight with 6 mol % of the catalyst to attain complete conversion of the starting material into **32** (66% yield).

Table 2. Substrate Scope of the Optimized Process



12-13, **17-26**

14, 27-41

n = 1, X = CH_2

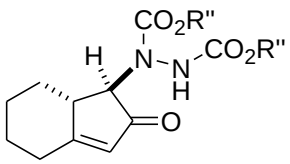
n = 1, X = *N*-Ts

n = 2, X = CH_2

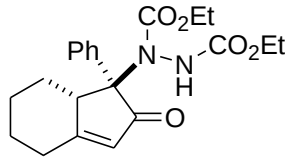
12-**13** R = R' = H
17 R = H, R' = Ph
18 R = H, R' = *n*-Bu
19 R = H, R' = -$(CH_2)_4$OTIPS
20 R = Me, R' = H
21 R = Me, R' = CO_2Me

22 R = R' = H

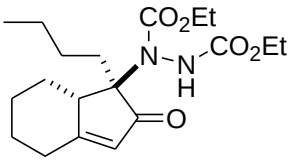
23 R = R' = H
24 R = H, R' = *n*-Bu
25 R = Me, R' = H
26 R = Me, R' = CO_2Me



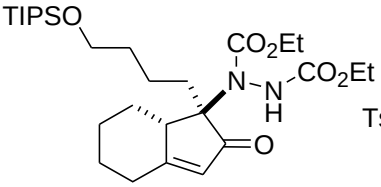
14 R'' = Et (82%)
27 R'' = *i*-Pr (53%)
28 R'' = Bn (84%)



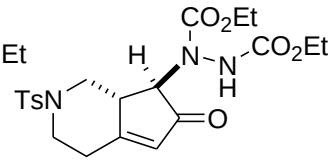
29 (50%)[a]



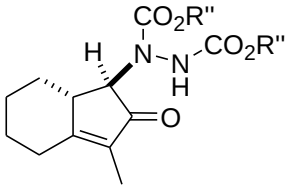
30 (98%)



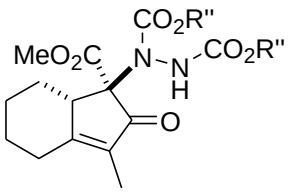
31 (90%)



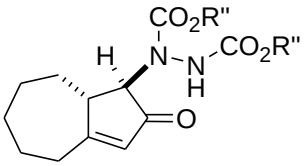
32 (66%)[b]



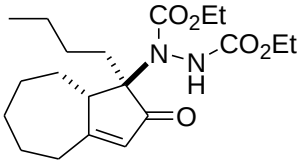
33 R'' = Et (76%)
34 R'' = *i*-Pr (63%)



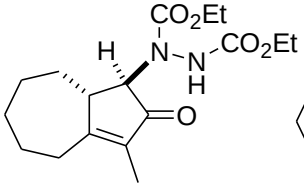
35 R'' = Et (79%)
36 R'' = *i*-Pr (58%)[c]



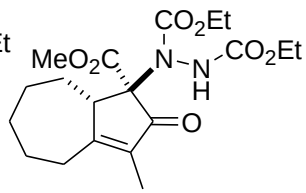
37 R'' = Et (70%)
38 R'' = *i*-Pr (59%)



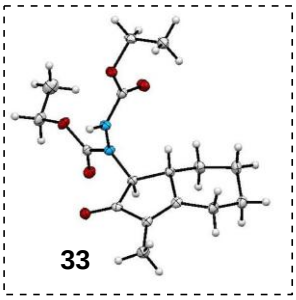
39 (76%)[b]



40 (29%)



41 (32%)[d]

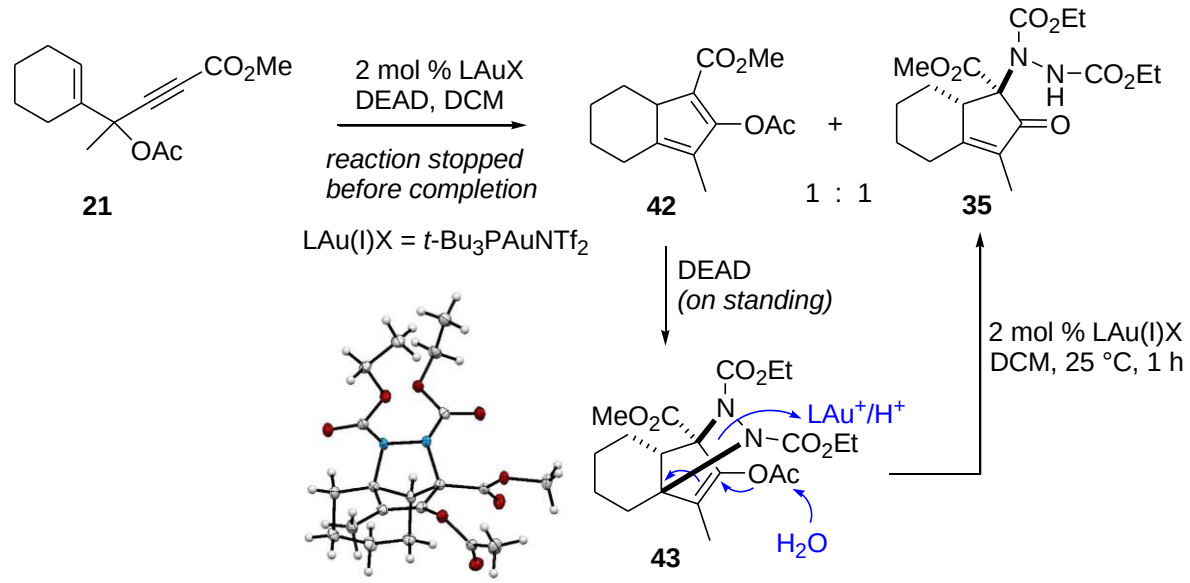


33

[a]In 14:1 ratio with the isomer deriving from the C1-N bond cleavage; [b]6 mol % of catalyst; [c]4 mol % of catalyst; [d]by ^{1}H-NMR of the crude reaction mixture. Not isolated.

Substrates bearing an alkyl (methyl) group at the carbinolic position such as **20** and **21** were suitable substrates for the process, as with DEAD they provided target compounds **33** and **35** in 76 and 79% yield, respectively, with complete facial selectivity. We managed to obtain an X-ray structure of **33** which confirmed both position and relative stereochemistry of the hydrazine appendage. No traces of the product deriving from the heterolytic C1-N bond cleavage were present in the crude reaction mixture of the latter (by ^{1}H NMR analysis) as the electron withdrawing CO_2Me group at C1 would markedly destabilize the positive charge that would form on this position.[18] The reaction of **21**, which was slower and required 45 min to reach completion, was repeated to isolate a less polar intermediate which was clearly visible by TLC when monitoring the reaction. So, the reaction was stopped before completion, filtered on a Celite layer and concentrated.

Scheme 4. Isolation and Reaction of the Cycloadduct Intermediate 43



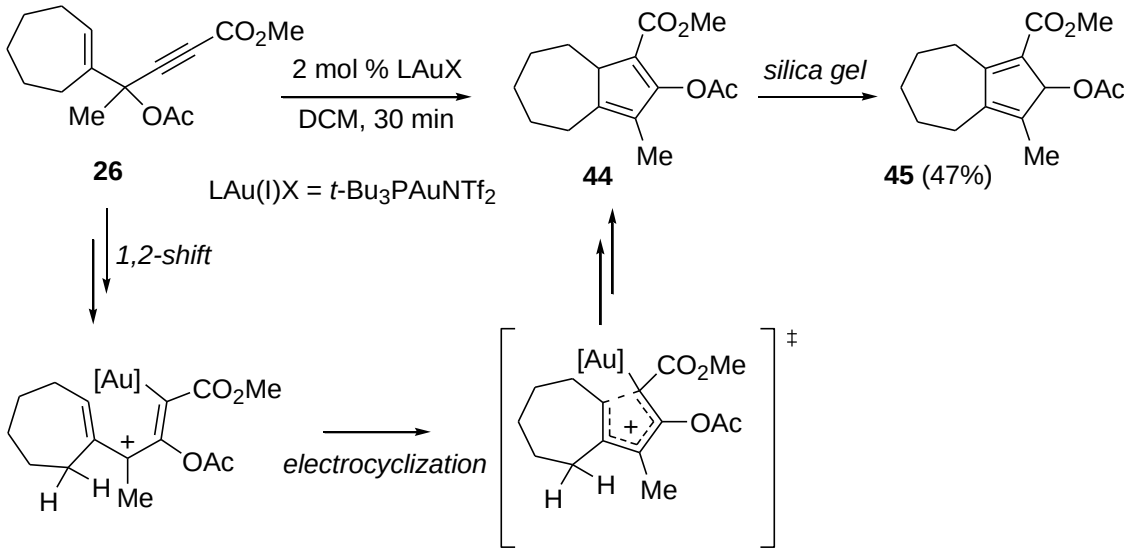
By ^{1}H NMR analysis it resulted containing a roughly 1:1 mixture of target product **35** and the unreacted Rautenstrauch reaction intermediate (**42**) (Scheme 4). On standing overnight the cycloaddition reached completion to form cycloadduct **43** as a single diastereomer of which we obtained suitable crystals for X-ray analysis. By adding the gold catalyst (2 mol %) to a solution of the latter in DCM, we observed complete ring opening in about 1 h to form **35**, which suggests that the catalyst has a role in activating the cycloadduct

intermediate towards the retro aza-Michael process, and water alone is not sufficient for the ring opening to occur. In the overall process, the gold catalyst plays therefore the dual role of π-Lewis acid for the activation of the triple bond and σ-Lewis acid to promote the retro aza-Michael process.

When we used DIAD as the heterodienophile, yields were generally lower (products **27**, **34**, and **36**, Table 2). In particular, the reaction of **21**, after the disappearance of the starting material, did not reach completion due to the slow rate of the cycloaddition step. Stopping the reaction after 5 h, compound **36** was obtained in 35% yield after chromatography, together with diene **42** (22%). The increase of steric hindrance in both the heterodienophile and diene **42**, and the decrease of electron density in the latter, should account for this result. Leaving the reaction overnight with the addition of a further 2 mol % of the catalyst resulted in almost complete conversion into **36** (58% yield after chromatography).[18]

When substrates bearing a cycloheptenyl moiety (**23**-**26**) were used, the yields were generally lower but still acceptable when R = H (70 and 59% for **37** and **38**, respectively). The cycloaddition step with DEAD was slow with substrate **24** (R' = *n*-Bu) having an internal triple bond and in this case the reaction was left overnight with more catalyst to provide **39** in 76% yield after chromatography. When the carbinolic position was occupied by a methyl group as in **25** and **26**, yields were quite low and only in one case we managed to isolate the final product (**40**) from a mixture of unidentified byproducts.

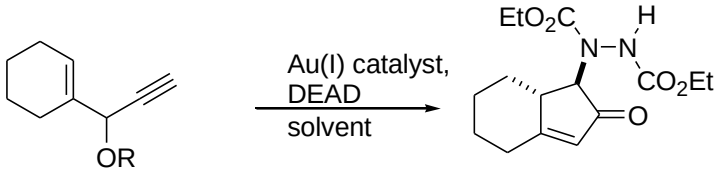
Scheme 5. The Rautenstrauch Reaction on Substrate 26



The Rautenstrauch reaction on this kind of substrates (large ring and alkyl substituted carbinolic position) has never been reported; so, to understand the reasons of the low yields, we subjected **26** to gold catalysis without DEAD (Scheme 5). We found that, albeit the starting material readily disappeared in 30 min, much degradation occurred (TLC) and the yield in the Rautenstrauch product **44** was quite low (47%) after chromatography (during which double bond isomerization to **45** occurred).[19] This suggests that it could be the Rautenstrauch process that limits the final yields with substrates **25** and **26**, probably due to augmented strains between the methyl group and the allylic protons in the transition state of the electrocyclization step.

Finally, to evaluate whether the presence of the heterodienophile could somehow interfere with the high chirality transfer observed by Toste in the Rautenstrauch rearrangement of propargyl esters,[7a] we carried out a few experiments on enantioenriched substrates **12**-**13** in the presence of DEAD (Table 3).[20-21]

Table 3. Chirality Transfer in the Reaction of Propargyl Esters in the Presence of DEAD



12 R = Ac
13 R = Piv

14

Entry	Substrate	e.e. (%)[a]	Conditions	Product (% yield)	e.e. (%)[b]
1	(*R*)-**12**	99.8	4 mol % *t*-$Bu_3PAuNTf_2$, CH_2Cl_2, 25 °C, 1 h	(1*R*, 7a*S*)-**14** (79)	53.2
2	(*S*)-**12**	93	4 mol % *t*-$Bu_3PAuNTf_2$, CH_2Cl_2, -20 °C, 28 h	(1*S*, 7a*R*)-**14** (69)	56.7
3	(*S*)-**13**	87.9	5 mol % $Ph_3PAuSbF_6$,[c] ACN, -20 °C, 46 h	(1*S*, 7a*R*)-**14** (9)[d]	86.7
4	(*S*)-**13**	87.9	5 mol % *t*-$Bu_3PAuNTf_2$, ACN, -15 °C, 24 h	(1*S*, 7a*R*)-**14** (47)[e]	59.9
5	(*R*)-**13**	99.9	5 mol % $Ph_3PAuSbF_6$,[c] CH_2Cl_2, -20 °C, 4 h	(1*R*, 7a*S*)-**14** (57)	87.0

[a]Determined by GLC with a β DEX™ 120 column; [b]Determined by HPLC on a Lux 5μ cellulose-4 column (see Supporting Information); [c]Prepared as reported in ref. 7a; [d]Most of the substrate was recovered unreacted; [e]Conversion uncomplete (65%).

The reaction of enantiopure (*R*)-**12** was first carried out (entry 1) under our standard conditions but provided (1*R*, 7a*S*)-**14** with low ee (53%). Even by decreasing the temperature to -20 °C[7a] we did not manage

to obtain the target product with much higher ee (57%) (entry 2). Switching to the conditions reported by Toste[7a] (entry 3), the reaction did occur with complete chirality transfer but, in the solvent used (ACN), the cycloisomerization step was very slow in our hand, with a conversion into the final product lower than 15% after 46 h. Repeating the reaction in acetonitrile with *t*-$Bu_3PAuNTf_2$ as the catalyst (entry 4), the reaction was slightly faster (65% conversion in 24 h) but again the ee dropped to about 60%. So $Ph_3PAuSbF_6$ seems to be the optimal catalyst for the chirality transfer and, in fact, by carrying out the last experiment with this catalyst in CH_2Cl_2 at -20 °C the reaction was complete in 4 h providing (1*R*, 7a*S*)-**14** with 87% ee starting from enantiopure (*R*)-**13**, with just a slight erosion (13%) of the initial optical purity.

Conclusions

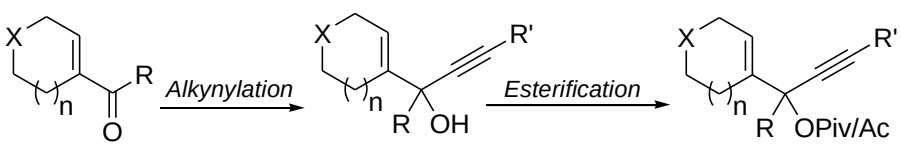
In conclusion, we have established a reliable method for the synthesis of α-hydrazineyl 2-cyclopentenones by trapping with dialkylazodicarboxylates the cyclopentadienyl ester intermediates which are formed in the gold(I)-catalyzed Rautenstrauch reaction of suitable propargyl acetates and pivalates and the consequent highly regioselective ring opening of the hetero-Diels-Alder cycloadducts. The presence of the right amount of water, as well as of the gold(I) catalyst, is essential to promote the latter step which occurs via a retro aza-Michael reaction. This tandem, one-pot process, which includes a sequence of four reactions (1,2-acyloxy migration, electrocyclization, hetero Diels-Alder, and retro aza-Michael addition), generally provides in moderate to excellent yields (50-98%) unprecedented, densely functionalized ring-fused 2-cyclopentenone derivatives. An example with an enantiomerically enriched substrate demonstrates that the whole process occurs with just a minimal erosion of the initial optical purity.

EXPERIMENTAL SECTION

General experimental methods. Anhydrous solvents were prepared accordingly to the standard techniques. Commercially available reagents were used without further purification. Melting points were recorded on a Büchi B-540 apparatus and are uncorrected. Chromatographic separations were performed under pressure on silica gel (Merck 70-230 mesh) by using flash column techniques; R_f values refer to TLC carried out on

0.25 mm silica gel plates (F_{254}) with the same eluent as indicated for column chromatography. ^{1}H NMR (200 or 400 MHz) and ^{13}C NMR (100.4 MHz) spectra were recorded either on Varian Inova (400 MHz) or Mercury (200 or 400 MHz) spectrometers in the specified deuterated solvent at 25 °C. Solvent reference lines were set at 7.26 and 77.00 ($CDCl_3$) in ^{1}H and ^{13}C NMR spectra, respectively. Mass spectra were recorded either by direct inlet of a 20 ppm solution in CH_3OH on a LCQ Fleet™ Ion Trap LC/MS system (Thermo Fisher Scientific) with electrospray ionization (ESI) interface in the positive ion mode or by electron ionization (EI) at 70 eV on a Shimadzu GC/MS-QP2020NX instrument equipped with a SH-Rxi-5ms Shimadzu column. Microanalyses were carried out with a ThermoScientific FlashSmart Elemental Analyzer CHNS/O. HPLC analyses were carried out with a Dionex Ulltimate 3000 HPLC system equipped with a Lux 5µ Cellulose-4 column, 250 x 4.60 mm and eluting at 0.5 mL/min flow rate in isocratic 50% IPA, 50% hexane. GLC analyses were carried out on a Shimadzu GC2014 instrument equipped with a Supelco β DEX™ 120, 30 m × 0.25 mm, 0.25 µm film column. 5-Hexynyloxytriisopropylsilane was prepared as reported.[22,23]

General Procedure for the Synthesis of Propargyl Esters.



X = CH_2
46: R = H, n = 1
47: R = Me, n = 1
48: R = H, n = 2
49: R = Me, n = 2
X = N-Ts
50: R = H, n = 1

51a-k

X = CH_2, R = H
13 R' = H, n = 1
17 R' = Ph, n = 1
18 R' = *n*-Bu, n = 1
19 R' = -$(CH_2)_4$OTIPS, n = 1
23 R' = H, n = 2
24 R' = *n*-Bu, n = 2
X = CH_2, R = Me
20 R' = H, n = 1
21 R' = CO_2Me, n = 1
25 R' = H, n = 2
26 R' = CO_2Me, n = 2
X = *N*-Ts
22 R = R' = H, n = 1

Compounds **46** and **47** are commercially available; compounds **48**[24] and **49**[25] were prepared as reported. For the synthesis of **50** see Supporting Infomation. Alcohol **51b** is known.[26] Acetate **20a**[8b] and pivalate **20b**,[7c] pivalates **13**,[7d] and **23**[7d] are known.

STEP 1: Alkynylation. Procedure A (R' = H). A solution of the aldehyde/ketone (2.0 mmol) in anhydrous THF (2.0 mL, 1.0 M) under nitrogen atmosphere was cooled at 0°C (ice bath) and ethynylmagnesium bromide

(0.5 M solution in THF, 6.0 mL, 3.0 mmol, 1.5 equiv) was dropwise added. The mixture was left under stirring at 0°C until complete consumption of the starting material (TLC monitoring). Satd $NaHCO_3$ (5 mL) was then added and the product extracted with Et_2O (3 x 5 mL). The combined organic extracts were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, the crude reaction mixture was purified by flash chromatography affording the corresponding intermediate alcohol **51**, which was used immediately in the next step. *Procedure B (R' ≠ H).* A solution of the terminal alkyne (2.0 mmol) in anhydrous THF (12.5 mL, 0.08 M) under nitrogen atmosphere was cooled at -78 °C (internal) and *n*-butyllitium (1.6 M in hexanes, 1.25 mL, 2.0 mmol) was dropwise added, maintaining the internal temperature below -70 °C during the addition. The mixture was allowed to warm to -60°C and left under stirring for 1 hour. After cooling at -78 °C, the aldehyde/ketone (1.0 mmol) was dropwise added and the temperature risen up to -50 °C. The mixture was left under stirring for 2 hours after which time the mixture was allowed to warm at 0°C and quenched by the addition of satd aqueous $NaHCO_3$ (12.5 mL). The product was extracted with Et_2O (3 x 15 mL) and the combined organic extracts washed with brine (25 mL) and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, the crude reaction mixture was purified by flash chromatography affording the corresponding intermediate alcohol **51**, which was used immediately in the next step.

STEP 2: Esterification. Alcohol **51** (1 mmol) was dissolved in anhydrous DCM (0.25 M for secondary alcohols or 0.5 M for tertiary alcohols) and freshly distilled Et_3N (3.0 or 4.0 mmol) and a catalytic amount of DMAP (0.05 mmol) were added. After cooling at 0 °C (ice bath), Ac_2O (1.5 mmol) or trimethylacetyl chloride (2.0 mmol) was dropwise added. After 10 minutes the ice bath was removed and the reaction mixture was left under stirring at room temperature until complete consumption of the starting material (TLC monitoring). *Work-up for acetates*: Aqueous satd $NaHCO_3$ (5 mL) was added and the product was extracted with DCM (2 x 5 mL); the combined organic extracts were dried over anhydrous Na_2SO_4. *Work-up for pivalates*: Methanol (1 mL) was added and the mixture left under stirring for 1 hour. The mixture was diluted with DCM (20 mL) and washed with aqueous satd $NaHCO_3$ (20 mL). After separation of the phases the product was extracted with DCM (2 x 20 mL) and the combined organic extracts dried over anhydrous Na_2SO_4. After filtration and

evaporation of the solvent, the crude reaction mixture was purified by flash column chromatography to give pure ester **12**-**13**, **17**-**22**.

*Acetic acid 1-cyclohexen-1-enylprop-2-ynyl ester (**12**).* Alcohol **51a** was prepared following procedure A, starting from 1-cyclohexene-1-carboxaldehyde (228 µL, 2.0 mmol) and ethynylmagnesium bromide (0.5 M solution in THF, 6 mL, 3.0 mmol). Purification by flash chromatography (EtOAc/*n*-hexane, 1:10; R_f = 0.15) afforder pure alcohol **51a** (210 mg, 77%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 5.93 (s, 1H), 4.73 (s, 1H), 2.54 (d, *J* = 2.2 Hz, 1H), 2.23 – 2.00 (m, 4H), 1.82 (br s, 1H), 1.73 – 1.56 (m, 4H). Acetylation of **51a** afforded **12**, which was purified by flash chromatography (EtOAc/*n*-hexane, 1:30; R_f = 0.23). Pure **12** (228 mg, 83%) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.00 (m, 1H), 5.76 (s, 1H), 2.52 (d, *J* = 2.0 Hz, 1H), 2.20 – 1.98 (m, 4H), 2.10 (s, 3H), 1.70 – 1.64 (m, 2H), 1.61 – 1.55 (m, 2H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 169.7, 132.9, 127.8, 79.8, 74.3, 67.5, 25.0, 24.2, 22.2, 21.8, 20.9. GCMS *m/z* (%): 178 ([M]$^+$, 6), 136 (54), 117 (100), 103 (46), 91 (71), 79 (82). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.13; H, 7.81.

*2,2-Dimethylpropionic acid 1-cyclohex-1-enyl-3-phenylprop-2-ynyl ester (**17**).* Alcohol **51b** was obtained as reported[26] and used in the next step without further purification. Pivalation of crude **51b** afforded **17** which was purified by flash chromatography (EtOAc/*n*-hexane, 1:40; R_f = 0.40). Pure **17** (260 mg, 88% over 2 steps) was obtained as a pale yellow thick oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.47 – 7.42 (m, 2H), 7.32 – 7.27 (m, 3H), 6.04 (m, 1H), 6.00 (s, 1H), 2.25 – 2.18 (m, 1H), 2.13 – 2.03 (m, 3H), 1.74 – 1.57 (m, 4H), 1.25 (s, 9H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 177.2, 133.7, 131.9 (2C), 128.5, 128.2 (2C), 126.9, 122.5, 85.8, 85.4, 68.0, 39.9, 27.1 (3C), 25.1, 24.5, 22.4, 22.1. MS (ESI) *m/z* (%): 615 ([2M + Na]$^+$, 18), 319 ([M + Na]$^+$, 100). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.04; H, 8.16.

*2,2-Dimethylpropionic acid 1-cyclohex-1-enylhept-2-ynyl ester (**18**).* Alcohol **51c** was prepared following procedure B, starting from 1-cyclohexene-1-carboxaldehyde (114 µL, 1.0 mmol) and 1-hexyne (230 µL, 2.0

mmol). The so obtained alcohol **51c** was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.88 – 5.86 (m, 1H), 4.71 (s, 1H), 2.23 (td, *J* = 6.8, 2.0 Hz, 2H), 2.08 – 2.02 (m, 2H), 1.70 – 1.62 (m, 4H), 1.61 – 1.54 (m, 2H), 1.53 – 1.45 (m, 2H), 1.43 – 1.35 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H). Pivalation of **51c** afforded **18**, which was purified by flash chromatography (EtOAc/*n*-hexane, 1:30; R_f = 0.17). Pure **18** (163 mg, 59% over 2 steps) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.95 – 5.93 (m, 1H), 5.74 (m, 1H), 2.22 (td, *J* = 6.8, 2.0 Hz, 2H), 2.14 – 1.95 (m, 4H), 1.68 – 1.56 (m, 4H), 1.53 – 1.36 (m, 4H), 1.21 (s, 9H), 0.90 (t, *J* = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 177.2, 134.1, 126.2, 86.8, 76.3, 68.0, 38.8, 30.6, 27.0 (3C), 25.0, 24.4, 22.4, 22.1, 21.8, 18.4, 13.5. MS (ESI) *m/z* (%): 575 ([2M + Na]$^+$, 53), 299 ([M + Na]$^+$, 100). Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.09; H, 8.90.

*Acetic acid 1-cyclohex-1-enyl-7-triisopropylsilanyloxyhept-2-ynyl ester (**19**).* Alcohol **51d** was prepared following procedure B, starting from 1-acetyl-1-cyclohexene (186 µL, 1.63 mmol) and 5-hexynyloxytriisopropylsilane[22] (829 mg, 3.3 mmol). Purification by flash chromatography (EtOAc/*n*-hexane, 1:20; R_f = 0.15) afforded pure **51d** (385 mg, 65%) as a thick colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.89 – 5.86 (m, 1H), 4.71 (d, *J* = 5.6 Hz, 1H), 3.70 (t, *J* = 6.0 Hz, 2H), 2.29 – 2.25 (m, 2H), 2.23 – 2.14 (m, 1H), 2.13 – 2.02 (m, 3H), 1.68 – 1.55 (m, 8H), 1.09 – 1.02 (m, 21H). Acetylation of **51d** (385 mg, 1.06 mmol) afforded **19**, which was purified by flash chromatography (EtOAc/*n*-hexane, 1:40; R_f = 0.26). Pure **19** (407 mg, 85%) was obtained as a thick colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.95 (m, 1H), 5.76 (m, 1H), 3.69 (t, *J* = 6.0 Hz, 2H), 2.29 – 2.26 (m, 2H), 2.19 – 2.09 (m, 1H), 2.08 (s, 3H), 2.07 – 1.96 (m, 3H), 1.68 – 1.54 (m, 8H), 1.05 (s, 18H), 1.04 (s, 3H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 169.9, 133.9, 127.0, 87.1, 76.3, 68.3, 62.8, 32.1, 25.0 (2C), 24.4, 22.3, 22.0, 21.1, 18.6, 18.0 (6C), 12.0 (3C). MS (ESI) *m/z* (%): 429 ([M + Na]$^+$, 100). Anal. Calcd for $C_{24}H_{42}O_3Si$: C, 70.88; H, 10.41. Found: C, 70.63; H, 10.33.

*4-Acetoxy-4-cyclohex-1-enylpent-2-ynoic acid methyl ester (**21**).* Alcohol **51f** was prepared following procedure B, starting from 1-acetyl-1-cyclohexene (193 µL, 1.5 mmol) and methyl propiolate (267 µL, 3.0

mmol). Purification by flash chromatography (EtOAc/*n*-hexane, 1:20; R_f = 0.16) afforded pure **51f** (228 mg, 73%) as a pale yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 6.06 – 6.01 (m, 1H), 3.78 (s, 3H), 2.14 – 2.04 (m, 4H), 1.73 – 1.57 (m, 4H), 1.60 (s, 3H). Acetylation of **51f** (228 mg, 1.09 mmol) afforded **21**, which was purified by flash chromatography (EtOAc/*n*-hexane, 1:20; R_f = 0.21). Pure **21** (187 mg, 69%) was obtained as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.06 – 6.04 (m, 1H), 3.77 (s, 3H), 2.12 – 2.03 (m, 3H), 2.05 (s, 3H), 1.99 – 1.89 (m, 1H), 1.72 (s, 3H), 1.68 – 1.52 (m, 4H). $^{13}C\{^1H\}$ NMR (100.4 MHz, $CDCl_3$) δ (ppm): 168.4, 153.7, 135.7, 124.5, 86.4, 77.9, 75.8, 52.6, 26.9, 24.9, 23.3, 22.5, 21.7, 21.3. MS (ESI) *m/z* (%): 523 ($[2M + Na]^+$, 100), 273 ($[M + Na]^+$, 86). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.12; H, 7.25.

*Acetic acid 1-[1-(toluene-4-sulfonyl)-1,2,3,6-tetrahydropyridin-4-yl]-prop-2-ynyl ester (**22**).* Alcohol **51g** was prepared following procedure A, starting from crude aldehyde **50** (111 mg, 0.42 mmol) and ethylmagnesium bromide (0.5 M solution in THF, 1.26 mL, 0.63 mmol). The so obtained alcohol **51g** was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.67 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.86 – 5.84 (m, 1H), 4.74 (s, 1H), 3.65 – 3.60 (m, 2H), 3.22 (t, *J* = 6.0 Hz, 2H), 2.53 (d, *J* = 2.4 Hz, 1H), 2.43 (s, 3H), 2.41 – 2.26 (m, 2H). Acetylation of **51g** afforded **22**, which was purified by flash chromatography (EtOAc/*n*-hexane, 1:4; R_f = 0.23). Pure **22** was obtained as a white solid (94 mg, 67% over 2 steps from **50**). M.p. 88.9 – 90.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.64 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.89 – 5.86 (m, 1H), 5.74 (s, 1H), 3.64 – 3.59 (m, 2H), 3.19 (t, *J* = 5.6 Hz, 2H), 2.51 (d, *J* = 2.4 Hz, 1H), 2.40 (s, 3H), 2.38 – 2.33 (m, 1H), 2.25 – 2.19 (m, 1H), 2.04 (s, 3H). $^{13}C\{^1H\}$ NMR (100.4 MHz, $CDCl_3$) δ (ppm): 169.4, 143.6, 132.9, 131.7, 129.6 (2C), 127.6 (2C), 122.5, 78.5, 75.1, 65.7, 44.4, 42.4, 24.5, 21.4, 20.8. MS (ESI) *m/z* (%): 689 ($[2M + Na]^+$, 100), 356 ($[M + Na]^+$, 57). Anal. Calcd for $C_{17}H_{19}NO_4S$: C, 61.24; H, 5.74; N, 4.20. Found: C, 61.23; H, 5.84; N, 4.20; S, 9.41.

*Acetic acid 1-cyclohept-1-enylhept-2-ynyl ester (**24**).* Alcohol **51i** was prepared following procedure B, starting from 1-cycloheptene-1-carboxaldehyde (135 mg, 1.09 mmol) and 1-hexyne (250 µL, 2.2 mmol). Purification by flash chromatography (EtOAc/*n*-hexane, 1:10; R_f = 0.38) afforded pure **51i** (171 mg, 76%) as a

pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.97 (t, *J* = 6.4 Hz, 1H), 4.71 – 4.69 (m, 1H), 2.31 – 2.25 (m, 2H), 2.22 (td, *J* = 6.8, 2.0 Hz, 2H), 2.17 – 2.12 (m, 2H), 1.77 – 1.71 (m, 2H), 1.54 – 1.35 (m, 8H), 0.90 (t, *J* = 7.6 Hz, 3H). Acetylation of **51i** (171 mg, 0.83 mmol) afforded **24**, which was purified by flash chromatography (EtOAc/*n*-hexane, 1:30; R_f = 0.25). Pure **24** (145 mg, 74%) was obtained as a colorless thick oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.03 (t, *J* = 6.4 Hz, 1H), 5.70 (s, 1H), 2.25 – 2.17 (m, 4H), 2.15 – 2.10 (m, 2H), 2.04 (s, 3H), 1.75 – 1.68 (m, 2H), 1.52 – 1.43 (m, 6H), 1.41 – 1.32 (m, 2H), 0.87 (t, *J* = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 169.8, 139.9, 132.0, 87.0, 76.2, 69.6, 32.3, 30.5, 29.1, 28.1, 26.9, 26.4, 21.8, 21.1, 18.4, 13.5. MS (ESI) *m/z* (%): 519 ([2M + Na]$^+$, 86), 271 ([M + Na]$^+$, 100). Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.32; H, 9.71.

*Acetic acid 1-cyclohept-1-enyl-1-methylprop-2-ynyl ester (**25**).* Alcohol **51j** was prepared following procedure A, starting from 1-acetyl-1-cycloheptene **49** (175 mg, 1.26 mmol) and ethynylmagnesium bromide (0.5 M solution in THF, 3.8 mL, 1.89 mmol). Purification by flash chromatography (Et_2O/*n*-hexane, 1:5; R_f = 0.30) afforded pure **51j** (137 mg, 65%) as a pale yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 6.22 (t, *J* = 6.6 Hz, 1H), 2.51 (s, 1H), 2.33 – 2.27 (m, 2H), 2.21 – 2.11 (m, 2H), 1.95 (br s, 1H), 1.83 – 1.71 (m, 2H), 1.55 (s, 3H), 1.53 – 1.41 (m, 4H). Acetylation of **51j** (136 mg, 0.82 mmol) afforded **25**, which was purified by flash chromatography (EtOAc/*n*-hexane, 1:20; R_f = 0.40). Pure **25** (125 mg, 74%) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.32 (t, *J* = 6.8 Hz, 1H), 2.66 (s, 1H), 2.22 – 2.14 (m, 4H), 2.04 (s, 3H), 1.77 – 1.71 (m, 2H), 1.67 (s, 3H), 1.51 – 1.42 (m, 4H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 168.8, 142.7, 128.5, 83.0, 77.4, 74.6, 32.7, 28.0, 27.6, 27.4, 26.8, 26.3, 21.7. MS (ESI) *m/z* (%): 435 ([2M + Na]$^+$, 100), 229 ([M + Na]$^+$, 74). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.57; H, 8.95.

*4-Acetoxy-4-cyclohept-1-enylpent-2-ynoic acid methyl ester (**26**).* Alcohol **51k** was prepared following procedure B, starting from 1-acetyl-1-cycloheptene **49** (213 mg, 1.54 mmol) and methyl propiolate (274 μL, 3.08 mmol). Purification by flash chromatography (EtOAc/*n*-hexane, 1:5; R_f = 0.44) afforded pure **51k** (172 mg, 50%) as a thick colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.20 (t, *J* = 6.8 Hz, 1H), 3.78 (s, 3H), 2.30

– 2.28 (m, 2H), 2.19 – 2.14 (m, 2H), 2.09 (br d, *J* = 7.2 Hz, 1H), 1.79 – 1.73 (m, 2H), 1.58 (s, 3H), 1.53 – 1.43 (m, 4H). Acetylation of **51k** (168 mg, 0.75 mmol) afforded **26**, which was purified by flash chromatography (EtOAc/*n*-hexane, 1:20; R_f = 0.16). Pure **26** (137 mg, 69%) was obtained as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.24 (t, *J* = 6.8 Hz, 1H), 3.75 (s, 3H), 2.25 – 2.09 (m, 4H), 2.02 (s, 3H), 1.75 – 1.69 (m, 2H), 1.68 (s, 3H), 1.51 – 1.39 (m, 4H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 168.5, 153.7, 141.6, 129.4, 86.4, 78.0, 76.6, 52.6, 32.5, 28.0, 27.6, 26.7, 26.6, 26.1, 21.4. MS (ESI) *m/z* (%): 551 ([2M + Na]$^+$, 60), 287 ([M + Na]$^+$, 100). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.13; H, 7.60.

General Procedure for the synthesis of compounds 14, 27-40 and 42-45. A solution of commercially available gold(I) complex ^{t}Bu$_3$PAuNTf$_2$ (2-6 mol%) was prepared in DCM (10 mL) under nitrogen atmosphere, and a solution of ester **12**-**13**, **17**-**26** (1.0 mmol) and the dienophile (1.0 - 1.5 equiv.) in DCM (10 mL; final concentration 0.05 M) was then added. The reaction mixture was stirred at 25 °C until complete consumption of the starting material (TLC monitoring). Aqueous satd $NaHCO_3$ (20 mL) was added and the reaction mixture vigorously stirred at 25 °C for 15 minutes; after separation of the phases, the product was extracted with DCM (20 mL) and the combined organic extracts dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, the oily residue was purified by flash chromatography.

*1-(N,N'-Dicarbetoxyhydrazino)-1,4,5,6,7,7a-hexahydroinden-2-one (**14**).* Compound **14** was prepared following the general procedure, starting from pivalate **13** (192 mg, 0.87 mmol) and DEAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 30 minutes. Purification by flash chromatography (EtOAc/*n*-hexane, 1:2; R_f = 0.20) afforded **14** (222 mg, 82%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.64 (br s, 1H, major), 6.47 (br s, 1H, minor), 5.86 (s, 1H), 4.36 – 4.07 (m, 5H), 2.96 – 2.85 (m, 1H), 2.79 (d, *J* = 14.4 Hz, 1H), 2.51 – 2.39 (m, 1H), 2.30 (td, *J* = 14.0, 6.0 Hz, 1H), 2.03 – 1.93 (m, 1H), 1.92 – 1.82 (m, 1H), 1.57 – 1.37 (m, 2H), 1.29 – 1.23 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 6H, minor), 1.25 (t, *J* = 7.2 Hz, 6H, major). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 202.7, 182.6, 156.3, 155.8, 125.1, 70.5, 62.7, 62.0, 45.1, 32.4, 31.0, 26.1, 24.8, 14.2 (2C). MS (ESI) *m/z* (%): 644

([2M + Na]$^+$, 100), 333 ([M + Na]$^+$, 29). Anal. Calcd for $C_{15}H_{22}N_2O_5$: C, 58.05; H, 7.15; N, 9.03. Found: C, 57.93; H, 7.04; N, 8.87.

*(1R,7aS)-1-(N,N'-Dicarbetoxyhydrazino)-1,4,5,6,7,7a-hexahydroinden-2-one [(1R,7aS)-**14**].* Catalyst Ph_3PAuCl (6.8 mg, 14 µmol, 5 mol%) and $AgSbF_6$ (4.7 mg, 14 µmol, 5 mol%) were mixed in DCM (0.5 mL) for 3 minutes and the suspension was filtered off over a celite plug into the reaction flask containing DCM (4 mL) and equipped with internal thermometer. After cooling at -20°C (internal), a pre-cooled solution of enantiopure pivalate (*R*)-**13** (61 mg, 0.28 mmol; e.e. > 99%) and DEAD (43 µL, 0.28 mmol) in DCM (1 mL) was added and the mixture left under stirring at -20 °C until completion of the Rautenstrauch rearrengement. After 2 h the mixture was allowed to warm to 0 °C over 1 h, after which time the cooling bath was removed and stirring was continued until completion (3 h). Recovery of the final product was performed as reported in the general procedure. Purification of the crude by flash chromatography (EtOAc/*n*-hexane, 1:2; R_f = 0.20) afforded (1*R*,7a*S*)-**14** (50 mg, 57%) as a colorless oil. Spectroscopical data are identical to those reported for the corresponding racemic compound. $[\alpha]_D^{23}$ + 45.8 (*c* 1.0, $CHCl_3$). e.e. 87% (by HPLC).

*1-(N,N'-Dicarbisopropoxyhydrazino)-1,4,5,6,7,7a-hexahydroinden-2-one (**27**).* Compound **27** was prepared following the general procedure, starting from pivalate **13** (42 mg, 0.19 mmol) and DIAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 30 minutes. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.13) afforded **27** (34 mg, 53%) as a foamy white solid. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.62 (br s, 1H), 5.84 (s, 1H), 4.99 – 4.82 (m, 2H), 4.29 (br s, 1H, major), 4.14 (br s, 1H, minor), 2.95 – 2.84 (m, 1H), 2.76 (d, *J* = 13.6 Hz, 1H), 2.49 – 2.35 (m, 1H), 2.34 – 2.19 (m, 1H), 2.01 – 1.89 (m, 1H), 1.89 – 1.77 (m, 1H), 1.56 – 1.32 (m, 3H), 1.23 – 1.19 (m, 12H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 202.9, 182.6, 156.1, 155.3, 125.2, 70.8, 70.5, 69.8, 45.2, 32.5, 31.1, 26.1, 24.8, 21.9 (4 C). MS (ESI) *m/z* (%): 699 ([2M + Na]$^+$, 31), 361 ([M + Na]$^+$, 100), 339 ([M]$^+$, 24). Anal. Calcd for $C_{17}H_{26}N_2O_5$: C, 60.34; H, 7.74; N, 8.28. Found: C, 60.26; H, 7.87; N, 8.16.

*1-(N,N'-Dicarbobenzyloxyhydrazino)-1,4,5,6,7,7a-hexahydroinden-2-one (**28**).* Compound **28** was prepared following the general procedure, starting from acetate **12** (98 mg, 0.55 mmol) and DBAD (1.5 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 20 minutes. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.12) afforded **28** (222 mg, 84%) as a thick colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 7.43 – 7.18 (m, 10H), 6.83 (br s, 1H, major), 6.60 (br s, 1H, minor), 5.87 (s, 1H, major), 5.81 (s, 1H, minor), 5.24 – 5.03 (m, 4H), 4.39 (br s, 1H, major), 4.26 (br s, 1H, minor), 2.91 (m, 1H), 2.81 – 2.72 (m, 1H), 2.53 – 2.36 (m, 1H), 2.35 – 2.18 (m, 1H), 2.03 – 1.93 (m, 1H), 1.92 – 1.80 (m, 1H), 1.68 – 1.62 (m, 1H), 1.49 – 1.25 (m, 2H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 202.6 and 202.3, 182.8 and 182.5, 156.5 and 156.2, 155.7, 135.53 and 135.48, 135.36 (2C), 128.42 and 128.37 (2C), 128.2 (2C), 128.1 and 128.0 (2C), 127.9 and 127.6 (2C), 125.2 and 125.0 (2C), 70.7 and 70.4, 68.6 and 68.2, 67.6, 45.3 and 45.1, 32.5 and 32.3, 31.0, 26.1 and 25.8, 24.8 and 24.5. MS (ESI) *m/z* (%): 891 ($[2M + Na]^+$, 100), 457 ($[M + Na]^+$, 11). Anal. Calcd for $C_{25}H_{26}N_2O_5$: C, 69.11; H, 6.03; N, 6.45. Found: C, 69.00; H, 5.95; N, 6.45.

*1-(N,N'-Dicarbetoxyhydrazino)-1-phenyl-1,4,5,6,7,7a-hexahydroinden-2-one (**29**).* Compound **29** was prepared following the general procedure, starting from pivalate **17** (83 mg, 0.28 mmol) and DEAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 2 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.21) afforded **29** (54 mg, 50%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 7.42 – 7.09 (m, 5H), 6.65 (br s, 1H), 6.10 (s, 1H, major), 5.99 (s, 1H, minor), 4.16 – 4.04 (m, 4H), 3.90 (dd, *J* = 12.8, 6.0 Hz, 1H, major), 3.64 (m, 1H, minor), 2.90 – 2.79 (m, 1H), 2.37 (td, *J* = 14.4, 6.4 Hz, 1H), 2.04 – 1.66 (m, 3H), 1.48 – 1.39 (m, 1H and 1H minor), 1.36 – 1.30 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.15 (t, *J* = 7.2 Hz, 3H), 0.35 (qd, *J* = 12.8, 3.2 Hz, 1H, major). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 208.5 and 203.5, 182.3, 157.5, 156.0, 136.0, 129.1 (2C), 127.7 and 127.6, 127.3, 127.1 and 127.0, 125.7 and 125.0, 78.6, 62.8 and 62.6, 62.0 and 61.5, 51.2, 31.37 and 31.34, 30.8, 26.2 and 25.4, 25.0 and 24.9, 14.4 and 14.3, 14.1. MS (ESI) *m/z* (%): 795 ($[2M + Na]^+$, 100), 409 ($[M + Na]^+$, 15). Anal. Calcd for $C_{21}H_{26}N_2O_5$: C, 65.27; H, 6.78; N, 7.25. Found: C, 65.01; H, 6.98; N, 7.43.

*1-(N,N'-Dicarbetoxyhydrazino)-1-butyl-1,4,5,6,7,7a-hexahydroinden-2-one (**30**).* Compound **30** was prepared following the general procedure, starting from pivalate **18** (52 mg, 0.19 mmol) and DEAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 30 minutes. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.16) afforded **30** (68 mg, 98%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.69 (br s, 1H, major), 6.62 (br s, 1H, minor), 5.82 (s, 1H), 4.24 – 4.00 (m, 4H), 3.27 – 3.15 (m, 1H, major), 3.13 – 3.04 (m, 1H, minor), 2.75 (d, *J* = 15.2 Hz, 1H), 2.38 – 2.23 (m, 1H), 2.05 – 1.96 (m, 1H, major), 1.93 – 1.80 (m, 2H and 1H minor), 1.71 – 1.63 (m, 1H), 1.53 – 1.31 (m, 3H), 1.28 – 1.04 (m, 11H), 0.83 (t, *J* = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers; major rotamer reported) δ (ppm): 204.5, 178.4, 156.8, 154.9, 124.4, 71.4, 62.4, 62.1, 50.2, 31.9, 30.5, 26.6, 25.6, 25.5, 24.7, 23.1, 14.4, 14.2, 13.8. MS (ESI) *m/z* (%): 755 ([2M + Na]$^+$, 100), 389 ([M + Na]$^+$, 55). Anal. Calcd for $C_{19}H_{30}N_2O_5$: C, 62.27; H, 8.25; N, 7.64. Found: C, 62.08; H, 8.18; N, 7.93.

*1-(N,N'-Dicarbetoxyhydrazino)-1-(4-triisopropylsilanyloxybutyl)-1,4,5,6,7,7a-hexahydroinden-2-one (**31**).* Compound **31** was prepared following the general procedure, starting from acetate **19** (158 mg, 0.39 mmol) and DEAD (1.2 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 2.5 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.29) afforded **31** (188 mg, 90%) as a thick colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.75 (br s, 1H, major), 6.50 (br s, 1H, minor), 5.84 (s, 1H), 4.28 – 4.03 (m, 4H), 3.71 – 3.60 (m, 2H), 3.30 – 3.21 (m, 1H, major), 3.18 – 3.08 (m, 1H, minor), 2.77 (d, *J* = 13.2 Hz, 1H), 2.43 – 2.28 (m, 1H), 2.07 – 1.99 (m, 1H), 1.96 – 1.82 (m, 2H), 1.77 – 1.66 (m, 1H), 1.57 – 1.24 (m, 8H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H), 1.09 – 1.03 (m, 21H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers; major rotamer reported) δ (ppm): 204.3, 178.4, 156.8, 155.0, 124.4, 71.4, 62.5, 62.4, 62.1, 50.3, 33.1, 31.6, 30.5, 25.6 (2C), 24.8, 20.5, 18.0 (6C), 14.5, 14.3, 11.9 (3C). MS (ESI) *m/z* (%): 1099 ([2M + Na]$^+$, 100), 561 ([M + Na]$^+$, 51). Anal. Calcd for $C_{28}H_{50}N_2O_6Si$: C, 62.42; H, 9.35; N, 5.20. Found: C, 62.31; H, 9.28; N, 5.25.

*7-(N,N'-Dicarbetoxyhydrazino)-2-(toluene-4-sulfonyl)-1,2,3,4,7,7a-hexahydro[2]pyrindin-6-one (**32**).* Compound **32** was prepared following the general procedure, starting from acetate **22** (78 mg, 0.24 mmol) and DEAD (1.2 equiv.) and using 6 mol% of the catalyst. The reaction was complete in 18 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:1; R_f = 0.25) afforded **32** (74 mg, 66%) as a white solid. M.p. 93.5 – 94.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 7.63 – 7.61 (m, 2H), 7.33 (d, *J* = 6.8 Hz, 2H), 6.60 (br s, 1H, major), 6.31 (br s, 1H, minor), 5.93 (s, 1H), 4.52 – 4.01 (m, 6H), 3.38 – 3.15 (m, 1H), 2.85 – 2.59 (m, 2H), 2.47 – 2.33 (m, 1H), 2.43 (s, 3H), 2.31 – 2.20 (m, 1H), 1.43 – 1.33 (m, 1H), 1.27 (m, 6H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 200.9, 175.6, 156.1 (2C), 143.8, 133.7, 129.8 (2C), 127.5 (2C), 126.7, 66.8, 63.1, 62.3, 50.6, 45.5, 43.5, 30.0, 21.5, 14.4 (2C). MS (ESI) *m/z* (%): 953 ([2M + Na]$^+$, 100), 488 ([M + Na]$^+$, 55). Anal. Calcd for $C_{21}H_{27}N_3O_7S$: C, 54.18; H, 5.85; N, 9.03; S, 6.89. Found: C, 54.18; H, 5.87; N, 8.98; S, 6.72.

*1-(N,N'-Dicarbetoxyhydrazino)-3-methyl-1,4,5,6,7,7a-hexahydroinden-2-one (**33**).* Compound **33** was prepared following the general procedure, starting from pivalate **20b** (60 mg, 0.26 mmol) and DEAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 50 minutes. Purification by flash chromatography (EtOAc/*n*-hexane, 1:4; R_f = 0.11) afforded **33** (64 mg, 76%) as a white solid. M.p. 108.2 – 109.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.78 (br s, 1H, major), 6.49 (br s, 1H, minor), 4.28 – 4.09 (m, 5H), 2.82 (d, *J* = 14.4 Hz, 1H), 2.84 – 2.71 (m, 1H), 2.45 – 2.33 (m, 1H, major), 2.32 – 2.23 (m, 1H, minor), 2.14 – 2.03 (m, 1H), 1.96 – 1.92 (m, 1H), 1.85 – 1.81 (m, 1H), 1.65 (s, 3H), 1.53 – 1.43 (m, 1H), 1.39 – 1.26 (m, 1H), 1.24 – 1.14 (m, 1H), 1.22 (t, *J* = 6.8 Hz, 3H), 1.21 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 203.0, 173.7, 156.7 and 156.2, 155.9, 131.6, 69.6, 62.7, 62.0, 43.9, 32.4, 28.1, 25.7, 24.9, 14.3 (2C), 7.6. MS (ESI) *m/z* (%): 671 ([2M + Na]$^+$, 100), 347 ([M + Na]$^+$, 15). Anal. Calcd for $C_{16}H_{24}N_2O_5$: C, 59.24; H, 7.46; N, 8.64. Found: C, 59.36; H, 7.26; N, 8.54.

*1-(N,N'-Dicarbisopropoxyhydrazino)-3-methyl-1,4,5,6,7,7a-hexahydroinden-2-one (**34**).* Compound **34** was prepared following the general procedure, starting from acetate **20a** (90 mg, 0.47 mmol) and DIAD (1.0

equiv.) and using 2 mol% of the catalyst. The reaction was complete in 30 minutes. Purification by flash chromatography (EtOAc/*n*-hexane, 1:4; R_f = 0.18) afforded **34** (104 mg, 63%) as a white solid. M.p. 115.1 – 116.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.52 (br s, 1H, major), 5.02 – 4.79 (m, 2H), 4.27 – 4.14 (m, 1H, major), 2.85 (d, *J* = 15.6 Hz, 1H), 2.88 – 2.74 (m, 1H, major), 2.72 – 2.60 (m, 1H, minor), 2.47 – 2.36 (m, 1H, major), 2.36 – 2.24 (m, 1H, minor), 2.19 – 2.05 (m, 1H), 2.02 – 1.91 (m, 1H), 1.91 – 1.79 (m, 1H), 1.68 (s, 3H), 1.56 – 1.43 (m, 1H), 1.41 – 1.30 (m, 1H), 1.26 – 1.21 (m, 13H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 203.1 and 202.9, 173.7 and 173.4, 156.4 and 156.0, 155.4, 131.6, 110.4, 70.6 and 70.4, 69.9 and 69.8, 44.4 and 43.9, 32.4, 28.1, 25.8, 24.9, 21.9 and 21.7 (4C), 7.7. MS (ESI) *m/z* (%): 727 ($[2M + Na]^+$, 100), 375 ($[M + Na]^+$, 85), 353 ($[M]^+$, 14). Anal. Calcd for $C_{18}H_{28}N_2O_5$: C, 61.34; H, 8.01; N, 7.95. Found: C, 61.23; H, 8.01; N, 7.97.

*1-(N,N'-Dicarbethoxyhydrazino)-1-carbomethoxy-3-methyl-1,4,5,6,7,7a-hexahydroinden-2-one (**35**).* Compound **35** was prepared following the general procedure, starting from acetate **21** (71 mg, 0.28 mmol) and DEAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 45 minutes. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.13) afforded **35** (85 mg, 79%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.69 (br s, 1H), 4.28 – 4.02 (m, 4H), 3.71 (s, 3H), 3.49 – 3.30 (m, 1H), 2.88 (d, *J* = 14.8 Hz, 1H), 2.32 – 2.07 (m, 2H), 2.02 – 1.93 (m, 1H), 1.93 – 1.82 (m, 1H), 1.77 – 1.64 (m, 1H), 1.69 (s, 3H), 1.58 – 1.32 (m, 2H), 1.28 – 1.18 (m, 6H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers; major rotamer reported) δ (ppm): 198.1, 177.0, 167.9, 156.6, 155.8, 130.1, 75.6, 62.9, 61.9, 53.3, 52.6, 29.1, 28.6, 25.8, 25.5, 14.3 (2C), 7.9. MS (ESI) *m/z* (%): 787 ($[2M + Na]^+$, 100), 405 ($[M + Na]^+$, 93). Anal. Calcd for $C_{18}H_{26}N_2O_7$: C, 56.53; H, 6.85; N, 7.33. Found: C, 56.53; H, 6.82; N, 7.22.

*1-(N,N'-Dicarbisopropoxyhydrazino)-1-carbomethoxy-3-methyl-1,4,5,6,7,7a-hexahydroinden-2-one (**36**).* Compound **36** was prepared following the general procedure, starting from acetate **21** (100 mg, 0.40 mmol) and DIAD (1.0 equiv.) and using 4 mol% of the catalyst. The reaction was complete in 18 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:4; R_f = 0.10) afforded **36** (95 mg, 58%) as a pale yellow oil. ^{1}H

NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.59 (br s, 1H), 5.03 – 4.73 (m, 2H), 3.70 (s, 3H), 3.50 – 3.13 (m, 1H), 2.86 (d, *J* = 13.6 Hz, 1H), 2.30 – 2.02 (m, 2H), 2.02 – 1.80 (m, 2H), 1.80 – 1.58 (m, 1H), 1.68 (s, 3H), 1.56 – 1.31 (m, 2H), 1.30 – 1.04 (m, 12H). $^{13}C\{^1H\}$ NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers; major rotamer reported) δ (ppm): 198.2, 177.2, 167.9, 156.2, 155.6, 130.0, 75.7, 70.9, 69.7, 53.3, 52.6, 29.2, 28.6, 25.9, 25.5, 22.0, 21.9, 21.8, 21.7, 7.9. MS (ESI) *m/z* (%): 843 ($[2M + Na]^+$, 100), 433 ($[M + Na]^+$, 32). Anal. Calcd for $C_{20}H_{30}N_2O_7$: C, 58.52; H, 7.37; N, 6.82. Found: C, 58.44; H, 7.27; N, 6.51.

*1-(N,N'-Dicarbethoxyhydrazino)-4,5,6,7,8,8a-hexahydro-1H-azulen-2-one (**37**).* Compound **37** was prepared following the general procedure, starting from pivalate **23** (65 mg, 0.28 mmol) and DEAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 2 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.19) afforded **37** (64 mg, 70%) as a white solid. M.p. 112.7 – 113.9 °C. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.65 (br s, 1H), 5.89 (s, 1H), 4.55 (br s, 1H, first rotamer), 4.39 (br s, 1H, second rotamer), 4.26 – 4.07 (m, 4H), 3.06 (br s, 1H), 2.75 – 2.68 (m, 2H), 2.09 (m, 1H), 1.82 – 1.46 (m, 7H), 1.25 (t, *J* = 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 202.7, 185.7, 156.2 (2C), 127.1, 70.5 and 70.0, 62.8, 62.1, 48.0, 33.5, 21.2, 29.9, 27.4 (2C), 14.34, 14.29. MS (ESI) *m/z* (%): 671 ($[2M + Na]^+$, 100), 347 ($[M + Na]^+$, 10), 325 ($[M]^+$, 21). Anal. Calcd for $C_{16}H_{24}N_2O_5$: C, 59.24; H, 7.46; N, 8.64. Found: C, 59.16; H, 7.43; N, 8.43.

*1-(N,N'-Dicarbisopropoxyhydrazino)-4,5,6,7,8,8a-hexahydro-1H-azulen-2-one (**38**).* Compound **38** was prepared following the general procedure, starting from pivalate **23** (76 mg, 0.32 mmol) and DIAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 2 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.26) afforded **38** (67 mg, 59%) as a white solid. M.p. 120.9 – 122.0 °C. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.52 (br s, 1H, major), 6.28 (br s, 1H, minor), 5.89 (s, 1H), 5.03 – 4.85 (m, 2H), 4.55 (br s, 1H, major), 4.36 (br s, 1H, minor), 3.12 – 2.92 (m, 1H), 2.71 – 2.59 (m, 2H), 2.16 – 1.98 (m, 1H), 1.81 – 1.48 (m, 7H), 1.27 – 1.22 (m, 12H). $^{13}C\{^1H\}$ NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 202.8, 185.6, 156.0, 155.7, 127.1, 70.8 and 70.6, 69.9 and 69.8, 48.0,

33.5, 31.2, 29.9, 29.7, 27.5 (2C), 21.93 and 21.89 (2C), 21.7 (2C). MS (ESI) *m/z* (%): 727 ([2M + Na]$^+$, 88), 375 ([M + Na]$^+$, 100), 353 ([M]$^+$, 12). Anal. Calcd for $C_{18}H_{28}N_2O_5$: C, 61.34; H, 8.01; N, 7.95. Found: C, 61.40; H, 7.97; N, 7.66.

*1-(N,N'-Dicarbethoxyhydrazino)-1-butyl-4,5,6,7,8,8a-hexahydro-1H-azulen-2-one (**39**).* Compound **39** was prepared following the general procedure, starting from acetate **24** (80 mg, 0.30 mmol) and DEAD (1.0 equiv.) and using 6 mol% of the catalyst. The reaction was complete in 18 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.25) afforded **39** (87 mg, 76%) as a white solid. M.p. 127.2 – 128.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.68 (br s, 1H, major), 6.50 (br s, 1H, minor), 5.88 (s, 1H), 4.26 – 4.07 (m, 4H), 3.43 – 3.33 (m, 1H, major), 3.31 – 3.24 (m, 1H, minor), 2.93 (dd, *J* = 17.2, 6.4 Hz, 1H), 2.43 – 2.35 (m, 1H), 2.04 – 1.89 (m, 3H), 1.85 – 1.63 (m, 2H), 1.57 – 1.38 (m, 2H), 1.35 – 1.12 (m, 11H), 1.11 – 0.99 (m, 2H), 0.82 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 204.7 and 204.2, 182.7 and 181.8, 157.0, 154.8 and 154.5, 126.0 and 125.7, 73.7, 62.4, 62.1, 54.2, 33.9 and 33.8, 32.0, 31.8 and 31.7, 30.4 and 30.0, 26.9 and 26.7, 26.5 and 26.3, 25.8, 23.1, 14.5 and 14.4, 14.3 and 14.2, 13.8. MS (ESI) *m/z* (%): 783 ([2M + Na]$^+$, 84), 403 ([M + Na]$^+$, 100). Anal. Calcd for $C_{20}H_{32}N_2O_5$: C, 63.13; H, 8.48; N, 7.36. Found: C, 63.10; H, 8.41; N, 7.75.

*1-(N,N'-Dicarbethoxyhydrazino)-3-methyl-4,5,6,7,8,8a-hexahydro-1H-azulen-2-one (**40**).* Compound **40** was prepared following the general procedure, starting from acetate **25** (63 mg, 0.30 mmol) and DEAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was complete in 1.5 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.21) afforded **40** (29 mg, 29%) as a white solid. M.p. 131.3 – 132.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 6.62 (br s, 1H, major), 6.33 (br s, 1H, minor), 4.46 (m, 1H, minor), 4.35 – 4.06 (m, 4H and 1H major), 3.04 – 2.83 (m, 1H), 2.65 – 2.50 (m, 2H), 2.16 – 2.04 (m, 1H), 1.83 – 1.46 (m, 7H), 1.68 (d, *J* = 2.0 Hz, 3H), 1.25 (t, J = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) (mixture of rotamers) δ (ppm): 202.9, 177.1, 156.2 (2C), 133.6, 69.5 and 69.0, 62.8, 62.1, 46.5, 31.4,

31.0, 30.8, 27.6, 26.7, 14.3 (2C), 7.9. MS (ESI) *m/z* (%): 699 ([2M + Na]$^+$, 72), 361 ([M + Na]$^+$, 100). Anal. Calcd for $C_{17}H_{26}N_2O_5$: C, 60.34; H, 7.74; N, 8.28. Found: C, 60.25; H, 7.62; N, 8.01.

*2-Acetoxy-3-methyl-4,5,6,7-terahydro-2H-indene-1-carboxylic acid methyl ester (**42**).* Compound **42** was isolated following the general procedure, starting from acetate **21** (100 mg, 0.40 mmol) and DIAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was stopped after 5 hours. Purification by flash chromatography (EtOAc/*n*-hexane, 1:4;) afforded **36** (R_f = 0.10; 58 mg, 35%) as a pale yellow oil and **42** (R_f = 0.52; 22 mg, 22%) as a white solid. M.p.79.2 – 80.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.71 (s, 3H), 2.95 (dd, *J* = 6.0, 1.2 Hz, 1H), 2.74 – 2.63 (m, 2H), 2.32 (s, 3H), 2.15 – 2.04 (m, 1H), 2.01 – 1.93 (m, 1H), 1.83 – 1.75 (m, 1H), 1.74 (t, *J* = 1.2 Hz, 3H), 1.46 (qt, *J* = 13.2, 3.2 Hz, 1H), 1.17 (qt, *J* = 13.2, 4.0 Hz, 1H), 0.88 (qd, *J* = 12.8, 3.2 Hz, 1H). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ (ppm): 167.9, 163.1, 160.5, 153.0, 127.1, 120.4, 50.9, 49.2, 32.4, 28.2, 26.6, 25.0, 20.8, 8.6. MS (ESI) *m/z* (%): 523 ([2M + Na]$^+$, 43), 273 ([M + Na]$^+$, 100). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.21; H, 7.24.

*11-Acetoxy-10-methyl-8,9-diazatricyclo[5.2.2.0^{1,6}]undec-10-ene-7,8,9-tricarboxylic acid 8,9-diethyl ester 7-methyl ester (**43**).* Compound **43** was isolated following the general procedure, starting from acetate **21** (181 mg, 0.72 mmol) and DEAD (1.0 equiv.) and using 2 mol% of the catalyst. The reaction was stopped before completion and the mixture filtered over a celite pad. The solvent was evaporated and the crude mixture analyzed by ^{1}H NMR, that showed a roughly 1 : 1 mixture of target compound **35** and intermediate **42**, together with unreacted DEAD. On standing overnight the cycloaddition on **42** completed to afford compound **43** which was isolated by purification by flash chromatography (EtOAc/*n*-hexane, 1:3; R_f = 0.29) and obtained as a white solid (125 mg, 41%), together with a small amount of **35** (32 mg, 12%). Crystals of **43** suitable for X Ray structure determination were obtained by slow evaporation of a diethyl ether solution. M.p. 72.1 – 73.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.22 – 4.07 (m, 4H), 3.77 (s, 3H), 2.78 (d, *J* = 12.4 Hz, 1H), 2.16 (s, 3H), 2.07 (dd, *J* = 11.2, 4.0 Hz, 1H), 2.00 – 1.91 (m, 1H), 1.89 – 1.77 (m, 2H), 1.70 (s, 3H), 1.68 – 1.61 (m, 1H), 1.55 – 1.41 (m, 1H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.16 – 1.05 (m, 2H). ^{13}C{^{1}H}

NMR (100.4 MHz, $CDCl_3$) δ (ppm): 169.2, 165.5, 158.5 (2C), 145.4, 132.0, 78.0, 76.2, 62.9, 62.1, 61.1, 52.3, 28.1, 23.7, 22.8, 22.5, 20.3, 14.3, 14.2, 9.4. MS (ESI) *m/z* (%): 871 ($[2M + Na]^+$, 100), 447 ($[M + Na]^+$, 30). Anal. Calcd for $C_{20}H_{28}N_2O_8$: C, 56.59; H, 6.65; N, 6.60. Found: C, 56.53; H, 6.73; N, 6.86.

*2-Acetoxy-3-methyl-2,4,5,6,7,8-hexahydroazulene-1-carboxylic acid methyl ester (**45**).* Compound **45** was isolated following the general procedure, starting from acetate **26** (44 mg, 0.17 mmol) and using 2 mol% of the catalyst, without the addition of the dienophile. The starting material disappeared in 30 minutes. After filtration and evaporation of the solvent, the crude was analyzed by ^1H NMR that showed the presence of compound **44**. ^1H NMR (200 MHz, $CDCl_3$) (diagnostic signals) δ (ppm): 3.73 (s, 3H, CO_2CH_3), 3.38 – 3.27 (m, 1H, 8a-*H*), 2.31 (s, 3H, CH_3CO), 1.70 (q, *J* = 1.2 Hz, 3H, 3-CH_3). Purification by flash chromatography (EtOAc/*n*-hexane, 1:10 + 1% Et_3N; R_f = 0.17) caused the isomerization of **44** to **45**, which was obtained as a white solid (21 mg, 47%). M.p. 113.9 – 115.2 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.19 (s, 1H, 2-H), 3.69 (s, 3H, CO_2CH_3), 3.10 – 2.96 (m, 1H, 8-H), 2.93 – 2.77 (m, 1H, 8-H'), 2.43 – 2.35 (m, 1H, 4-H), 2.31 – 2.22 (m, 1H, 4-H'), 2.13 (s, 3H, CH_3CO), 1.77 (s, 3H, 3-CH_3), 1.75 – 1.67 (m, 2H), 1.67 – 1.50 (m, 4H). $^{13}C\{^1H\}$ NMR (100.4 MHz, $CDCl_3$) δ (ppm): 170.5, 165.9, 164.1, 143.5, 140.0, 124.4, 78.4, 50.8, 32.1, 29.0, 28.4, 28.3, 26.7, 20.9, 11.2. MS (ESI) *m/z* (%): 551 ($[2M + Na]^+$, 100), 287 ($[M + Na]^+$, 42). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.21; H, 7.59.

Associated content.

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://....

Experimental procedures, NMR spectra, and X-ray crystallography details (PDF)

Accession Codes. CCDC 2361196−2361197 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Notes

The authors declare no competing financial interest.

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Graphical Abstract