A Rh(I)-Catalyzed Cycloisomerization Reaction Affording Cyclic Trienones

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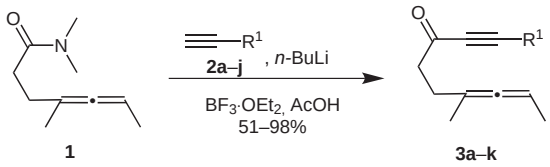
Abstract: A Rh(I)-catalyzed carbocyclization reaction of allene-ynones affords functionalized 2-alkylidene-3-vinylcyclohexenones and 2-alkylidene-3-vinylcyclopentenones. The scope, limitations, and utility of this triene-forming protocol have been examined and the results reported within.

Key words: allenes, alkynes, Rh(I), cycloisomerization, triene

Selective and concise entry into molecular complexity via carbocyclization reactions of unsaturated carbon–carbon bonds is an important area in organometallic chemistry.[1] Recently, it was demonstrated that Rh(I)-catalyzed cycloisomerization reactions of allenes lead to trienyl-containing carbocycles,[2] heterocycles,[2] δ- and ε-lactams,[3] and δ-lactones.[4] Combining these functional motifs with a cross-conjugated trienyl moiety provides functionally dense substructures and if chemical reactivity can be controlled, a means of gaining rapid access to molecular complexity.

Using cross-conjugated trienes in complexity generating reactions requires novel approaches to controlling double-bond selectivity.[5] It was this control element that led us to consider the carbocyclization reactions of alkynones[6] because the resulting trienones would possess double bonds that are sterically biased and electronically differentiated by the carbonyl group. In this Letter we report on the assembly of the allene-ynones and their participation in Rh(I)-catalyzed carbocylization reactions to produce trienones. Selective reactions of the double bonds of the trienones were briefly investigated and also reported on.

Allene-ynones **3a**–**j**[7] were conveniently prepared by addition of the corresponding lithium acetylides **2a**–**j** to amide **1** (Scheme 1). Compound **3k**, possessing a terminal alkynone, was obtained by removal of the TMS group from **3e**.[7c] Subjecting allene-ynone **3e** to the standard reaction protocol developed in our group for the Rh(I)-catalyzed cycloisomerization reaction {10 mol% $[Rh(CO)_2Cl]_2$, r.t.} afforded a 10% yield of **4e**. Reasoning that alkynone **3e** was either more reactive and/or trienone **4e** less stable, the reaction was performed at 0 °C using only 3 mol% of catalyst.[8] To our delight, trienone **4e** was obtained in 95% yield after only five minutes at 0 °C (entry 5, Table 1).



3a R^1 = Me, 93%
3b R^1 = $(CH_2)_3$OTBS, 51%
3c R^1 = $(CH_2)_2$OTBS, 99%
3d R^1 = $(CH_2)_2$OTHP, 98%
3e R^1 = TMS, 64%
3f R^1 = 1-cyclohexenyl, 97%
3g R^1 = Ph, 98%
3h R^1 = 4-$MeOC_6H_4$, 93%
3i R^1 = 4-$F_3CC_6H_4$, 90%
3j R^1 = OEt, 83%
3k R^1 = H, 90%

Scheme 1 Formation of allenyl alkynones **3a**–**k**

Next, the scope and limitations of this reaction were examined by varying the substituents on the alkyne. These variations had a significant impact on the rate and yields of these cycloisomerization reactions. For example, if R^1 = Me (**3a**) or a TBS-protected propanol **3b**, conversion to **4a** or **4b** required 90 minutes (entries 1 and 2, Table 1). Interestingly, shortening the tether between the protected alcohol and the alkyne from three to two methylene units dramatically reduces the reaction time to ca. 20 minutes (entries 3 and 4, Table 1).[9] Alternatively, placing an aromatic ring on the alkyne terminus slows the reaction, requiring that substrate **3g** be heated to 50 °C and 8 mol% of Rh(I) catalyst to effect the formation of trienone **4g**. An electron-withdrawing or electron-donating group on the *para*-position of the aryl ring had a negligible effect on this reaction; since each of these reactions occurred within five minutes and the corresponding products were obtained in similar yields (entries 7–9). An ethoxy group on the alkyne terminus furnished a product that quickly decomposed before it could be characterized (entry 10, Table 1). Terminal alkynes were not tolerated under the reaction conditions since complete decomposition was observed immediately upon addition of the Rh(I) catalyst (entry 11).[10,11]

Interestingly, the reaction of **3f**, possessing a cyclohexenyl group on the alkyne terminus, affords the tricyclic compound **7** in 29% yield.[12] The proposed reaction pathway to account for the formation of **7** involves a carbocyclization of allene **3f** to give trienone **5**, then an electrocyclization leading to **6** and an oxidative aromatization reaction to give **7** (Scheme 2).

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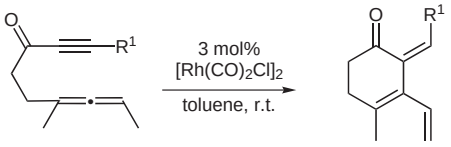
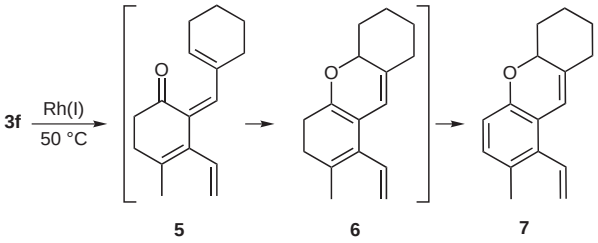
Table 1 Formation of 2-Alkylidene-3-cyclohexenones



3a–k **4a–k**

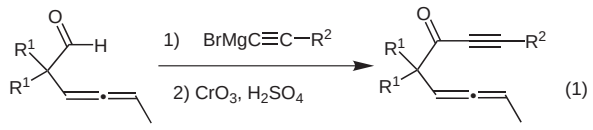
Entry	Reaction	R^1	Time (min)	Yield (%)
1	**3a** → **4a**	Me	90	75
2	**3b** → **4b**	$(CH_2)_3OTBS$	90	80
3	**3c** → **4c**	$(CH_2)_2OTBS$	20	88
4	**3d** → **4d**	$(CH_2)_2OTHP$	15	93
5[a]	**3e** → **4e**	TMS	5	95
6[b]	**3f** → **4f**	cyclohexenyl	–	–
7[c]	**3g** → **4g**	Ph	5	81
8[c]	**3h** → **4h**	4-MeOAr	5	77
9[c]	**3i** → **4i**	4-CF_3Ar	5	79
10[d]	**3j** → **4j**	OEt	45	–
11[e]	**3k** → **4k**	H	–	–

[a] Reaction performed at 0 °C.
[b] See the discussion below and Scheme 2.
[c] Reaction performed at 50 °C using 8 mol% catalyst.
[d] Obtained an unstable compound that could not be characterized.
[e] Immediate decomposition of starting material.



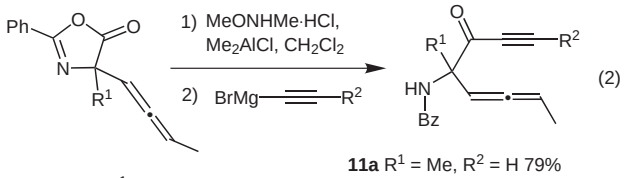
Scheme 2 A Rh(I)-catalyzed cascade reaction

Encouraged by the results in Table 1, the formation of 2-alkylidene-3-vinylcyclopentenones was investigated. Construction of the corresponding allene-ynones was carried out by the addition of alkynyl magnesium bromides to allenic aldehydes **8a–c** and subsequent oxidation of the alcohols to afford **9a–g** (equation 1, Scheme 3).[13] Alternatively, allenic oxazolidiones[14] **10a–c** were reacted with methylmethoxylamine to afford the allenic Weinreb amide intermediate, and without purification, the amide was then transformed into the allene-ynones **11a–f** by addition of the corresponding Grignard reagents[15] to afford cyclization precursors possessing an unsymmetrically substituted quaternary carbon and a benzamide group (equation 2, Scheme 3).[16] For each of these substrates, the quaternary carbon between the carbonyl and allene prevented isomerization of the 1,2-diene of the allene to a 1,3-diene during the preparation of these substrates.



8a R^1 = Me
8b R^1 = Et
8c R^1–R^1 = $(CH_2)_5$

9a R^1 = Me, R^2 = *n*-Bu 55%[a]
9b R^1 = Me, R^2 = Me 44%
9c R^1 = Me, R^2 = Ph 54%
9d R^1 = Me, R^2 = 2-Py 42%[b]
9e R^1 = Et, R^2 = Me 79%
9f R^1 = Et, R^2 = H 82%
9g R^1–R^1 = $(CH_2)_5$, R^2 = Me 65%



10a R^1 = Me
10b R^1 = Bn
10c R^1 = *i*-Bu

11a R^1 = Me, R^2 = H 79%
11b R^1 = Me, R^2 = Me 97%
11c R^1 = Me, R^2 = Ph 80%
11d R^1 = Me, R^2 = CH_2OMe 80%
11e R^1 = Bn, R^2 = Ph 23%
11f R^1 = *i*-Bu, R^2 = Me 76%

[a] 1-Hexynyl lithium was used instead of the corresponding magnesium bromide salt
[b] MnO_2, CH_2Cl_2 used instead of CrO_3, H_2SO_4

Scheme 3 Synthesis of allenic alkynones **9a–g** and **11a–f**

The $[Rh(CO)_2Cl]_2$-catalyzed cycloisomerization reactions of **9a–g** and **11a–f** proceed smoothly at room temperature to afford the cyclopentenones **12a–m** (Table 2). These trienones were found to be stable on the bench top for several months.[17] Interestingly, the carbocyclization reaction was tolerant of coordinating heteroatoms, evidenced by obtaining **12d** in 50% yield (entry 4, Table 2); and the methoxymethyl ether **12k** in 53% yield (entry 11, Table 2). Terminal alkynes are compatible with the reaction conditions evidenced by the isolation of **12f** and **12i** in 61% and 83% yield, respectively.[18] A control experiment was performed where allene-ynones **11b** and **11c** were simply heated (no catalyst) in toluene at 100 °C for one hour; trienones **12b** and **12c** were afforded in 63% and 68% yield, respectively. However, the products were contaminated with trace quantities of inseparable impurities. Heating **9a** in toluene at 100 °C afforded an unidentified isomerization product in 71% yield. Based upon these results, the Rh(I)-catalyzed conditions were deemed more reliable.

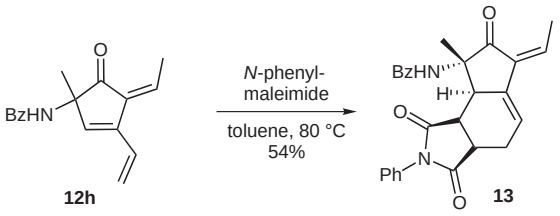
The highly functionalized cyclopentenones **12h–m** serve as ideal candidates for accessing compounds possessing other interesting arrays of functionality. For example, reaction of **12h** with *N*-phenyl maleimide in toluene at 80 °C affords the Diels–Alder adduct **13** in 54% yield as a single diastereomer (Scheme 4).[19,20] The ketone functionality prevents the newly formed 1,3-diene in **13** from

Table 2 Formation of 2-Alkylidene-3-cyclopentenones

9 or **11** **12**

Entry[a]	Reaction	R^1	R^2	R^3	Yield (%)
1	**9a** → **12a**	Me	*n*-Bu	Me	73
2	**9b** → **12b**	Me	Me	Me	66
3	**9c** → **12c**	Me	Ph	Me	80
4	**9d** → **12d**	Me	2-pyridyl	Me	50
5	**9e** → **12e**	Et	Me	Et	94[b]
6	**9f** → **12f**	Et	H	Et	61
7	**9g** → **12g**	$(CH_2)_5$	Me		65
8	**11a** → **12h**	Me	Me	BzNH	78[b]
9	**11b** → **12i**	Me	H	BzNH	83
10	**11c** → **12j**	Me	Ph	BzNH	68[b]
11	**11d** → **12k**	Me	CH_2OMe	BzNH	53
12	**11e** → **12l**	Bn	Me	BzNH	79
13	**11f** → **12m**	*i*-Bu	Me	BzNH	88

[a] Reaction time 1–2 h.
[b] Designates reactions that were scaled up to multigram scale with no loss of yield.



Scheme 4 Selective Diels–Alder reaction of trienone **12h**

undergoing a second Diels–Alder reaction with the same dienophile.

Furthermore, a selective cyclopropanation reaction of the vinyl group of trienone **12e** occurs when reacted with diethyl 4-diazo-2-pentenedioate and rhodium acetate (Scheme 5).[21] The corresponding *cis*-divinylcyclopropane[22] undergoes a Cope rearrangement to provide **14** which is subsequently reacted with maleic anhydride in toluene at 80 °C to afford the Diels–Alder adduct **15** as a single diastereomer in 60% yield. The stereochemistry of **15** has been assigned by X-ray crystallographic analysis of a related compound and this information will be published in its entirety in the future.

In summary, a Rh(I)-catalyzed allenic cycloisomerization reaction of alkynones affords 2-alkylidene-3-vinyl-3-cyclopentenones and 2-alkylidene-3-vinyl-3-cyclohexenones. This scope and limitations study demonstrate that the reactions conditions are compatible with amides, ethers, and terminal alkynes; and that the highly unsaturated products are stable and undergo selective cycloaddition and cycloisomerization reactions. Further research on these functionally rich trienones will be reported in due course.

Acknowledgment

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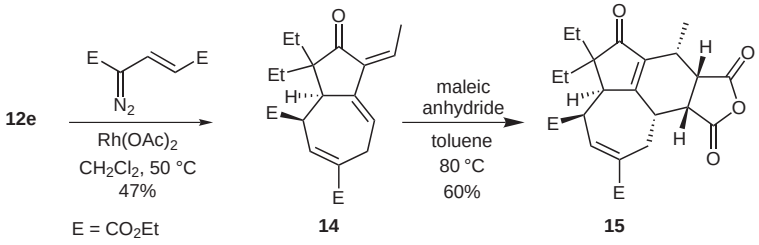

Scheme 5 Selective cyclopropanation reaction of the trienone **12e**

(6) Metal-catalyzed carbocyclization reactions of enynones have been previously reported, for leading references, see: Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025.

(7) **General Procedure for the Preparation of Allene-ynones 3**

(a) In a manner entirely analogous to that reported by Trost:[7b] A solution of the alkyne (1.08 mmol) in THF (2.4 mL) was cooled to –78 °C and a solution of *n*-BuLi (0.6 mL of a 1.6 M solution in hexanes, 0.96 mmol) was added rapidly via syringe. After 5 min $BF_3{\cdot}OEt_2$ (128 μL, 1.02 mmol) was added. The resultant solution/mixture was stirred for 15 min then a solution of the allenyl amide **1** (100 mg, 0.60 mmol) in THF (3 mL) was added via cannula. After 1.5 h, more $BF_3{\cdot}OEt_2$ (128 μL, 1.02 mmol) and AcOH (58 μL, 1.02 mmol) were added. The reaction was allowed to warm to –20 °C and quenched with sat. aq NH_4Cl (2.1 mL). After warming to r.t., the reaction mixture was diluted with Et_2O and H_2O. The layers were separated and the aqueous layer was extracted with Et_2O (3×). The combined organic layers were washed with H_2O (2×) and dried over $MgSO_4$. This mixture was filtered through a pad of silica gel and concentrated under vacuum. The crude residue was purified by column chromatography on silica gel to give the product as a faint yellow to clear oil.

Data for **3e**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.06–4.98 (m, 1 H), 2.62 (dd, *J* = 6.7, 7.5 Hz, 2 H), 2.28–2.21 (m, 2 H), 1.66 (d, *J* = 2.7 Hz, 3 H), 1.57 (d, *J* = 7.0 Hz, 3 H), 0.21 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.6, 187.1, 101.9, 97.5, 97.1, 87.0, 43.0, 27.8, 19.3, 14.6, –0.9. IR (thin film): ν = 2962, 2900, 2151, 1967, 1679, 1252, 847 cm^{-1}. MS: *m/z* (%) = 220 (16) [M$^+$], 219 (6), 205 (8), 178 (12), 163 (29), 73 (100), 61 (100). HRMS (EI): *m/z* calcd for $C_{13}H_{20}OSi$ [M$^+$]: 220.1283; found: 220.1289.

Data for **3h**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.9 Hz, 2 H), 6.90 (d, *J* = 8.9 Hz, 2 H), 5.11–5.04 (m, 1 H), 3.85 (s, 3 H) 2.76 (dd, *J* = 6.8, 8.1 Hz, 2 H), 2.39–2.31 (m, 2 H), 1.73 (d, *J* = 2.8 Hz, 3 H), 1.62 (d, *J* = 6.9 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.7, 187.2, 161.5, 134.9, 114.2, 111.8, 97.6, 91.4, 87.6, 86.8, 55.2, 43.2, 28.1, 19.3, 14.6. IR (thin film): ν = 2979, 2899, 2849, 2553, 2197, 1965, 1665, 1254, 1092 cm^{-1}. MS: *m/z* (%) = 254 (27) [M$^+$], 253 (16), 239 (40), 237 (53), 211 (54), 197 (54), 165 (47), 159 (100), 144 (44), 116 (47), 77 (47). HRMS (EI): *m/z* calcd for $C_{17}H_{18}O_2$ [M$^+$]: 254.1307; found: 254.1282. (b) Trost, B. M.; Li, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6625. (c) Walton, D. R. M.; Waugh, F. *J. Organomet. Chem.* **1972**, *37*, 45.

(8) We have seen similarly facile reactions when the cycloisomerization substrate possesses an aminoester tether. See ref. 2c.

(9) Chelation of the tethered oxygen of **3c** or **3d** to the Rh(I) catalyst may be responsible for the rate enhancement by facilitating the oxidative addition step of the cycloisomerization process. Trost observed a similar effect in a palladium-catalyzed enyne cycloisomerization reaction, see: Trost, B. M.; Romero, D. L.; Rise, F. *J. Am. Chem. Soc.* **1994**, *116*, 4268.

(10) Terminal ynones have been reported to undergo decomposition in palladium-catalyzed cycloisomerization reactions, see: Trost, B. M.; Phan, L. T. *Tetrahedron Lett.* **1993**, *34*, 4735.

(11) **General Procedure for the Preparation of Trienone 4**

A 2-dram vial, equipped with a stir bar was charged with allene-ynone **3** (0.1 mmol) and toluene (0.33 mL), sealed with a septum, and degassed (degassing was accomplished by bubbling argon through the stirred solution for 20 min). Rhodium biscarbonyl chloride dimer {$[Rh(CO)_2Cl]_2$, 3 mol%} was then added and the reaction progress was monitored by TLC. Upon completion of the reaction, the mixture was diluted with a 10% EtOAc–hexanes solution and filtered through a pad of silica gel, further eluting with 10% EtOAc–hexanes solution. The resultant yellow solution was concentrated under vacuum to yield the products as yellow oils without further purification.

Data for **4e**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.27 (dd, *J* = 11.3, 17.7 Hz, 1 H), 6.01 (s, 1 H), 5.45 (dd, *J* = 2.1, 11.3 Hz, 1 H), 5.15 (dd, *J* = 2.1, 17.7 Hz, 1 H), 2.61–2.51 (m, 4 H), 1.95 (s, 3 H), 0.13 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.6, 145.6, 139.1, 135.3, 134.0, 133.7, 119.8, 37.8, 30.8, 21.8, –0.2. IR (thin film): ν = 2945, 1701, 1542, 1245, 856 cm^{-1}. MS: *m/z* (%) = 220 (1) [M$^+$], 205 (40), 75 (13). HRMS (EI): *m/z* calcd for $C_{13}H_{20}OSi$ [M$^+$]: 220.1283; found: 220.1281.

Data for **4h**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.7 Hz, 2 H), 6.83 (d, *J* = 8.8 Hz, 2 H), 6.61(s, 1 H), 6.34 (dd, *J* = 11.2, 17.7, 1 H), 5.49 (dd, *J* = 2.1, 11.2 Hz, 1 H), 5.27 (dd, *J* = 2.1, 17.8 Hz, 1 H), 3.81 (s, 3 H), 2.71–2.59 (m, 4 H), 1.94 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.6, 159.5, 133.7, 133.6, 132.7, 132.5, 131.3, 128.4, 119.7, 113.3, 55.1, 39.6, 32.3, 21.1. IR (thin film): ν = 3081, 2908, 2836, 1698, 1603, 1509, 1254, 1032, 829 cm^{-1}. MS: *m/z* (%) = 277 (32) [M + ^{23}Na$^+$], 255 (17). ES-HRMS: *m/z* calcd for $C_{17}H_{18}O_2$ [M + ^{23}Na$^+$]: 277.1204; found: 277.1215.

(12) **Preparation of 6,7,8,10a-Tetrahydro-2-methyl-1-vinyl-5*H*-xanthene (7)**

Following the general procedure for the preparation of trienone **4**: toluene (2.8 mL), allene-ynone **3f** (32 mg, 0.140 mmol), $[Rh(CO_2)Cl]_2$ (1.6 mg, 0.004 mmol, 5 mol%), purification by silica gel column chromatography eluting with 2% EtOAc–hexanes (column pretreated with a 1% solution of Et_3N in hexanes) to afford **7** as a green solid (9 mg, 29%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.85 (d, *J* = 8.1 Hz, 1 H), 6.63 (dd, *J* = 11.4, 17.8 Hz, 1 H), 6.56 (d, *J* = 8.1 Hz, 1 H), 6.39 (s, 1 H), 5.58 (dd, *J* = 2.0, 11.4 Hz, 1 H), 5.23 (dd, *J* = 2.0, 17.8 Hz, 1 H), 4.86 (dd, *J* = 5.7, 10.9 Hz, 1 H), 2.60–1.19 (m, 8 H), 2.18 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.3, 137.5, 134.4, 133.7, 128.8, 127.8, 120.4, 119.1, 114.9, 113.5, 76.1, 34.7, 33.2, 26.5, 24.2, 19.8. IR (thin film): ν = 3078, 3058, 2932, 2857, 1582, 1468, 1235, 1041, 811 cm^{-1}. MS: *m/z* (%) = 226 (100) [M$^+$], 225 (90), 223 (82), 198 (61), 197 (60), 145 (43), 128 (44), 115 (60). HRMS (EI): *m/z* calcd for $C_{16}H_{18}O$ [M$^+$]: 226.1358; found: 226.1353.

(13) **Preparation of Allenyl Alkynone 9e**

A flame-dried 100 mL round-bottomed flask was charged with 2,2-diethylhexa-3,4-dienal (**8b**, 1.52 g, 10.0 mmol) and THF (40 mL). After cooling to 0 °C, 1-propynylmagnesium bromide (24 mL, 0.5 M in THF, 12 mmol) was slowly added via syringe and the mixture was stirred at 0 °C for 2 h. The reaction mixture was quenched with sat. NH_4Cl (20 mL). The mixture was partitioned between Et_2O (30 mL) and H_2O (30 mL). The layers were separated and the aqueous phase was extracted with Et_2O (2 × 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to afford a light yellow oil (1.65 g). A portion of the oil (452 mg) was transferred into a 50 mL round-bottomed flask fitted with a Teflon-coated stirring bar and dissolved in acetone (20 mL). After cooling to 0 °C, freshly prepared Jones reagent was added dropwise via a pipette until an orange color persisted. The reaction mixture was then poured into Et_2O (20 mL) and H_2O (10 mL). The layers were separated and the aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$,

and concentrated under reduced pressure. Purification of the yellow oil by flash chromatography (10% EtOAc–hexanes) afforded the title compound **9e** (425 mg, 79%) as a light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.28–5.19 (m, 2 H), 2.04 (s, 3 H), 1.78–1.70 (m, 4 H),1.68 (dd, *J* = 6.6, 3.6 Hz, 3 H), 0.83 (t, *J* = 7.4 Hz, 3 H), 0.82 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.1, 191.4, 92.4, 90.6, 88.2, 78.8, 56.5, 27.5, 14.1, 8.5, 4.1. IR (thin film): ν = 2968, 2938, 2218, 1963, 1666 cm^{-1}. MS: *m/z* (%) = 190 (15) [M$^+$], 175 (28), 161 (95), 147 (65), 81 (100). HRMS: *m/z* calcd for $C_{13}H_{18}O$ [M$^+$]: 190.1357; found: 190.1358.

(14) (a) Castelhano, A. L.; Pliura, D. H.; Taylor, G. J.; Hsieh, K. C.; Krantz, A. *J. Am. Chem. Soc.* **1984**, *106*, 2734.
(b) Castelhano, A. L.; Horne, S.; Taylor, G. J.; Billedeaux, R.; Krantz, A. *Tetrahedron* **1988**, *44*, 5451.

(15) Tice, C. M.; Hormann, R. E.; Thompson, C. S.; Friz, J. L.; Cavanaugh, C. K.; Michelotti, E. L.; Garcia, J.; Nicolas, E.; Albericio, F. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 475.

(16) **Preparation of Allenyl Alkynone 11b**
A flame-dried 25 mL round-bottomed flask was charged with *N*-[2-(*N*-methoxy-*N*-methylcarbamoyl)hexa-3,4-dien-2-yl]benzamide (268 mg, 0.93 mmol) and THF (15 mL). After cooling to 0 °C, 1-propynylmagnesium bromide (4.4 mL, 0.5 M in THF, 2.2 mmol) was slowly added via syringe and the mixture was stirred at 0 °C for 3 h. The reaction mixture was quenched with sat. NH_4Cl (10 mL). The mixture was partitioned between Et_2O (15 mL) and H_2O (15 mL). The layers were separated and the aqueous phase was extracted with Et_2O (2 × 15 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to afford a white solid. The solid was purified via silica gel column chromatography (50% EtOAc–hexanes) to give the title compound **11b** (242 mg, 97%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81–7.78 (m, 2 H), 7.54–7.41 (m, 3 H), 7.21 (br s, 0.3 H),* 7.11 (br s, 0.7 H), 5.24 (p, *J* = 7.1 Hz, 1 H), 5.40–5.32 (m, 1 H), 2.02 (s, 1 H),* 1.99 (s, 2 H), 1.81 (s, 1 H),* 1.78 (s, 2 H), 1.74 (dd, *J* = 7.0, 3.2 Hz, 2 H), 1.72 (dd, *J* = 7.0, 3.2 Hz, 1 H)*. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.4, 204.2,* 185.9, 166.6, 165.3,* 134.7, 134.6,* 131.8, 131.7,* 128.8, 127.1, 93.8,* 93.6, 93.5,* 93.0, 91.9, 91.7,* 77.4,* 77.3, 63.7,* 63.5, 21.9, 14.1,* 14.0, 4.50,* 4.42. IR (thin film): ν = 3280, 2211, 1966, 1688, 1627 cm^{-1}. MS: *m/z* (%) = 267 (10) [M$^+$], 253 (28), 105 (100), 77 (65). HRMS: *m/z* calcd for $C_{17}H_{17}NO_2$ [M$^+$]: 267.1259; found: 267.1263. *Denotes the minor diastereomer.

(17) With the exception of **12b**, which had to be stored in benzene at –20 °C, the only literature report on the formation of five-membered cross-conjugated triene stressed product instability. For details, see: Yamazaki, T.; Urabe, H.; Sato, F. *Tetrahedron Lett.* **1998**, *39*, 7333.

(18) **General Procedure for the Preparation of Trienones 12**
A flame-dried test tube equipped with a Teflon-coated stir bar was charged with allene-ynone **9** or **11** (1.0 mmol, 1 equiv) and toluene (10 mL) under an atmosphere of N_2. After adding $[Rh(CO)_2Cl]_2$ (0.05 mmol, 0.05 equiv), the reaction mixture was stirred at r.t. until complete consumption of starting material (as observed by TLC). The solution was concentrated under reduced pressure and the residue was purified via silica gel column chromatography (10% EtOAc–hexanes) to afford trienone **12**.
Data for **12a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.44 (dd, *J* = 17.6, 11.1 Hz, 1 H), 6.16 (t, *J* = 7.4 Hz, 1 H), 6.12 (s, 1 H), 5.62 (dd, *J* = 17.6, 1.6 Hz, 1 H), 5.28 (dd, *J* = 11.1 1.6 Hz, 1 H), 2.78 (q, *J* = 7.5 Hz, 2 H), 1.45–1.36 (m, 4 H), 1.12 (s, 6 H), 0.92 (t, *J* = 6.9 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.8, 139.5, 137.5, 136.2, 134.9, 129.8, 116.8, 48.3, 31.7, 27.2, 23.6, 22.5, 13.9. IR (thin film): ν = 2959, 2932, 2871, 1708 cm^{-1}. MS: *m/z* (%) = 204 (43) [M$^+$], 189 (15), 175 (25), 119 (88), 91 (100). HRMS: *m/z* calcd for $C_{14}H_{20}O$ [M$^+$]: 204.1514; found: 204.1514.
Data for **12c**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94 (dd, *J* = 7.8, 2.1 Hz, 2 H), 7.43–7.32 (m, 3 H), 6.85 (s, 1 H), 6.56 (ddd, *J* = 17.4, 11.1, 1.2 Hz, 1 H), 6.29 (s, 1 H), 5.74 (dd, *J* = 17.4, 1.5 Hz, 1 H), 5.38 (dd, *J* = 11.1, 1.5 Hz, 1 H), 1.20 (s, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.6, 141.7, 137.8, 135.2, 134.8, 133.0, 131.1, 130.5, 130.0, 129.6, 128.2, 117.9, 48.6, 24.0. IR (thin film): ν = 2942, 1708 cm^{-1}. MS: *m/z* (%) = 224 (40) [M$^+$], 196 (50), 181 (65), 129 (100). HRMS (EI): *m/z* calcd for $C_{16}H_{16}O$ [M$^+$]: 224.1201; found: 224.1198.
Data for **12e**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.44 (ddd, *J* = 17.6, 11.2, 0.9 Hz, 1 H), 6.19 (dq, *J* = 7.6, 0.7 Hz, 1 H), 6.04 (s, 1 H), 5.63 (dd, *J* = 17.6, 1.6 Hz, 1 H), 5.27 (dd, *J* = 11.2, 1.6 Hz, 1 H), 2.25 (dd, *J* = 7.6, 0.7 Hz, 3 H), 1.66 (dq, *J* = 13.6, 7.5 Hz, 2 H), 1.50 (dq, *J* = 13.6, 7.5 Hz, 2 H), 0.74 (t, *J* = 7.5 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 212.1, 142.4, 137.9, 133.2, 130.5, 129.9, 116.7, 57.3, 29.6, 14.1, 9.3. IR (thin film): ν = 2963, 2929, 1720 cm^{-1}. MS: *m/z* (%) = 190 (54) [M$^+$], 161 (80), 133 (86), 84 (100). HRMS (EI): *m/z* calcd for $C_{13}H_{18}O$ [M$^+$]: 190.1357; found: 190.1355.

(19) The stereochemistry has been assigned based upon X-ray crystal data of a similar compound. This information will be published in the near future.

(20) **Preparation of *N*-{(1*Z*,3a*S*,8*S*,8a*R*,8b*R*)-6-Ethylidene-1,2,3,3a,4,6,7,8,8a,8b-decahydro-8-methyl-1,3,7-trioxo-2-phenylcyclopenta[*e*]isoindol-8-yl}benzamide (13)**
A flame-dried test tube equipped with a Teflon-coated stirring bar was charged with *N*-[(13*Z*)-4-ethylidene-1-methyl-5-oxo-3-vinylcyclopent-2-enyl]benzamide (**12h**, 100 mg, 0.37 mmol) and 1-phenyl-1*H*-pyrrole-2,5-dione (68 mg, 0.39 mmol). After adding toluene (4 mL), the test tube was placed into a preheated 80 °C oil bath until complete consumption of starting materials (as observed by TLC). The solution was directly purified via silica gel column chromatography (50% EtOAc–hexanes) to afford the title compound **13** (87.4 mg, 54%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89–7.85 (m, 2 H), 7.54–7.30 (m, 7 H), 7.06–7.03 (m, 2 H), 6.70 (q, *J* = 7.6 Hz, 1 H), 6.19–6.11 (m, 1 H), 3.58 (dd, *J* = 8.3, 4.3 Hz, 1 H), 3.40 (t, *J* = 8.3 Hz, 1 H), 3.26–3.22 (m, 1 H), 2.92 (dd, *J* = 7.5 and 1.0 Hz, 1 H), 2.57–2.47 (m, 1 H), 2.30 (d, *J* = 7.6 Hz, 3 H), 1.74 (s, 3 H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 204.1, 178.7, 177.5, 167.3, 140.5, 137.1, 135.1, 132.3, 131.9, 131.1, 129.3, 128.9, 128.6, 127.4, 126.9, 116.8, 63.3, 46.4, 43.6, 41.7, 27.0, 25.9, 15.1. IR (thin film): ν = 3425, 2975, 1773, 1708, 1654, 1522 cm^{-1}. MS: *m/z* (%) = 441 (100) [M$^+$ + 1], 308 (38). HRMS (EI): *m/z* calcd for $C_{27}H_{25}N_2O_4$ [M$^+$]: 441.1814; found: 441.1812.

(21) Davies, H. M. L.; Walji, A. M. *Rhodium(II)-Stabilized Carbenoids Containing Both Donor and Acceptor Substituents, In Modern Rhodium Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, **2005**, 301.

(22) **Preparation of Adduct 15**
To a refluxing solution of (5*Z*)-2,2-diethyl-5-ethylidene-4-vinylcyclopent-3-enone (**12e**, 28 mg, 0.15 mmol) and $Rh(OAc)_2$ (3.3 mg, 0.0075 mmol) in CH_2Cl_2 (1.5 mL) was added a CH_2Cl_2 (1 mL) solution of diethyl 4-diazo-2-pentenedioate (48 mg, 0.23 mmol) over 10 min under argon. After 30 min, TLC showed complete consumption of **12e**. The solvent was removed and the crude mixture was purified via silica gel flash chromatography (10% EtOAc–hexanes) to give **14** (26 mg, 47%) together with the *trans*-

divinylcyclopropane (*cis*/*trans* = 7:1). A test tube was charged with **14** (19 mg, 0.051 mmol) and maleic anhydride (7.5 mg, 0.077 mmol) and purged with N_2 for 5 min. Toluene (0.8 mL) was added and the test tube was placed into a preheated oil bath (80 °C). After 3 h, the reaction mixture was cooled to r.t. and directly applied to silica gel flash chromatography (35% EtOAc–hexanes) to give **15** (14 mg, 60%) as a single diastereomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.04 (dd, *J* = 7.2, 2.1 Hz, 1 H), 4.30–4.22 (m, 2 H), 4.12–4.00 (m, 2 H), 3.81 (dd, *J* = 7.1, 2.8 Hz, 1 H), 3.60–3.57 (m, 1 H), 3.51 (q, *J* = 7.3 Hz, 1 H), 3.29–3.25 (m, 2 H), 3.12 (t, *J* = 2.7 Hz, 1 H), 2.94–2.88 (m, 1 H), 1.69–1.62 (m, 2 H), 1.54–1.52 (m, 1 H), 1.48 (q, *J* = 7.4 Hz, 4 H), 1.39–1.27 (m, 2 H), 1.34 (t, *J* = 7.1 Hz, 3 H), 1.01 (t, *J* = 7.4 Hz, 3 H), 0.91–0.84 (m, 2 H), 0.73 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.1, 171.0, 170.8, 170.6, 170.2, 167.4, 137.5, 136.6, 134.9, 61.9, 53.3, 49.8, 46.9, 46.3, 45.2, 36.7, 31.8, 29.6, 27.7, 27.4, 22.9, 21.8, 14.7, 14.5, 14.1, 8.8, 8.6. IR (thin film): ν = 2969, 2937, 1781, 1699, 1461 cm^{-1}. MS: *m/z* (%) = 472 (100) [M$^+$], 426 (71), 398 (84). HRMS (EI): *m/z* calcd for $C_{26}H_{32}O_8$ [M$^+$]: 472.2097; found: 472.2101.

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