European Journal of Organic Chemistry

EurJOC
European Journal of Organic Chemistry

Chemistry Europe
European Chemical Societies Publishing

RESEARCH ARTICLE OPEN ACCESS

One-Pot Gold(I)-Catalyzed Rautenstrauch Rearrangement/Nitrosocarbonyl Hetero-Diels–Alder Reaction Sequence for the Synthesis of α-Hydroxylated Cyclopentenones

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Received: 26 March 2026 | **Revised:** 18 May 2026 | **Accepted:** 28 May 2026

Keywords: cycloaddition | fused-ring systems | gold(I)-catalysis | nitrosocarbonyl compounds | rearrangement

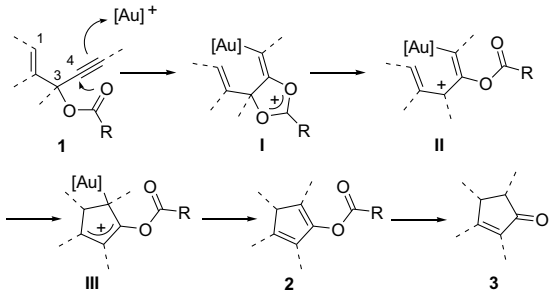
ABSTRACT

The synthesis of densely functionalized, ring-fused α-hydroxy-2-cyclopentenone precursors is achieved by one-pot gold(I)-catalyzed Rautenstrauch/hetero Diels–Alder/ring opening sequential reactions of suitable propargyl esters. The 1,2-acyloxy migration/cyclization process (Rautenstrauch reaction) leads to cyclopentadienyl ester intermediates which are stereo- and regioselectively trapped by the nitrosocarbonyl reagent generated in situ by adding a hydroxamic acid (e.g., Boc-NHOH) and an oxidant (n-Bu_4NIO_4) to the reaction mixture after the Au(I)-catalyzed cycloisomerization step. This provides strained intermediates, which undergo highly regioselective ring opening by a retro-aza-Michael reaction triggered by hydrolysis of the acetate group, eventually yielding the precursors of racemic, ring-fused α-hydroxy-2-cyclopentenone compounds in 46%–90% yield. The target six-, seven-, and eight-membered ring-fused cyclopentenones bearing a tertiary α-hydroxy group can be then obtained in moderate to good yield (42%–84%) by N-O cleavage in the presence of $Mo(CO)_6$.

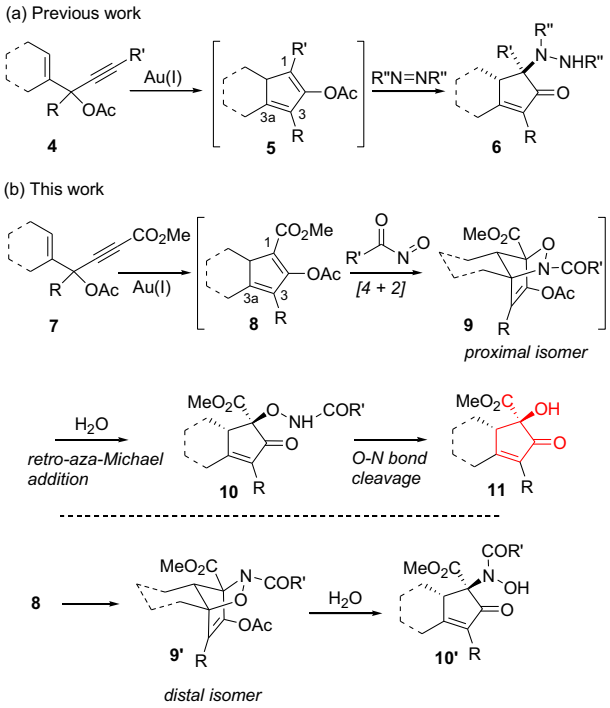
1 | Introduction

The transition metal-catalyzed rearrangement of 3-acyloxy-1,4-enynes **1** to 1,3-cyclopentadienyl esters **2**, occurring via initial 1,2-shift of the acyloxy group, and evolving to the corresponding cyclopentenone products **3** (Scheme 1), was originally reported to take place under Pd(II)-catalysis by Rautenstrauch [1–3]. In 2005, Toste and Gagosz independently demonstrated that gold(I)-complexes were able to promote the same reaction [4, 5], thus spurring an increasing interest toward the Au(I)-catalyzed Rautenstrauch rearrangement [6–12]. Since then, this process has in fact become a reliable tool to build a conjugated cyclopentenone moiety during the synthesis of natural compounds [13–16], as well as to increment the molecular complexity of the products through cascade processes involving any of the rearrangement intermediates [17–23].

In continuation of our studies on cascade processes involving Au(I)-catalyzed rearrangements of propargyl alcohol derivatives [24–27], we recently reported that 2-acyloxy-1,3-dienes **5** (Scheme 2a) obtained from propargyl esters **4** can be trapped by dialkyl azodicarboxylates present in the reaction medium as soon as generated by the Rautenstrauch rearrangement, forming highly strained cycloadducts [28]. These spontaneously undergo a retro-aza-Michael reaction forming ring-fused cyclopentenones **6** bearing a α-tertiary hydrazino group. Following the same approach, we embarked in the investigation of the Rautenstrauch rearrangement/nitroso-Diels–Alder reaction sequential process of propargyl esters **7** as a conceivable route to the synthesis of the corresponding α-hydroxy-2-cyclopentenones **11** (Scheme 2b). We envisaged that, after a stereo- and regioselective cycloaddition step, the retro-aza-Michael reaction on cycloadducts **9** and the subsequent N—O bond cleavage in hydroxylamine derivatives **10** would provide our target ring-fused cyclopentenones **11** bearing a tertiary hydroxyl group at C1, i.e., at the adjacent position to the ring junction [29–34]. Reverse regioselectivity in the cycloaddition step would instead lead to the



SCHEME 1 | The gold(I)-catalyzed Rautenstrauch rearrangement.



SCHEME 2 | (a) Previous and (b) current work.

wrong "distal" isomers **9**′ and presumably to N-acylhydroxylamine derivatives **10**′ after a retro-oxa-Michael step.

α-Hydroxy-substituted 2-cyclopentenones, and structurally similar tertiary alcohol-containing bicyclic moieties, are present in many natural and bioactive compounds (Figure 1). To our knowledge, only one general approach to the synthesis of compounds **11** (as acetates), with the same relative stereochemistry, and based on the initial Pt(II)-catalyzed 1,2-rearrangement of propargyl esters, has been reported so far [29]. Consequently, if successful, our approach would constitute an alternative and quick access to densely functionalized, six-, seven-, and eight-membered ring-fused compounds **11** as intermediates in the synthesis of natural compounds.

The choice of compounds **7** for the initial Rautenstrauch rearrangements stems from regioselective issues in the cycloaddition of nitroso compounds [35–37]. Since steric and electronic effects influence the outcome in Diels–Alder reaction of nitroso reagents [35–38], predicting the regioselectivity in the case of densely substituted dienes such as **8** (Scheme 2) is not easy. However,

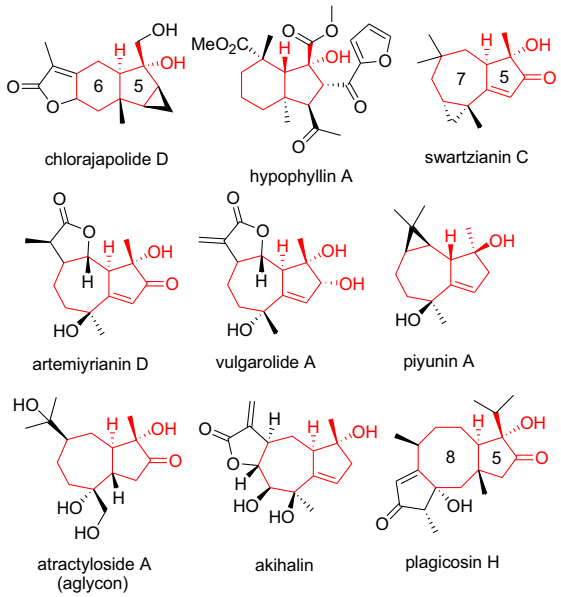
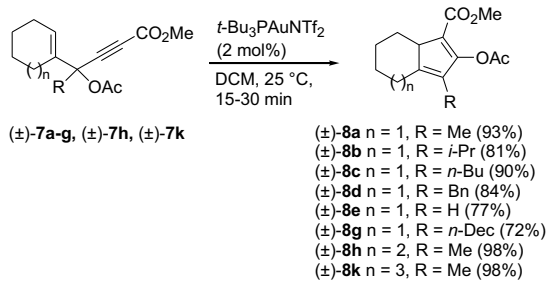


FIGURE 1 | Selected natural compounds containing the target bicyclic moieties (in red).

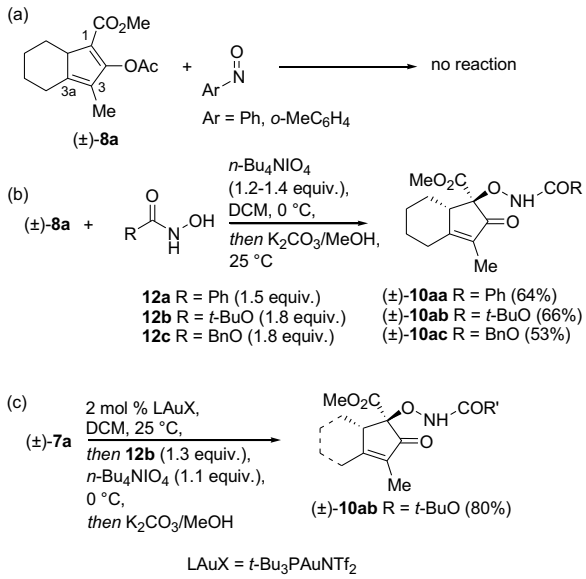
according to Houk's prediction on monosubstituted acyclic butadienes [39] and based on the results reported by Stachulski [40] and Kouklowski [38] on disubstituted acyclic butadienes, we hoped that the simultaneous presence of the electron-withdrawing ester group at position 1 and the acyloxy group at position 2 would override any other effect exerted by other substituents (at C3 and C3a) on the five-membered ring, thus strongly favoring the formation of "proximal" isomer **9**. The presence of the CO_2Me group at position 1 brings two further benefits: from the perspective of elaborating products **11** into a particular target, the ester group at C1 should be easily manipulated. Moreover, based on our experience, 2-acyloxy dienes **8** bearing the CO_2Me group at C1 are, generally, hydrolytically stable under the Au(I)-catalyzed reaction conditions [28, 41]. This would allow one to carry out the cycloaddition step after the completion of the gold(I)-catalyzed Rautenstrauch rearrangement, as trapping intermediates **8** while they are formed during the latter process with very labile acyl- or acyloxynitroso compounds is not possible [42].

2 | Results and Discussion

Although our final objective was to perform all steps (from the rearrangement to the retro-Michael addition) to products **10** in one pot, because there are only very few examples of Rautenstrauch rearrangement of 3-acyloxy-1,4-enynes of type **7** bearing an EWG group on the triple bond [2, 7, 28, 43], we preliminarily carried out the cycloisomerization reaction under optimized conditions (2 mol % of *t*-$Bu_3PAuNTf_2$ in freshly distilled CH_2Cl_2 at 25 °C, 15–30 min) [28] on a number of racemic substrates to fully characterize the corresponding acyloxy intermediate products (**8,** Scheme 3). All these products proved hydrolytically stable (to possible adventitious water) during the reaction. However, as we have already shown [28], when a large cycle was fused to the five-membered ring these products could not be chromatographed on silica gel as they readily underwent double bond migration inside and outside the smaller ring. Nonetheless, two representatives of 7–5



SCHEME 3 | Synthesis of 2-acyloxydienes **8**.



SCHEME 4 | (a) Studies on the hetero-Diels–Alder with arylnitroso reagents and (b)–(c) with nitrosocarbonyl reagents.

and 8–5 membered-ring fused acyloxy dienes (**8h** and **8k**, respectively) (Scheme 3), were isolated to be fully characterized as crude reaction mixtures. Instead, the cycloisomerization of acetates (**7a**-**e** and **7g**) bearing the double bond inside a six-membered carbocycle allowed us to isolate chromatographically stable 2-acetoxydienes **8**.

Initial studies on the nitroso-Diels–Alder reaction carried out with commercial nitrosobenzene and *o*-nitrosotoluene (Scheme 4a, and Table 1, entries 1–2) on isolated diene **8a** under various conditions were disappointing. The reaction never led to the formation of any cycloaddition product, and the recovery of the starting material, together with its product of hydrolysis, was always complete [44].

Switching to the more reactive acyl- and acyloxynitroso compounds [35] was instead successful, but it required their preparation in situ, which was carried out by oxidizing their hydroxamic acid precursors **12a-c** with *n*-Bu_4NIO_4 in the presence of diene **8a** in dichloromethane (Scheme 4b) [45]. Initial studies were carried out with benzhydroxamic acid **12a** (Table 1, entries 3–4). Under the best conditions, **8a** was mixed with 1.5 equiv. of **12a** in anhydrous DCM followed by drop-wise addition of a dichloromethane solution of the oxidant (1.2 equiv.) at 0 °C. After disappearance of the diene (by TLC) (11 min) we stopped the reaction and tried to isolate the cycloadduct intermediate. However, this proved not feasible as the cycloadduct quickly decomposed after work up [46, 47]. For this reason, we decided to promote the retro-Michael addition step by the hydrolysis of the acetate group [27, 28] just after completion of the cycloaddition. This would provide either of the α-substituted cyclopentenones **10aa** (from proximal HDA and next retro-aza-Michael) and **10aa'** (from distal HDA and retro-oxa-Michael, see Scheme 2b) or both. The hydrolysis was thus carried out by adding a saturated K_2CO_3 solution in MeOH at 25 °C, which caused the almost immediate disappearance of the cycloaddition product and the formation of a new product as a single isomer (Table 1, entry 4). Although purification by chromatography was not easy (as with all compounds **10**) because of the excess of reagents used, that could be isolated (64% yield) and fully characterized and, gratifyingly, corresponded to **10aa** [48]. Thus, similarly to the reactions with dialkyl azodicarboxylates [28], the facial selectivity in the cycloaddition step was very high and, moreover, only the hoped-for proximal regioselectivity was observed.

The hetero-Diels–Alder reaction of **8a** with acyloxynitroso reagents prepared from *N*-Boc hydroxylamine **12b** (commercial) and *N*-(benzyloxycarbonyl) hydroxylamine **12c** (freshly prepared) was carried out under the same conditions (Table 1, entries 5–7). We found that with the acyloxynitroso reagents the hetero Diels–Alder step was slightly slower. By TLC monitoring, it was complete in 30 min with **12b** and in 10 min when increasing the relative amount of **12b** (1.8 equiv.) and oxidant (1.4 equiv.), under which conditions the final product **10ab**

TABLE 1 | Initial studies on the nitroso-Diels–Alder reaction on isolated diene **8a**.

Entry	Nitroso reagent, equiv.	*n*-Bu_4NIO_4, equiv.	Solvent	*T*, °C	*t*, min	Product, %[a]
1	PhNO (2.0)	—	CH_2Cl_2	0	60	—[b]
2	*o*-MeC_6H_4NO (2.0)	—	CH_2Cl_2	25 °C	90	—[b]
3[c]	**12a** (1.5)	1.2	CH_2Cl_2	0	11	—
4[d]	**12a** (1.5)	1.2	CH_2Cl_2	0	11	**10aa** (64)
5[d]	**12b** (1.5)	1.2	CH_2Cl_2	0	30	**10ab** (43)
6[d]	**12b** (1.8)	1.4	CH_2Cl_2	0	10	**10ab** (66)
7[d]	**12c** (1.8)	1.4	CH_2Cl_2	0	15	**10ac** (53)

[a]Yield of **10** after chromatography.
[b]The product deriving from hydrolysis of **8a** was observed in the ^1H NMR spectrum of the crude reaction mixture.
[c]Reaction carried out in the attempt of isolating the cycloadduct intermediate.
[d]Treatment with K_2CO_3/MeOH at 25 °C after completion of the cycloaddition step.

was obtained, as a single isomer, in 66% yield after hydrolysis (entry 6). Under the latter conditions, with **12c** the hetero Diels–Alder step was complete in 15 min and provided, after the usual work-up, **10ac** in 53% yield, again as a single isomer (entry 7). Both **10ab** and **10ac** were fully characterized to assign their structure.

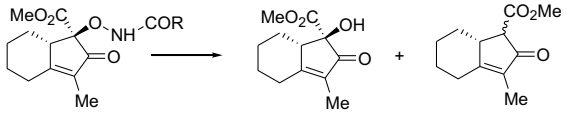
To establish a one-pot protocol, i.e., to avoid the isolation of acyloxydienes **8**, we tried the addition of the hydroxamic acid (we used **12b**) and the oxidant to the cycloisomerization reaction mixture just after complete conversion (15 min) of propargyl acetate **7a** into diene intermediate **8a** (Scheme 4c). We found that under these conditions the hetero-Diels–Alder step was slower and it was complete in 55 min when using 1.8 equiv. of **12b** and 1.4 equiv. of oxidant. By lowering the amount of both oxidant (1.1 equivalent) and **12b** (1.3 equiv.), albeit slowing down the reaction rate (complete in 2.5 h), the whole sequence encompassing cycloisomerization, cycloaddition of the nitroso reagent, and the retro-aza-Michael addition, on the other hand provided **10ab** in an excellent 80% yield after chromatography. In the evaluation of the scope (see below), for all substrates **7** we then employed this one-pot protocol, with just an exception, regardless of the regiochemical stability of diene intermediates **8**.

The last problem to face was the N—O cleavage, for which we tried conditions that in principle would leave the double bond in the five-membered ring unaltered (Table 2) so to conserve the highest degree of functionalization. As shown, the formation of byproduct **13a** *via* C—O bond cleavage was an obstacle when using Zn in acetic acid (entry 1) [49], and SmI_2 (entries 2–3) [50], while CuCl in MeOH [51] (entry 4) left the starting material unreacted. Eventually we found that refluxing a 15:1 $MeCN/H_2O$ solution of **10aa** in the presence of $Mo(CO)_6$ (0.7 equiv., entry 5) [52] cleanly provided tertiary alcohol **11a** in 65% yield after work-up and chromatographic purification. Analogous results were obtained with substrates **10ab** and **10ac** (entries 6 and 7). Of course, the presence of the OH group on the ring was the unequivocal demonstration of the regiochemical outcome of the cycloaddition step (see Supporting Information).

Having established a protocol for the synthesis of compound **11a**, we proceeded with the extension of the procedure to differently substituted substrates **7b-l**, which were prepared from the corresponding α,β-unsaturated ketones **14** (Scheme 5). As with **7a**, all these substrates were prepared in racemic form. With a single exception, all reactions were carried out with *N*-Boc hydroxylamine **12b** for the generation of the nitroso reagent (Table 3). Because of the difficulties encountered in their purification, products **10** obtained in the cascade process were chromatographed just to remove the excess of the reagents present in the crude reaction mixtures and then directly subjected to N–O cleavage. Besides **10aa-ac**, only for two more compounds (**10hc** and **10kb**) we repeated the chromatography to attain a sufficiently pure sample of the two representative seven- and eight-membered ring-fused compounds for the full characterization (see Supporting Information). Instead, all final products **11** could be properly purified by chromatography and thus fully characterized.

We first evaluated the effect of the substituent at C3 on reaction rate, regio- and stereoselectivity of the one-pot process to compounds **10**. The formation of intermediates **10** occurred smoothly with propargyl esters **7** bearing a six-membered ring (**7a-d**, **7g**) as they were obtained in high yield (70%–90%) over the three steps. The cycloaddition step was complete in 1–3 h before proceeding with the hydrolysis. In all cases, the substituents at C3 did not affect either the regio- or the facial selectivity as the products were all obtained as single isomers. The same was true for products **10eb** (R = H) and **10fb** (R = Ph), although in these two cases the one-pot process provided lower yields (46%). In the first case the lack of a substitution at C3 (on the five-membered ring) perhaps determined a higher susceptibility of either **10eb** or its diene precursor to the oxidant, whereas for the Ph-substituted compound we noted a certain propensity of diene intermediate **8f** to double bond isomerization. Interestingly, the regioselectivity

TABLE 2 | Studies on the N–O cleavage.



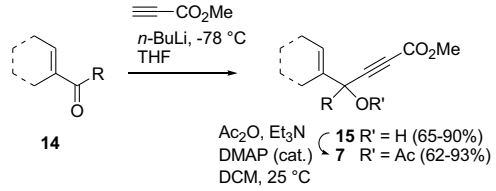
(±)-**10aa** R = Ph
(±)-**10ab** R = *t*-BuO
(±)-**10ac** R = BnO

(±)-**11a**

13a

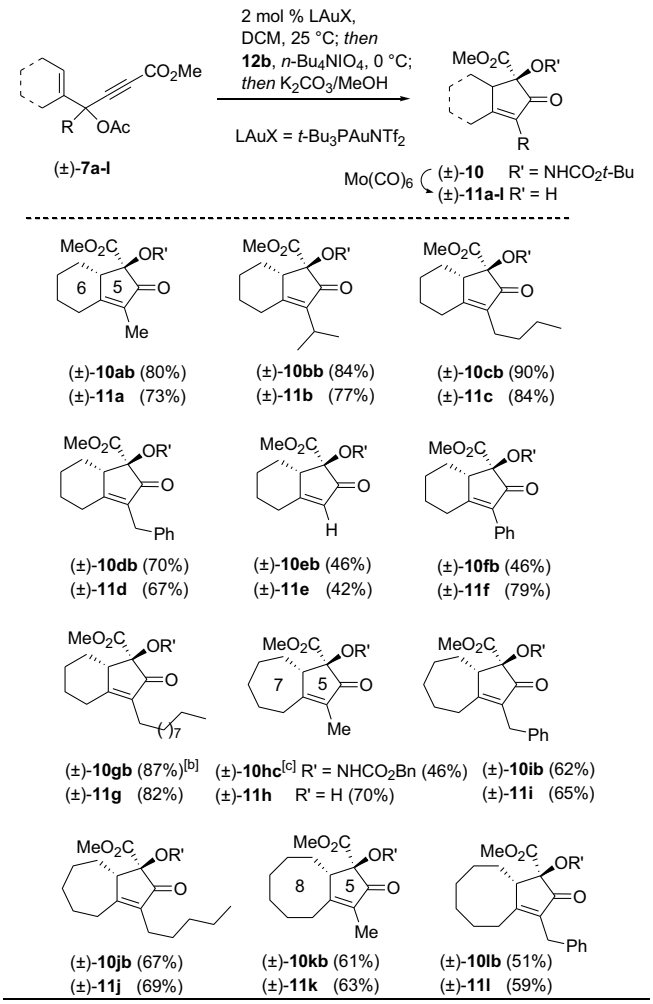
Entry	Substrate	Reagent, equiv.	Solvent	*T*, °C	*t*, min	**11a**[a], %[b]	**13a**[a]
1	**10aa**	Zn (4.2)	$AcOH/H_2O$ 2:1	70	180	—	100
2	**10aa**	SmI_2 (2)	THF	25	30	—	100
3	**10aa**	SmI_2 (1)	THF	25	15	—	100
4	**10aa**	CuCl (1)	MeOH	25	50	—	—
5	**10aa**	$Mo(CO)_6$ (0.7)	$MeCN/H_2O$ 15:1	Reflux	50	100 (65)	—
6	**10ab**	$Mo(CO)_6$ (0.7)	$MeCN/H_2O$ 15:1	Reflux	60	100 (73)	—
7	**10ac**	$Mo(CO)_6$ (0.7)	$MeCN/H_2O$ 15:1	Reflux	30	100 (70)	—

[a]Conversion of **10** into **11a** or **13a**.
[b]Yield of **11a** after chromatography.



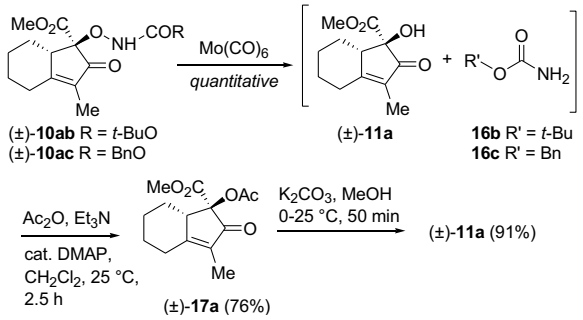
SCHEME 5 | Synthesis of the acetates **7**.

TABLE 3 | Evaluation of the substrate scope.[a]



[a]Reactions carried out with 1.3 equiv. of **12b** and 1.1 equiv. of n-Bu_4IO_4.
[b]Carried out on 1 mmol.
[c]*N*-(benzyloxycarbonyl)hydroxylamine **12c** (1.8 equiv) and 1.2 equiv. of oxidant were used in this experiment.

in the cycloaddition of **8e** to form **10eb** remained unchanged, confirming that the presence of a group at C3 is irrelevant in determining the approach of the nitroso reagent to the diene. The effect of the size of the carbocycle bearing the double bond in **7** was evaluated next. Apparently, with the larger cycles the yields of the one-pot process to intermediates **10** were lower. We found that adding, after 1 h, another 0.5 equiv. of hydroxamic acid **12b** ameliorated the yields so to render them acceptable for a three-step process (51%–62%). Only **10hc** was obtained in a lower (46%) yield, but in this case the reaction was carried out in the presence of hydroxamic acid **12c**. Stereo- and regioselectivity did not change, however. The next N—O cleavage occurred efficiently



SCHEME 6 | Acetylation of product **11a** and successive hydrolysis.

with all compounds **10**, with the only exception of **10eb** which furnished tertiary alcohol **11e** in 42% yield, only.

In a few cases, chromatographic separation of products **11** from carbamates **16** (Scheme 6) deriving from the N—O bond cleavage was difficult. In such cases we proceeded in two different ways. When *N*-(benzyloxycarbonyl)hydroxylamine **12c** was used as the source of the nitroso reagent, the product obtained following N—O cleavage (e.g., **11a**, Scheme 6) was selectively acetylated, which allowed us to obtain less polar product **17a** easily separated from **16c** by chromatography. Subsequent hydrolysis then regenerated **11a**. When the byproduct of the process was carbamic acid *t*-butyl ester **16b** (R′ = *t*-Bu) the best solution was to destroy it after either the work-up or chromatography of the N—O cleavage reaction mixture by treatment with TFA (see Experimental section).

3 | Conclusion

In conclusion, we have established a reliable, one-pot method for the synthesis of functionalized racemic α-hydroxy-2-cyclopentenones by stereo- and regioselectively trapping with nitrosocarbonyl reagents the cyclopentadienyl ester intermediates which are formed in the gold(I)-catalyzed Rautenstrauch rearrangement of suitable propargyl acetates, followed by ring opening of the hetero-Diels–Alder cycloadducts and eventual N—O cleavage. The addition of an alkaline methanolic solution was essential to promote the ring-opening step which occurs via a retro aza-Michael reaction. The nitrosocarbonyl reagents were prepared in situ by adding the hydroxamic acid precursor and the oxidant to the reaction mixture after the Au(I)-catalyzed cycloisomerization step. This sequential process, which includes four reactions (cycloisomerization, generation of the nitroso reagent, hetero Diels–Alder, and retro aza-Michael addition), generally provides in moderate to excellent yields (46%–90%) the precursors of ring-fused α-tertiary hydroxy 2-cyclopentenone derivatives, in turn obtained by N—O cleavage, whose skeleton is part of many natural compounds.

4 | Experimental Section

4.1 | Representative Procedure for the Synthesis of Compounds 11 Starting from Acetates 7

(±)-*3-Decyl-1-hydroxy-2-oxo-2,4,5,6,7,7a-hexahydro-1H-indene-1-carboxylic acid methyl ester* **(11g).** A solution of commercially

available gold(I) complex $^{t}Bu_3PAuNTf_2$ (15.4 mg, 22.6 μmol, 2 mol%) was prepared in anhydrous DCM (11.3 mL) under nitrogen atmosphere, and a solution of acetate **7g** (426 mg, 1.13 mmol) in anhydrous DCM (11.3 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; 25 min) and then cooled to 0 °C (ice bath). Reagent **12b** (196 mg, 1.3 equiv.) was added, immediately followed by a solution of $n Bu_4NIO_4$ (539 mg, 1.1 equiv.) in anhydrous DCM (1.2 mL, 1 M). The resulting mixture was stirred at 0 °C until disappearance of the intermediate diene (TLC monitoring; 2 h). Satd methanolic K_2CO_3 solution (22 mL) was added and the mixture left under vigorous stirring at room temperature for 10 min, after which time it was poured into water (160 mL) and the product extracted with Et_2O (5 × 70 mL). The combined organic extracts were washed with satd aqueous $Na_2S_2O_3$ (120 mL), satd aqueous $NaHCO_3$ (120 mL) and brine (120 mL), and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, crude **10gb** was obtained. Flash chromatography (eluent: *n*-hexane/EtOAc, 4:1, $R_f = 0.26$) of the crude reaction mixture afforded **10gb** (458 mg, 87%) as a pale-yellow oil. ^{1}H NMR (400 MHz, CD_2Cl_2) δ (ppm): 7.71 (s, NH, 1H), 3.72 (s, 3H), 2.98–2.88 (m, 2H), 2.23–2.12 (m, 3H), 2.01–1.93 (m, 2H), 1.90–1.83 (m, 1H), 1.54–1.36 (m, 4H), 1.43 (s, 9H), 1.34–1.20 (m, 15H), 0.88 (t, J = 6.8 Hz, 3H). A solution of compound **10gb** (450 mg, 0.97 mmol) in acetonitrile-water, 15:1 (16 mL) was prepared and $Mo(CO)_6$ (179 mg, 0.68 mmol) was added. The resulting mixture was heated under reflux for 50 min, after which time the dark warm suspension was gently poured onto a thin layer of silica gel (2.9 g) and left to concentrate to dryness. The dry silica gel was transferred onto a celite layer (10 mm height) in a gooch funnel and the cake washed under *vacuum* with portions of EtOAc (50 mL total volume). Solvent was evaporated and the oily residue purified by flash chromatography (eluent: *n*-hexane/EtOAc, 4:1, R_f = 0.24) and the so obtained compound **11g** was then dissolved in DCM (16 mL, 0.05 M) containing TFA (1.6 mL, 10% v/v) and stirred at room temperature. After 20 min the solvent was evaporated, DCM added (16 mL) to the residue and the organic layer washed once with satd aqueous $NaHCO_3$ (16 mL) and then dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, pure compound (±)-**11g** (278 mg, 82%) was obtained as a waxy white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.73 (s, 3H), 2.94–2.87 (m, 1H), 2.76–2.71 (m, 1H), 2.23–2.09 (m, 3H), 2.01–1.93 (m, 2H), 1.91–1.85 (m, 1H), 1.53–1.45 (m, 1H), 1.42–1.31 (m, 3H), 1.28–1.19 (m, 15H), 0.86 (t, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.4 MHz, $CDCl_3$) δ (ppm): 202.9 (C), 173.0 (C), 171.6 (C), 135.9 (C), 81.7 (C), 52.6 (CH_3), 51.8 (CH), 31.9 (CH_2), 29.59 (CH_2), 29.57 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.2 (CH_2), 28.1 (CH_2), 27.2 (CH_2), 25.4 (CH_2), 24.8 (CH_2), 22.8 (CH_2), 22.6 (CH_2), 14.1 (CH_3). MS (ESI) *m/z* (%): 723 ([2M + Na]$^+$, 100), 373 ([M + Na]$^+$, 8). HRMS (ESI Orbitrap) *m/z*: [M + H]$^+$ calcd for $C_{21}H_{35}O_4$: 351,2535. Found: 351,2524.

Acknowledgements

This study was supported by MUR and European Union – "Next Generation EU" (PRIN2022 "Achieving Molecular Diversity by Metal-Catalyzed Tandem Reactions – AMODIVE", project n. 2022R2FYE3; CUP: B53D2301−5620006). The authors thank MUR-Department of Excellence 2023-2027 n. 58503_DIPECC_23_27, and Centro di Servizi di Spettrometria di Massa – CISM (University of Florence).

Open access publishing facilitated by Universita degli Studi di Firenze, as part of the Wiley - CRUI-CARE agreement.

Funding

This study was supported by Ministero dell'Università e della Ricerca (2022R2FYE3).

Conflicts of Interest

The authors declare no conflicts of interest.

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46. Liu has recently reported on a rare [2 + 2]-nitroso/alkene cycloaddition with 2-acyloxycyclopentadienes as the substrates. It is possible that the mechanism proposed by Liu applies to our substrates, too, although in a regioselective manner. However, we tend to discard it for the following reasons: the [2 + 2] cycloaddition proposed by Liu occurs under special conditions only (with 10 mol% NaBArF in toluene at 50°C for 18 h), which are quite different from our reaction conditions. Moreover, we have never observed the formation of the piperidone which should be obtained by the subsequent intramolecular rearrangement of the [2 + 2] cycloaddition product. On the other hand, Zhang (ref. [44]) has subsequently demonstrated the [4 + 2] mechanism for the nitroso cycloaddition to 2-acyloxypentadienes like those employed by Liu by isolating the cycloaddition product. Moreover, the [4 + 2] cycloaddition intermediates between 1-acyloxycyclopentadienes and acyloxynitroso reagent **12c** were previously isolated by Grieco (see ref. [47]). We also managed to record a ^{1}H NMR spectrum of the cycloadduct intermediate by adding N-Boc-hydroxylamine **12b** and the oxidant to a solution of **8a** (10 mg) in CD_2Cl_2 in an NMR tube. Monitoring by NMR, under these conditions the reaction was complete in about 2 h and provided a product whose signals were consistent with those of [4 + 2] cycloadduct **9** (see Supporting Information). J.-X. Chen, P. D. Jadhav, C.-N. Chen, and R.-S. Liu, "Development of a [2 + 2]-Nitroso/Alkene Cycloaddition Using Sodium Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate Catalyst: Controlled Chemoselectivity of Two Equilibrating Isomeric Intermediates," *Organic Letters* 23 (2021): 6246–6251.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.