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Rh(I)-Catalyzed Cyclocarbonylation of Allenol Esters To Prepare Acetoxy 4-Alkylidenecyclopent-3-en-2-ones

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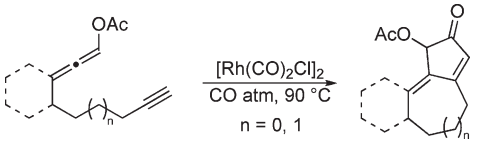

A Rh(I)-catalyzed cyclocarbonylation reaction of allenol esters has been examined and its synthetic viability established for the conversion of trisubstituted allenes to bicyclo[4.3.0] and -[5.3.0] skeletons possessing an α-acetoxy cyclopentadienone. Tetrasubstituted allenol acetates gave elimination products, providing examples of a cyclocarbonylation reaction between an alkyne and a latent cumulene or cumulene equivalent. Cleavage of the acetate affords a free hydroxyl group illustrating the utility of this method for accessing α-hydroxy carbonyls from allenol esters.

Introduction

α-Hydroxy carbonyls are important building blocks in organic synthesis and are present in a number of biologically active molecules.[1] A variety of methods exist for forming α-hydroxyl carbonyls, the most commonly used protocol being the oxidation of enol ethers.[1c] In view of incompatibilities of some functional groups to these oxidation conditions,[1b] the regioselectivity requirements for the enolization step,[2] and redox economy considerations,[3] synthetic alternatives to this late stage enolization/oxidation strategy would be useful.

The Pauson−Khand reaction provides a powerful method for the preparation of highly functionalized cyclopentenone-containing compounds.[4] However, missing from the cyclocarbonylation reaction arsenal is an efficient way of accessing an α-hydroxycarbonyl moiety via an enol ether or vinyl ester precursor. Shore demonstrated that alkoxycyclopentenones could be prepared from enol ether precursors[5] using a Pauson−Khand reaction, and subsequently a number of groups have rendered this reaction asymmetric.[6] However, relatively harsh conditions are required for the conversion of the alkoxycyclopentenone to a hydroxycyclopentenone, thus the alkoxy group serves as a control element in the reaction and then is typically removed.[6] The $Co_2(CO)_8$-mediated Pauson−Khand reaction of vinyl esters to form an α-acetoxy- or α-benzyloxycyclopentenones, results in concurrent loss of the ester moiety through a proposed single electron reduction.[7]

The Rh(I)-catalyzed cyclocarbonylation reaction[8] of allene-ynes is an efficient method for synthesizing a variety

(1) For selected examples, see: (a) Ball, M.; Andrews, S. P.; Wierschem, F.; Cleator, E.; Smith, M. D.; Ley, S. V. *Org. Lett.* **2007**, *9*, 663–666. (b) Ley, S. V.; Antonello, A.; Balskus, E. P.; Booth, D. T.; Christensen, S. B.; Cleator, E.; Gold, H.; Högenaur, K.; Hünger, U.; Myers, R. M.; Oliver, S. F.; Simic, O.; Smith, M. S.; Søhoel, H.; Woolford, J. A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12073–12078. (c) Chen, B.-C.; Zhou, P.; Davies, F. A.; Ciganek, E. *Org. React.* **2003**, *62*, 1 and references cited therein. (d) Tang, Y.-Q.; Sattler, I.; Thiericke, R.; Grabley, S.; Feng, X.-Z. *Eur. J. Org. Chem.* **2000**, 2401–2406.

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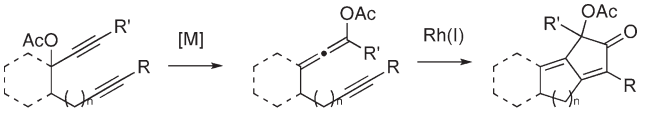
of alkylidenecyclopentenones including bicyclo[5.3.0]undecadienones, a long-sought-after ring system previously inaccessible to cyclocarbonylation methodologies.[9] It was hypothesized that a Rh(I)-catalyzed cyclocarbonylation reaction of allenol acetates affording α-acetoxy cyclopentadienones may be possible due to the mildness of the reaction conditions and the unlikely prospect of the rhodium(I) catalyst participating in a single electron transfer process under these reaction conditions.[10] Moreover, allenol acetates are well-known and are prepared via a formal [3,3]-sigmatropic rearrangement of a propargyl acetate using a variety of transition-metal catalysts such as Ag, Au, Cu, Pt, and Rh.[11] Thus, readily available allenol acetates afford an opportunity to directly access α-acetoxy cyclopentadienones, which in turn can be used as precursors to α-hydroxycarbonyl-containing compounds. Herein, a Rh(I)-catalyzed cyclocarbonylation reaction to form α-acetoxycyclopentadienones is reported.

Results and Discussion

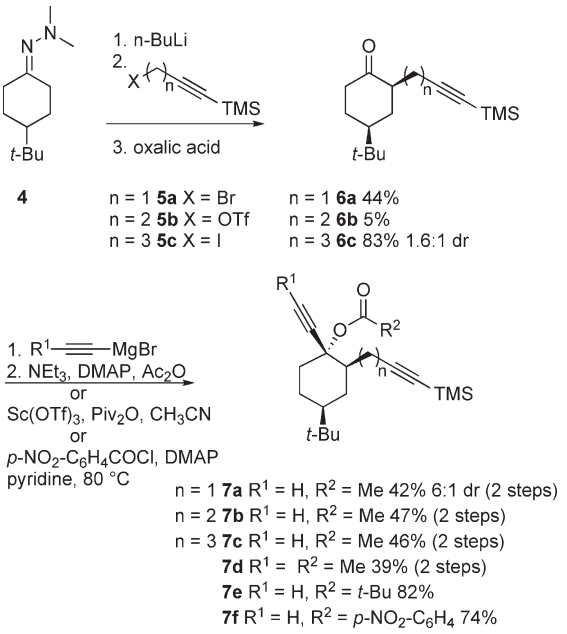
Substrate Design. Once the feasibility of the cyclocarbonylation reaction of allenol acetates to produce α-acetoxy carbonyls has been established, our research objective is to examine several cycloaddition substrates. Guided by a plethora of natural product substructures that would benefit from this reaction: (1) the chain length of the tether between the allene and alkyne will be varied (n = 1−4); (2) substitution on the allene, alkyne and tether altered; and (3) stereochemical consequences of the [3,3]-sigmatropic rearrangement of **1** to give **2** and the cyclocarbonylation reaction to give **3** will be examined (Scheme 1). Furthermore, imbedding the allene into a conformationally anchored cyclohexane ring will serve as an effective method for examining diastereoselectivity issues.

SCHEME 1. Substrate Design



Preparation of Propargyl Acetates. Propargyl acetates were prepared using two general procedures. Preparation of cyclohexane-based substrates began by alkylating the lithium enolate of dimethyl hydrazone **4**, with the corresponding halides or triflates **5a**−**c** (Scheme 2).[12] Acidic hydrolysis with oxalic acid gave ketones **6a** and **6c** (n = 1, 3) in 44% and 83% yield.[13] Ketone **6b** was obtained in only 5% yield, possibly due to a competing E2 elimination of the triflate to form an enyne. The diastereomers of **6a**−**c** were separated via column chromatography, and the major diastereomer was carried forward. Addition of ethynyl or 1-propynylmagnesium bromide to **6a**−**c** gave the corresponding propargyl alcohols in 63−90% yields with diastereoselectivities ranging from 1:1 to 3:1. The major diastereomers were assigned on the basis of the predisposition of small nucleophiles to add axially to substituted cyclohexanones.[14] Separation of the two diastereomers was readily accomplished via column chromatography. The major diastereomers were acetylated using triethylamine, DMAP, and acetic anhydride yielding a single diastereomer of propargyl acetates **7a**−**d** in 39−47% yield from ketones **6a**−**c**. Two substrates were prepared to examine electronic and steric effects of the carboxy group. A bulky pivaloyl group was appended to the corresponding propargyl alcohol from **6c** using trimethylacetic anhydride and catalytic $Sc(OTf)_3$ to give **7e** in 82% yield.[15] An electron-withdrawing *p*-nitrobenzoate was attached to the same propargyl alcohol using 4-nitrobenzoyl chloride and DMAP to give **7f** in 74% yield.[16]

SCHEME 2. Preparation of Propargyl Acetates 7a−f



Linear propargyl acetates were prepared using two different methods (Scheme 3). Propargyl acetates **9a**−**d** (n = 1, 2) were prepared by addition of ethynylmagnesium bromide or 1-propynylmagnesium bromide to aldehyde **8a** or ketones **8b**,**c** followed by in situ acetylation with acetyl chloride furnishing the desired products in 55−83% yields.[17] For

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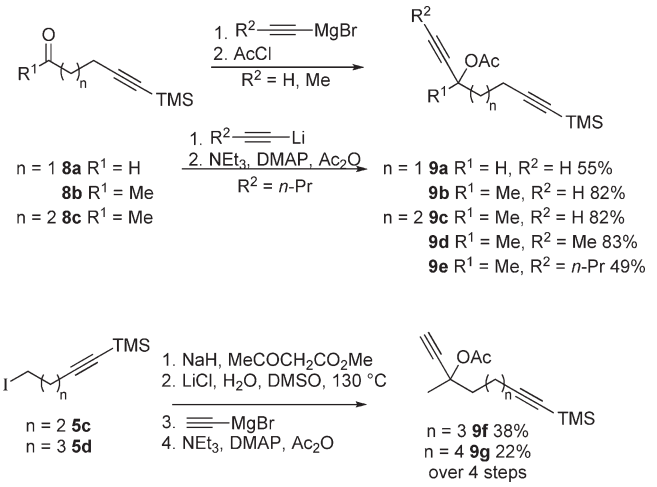
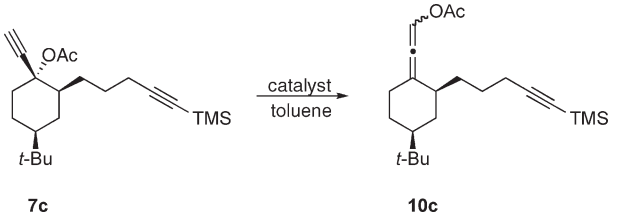
SCHEME 3. Preparation of Propargyl Acetates 9a−g



propargyl acetate **9e** (R^2 = *n*-Pr), addition of the lithium acetylide of 1-pentyne to ketone **8c** gave the propargyl alcohol, which was then acetylated using triethylamine, DMAP, and acetic anhydride to obtain propargyl acetate **9e** in 49% yield over two steps. Propargyl acetates **9f**,**g** were prepared by reacting a slight excess of the sodium salt of methyl acetoacetate with iodides **5c** and **5d**.[18] After an aqueous workup, the crude material was subjected to Krapcho decarboxylation by heating the ketoester to 130 °C with lithium chloride in wet DMSO to obtain 8-(trimethylsilyl)-oct-7-yn-2-one or 9-(trimethylsilyl)non-8-yn-2-one.[19] Purification of the ketones proved impractical and as a result the crude material was subjected to alkynylation with ethynylmagnesium bromide. After chromatographic purification, the alcohols were acetylated using triethylamine, DMAP, and acetic anhydride to obtain propargyl acetates **9f** and **9g** in 38 and 22% yields over four steps.

Formation of Allenol Acetates from Propargyl Acetates. Previously reported conditions to form allenol acetates were screened for efficiency and diastereoselectivity. Reacting a single diastereomer of **7c** with $AuCl_3$ at 60 °C (entry 1, Table 1) gave complete conversion to the allene-yne **10c** in 30 min in a 1:1 diastereomeric ratio (dr).[11k] Performing this same reaction at room temperature with $AuCl_3$ gave **10c** as a 1:1 mixture of diastereomers in 30 min (entry 2). Upon lowering the temperature to −30 °C, the reaction took 5 h to go to 55% completion and afforded **10c** in a 1:1 dr (entry 3). Increasing the temperature to 90 °C decreased the reaction time to give full conversion to allenol acetate **10c** in 12 min in a 1:1 dr (entry 4). Two Ag(I) catalysts, $AgBF_4$ and $AgSbF_6$, were examined (entries 5−8) with no significant changes in diastereoselectivity, but significant loss of the TMS group was observed.[11f,i] Using $[Rh(OCOCF_3)_2]_2$ gave only a trace amount of product after 14 h (entry 9).[11j] Using the $PtCl_2$ conditions reported by Malacria,[11h] clean conversion to **10c** was observed with a 1:1 dr (entry 10). Among the conditions examined, $AuCl_3$ afforded the allenol acetates in the highest yield, and shortest reaction times. The reaction temperature of the $AuCl_3$-catalyzed process had no effect on the diastereoselectivity.

TABLE 1. Catalyst Screening for Rearrangement

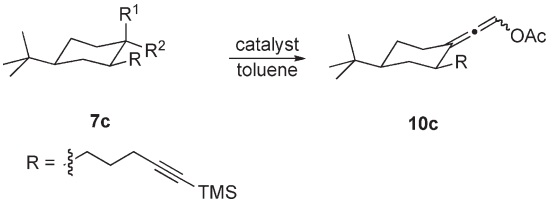


entry	catalyst	mol %	temp (°C)	time (h)	conversion (%) (isolated yield (%))[a]	dr[b]
1	$AuCl_3$	10	60	0.5	100 (71)	1:1
2	$AuCl_3$	10	rt	0.5	100 (74)	1:1
3	$AuCl_3$	20	−30	5	55	1:1
4	$AuCl_3$	10	90	0.2	100 (62)	1:1
5	$AgBF_4$	50	rt	4	84[c]	1:1
6	$AgSbF_6$	10	60	3	83	2:1
7	$AgSbF_6$	10	rt	19	90[c]	1:1
8	$AgSbF_6/PPh_3$	20	rt	17	73	1:1
9	$[Rh(OCOCF_3)_2]_2$	2	60	14	2	1:1
10	$PtCl_2$	10	40	96	100	1:1

[a]Conversion determined by ^{1}H NMR. [b]Diastereomeric ratio determined comparing allenyl protons by ^{1}H NMR. [c]Significant loss of TMS observed by ^{1}H NMR.

Interestingly, reacting both diastereomers of **7c** independently with $AuCl_3$ at room temperature showed little difference in reaction time, yield, or dr (entries 1 and 2, Table 2). However, when using $[Rh(OCOCF_3)_2]_2$ significant differences in reactivity for the two diastereomers were observed (compare entries 3 and 4). With the alkyne cis to the *tert*-butyl group only trace amounts of product were observed after 72 h (entry 3). Conversely, the trans diastereomer showed complete conversion to **10c** in 4 h in 94% yield (entry 4).

TABLE 2. Au(III)- and Rh(II)-Catalyzed Rearrangement



entry	R^1	R^2	catalyst (mol %)	time (h)	yield (%)	dr
1	CCH	OAc	$AuCl_3$ (10)	0.5	74	1:1
2	OAc	CCH	$AuCl_3$ (10)	0.5	81	1:1
3	CCH	OAc	$[Rh(OCOCF_3)_2]_2$ (2)	72	2[a]	1:1
4	OAc	CCH	$[Rh(OCOCF_3)_2]_2$ (2)	4	94	1:1

[a]Approximate conversion by ^{1}H NMR.

Similar results were seen when **11** (7:1 dr) was reacted with $[Rh(OCOCF_3)_2]_2$ (Scheme 4). After 5 h at 60 °C, the minor diastereomer possessing a trans relationship between the alkyne and the *tert*-butyl group was completely converted to allene **12**, whereas no change was observed for the major diastereomer of **11**, based upon ^{1}H NMR. Thus, the

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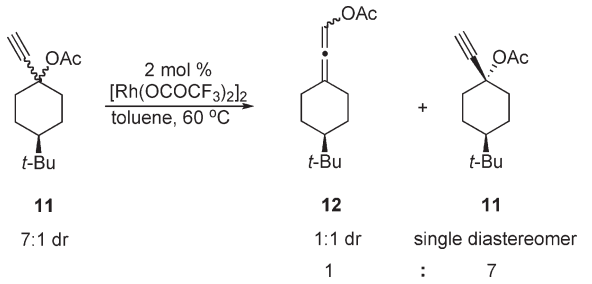
SCHEME 4. [Rh(OCOCF$_3$)$_2$]$_2$-Catalyzed Rearrangement of 11



11 7:1 dr **12** 1:1 dr **11** single diastereomer

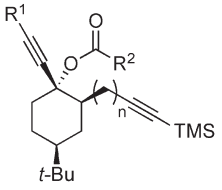
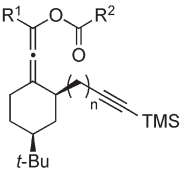
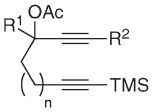
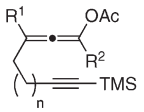
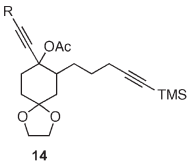
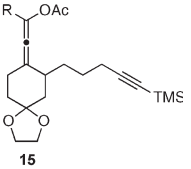
1 : 7

stereochemistry of the propargyl acetate significantly impacts the reaction time and efficiency of the rearrangement when using [Rh(OCOCF$_3$)$_2$]$_2$, with the axially oriented alkyne being the slowest and least efficient. It is postulated that developing 1,3-diaxial interactions of the alkyne coordinated to [Rh(OCOCF$_3$)$_2$]$_2$ slow this reaction.

With optimized rearrangement conditions in hand, propargyl acetates **7a**−**c** were transformed to the trisubstituted allenol acetates **10a**−**c** using $AuCl_3$ in 74−84% yield as 1:1 mixtures of diastereomers (entries 1−3, Table 3). Tetrasubstituted allenol acetate **10d** was isolated in 53% yield due to the incomplete consumption of starting material and the relative instability of **10d** evidenced by decomposition within 4 h of standing in $CDCl_3$ at rt (entry 4). Reacting pivaloate ester **7e** to $AuCl_3$ readily formed allene-yne **10e** in 1 h (91%, 1.4:1 dr, entry 5). Subjecting *p*-nitrobenzoate ester **7f** to $AuCl_3$-catalyzed conditions gave allene-yne **10f** in 87% yield in a 1.4:1 dr (entry 6). Reacting the acyclic secondary propargyl acetate **9a** to the $AuCl_3$-catalyzed reaction conditions yielded only trace amounts of 1,3-disubstituted allene even if the reaction temperature was increased to 60 °C; [Rh(OCOCF$_3$)$_2$]$_2$ and $PtCl_2$ conditions were also tried, but to no avail (entry 7). Tertiary acyclic propargyl acetates **9b** and **9c** (entries 8 and 9) rearranged to give the desired allenol acetates **13b** and **13c** in 46% and 67% yields. Longer reaction times were required when compared to the analogous cyclohexane based propargyl acetates (compare entries 1 and 2 to entries 8 and 9). Substituting an alkyl group for the proton on the terminus of the alkyne had little effect on the yield for the rearrangement of the linear system compared to the analogous cyclohexane-based system (compare entries 9 and 10 to 14 and 15). Propargyl acetates **9f** and **9g** (n = 3, 4) reacted in significantly shorter reaction times and gave **13f** and **13g** in 79 and 77% yields, respectively (entries 12 and 13). The reaction time was dependent upon the tether length; for example, the more removed the appended alkyne from the propargyl acetate, the faster the reaction. It is postulated that increasing the distance of the appended alkyne from the ring minimizes coordination of the gold catalyst allowing for more rapid catalyst turnover. Reacting propargyl acetate **14a** (R = H)[9a] to $AuCl_3$ gave allene-yne **15a** in near quantitative yield as a 1.3:1 dr (entry 14). However, treating propargyl acetate **14b** (R = Me)[9a] to $AuCl_3$ gave allene-yne **15b** in a 43% yield (entry 15). The low yield is attributed to long reaction times because after 19 h propargyl acetate 14b was still observed in the crude ^{1}H NMR along with the appearance of a byproduct containing alkene resonances.

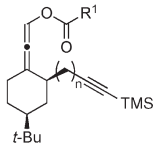
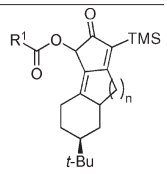
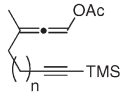
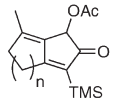
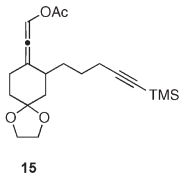
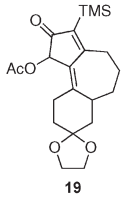
Rh(I)-Catalyzed Cyclocarbonylation Reaction of Allenol Acetates To Form α-Acetoxy Cyclopentadienones. Next, the feasibility, scope, and limitation studies of the Rh(I)-catalyzed cyclocarbonylation reaction of allenol acetates for the formation of bi- and tricyclic ring systems were explored (Table 4). Previously developed and optimized conditions were used to effect the cyclocarbonylation reaction of allenol acetates.[9] Reaction of allenol acetate **10a** to the standard Rh(I) cyclocarbonylation conditions gave only a 19% yield of **16a** after 8 h (entry 1). Allene-ynes **10b** and **10c** underwent cyclocarbonylation to produce **16b** and **16c** in 67% and 76% yields, respectively (entries 2 and 3). Formation of the

TABLE 3. Preparation of Allenol Acetates[a]

entry	propargyl acetate	time (h)	isolated yield (%)	dr[c]
	 **7**		 **10**	
1[b]	**7a** n = 1 R^1 = H, R^2 = Me	3	84	1:1
2[b]	**7b** n = 2 R^1 = H, R^2 = Me	0.5	80	1.1:1
3[b]	**7c** n = 3 R^1 = H, R^2 = Me	0.5	74	1:1
4[b]	**7d** n = 3 R^1 = Me, R^2 = Me	5	53	1.2:1
5	**7e** n = 3 R^1 = H, R^2 = *t*-Bu	1	91	1.4:1
6	**7f** n = 3 R^1 = H, R^2 = *p*-NO_2-C_6H_4	16	87	1.4:1
	 **9**		 **13**	
7	**9a** n = 1, R^1 = H, R^2 = H	20	trace[c]	NA
8	**9b** n = 1, R^1 = Me, R^2 = H	19	46	NA
9	**9c** n = 2, R^1 = Me, R^2 = H	4	67[d]	NA
10	**9d** n = 2, R^1 = R^2 = Me	1.5	64	NA
11	**9e** n = 2, R^1 =Me, R^2 =*n*-Pr	1.5	58	NA
12	**9f** n = 3, R^1 = Me, R^2 = H	0.5	79	NA
13	**9g**, n = 4, R^1 = Me, R^2 = H	0.5	77	NA
	 **14**		 **15**	
14[e]	**14a** R = H	4	quant	1.3:1
15[f]	**14b** R = Me	19	43	1.5:1

[a]Conditions: $AuCl_3$ (10 mol %), toluene, rt. [b]Reacted as a single diastereomer. [c]Observed by ^{1}H NMR. [d]Contaminated with unknown impurity. [e]Reacted as a 4:1 dr. [f]Reacted as a 5:1 dr.

TABLE 4. $[Rh(CO)_2Cl]_2$-Catalyzed Cyclocarbonylation Reactions[a]

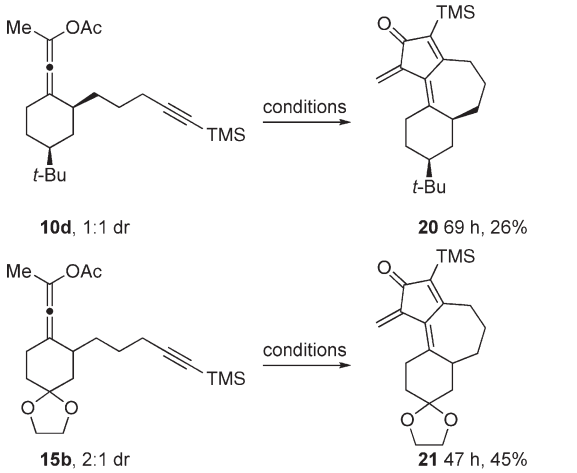
entry	allene-yne	time (h)	yield (%)	dr[b]
	 **10**		 **16**	
1	**10a** n = 1, R^1 = Me 1:1 dr	8	19	1.3:1
2	**10b** n = 2, R^1 = Me 1.1:1 dr	1	67	1:1.2
3	**10c** n = 3, R^1 = Me 1:1 dr	17	76	1.9:1
4	**10e** n = 3, R^1 = *t*-Bu 2:1 dr	18	51	2.3:1
5	**10f** n = 3, R^1 = *p*-NO_2-C_6H_4 1.4:1 dr	18	35	1.8:1
	 **13**		 **17**	
6	**13b** n = 1	22	28	NA
7	**13c** n = 2	2	53	NA
8	**13f** n = 3	46	62	NA
9	**13g** n = 4	120	trace[c]	NA
	 **15**		 **19**	
10	**15a** 1.3:1 dr	19	74	2.3:1

[a]Conditions: $[Rh(CO)_2Cl]_2$ (10 mol %), CO(g) (1 atm), toluene, 90 °C. [b]Diastereomeric ratio determined comparing proton resonances by ^{1}H NMR. [c]Observed by ^{1}H NMR.

[6−7−5] ring system took significantly longer than the analogous [6−6−5] ring system (17 h vs 1 h). Subjecting **10e** to cyclocarbonylation conditions gave a 2.3:1 dr of α-acetoxy 4-alkylidene cyclopentadienone **16e** in 51% yield (entry 4). Cyclocarbonylation of **10f** gave the cyclized product **16f** as a 1.8:1 mixture of diastereomers in 35% yield (entry 5). Thus, it appears that neither steric nor electronic changes in the carboxy group significantly impact the diastereomeric ratio of the products. Reaction of linear allene-yne **13b** (entry 6) gave **17b** in 28% yield along with significant decomposition products, indicating that either the starting material or the bicyclic [5−5] ring systems are unstable to the reaction conditions. Cyclocarbonylation of allene-yne **13c** and **13f** are readily accomplished giving **17c** and **17f** in 53% and 62% yields, respectively (entries 7 and 8). The reaction of **13g** to produce an [8−5] ring system resulted in only trace amounts of the product with the majority of allenol ester rearranging to the conjugated dienol acetate (entry 9).[20] Cyclocarbonylation of allenol-acetate **15a** gave the α-acetoxy 4-alkylidene cyclopentenone **19a** in 19 h and 74% yield.

Cyclocarbonylation reactions of tetrasubstituted allenes **10d** and **15b** afforded a 26% yield of **20** in 69 h and a 45% yield of **21** in 47 h, respectively (Scheme 5). Linear allenol acetate **13d** gave a 49% yield of trienone **22d**, along with a trace amount of the desilylated product observed in the crude ^{1}H NMR. Similarly, allenol acetate **13e** afforded triene **22e** in 42% yield along with desilyated **22e′** in 13% yield. Compounds **20**, **21**, and **22d**,**e** proved relatively unstable with observable decomposition by ^{1}H NMR after 24 h in a freezer. *These are examples of a cyclocarbonylation reaction between an alkyne and a latent cumulene or cumulene equivalent*. Two possible mechanisms for the formation of these compounds have been considered. One involves elimination of the acetoxy group prior to cyclocarbonylation and the other mechanism involves elimination of the acetoxy group after the cyclocarbonylation process. Studies are underway to elucidate the reaction pathway and synthetic utility of this transformation.

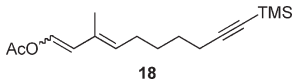
SCHEME 5. $[Rh(CO)_2Cl]_2$-Catalyzed Cyclocarbonylation Reaction of Tetrasubstituted Allenol Esters[a]



[a]Conditions: $[Rh(CO)_2Cl]_2$ (10 mol%), CO(g) (1 atm), toluene, 90 °C.

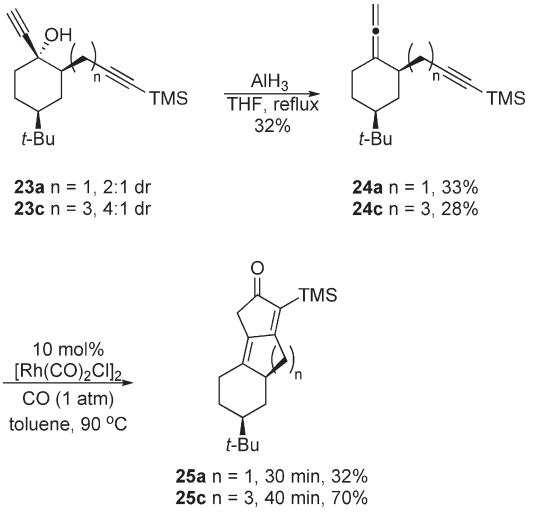
The cyclocarbonylation of allene-ynes **24a** and **24c** gave cycloadducts **25a** and **25c** in 32% and 70% yields (Scheme 6), paralleling the yields obtained for analogous [6−5−5] and [6−7−5] ring systems **16a** and **16c** (Table 4, entries 1 and 3) and suggesting that the acetoxy group has little influence on the yields of the cyclocarbonylation. Conversely, the

(20) Conjugated dienol acetate **18** was observed in an ~1:1 *E*/*Z* ratio:



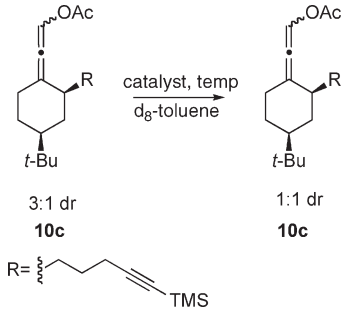
18

SCHEME 6. Preparation and Cyclocarbonylation of Allene-ynes 24a and 24c



reaction times for the cyclocarbonylation of **24a** and **24c** were 30 and 40 min, compared to 8 and 17 h for **16a** and **16c**, showing that the acetoxy group slowed the cyclocarbonylation reaction considerably.

TABLE 5. Isomerization of Allenol Acetate 10c



entry	starting dr (major/minor)	catalyst (mol %)	temp (°C)	time[a]
1	3:1	10	90	40 min[b]
2	1:3	10	90	40 min[b]
3	3:1	10	rt	7 h[b]
4	1:3	10	rt	7 h[b]
5	3:1	0	90	[c]
6	1:3	0	90	[c]

[a]Time indicating a 1:1 dr. [b]Performed under 1 atm of CO. [c]No isomerization observed after 24 h under Ar.

Diastereoselective Considerations. To probe the origin of the slight increase in diastereomeric ratios (1:1 to 2:1) in the transformation of **10c** to **16c**, the cyclocarbonylation of diastereomerically enriched allene-yne **10c** was performed in toluene-d_8 and monitored via ^{1}H NMR (Table 5). Starting with 3:1 dr (or 1:3) of **10c**, rapid isomerization of the allenol acetate was observed giving a 1:1 mixture of allenol acetates in 40 min with no evidence of **16c** (entries 1 and 2). Performing the reaction at room temperature slowed the rate of isomerization but still resulted in a 1:1 dr of **10c** after 7 h with no evidence of **16c** (entries 3 and 4). Heating allene **10c** in the absence of rhodium catalyst for 24 h at 90 °C resulted in no change in dr. Thus, under the Rh(I)-catalyzed cyclocarbonylation reaction conditions, rapid isomerization of the allene of **10c** is occurring. Moreover, subjecting a 5:1 dr of **16c** to the cyclocarbonylation reaction conditions afforded **16c** with no change in the dr after 24 h. Therefore, the diastereoselectivity occurs by a selective transformation of one allenol acetate to the cyclocarbonylation product over the other.

Finally, reacting acetate **17c** with K_2CO_3 in MeOH/H_2O gave alcohol **26** in 59% yield (Scheme 7), thus demonstrating the synthetic utility of the Rh(I)-catalyzed allenic cyclocarbonylation reaction for accessing α-hydroxy containing cyclopentadienones.

SCHEME 7. Deprotection of 17c

Conclusions

We have demonstrated the first Rh(I)-catalyzed cyclocarbonylation reaction for the formation of α-acetoxy 4-alkylidene cyclopentenones from both cyclohexane derived and linear allene-ynes. Cyclohexane and linear allene-yne [6−5] and [7−5] ring systems were prepared in good yields; however, [5−5] ring systems proved less successful. Control experiments confirmed that yields for the cyclocarbonylation reactions for acetoxy-containing allenes parallel that of hydrocarbon-only allenes but that the former reactions are significantly decelerated. Liberation of the acetate to the free alcohol was also readily accomplished yielding an α-hydroxy ketone. Studies are underway to expand the scope of this reaction and to render the cyclocarbonylation reaction stereoselective.

Experimental Section

General Procedure for the $AuCl_3$-Catalyzed Allenol Ester Formation. A flame-dried, 5 mL round-bottomed flask equipped with a Teflon-coated stir-bar was charged with $AuCl_3$ (0.1 equiv) in a nitrogen-filled glovebox. The flask was removed from the glovebox, wrapped in aluminum foil, and placed under N_2. A solution of propargyl acetate in toluene (0.2 M, toluene degassed by bubbling with nitrogen for ∼5 min) was added rapidly via cannula. The reaction was stirred at rt in a darkened hood. When the reaction was complete as observed by TLC, the mixture was passed through a plug of silica gel using hexanes/EtOAc and concentrated in vacuo.

3-Methyl-9-(trimethylsilyl)nona-1,2-dien-8-ynyl Acetate (13f). Following the general procedure for the $AuCl_3$-catalyzed allenol ester formation, $AuCl_3$ (4 mg, 0.01 mmol) and propargyl acetate **9f** (32 mg, 0.12 mmol) were reacted in toluene (0.61 mL) for 30 min. Purification via flash chromatography (hexanes/EtOAc, 9:1, v/v) afforded the title compound (25 mg, 79%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (sext, J = 2.1 Hz, 1H), 2.26−2.20 (m, 2H), 2.16−2.02 (m, 2H), 2.13 (s, 3H), 1.83 (d, J = 2.1 Hz, 3H), 1.61−1.49 (m, 4H), 0.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.4, 168.8, 115.7, 109.7, 107.2, 84.6, 34.6, 28.0, 26.3, 20.9, 20.4, 19.6, 0.1; IR 3065, 2943, 2862, 2174, 1976, 1750, 1456, 1369, 1249, 1215, 1066, 1039, 843 cm^{-1}; MS m/z (relative intensity) 249 (36, M − CH_3), 222 (26), 117 (100),

84 (88), 75 (79), 73 (95); HRMS-EI (*m*/*z*) $[M - CH_3]^+$ calcd for $C_{14}H_{21}O_2Si$ 249.1311, found 249.1308.

General Procedure for the $[Rh(CO)_2Cl]_2$-Catalyzed Cyclocarbonylation Reaction. A flame-dried test tube (10 × 100 mm) equipped with a Teflon-coated stir-bar was charged with allene-yne and toluene (0.1 M). The tube was evacuated for 3−5 s and refilled with CO(g) (3×). To the allene-yne solution was added $[Rh(CO)_2Cl]_2$ (0.10 equiv) in one portion, and the test tube was evacuated and refilled with CO(g) (3×). The test tube was placed in a preheated 90 °C oil bath and stirred under CO(g). After the reaction was complete by TLC, the mixture was cooled to rt, passed through a short plug of silica gel using hexanes/EtOAc, and concentrated in vacuo. The crude material was purified by flash chromatography.

(8*E*)-1,2,4,5,6,7-Hexahydro-8-methyl-3-(trimethylsilyl)-2-oxoazulen-1-yl acetate (17f). Following the general procedure for the $[Rh(CO)_2Cl]_2$-catalyzed cyclocarbonylation reaction, allene-yne **13f** (27 mg, 0.10 mmol) and $[Rh(CO)_2Cl]_2$ (3 mg, 0.008 mmol) were reacted in toluene (1.0 mL) for 46 h. Purification via flash chromatography (hexanes/EtOAc, 95:5, v/v) afforded the title compound (18 mg, 62%) as a slightly yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.73 (s, 1H), 2.87 (dt, J = 14.7, 5.4 Hz, 1H), 2.81−2.70 (m, 1H), 2.51−2.32 (m, 2H), 2.15 (s, 3H), 1.94−1.72 (m, 4H), 1.85 (s, 3H), 0.25 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.4, 181.8, 170.0, 143.5, 136.8, 134.5, 73.5, 34.1, 30.6, 25.9, 24.1, 23.7, 20.7, −0.2; IR 2937, 2865, 1746, 1697, 1528, 1369, 1246, 1224, 1049, 842.1 cm^{-1}; MS *m*/*z* (relative intensity) 292 (14, M^+), 266 (24), 249 (21), 232 (71), 217 (28), 117 (51), 75 (88), 73 (100); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{24}O_3Si$ 292.1495, found 292.1485.

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Supporting Information Available: Full experimental protocols and characterization of new compounds. This information is available free of charge via the Internet at http://pubs.acs.org.