Ring-Enlarging Annulations. A One-Step Conversion of Cyclic Silyl Acyloins and ω-Alkynyl Acetals to Polycyclic Enediones

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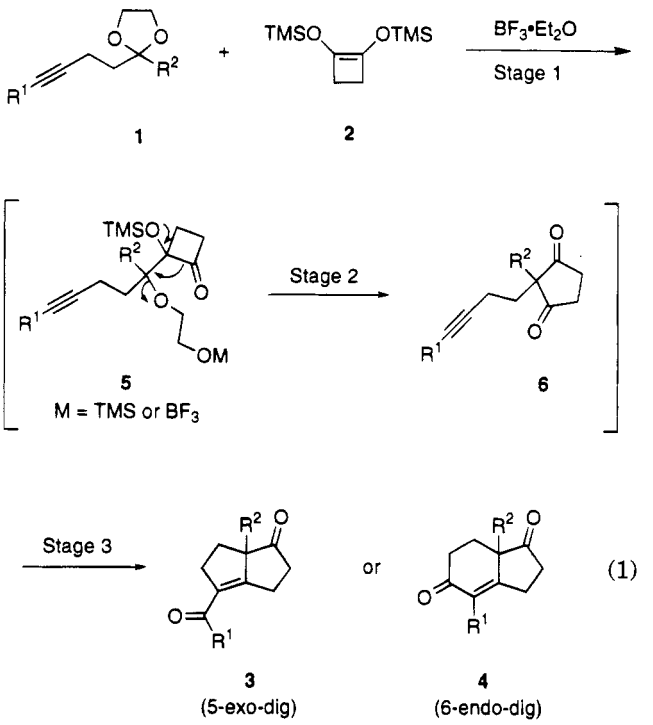
A new sequence of cationic reactions that converts cyclic silyl acyloins and ω-alkynyl acetals to polycyclic enediones is reported. For example, treatment of bis-1,2-((trimethylsilyl)oxy)cyclobutene and 2-(ethylenedioxy)-5-heptyne with excess boron trifluoride etherate in methylene chloride for 2 days provides 4-acetyl-3,5,6,6a-tetrahydro-6a-methyl-1-(2*H*)-pentalenone in 58% yield. This product is formed via a sequence involving a Mukaiyama aldol reaction, a pinacol ring expansion, and a 5-*exo-dig* alkynyl ketone cyclization. In the case of terminal alkynes, the last cyclization occurs in a 6-*endo-dig* fashion. The scope and limitations of this process are studied, and a number of bi- and tricyclic ring systems are formed.

Introduction

Tandem reactions are among the most powerful strategic tools available to the synthetic organic chemist[1] because they rapidly increase the complexity of a substrate while at the same time making economical use of available functional groups.[2] Tandem cationic reactions are featured in the biosynthesis of important natural products, and synthetic applications of both biomimetic and nonbiomimetic tandem cationic reactions have been widely developed.[3] Herein, we present full details of our recent discovery and development of a new class of tandem cationic ring enlarging annulation: the one-step condensation of cyclic silyl acyloins and ω-alkynyl acetals in the presence of excess boron trifluoride etherate to provide polycyclic enediones. This transformation has considerable synthetic potential, and in the accompanying paper[4] we expand its scope and alter its selectivity by conducting reactions in the presence of added nucleophilic reagents.

The new ring-enlarging annulation[5] is generically outlined in eq 1. Treatment of an alkynyl acetal **1** and a 1,2-*bis*((trimethylsilyl)oxy)cycloalkene (acyloin) **2** with excess BF_3·Et_2O provides either bicyclic dione **3** or **4**, depending on the nature of the alkyne substituent R^1. The tandem process occurs in three stages through the intermediacy of **5** and **6**. Each stage requires BF_3·Et_2O. The first stage is a Mukaiyama-aldol reaction to provide an α-(silyloxy)cycloalkanone **5**. In situ pinacol ring enlargement, stage 2, then occurs to provide dialkylated cyclopentanedione **6**. This intermediate dione **6** can usually be observed by TLC and is sometimes isolated. In stage 3, BF_3·Et_2O-promoted cyclization of the alkynyl



(1)

ketone **6** occurs in either a 5-*exo-dig* fashion to provide **3** (if $R^1 \neq H$) or in a 6-*endo-dig* fashion to provide **4** (if $R^1 = H$). This completes the annulation of the second ring.

Each of the individual stages in the new tandem sequence in eq 1 is precedented. In 1977, Nakamura and Kuwajima reported the two-step conversion of acyclic acetals related to **1** to dialkylated cyclopentanediones like **6**.[6] Stable products similar to **5** were first generated by a BF_3·Et_2O mediated Mukaiyama-aldol reaction. After isolation, these products were then exposed to TFA to induce the pinacol ring expansion. In 1988/89, Burnell and Wu[7] and Ayyangar[8] each reported the streamlining of the original two-step Kuwajima/Nakamura procedure to one step by exposing cyclic acetals to large excesses (5–15 equiv) of BF_3·Et_2O. Our reaction conditions are modeled after those of Burnell and co-workers.[7]

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(1) (a) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 31. (b) Ho, T.-L. *Tandem Organic Reactions*; Wiley-Interscience: New York, 1992. (c) Curran, D. P. *Synlett* **1991**, 63.

(2) Definitions of "tandem" (and its synonyms "serial", "cascade", and "domino") have been somewhat elusive. We consider that tandem reactions occur when the precursor for a subsequent step in a sequence of reactions is generated in the step that immediately precedes it. A tandem process requires only one initial precursor, regardless of the number of steps. This is differentiated from consecutive reactions, where the number of precursors is equal to the number of reactions in the sequence (see ref 1c).

(3) Sutherland, J. K. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming I., Eds.; Pergamon: Oxford, 1991; Vol. 3, p 341.

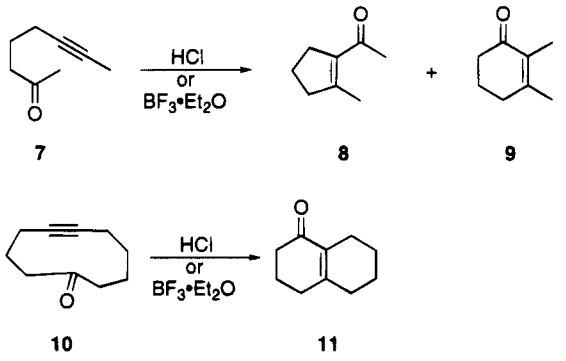
(4) Balog A.; Geib, S. V.; Curran, D. P. *J. Org. Chem.* **1995**, *60*, 345.

(5) Preliminary communication: Sisko, J.; Balog, A.; Curran, D. P. *J. Org. Chem.* **1992**, *57*, 4341.

(6) (a) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 961. (b) Shimada, J.; Hashimoto, K.; Kim, B. H.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 1759. (c) Nakamura, E.; Kuwajima, I. *Organic Syntheses*; Wiley: New York, 1993; Collect. Vol. VIII, p 579.

0022-3263/95/1960-0337$09.00/0

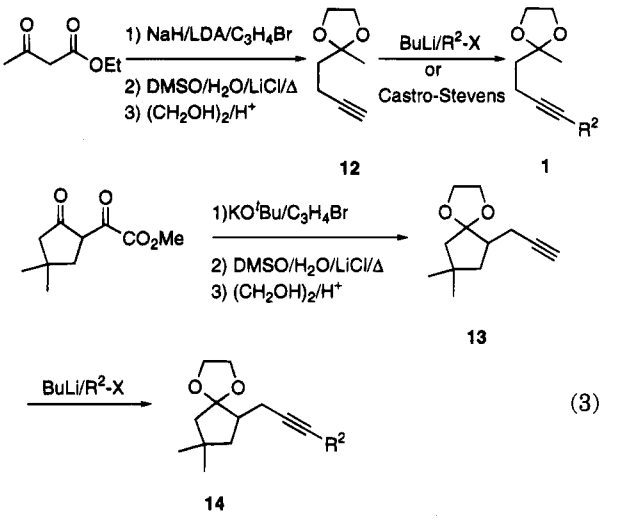
Sparse but solid precedent also exists for the BF_3·Et_2O-promoted cyclization of alkynyl diones **6** (stage 3) to provide **3** and **4**. While the use of alkynes as nucleophiles in cationic processes is well established,[9] we found only two examples where "Prins-type" reactions occur with activated carbonyls. Early studies by Weiler, Hanack, and others showed that alkynyl ketones **7** and **10** undergo both Brønsted and Lewis acid promoted cyclizations, as shown in eq 2.[10] Though the mechanisms of these



(2)

reactions have not been fully resolved, the observed products under Lewis acid conditions are consistent with vinyl cation reactive intermediates.

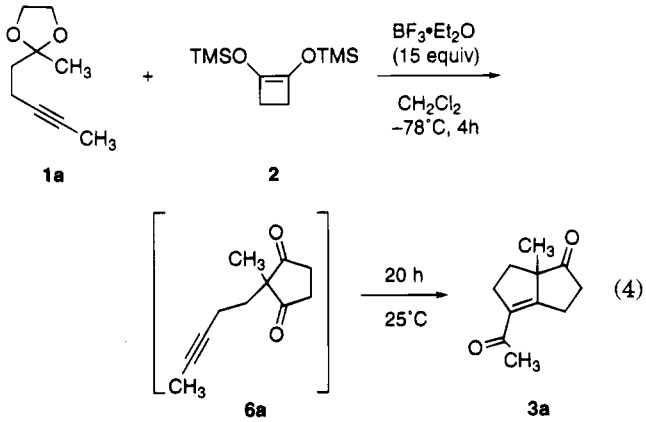
Synthesis of Ketals. The synthetic routes to the ketals used in this study are summarized in eq 3 and are presented in detail in the Experimental Section. The ketals of acyclic ketones were produced starting from methyl acetoacetate. Propargylation of the dianion,[11] followed by standard decarboxylation[12] and ketalization,[13] provided key intermediate **12**. While propargylation of the monoanion might seem more straightforward, problems with dialkylation of this intermediate make the dianion pathway superior. Subsequent introduction of a variety of R^1 groups was accomplished either through the acetylide anion (R^1 = alkyl, SR, SiR_3) or by a Castro–Stevens coupling (R^1 = Ar).[14] Preparation of ketals from cyclic ketones followed a modified route, as the conversion



(3)

of methyl 4,4-dimethylcyclopentanone-2-carboxylate (**13**) to **15** illustrates. In these cases, propargylation of the monoanion is suitable since dialkylation is not possible. Decarboxylation and ketalization then provided **14**, which could be functionalized as above to give **15**. Crude ketals were generally characterized by ^1H NMR and were often used without purification. Ring-enlarging annulation products were purified and fully characterized.

Ring Enlarging Annulations. After some optimization, we selected a standard procedure for cyclization that is similar to Burnell and Wu's procedure for cyclopentanedione synthesis.[7] This is illustrated in eq 4 for the



(4)

coupling of ketal **1a** and commercially available 1,2-bis-((trimethylsilyl)oxy)cyclobutene (**2**). A 0.1 M solution of **1a** in CH_2Cl_2 was cooled to −78 °C, and 15 equiv of distilled BF_3·Et_2O was added by syringe. After 10 min, neat succinoin **2** was added. After 4 h at −78 °C, the reaction was allowed to warm slowly to 25 °C. At this point, TLC analysis indicated the clean formation of the intermediate dione **6a**. Allowing the reaction to stand at 25 °C for an additional 20 h effected smooth conversion of **6a** to **3a**. Standard extractive workup and flash chromatography provided acetyl bicyclooctenone **3a** in 58% yield. The reaction could be interrupted by quenching shortly after the temperature reached 25 °C, and standard aqueous workup provided dione **6a** in 50% yield. Resubjection of this purified dione to the reaction conditions for 24 h at 25 °C provided **3a** in nearly quantitative yield.

The results for all the substrates that were studied are summarized in Table 1 (ketals of acyclic ketones with **2**), Table 2 (ketals of cyclic ketones with **2**), and Table 3

(7) (a) Wu, Y.-J.; Burnell, D. J. *Tetrahedron Lett.* **1988**, *29*, 4369. (b) Burnell, D. J.; Wu., Y.-J. *Can. J. Chem.* **1988**, *67*, 816. (c) Wu, Y.-J.; Burnell, D. J. *Tetrahedron Lett.* **1989**, *30*, 1021. (d) Burnell, D. J.; Wu, Y.-J. *Can. J. Chem.* **1990**, *68*, 804. (e) Wu, Y.-J.; Strickland, D. W.; Jenkins, T. J.; Liu, P.-Y.; Burnell, D. J. *Can. J. Chem.* **1993**, *71*, 1311. (f) Jenkins, T. J.; Burnell, D. J. *J. Org. Chem.* **1994**, *59*, 1485.

(8) Pandey, B.; Khire, U. R.; Ayyangar, J. R. *Synth. Commun.* **1989**, *19*, 2741.

(9) (a) Hanack, M. *Acc. Chem. Res.* **1975**, 304. (b) Stang, P.; Rappaport Z.; Hanack, M.; Subramaninian, L. R. *Vinyl Cations*; Academic Press: New York, 1979. (c) Overman, L. E.; Rodriguez-Campos, I. M. *Synlett* **1992**, 995. (d) Overman, L. E.; Sharp, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 612. (e) Overman, L. E.; Sharp, M. J. *Tetrahedron Lett.* **1988**, *29*, 901. (f) Johnson, T. O.; Overman, L. E. *Tetrahedron Lett.* **1991**, *32*, 7361. (g) Shoemaker, H. E.; Boer-Terpstra, T.; Dijkink, J.; Speckamp, W. N. *Tetrahedron* **1980**, *36*, 143. (h) Boer-Terpstra, Dijkink, J.; Shoemaker, H. E.; Speckamp, W. N. *Tetrahedron Lett.* **1977**, 939.

(10) (a) Harding, C. E.; Hanack, M. *Tetrahedron Lett.* **1971**, 1253. (b) Balf, R. J.; Rao, B.; Weiler, L. *Can. J. Chem.* **1971**, *49*, 315. (c) Hanack, M.; Harding, C. E.; Derocque, J.-L. *Chem. Ber.* **1972**, *105*, 421. (d) Chandy, M. J.; Hanack, M. *Arch. Pharmaz.* **1975**, *308*, 578. (e) Harding, C. E.; Stanford, Jr., G. R. *J. Org. Chem.* **1989**, *54*, 3054. (f) Harding, C. E.; King, S. L. *J. Org. Chem.* **1992**, *57*, 883. (g) Grunwell, J. R.; Wempe, M. F.; Mitchell, J. Grunwell, J. R. *Tetrahedron Lett.* **1993**, *34*, 7163.

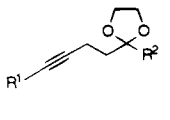
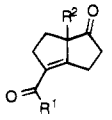
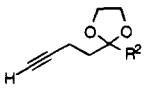
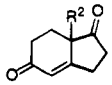
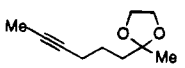
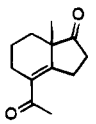
(11) Hayakawa, K.; Yodo, M.; Ohsuki, S.; Kanematsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 6753.

(12) Krapcho, A. P. *Synthesis* **1982**, 805.

(13) Caserio, F. F. Jr.; Roberts, J. D. *J. Am. Chem. Soc.* **1958**, *80*, 5837.

(14) Sonogashira, K.; Tohda, Y.; Hagihava, N. *Tetrahedron Lett.* **1975**, 4467.

Table 1. Ring-Enlarging Annulations of Ketals from Acyclic Ketones

Entry	Ketal	Product	Yield	Time (days)	Dione Detected (Isolated)
					
	1	**3**			
a	R^1 = Me	R^2 = Me	58%	1	yes
b	Bu	Me	56%	2	yes
c	Bu	$MeO_2C(CH_2)_3$	50%	1	yes
d	$PhCH_2$	Me	20%	1	yes
e	C_6H_5	Me	0	2	no
f	*o*-$NO_2C_6H_4$	Me	0	6	yes
g	MeS	Me	50%	1	yes
h	PhS	Me	0	2	no
i	*i*PrS	Me	0	2	no
j	TMS	Me	0	1	yes
k	TIPS	Me	0	1	yes
l	CO_2Me	Me	0	1.5	yes
					
	12m,n	**4m,n**			
m	—	R^2 = Me	66%	2	yes
n	—	$R^2 = (CH_2)_3CO_2Et$	41%	4	yes
o			87%	6	yes
	17	**18**			

(acyloins other than **2**). Yields of the ring-expanding annulation products ranged from 0 to 87%. Successful substrates typically exhibited a behavior similar to **1a**. An initial rapid conversion to a cyclopentanedione **6** was observed by TLC, followed by a slower (1−6 day) conversion to the final product. Though it was only demonstrated for a few cases, we believe that it is generally possible to interrupt the reaction at short reaction time if the dione **6** is the desired product.

Table 1 shows the results of the reactions of acetals derived from acyclic ketones with succinoin **2**. Alkyl-substituted acetals **1a** and **1b** gave the enones **3a** and **3b** derived from 5-*exo-dig* cyclization in 58 and 56% yields, respectively. None of the enone analogous to **4** that would result from a 6-*endo-dig* cyclization was formed in these reactions. In contrast, Hanack and Harding observed a mixture of 5-*exo-dig* and 6-*endo-dig* products **8** and **9** when they formed monocyclic enones, as shown in eq 2.[10] Acetal **1c** bearing an ester in the ketal side-chain cyclized without event to afford **3c** in 50% yield. The benzyl-substituted acetal **1d** also provided the product **3d**, though for this substrate the isolated yield was only 20%.

Though variations in the R^2 substituent will probably be well tolerated, the nature of the R^1 substituent is limited. The acetal **1e** was prepared with the notion that a phenyl-stabilized vinyl cation might improve the reaction. This idea proved to be wrong. When **1e** was treated under the standard reaction conditions, the dione **6e** was not detected by TLC or by GC. Because the dione was never detected, it was not possible to determine at which stage the reaction failed.

The *o*-nitro-substituted phenyl alkyne **1f** was prepared to see the effect of a destabilizing group on the aryl ring toward the vinyl cation intermediate. When **1f** was subjected to the standard reaction conditions, only one spot corresponding to the dione **6f** appeared on TLC after warming to 25 °C. After 6 days, the reaction was worked up, and this dione was isolated in 74% yield. The nitro group destabilizes the vinyl cation enough so that the Prins cyclization does not occur.

Acetals **1g**, **1h**, and **1i** were prepared with the goal of forming products in the carboxylic acid oxidation state. When the phenyl sulfide **1h** was subjected to the standard reaction conditions, a complex mixture of products was formed. As in the phenylalkyne case (**1e**), dione formation was not detected by TLC or GC after the reaction reached 25 °C. The (methylthio)alkynyl acetal **1g** did, however, give the expected thioester **3g** in 50% yield after 1 day. This substituent increases the functionality of the products that can be formed by the annulative ring expansion. The isopropyl sulfide **1i** was also tried in an effort to increase yields in the cyclization, but enone **3i** was not formed.

Table 2. Ring-Enlarging Annulations of Ketals from Cyclic Ketones

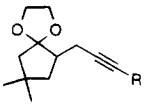
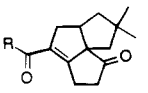
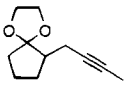
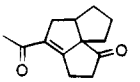
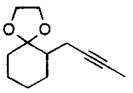
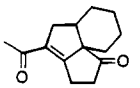
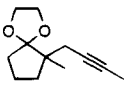
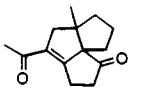
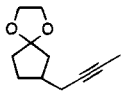
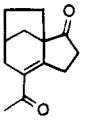
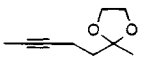
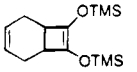
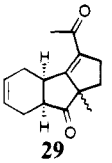
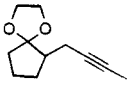
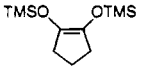
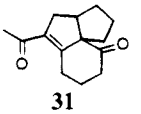
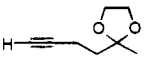
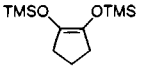
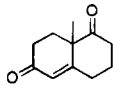
Entry	Acetal	Product	Isolated Yield (%)	Reaction Time (d)
				
	15a,b	**19a,b**		
a	R = Me	R = Me	62	4
b	R = SMe	R = SMe	20	2
c	 **20**	 **21**	69	2
d	 **22**	 **23**	0	6
e	 **24**	 **25**	0	6
f	 **26**	 **27**	0	6

Table 3. Ring-Enlarging Annulations of Bis(silyloxy)cycloalkenes

Acetal	Acyloin	Product	Isolated Yield (%)	Isolated Reaction Time (d)
 **1a**	 **28**	 **29**	44	2
 **20**	 **30**	 **31**	64	2
 **12m**	 **30**	 **32**	55	2

Cyclizations of TMS- and TIPS-substituted alkynes **1j** and **1k** were attempted, but these reactions gave no characterizable products. In both of these cases, an intermediate dione could be detected by TLC, but it was not transformed to the products **3**. The ester-substituted alkynyl acetal **1l** also gave none of the expected product **31**. In this case, the dione intermediate was isolated after 144 h. The vinyl cation produced by the cyclization is destabilized by the electron-withdrawing ability of the ester, and this apparently prevents the alkyne addition to the activated ketone.

Compounds **12m** and **12n** are terminal alkynyl acetals (entries m and n). Both acetals gave the enones (**4m** and **4n**) derived from a 6-*endo-dig* ring closure. None of the 5-*exo-dig* product **3** was detected in the ^{1}H NMR spectrum. Diagnostic of the structures of products **4m,n** were the vinyl proton resonances at 6.0 ppm in the ^{1}H NMR spectrum. Compound **4m** is known,[15] and our spectra were identical to the published data.

In order to test the possibility of a 6-*exo-trig* cyclization, acetal **17**, which has the alkyne chain extended by one carbon, was prepared (entry o). Although the reaction time was the longest of any acetal (6 days), the expected product **18** formed in the highest yield in this study (87%). The enone **18** could be more stable to the reaction conditions than other enones formed, allowing for higher yields even though the reaction time is long.

Table 2 shows annulative ring expansions with acetals derived from cyclic ketones. The products of these reactions are tricycles. Ketals **15a** and **15b** were made

(15) Rychnovsky, S. D.; Mickus, D. E. *J. Org. Chem.* **1992**, *57*, 2732.

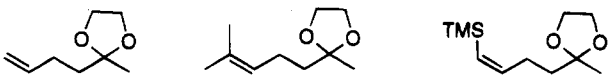


Figure 1.

for a projected synthesis of the angular triquinane natural product pentalenene.[16] The methylalkyne **15a** gave the expected tricycle **19a** in 62% yield. As before, the alkyl-substituted alkyne gave a 5-*exo-dig* cyclization product with no observable 6-*endo-dig* product. The methyl sulfide **14b** was cyclized in order to achieve the carboxylic acid oxidation state in the final product. Unfortunately, the isolated yield of **19b** was poor (20%) after purification. Ketal **20**, lacking the geminal dimethyl group, provided angular triquinane **21** in 69% yield. Homologous cyclohexanone ketal **22** did not provide tricyclic product **23**, nor did cyclopentanone ketal **24** bearing a quarternary carbon. An attempt to form a bridged tricyclic ring **27** from **26** also failed. When **26** was subjected to standard reaction conditions, only the corresponding dione was isolated after prolonged reaction time. Presumably, the increased strain in the bridged product **27** retards the Prins cyclization.

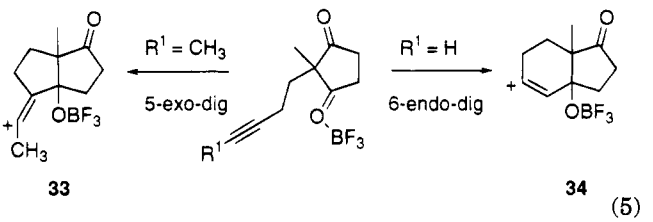
Table 3 gives the results from annulative ring expansions where acyloins other than **2** were used. Acyloins of varying ring size and functionality can be formed by reduction of a variety of diesters in a relatively good yields.[17] Acyloin **28** gave the tricyclic product **29** as a 1:1 mixture of diastereomers (44%) when it was reacted with acetal **1a**. Acyloin **30** gave the six-membered cyclic enone products **31** and **32** when reacted with alkynyl acetal **20** and **12m** under the standard conditions. When **30** was reacted with ketal **20**, the tricycle **31** was produced in good yield (64%). When **12m** was used, the Weiland–Miescher ketone **32** was formed in 55% yield. Both reactions with acyloin **30** were not as clean as the reactions with **2** and **28**. The crude product from the cyclizations with acyloin **30** was usually a black tar that was difficult to purify by flash chromatography.

Burnell and Wu have reported the cyclization of an electron rich styrenyl dione in a Torgo cyclization.[7b] Therefore, a few alkenyl acetals were also tried under standard conditions to see if alkenes would add to the diones in a similar manner (Figure 1). Each of the substrates shown appeared to form the dione intermediate analogous to **6a** by TLC. After dione formation, no evidence of formation of cyclized product was seen from any of the alkenes, and ultimately, no characterizable products could be isolated.

Discussion

The examples in Tables 1–3 begin to provide a reasonable overview of the scope and limitations of the ring enlarging annulation. The reaction will probably tolerate a variety of substituents R^2 on the ketal carbon, provided that the functional groups present are stable to prolonged exposure to $BF_3{\cdot}Et_2O$. Both four- and five-membered ring acyloins can be used, and the length of the tether between the ketal and the alkyne can be varied, thereby providing access fused 5,5-, 5,6-, 6,5-, and 6,6-bicyclic enones. The reactions with four-membered acyloins are cleaner, and the products are easier to purify. The use of ketals of cyclic ketones provides tricyclic products. As steric crowding in the vicinity of the ketal carbon increases, the reactions fail. It is likely that these failures are caused by a breakdown in the first stage of the reaction (the Mukaiyama-aldol step) since no dione is detected and since Burnell and c-oworkers encountered very similar limitations in their study of the synthesis of cyclopentanediones.[7e,f] The most serious limitation lies in the lack of diversity in the terminating groups on the alkyne that can be used. Terminal and internal alkynes and some alkylthio-substituted alkynes serve well, but other substituents such as aryl and silyl groups are not tolerated. Outside of alkynes, no other useful terminating groups have yet been identified. Importantly, the substrates that do work provide useful types of products that are well suited for further transformations.

The results are generally consistent with the sequence of events proposed in eq 1. While the initial Mukaiyama-aldol adducts **5** were never observed in this work, their intermediacy is virtually certain given the prior work of Kuwajima and co-workers.[6] The slow step in the process is the alkynyl ketone cyclization, and diones **6** were frequently observed by TLC and sometimes were isolated. The mechanism of the alkynyl ketone cyclization is not entirely clear. The regioselectivity of the reactions is consistent with vinyl cation intermediates, as summarized in eq 5. Terminal alkynes eschew the normal



33 **34** (5)

5-*exo-dig* cyclization pathway in favor of a 6-*endo-dig* pathway, presumably because a more stable cation is generated in the 6-*endo-dig* cyclization.

The pathway for conversion of vinyl cations **33** and **34** to the final products is not clear. The regioselectivity in our reactions is very faithful,[18] thus ruling out a number of mechanisms that have been considered for Brønsted acid-promoted cyclizations of a symmetrical substrate.[10] Harding suggests that these cations close to form oxetenes,[10e,f] which subsequently open to products. However, we view this as unlikely since several of the substrates in our study would provide highly strained oxetenes (**4m,n**, Table 1, would pass through oxetenes with double bonds in violation of Bredt's rule). Attack by adventitious water followed by dehydration is a possibility, though this also seems unlikely since we took pains to ensure that the reactions were dry. Even more compelling, Harding[10e] has shown in a related protic acid-promoted reaction that an oxygen atom from ^{18}O-labeled water is not incorporated into the products. Our own control experiments with isolated diones showed that addition of small amounts of water accelerated the reaction. This acceleration cannot be accounted for within the framework of eq 5 because cyclization to form the vinyl cations must be the rate-limiting step. Therefore, addition of water may cause a change in mechanism,

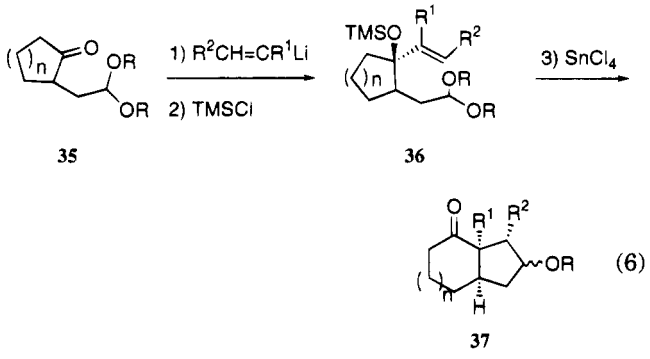
(16) Leading references: (a) Wu, Y.-J.; Zhu, Y.-Y.; Burnell, D. J. *J. Org. Chem.* **1994**, *59*, 104. (b) Frank-Neuman, M.; Miesch, M.; Gross, L. *Tetrahedron Lett.* **1992**, *27*, 3879. (c) Rowley, E. G.; Schore, N. E. *J. Org. Chem.* **1992**, *57*, 6853.

(17) Ruhlmann, K. *Synthesis* **1971**, 236.

(18) The β-enone carbon always derives from a dione carbonyl carbon, and the enone carbonyl carbon always derives from an alkyne carbon.

and it then becomes difficult to interpret the results of "control" experiments in the presence of added water. Although these experiments did not address the mechanistic role of adventitious water, they did lead to new procedures that expand the scope of the reaction, as the accompanying paper[4] describes. In short, though the observations seem to support vinyl cation intermediates like **33** and **34**, it is not clear how these intermediates are converted to the products, and it is therefore premature to exclude other mechanisms that do not go through vinyl cations.

It is worthwhile in closing to place the new ring-enlarging annulation in perspective with past work. In many respects, our method nicely complements the ring-enlarging annulation recently introduced by Overman and Sharp.[9e] This three-step protocol (eq 6) starts with



(6)

addition of a vinyl anion to a ketone **36** contained in the ring to be enlarged. This is followed by silylation to give **36**. The tandem ring enlarging annulation is then completed by exposure of **36** to $SnCl_4$. In this transformation of **35** to **37**, an addition of an alkyne to an oxonium ion completes the annulation, and this precedes a pinacol-type ring enlargement. Our one-step method (eq 1) starts with an aldol addition to a ketone of an acyloin contained in the ring to be enlarged. After the ring enlargement, the annulation is completed by an alkyne addition to an oxonium ion. The "building blocks" (functional groups and reactions) for the two transformations are quite similar. However, the juxtapositions of both the locations of the functional groups and the timing of the reactions suggest completely different kinds of strategic applications for these ring-enlarging annulations in synthesis.

The scope of this class of ring-enlarging annulation is considerably altered and expanded by the addition of nucleophiles, and these extensons are described in the following paper.

Experimental Section

General. All reactions were performed under an atmosphere of nitrogen or argon. Methylene chloride, chlorotrimethylsilane, $BF_3{\cdot}Et_2O$, and triethylamine were distilled from CaH, and toluene, diethyl ether, and THF were distilled from sodium/benzophenone. IR spectra were recorded as thin films. All ^1H NMR spectra were recorded in $CDCl_3$ at 300 MHz, and all ^{13}C NMR spectra were recorded in $CDCl_3$ at 75 MHz.

Methyl 3-Oxo-6-heptynoate. Methyl acetoacetate (18.4 mL, 170 mmol) was slowly added to a suspension of NaH (6.80 g, 80%, 227 mmol) in THF (300 mL) by syringe. The solution was cooled to 0 °C, and BuLi (113 mL, 1.5M in hexanes, 170 mmol) was added slowly to control the exothermic reaction. After 15 min, the reaction was cooled to −78 °C, and propargyl bromide (18.0 mL, 80% in toluene, 162 mmol) was then added very quickly. After 15 min, the reaction was warmed to 25 °C and quenched very slowly with water (200 mL). The solution was then extracted with ethyl acetate (3 × 150 mL). The combined organics were washed with brine (100 mL) and dried over $MgSO_4$. The solvent was evaporated to give the crude propargylated product as a brown oil. This material was used in subsequent reactions without purification: ^1H NMR δ 3.76 (3 H, s), 2.99 (2 H, s), 2.81 (2 H, t, J = 7.7 Hz), 2.48 (2 H, dt, J = 7.7, 2.6 Hz), 1.96 (1 H, t, J = 2.6 Hz).

Propargylation of Cyclic β-Keto Esters. The Sodium Hydride Method: Methyl 1-(2-Propynyl)-2-oxo-4,4-dimethylcyclopentanecarboxylate. Methyl 2-oxo-4,4-dimethylcyclo-pentanecarboxylate (**13**) (5.27 g, 33.7 mmol) was added slowly to a suspension of NaH (1.42 g, 80%, 47.2 mmol) in dry THF (150 mL). After 30 min, propargyl bromide (4.13 mL, 80% in toluene, 37.1 mmol) was added. After 4 h, the reaction was quenched very slowly with water (100 mL) and extracted with Et_2O (3 × 150 mL). The combined organics were washed with brine (30 mL) and dried over $MgSO_4$. Solvent evaporation gave 77% of the crude propargylated product, which was used without further purification: IR 3283, 1751, 1734 cm^{-1}; ^1H NMR δ 3.73 (3 H, s), 2.79 (1 H, dd, J = 2.6, 16.7 Hz), 2.61 (1 H, dd, J = 2.6, 16.7 Hz), 2.55 (2 H, dd, J = 6.2, 13.7 Hz), 2.20 (2 H, m), 2.01 (1 H, t, J = 2.6 Hz), 1.16 (6 H, s); ^{13}C NMR δ 213.26, 171.20, 80.24, 70.89, 60.28, 53.52, 52.97, 45.49, 33.26, 31.00, 30.12, 25.56; MS m/e 208, 180, 165, 152, 124, 107, 93, 83, 73; exact mass calcd for $C_{12}H_{18}O_2$ 194.1252, found 194.1257.

Propargylation of Cyclic β-Keto Esters. The KOtBu Method: Methyl 1-(2-Propynyl)-2-oxo-4,4-dimethylcyclopentanecarboxylate. Potassium (0.161 g, 4.13 mmol) was added to t-BuOH (10 mL), and the mixture was heated to reflux. Once all of the potassium was consumed, methyl 2-oxo-4,4-dimethylcyclopentane carboxylate (**13**) (0.533 g, 3.75 mmol) was added slowly. After 20 min, propargyl bromide (0.412 mL, 80% in toluene, 3.75 mmol) was added over a 30 min period and the reaction refluxed for an additional 30 min. The reaction was then cooled to 25 °C and poured into ice. The ice solution was extracted with $CHCl_3$ (3 × 50 mL). The combined organics were washed once with brine (30 mL) and dried over $MgSO_4$. Solvent evaporation gave the crude propargylated product (see above) in 91% yield.

Standard Decarboxylation Procedure:[12] 2-(2-Propynyl)-4,4-dimethylcyclopentanone. The crude ester (6.84 g, 38.0 mmol) was dissolved in DMSO (25 mL). H_2O (0.68 g, 38.0 mmol) and LiCl (3.19 g, 76.0 mmol) were added, and the reaction was heated at reflux for 2 h. The cooled mixture was diluted with water (500 mL) and extracted with Et_2O (4 × 150 mL). The combined organics were washed twice with water (200 mL) and once with brine (100 mL) and dried over $MgSO_4$. The dried solution was filtered through a 4 in. plug of silica gel followed by solvent evaporation. The crude ketone was briefly dried under high vacuum before use in subsequent reactions: ^1H NMR δ 2.52 (2 H, m), 2.38 (1 H, dd, J = 2.6, 5.5 Hz), 2.15 (1 H, t, J = 14.1 Hz), 2.05 (2 H, m), 1.92 (1H, t, J = 2.6 Hz), 1.71 (1H, t, J = 12.0 Hz), 1.20 (3 H, s), 1.06 (3 H, s); ^{13}C NMR δ 218.56, 81.46, 69.50, 53.06, 46.49, 42.35, 33.75, 29.51, 27.83, 18.89.

Standard Ketalization Procedure for Cyclic Ketones:[13] 2-(Ethylenedioxy)-5-hexyne (12m). Crude 5-hex-2-enyne (4.23 g, 43.2 mmol) was added to a solution of ethylene glycol (18.7 g, 302 mmol) and trimethyl orthoformate (13.7 g, 129 mmol), followed by addition of p-toluenesulfonic acid (0.5 g). After 2 h, the reaction was diluted with Et_2O (50 mL) and quenched very slowly with saturated $NaHCO_3$ (20 mL). The mixture was then diluted with H_2O (50 mL) and extracted with Et_2O (3 × 100 mL). The organics were washed twice with water (30 mL) and once with brine (20 mL) and dried over $MgSO_4$. Solvent evaporation gave the crude ketal **12m** as a brown oil. Bulb-to-bulb distillation (80 °C, 1.0 mmHg) gave the ketal **12m** as a clear oil: ^1H NMR δ 3.93 (4 H, m), 2.27 (2 H, m), 1.92 (3 H, m), 1.32 (3 H, s); ^{13}C NMR δ 108.60, 83.92, 67.81, 64.38, 37.63, 23.48, 12.88.

Ethyl 5-(Ethylenedioxy)-8-nonynoate (12n). This was isolated by silica gel chromatography eluting with hexanes/ethyl acetate (3:1): ^1H NMR δ 4.11 (2 H, q, J = 6.2 Hz), 3.93 (4 H, m), 1.89 (3 H, m), 1.64 (4 H, m), 1.24 (3 H, t, J = 6.2 Hz).

6-(2-Propynyl)-8,8-dimethyl-1,4-dioxaspiro[4.4]-nonane (14) was isolated by silica gel chromatography eluting with hexanes/ethyl acetate (6:1): IR 3296, 1269, 1107; ^{1}H NMR δ 3.87 (4 H, m), 2.36 (1 H, m), 2.30 (1 H, dd, J = 2.7, 5.5 Hz), 2.16 (1 H, m), 1.91 (1 H, t, J = 2.7 Hz), 1.81 (1 H, dd, J = 7.3, 12.8 Hz), 1.68 (2 H, s), 1.36 (1 H, t, J = 11.6 Hz), 1.07 (3 H, s), 1.05 (3 H, s); ^{13}C NMR δ 116.82, 83.66, 68.03, 64.31, 50.96, 45.52, 44.91, 34.10, 30.71, 29.80, 17.80.

General Procedure for the Alkylation of Terminal Alkynes: 2-(Ethylenedioxy)-5-heptyne (1a): Alkyne **12m** (1.546 g, 11.04 mmol) was added to dry THF (70 mL), and the mixture was cooled to −78 °C. BuLi (7.59 mL, 1.6 M in hexanes, 12.15 mmol) was then slowly added. After 30 min, MeI (0.687 mL, 11.04 mmol) was added, and the reaction was kept at −78 °C for 3 h. The reaction was then slowly warmed to 25 °C and after 2 h was quenched with water (30 mL). The solution was extracted with Et_2O (3 × 30 mL). The combined organic phases were washed with brine (20 mL) and dried over $MgSO_4$. Evaporation of the solvent gave the crude substituted alkyne. Purification was accomplished by silica gel chromatography eluting with hexanes/ethyl acetate (8:1) to give 87% of **1a**: ^{1}H NMR δ 3.92 (4 H, m), 2.21 (2 H, m), 1.86 (2 H, t, J = 7.7 Hz), 1.75 (3 H, t, J = 2.6 Hz), 1.30 (3 H, s); ^{13}C NMR δ 108.51, 78.28, 74.44, 64.10, 38.03, 23.10, 12.98, 2.69.

2-(Ethylenedioxy)-5-decyne (1b): ^{1}H NMR δ 3.70 (4 H, s), 2.15 (2 H, t, J = 7.4 Hz), 1.97 (2 H, m), 1.55 (2 H, t, J = 7.4 Hz), 1.37 (3 H, s), 1.26 (4 H, m), 0.75 (3 H, t, J = 7.6 Hz).

Methyl 4-(Ethylenedioxy)-7-dodecynoate (1c). This was isolated by silica gel chromatography eluting with hexanes/ethyl acetate (5:1): ^{1}H NMR δ 3.78 (4 H, s), 3.52 (3 H, s), 2.18 (2 H, t, J = 7.2 Hz), 1.97 (4 H, m), 1.68 (2 H, t, J = 7.2 Hz), 1.52 (4 H, m), 1.26 (4 H, m), 0.75 (3 H, t, J = 7.2 Hz).

2-(Ethylenedioxy)-7-phenyl-5-heptyne (1e): ^{1}H NMR δ 7.35 (4 H, m), 7.21 (1 H, m), 3.93 (4 H, m), 2.30 (2 H, dt, J = 2.7, 8.0 Hz), 1.93 (2 H, t, J = 8.0 Hz), 1.33 (3 H, s).

2-(Ethylenedioxy)-6-(2-nitrophenyl)-5-hexyne (1f): ^{1}H NMR δ 7.95 (1 H, dd, J = 0.8, 8.2 Hz), 7.53 (2 H, m), 7.38 (1 H, dt, J = 1.7, 8.2 Hz), 3.97 (4 H, m), 2.58 (2 H, t, J = 8.2 Hz), 2.03 (2 H, t, J = 8.2 Hz), 1.36 (3 H, s).

2-(Ethylenedioxy)-6-(methylthio)-5-hexyne (1g). This was purified by silica gel chromatography eluting with hexanes/ethyl acetate (7:1): ^{1}H NMR δ 3.93 (4 H, m), 2.37 (2 H, t, J = 7.7 Hz), 2.33 (3 H, s), 1.85 (2 H, t, J = 7.7 Hz), 1.31 (3 H, s).

2-(Ethylenedioxy)-6-(phenylthio)-5-hexyne (1h): ^{1}H NMR δ 7.40 (2 H, d, J = 7.4 Hz), 7.32 (2 H, t, J = 7.4 Hz), 7.20 (1 H, t, J = 7.4 Hz), 3.95 (4 H, m), 2.54 (2 H, t, J = 7.6 Hz), 2.01 (2 H, t, J = 7.6 Hz), 1.35 (3 H, s).

2-(Ethylenedioxy)-6-(isopropylthio)-5-hexyne (1i): ^{1}H NMR δ 3.93 (4 H, m), 3.11 (1 H, m), 2.42 (2 H, t, J = 8.0 Hz), 1.91 (2 H, t, J = 8.0 Hz), 1.33 (3 H, s), 1.33 (6 H, d, J = 7.2 Hz).

2-(Ethylenedioxy)-6-(trimethylsilyl)-5-hexyne (1j). This was purified by silica gel chromatography eluting with hexanes/ethyl acetate (8:1): ^{1}H NMR δ 3.93 (4 H, m), 2.31 (2 H, t, J = 7.7 Hz), 1.89 (2 H, t, J = 7.7 Hz), 1.31 (3 H, s), 0.13 (9 H, s).

2-(Ethylenedioxy)-6-(triisopropylsilyl)-5-hexyne (1k): ^{1}H NMR δ 3.95 (4 H, m), 2.38 (2 H, t, J = 7.4 Hz), 1.92 (2 H, t, J = 7.4 Hz), 1.35 (3 H, s), 1.08 (21 H, br, s).

Methyl 6-(Ethylenedioxy)-2-heptynoate (1l). This was purified by silica gel chromatography eluting with hexanes/ethyl acetate (5:1): ^{1}H NMR δ 3.94 (4 H, m), 3.76 (3 H, s), 2.41 (2 H, t, J = 7.7 Hz), 1.93 (2 H, t, J = 7.7 Hz), 1.31 (3 H, s).

6-(2-Butynyl)-8,8-dimethyl-1,4-dioxaspiro[4.4]-nonane (15a). This was purified by silica gel chromatography eluting with hexanes/ethyl acetate (6:1): ^{1}H NMR δ 3.86 (4 H, m), 2.29 (2 H, m), 2.05 (1 H, m), 1.80 (1 H, dd overlap with neighboring signal, J = 7.3 Hz), 1.77 (3 H, broad s), 1.67 (2 H, s), 1.32 (1 H, t, J = 12.1 Hz), 1.05 (6 H, d, J = 6.0 Hz).

6-(3-(Methylthio-2-propynyl)-8,8-dimethyl-1,4-dioxaspiro[4.4]nonane (15b) was purified by silica gel chromatography eluting with hexanes/ethyl acetate (5:1): IR 1435, 1221, 1269; ^{1}H NMR δ 3.86 (4 H, m), 2.40 (2 H, m), 2.34 (3 H, s), 2.25 (1 H, m), 1.75 (1 H, dd, J = 5.5, 9.0 Hz), 1.67 (2 H, s), 1.32 (1 H, t, J = 11.5 Hz), 1.06 (3 H, s), 1.04 (3 H, s); ^{13}C NMR δ 117.08, 92.45, 69.56, 64.50, 51.15, 45.98, 45.20, 34.30, 30.84, 29.90, 19.71, 19.19; MS m/e 240, 225, 193, 127, 113; exact mass calcd for $C_{13}H_{20}O_2S$ 240.1201, found 240.1203.

6-(2-Butynyl)-6-methyl-1,4-dioxaspiro[4.4]nonane (24). This was purified by silica gel chromatography eluting with hexanes/ethyl acetate (7:1): ^{1}H NMR δ 3.89 (4 H, m), 1.86 (2H, m), 1.83 (2 H, m), 1.78 (3 H, t, J = 2.6 Hz), 1.61 (4 H, m), 1.06 (3 H, s).

Standard Procedure for Ring-Expanding Annulations: 4-(1-Oxopentyl)-3,5,6,6a-tetrahydro-6a-((methoxycarbonyl)propyl)-1(2*H*)-pentalenone (3c). Ketal **1c** (0.39 g, 1.38 mmol) was dissolved in dry CH_2Cl_2 (10 mL), and the mixture was cooled to −78 °C. $BF_3{\cdot}Et_2O$ (2.55 mL, 20.7 mmol) was added slowly. After 10 min, succinoin **2** (0.44 mL, 1.73 mmol) was added slowly. The reaction was kept at −78 °C for 3 h and warmed to 25 °C. After 48 h, the mixture was diluted with Et_2O (40 mL) and H_2O (40 mL) and then extracted with Et_2O (3 × 20 mL). The organic layer was washed with H_2O (30 mL) and with brine (20 mL) and dried over $MgSO_4$. Evaporation of this solvent gave the crude product as a brown oil. The product was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (2:1): IR 1740, 1661 cm^{-1}; ^{1}H NMR δ 3.62 (3 H, s), 3.10 (1 H, m), 2.80 (4 H, m), 2.52 (3 H, m), 2.28 (2 H, m), 1.90 (2 H, m), 1.59 (6 H, m), 1.30 (2 H, m), 0.88 (3 H, t, J = 7.3 Hz); ^{13}C NMR δ 215.20, 198.70, 173.23, 160.49, 135.01, 67.74, 51.51, 41.63, 39.96, 34.49, 33.75, 33.65, 28.55, 25.69, 23.13, 22.29, 19.60, 13.85; MS m/e 306, 275, 237, 222, 191, 149, 135, 119, 105; exact mass calcd for $C_{18}H_{26}O_4$ 306.1831, found 306.1834.

4-Acetyl-3,5,6,6a-tetrahydro-6a-methyl-1(2*H*)-pentalenone (3a) was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (2:1): IR 1742, 1659 cm^{-1}; ^{1}H NMR δ 3.11 (1 H, m), 2.83 (4 H, m), 2.55 (1 H, m), 2.28 (3 H, s), 1.86 (2 H, m), 1.23 (3 H, s); ^{13}C NMR δ 216.23, 196.09, 162.89, 134.61, 63.87, 39.99, 33.62, 31.55, 29.61, 23.01, 20.58; MS m/e 178, 163, 149, 136, 93; exact mass calcd for $C_{11}H_{14}O_2$ 178.0994, found 178.0991.

4-(1-Oxopentyl)-3,5,6,6a-tetrahydro-6a-methyl-1(2*H*)-pentalenone (3b) was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (2:1): IR 1742, 1655 cm^{-1}; ^{1}H NMR δ 3.10 (1 H, m), 2.81 (4 H, m), 2.50 (3 H, m), 1.86 (2 H, m), 1.53 (2 H, m), 1.30 (2 H, m), 1.19 (3 H, s), 0.86 (3 H, t, J = 7.3 Hz); ^{13}C NMR δ 216.43, 198.74, 162.08, 134.07, 63.61, 41.48, 39.93, 33.53, 31.59, 25.69, 23.00, 22.27, 20.49, 13.85; MS m/e 220, 204, 192, 188, 163, 136, 121; exact mass calcd for $C_{14}H_{20}O_2$ 220.1653, found 220.1643.

2,3,3a,4,5,6-Hexahydro-3a-methyl-4-oxo-*S*-methyl-1-pentalenecarbothioic acid (3g) was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (2:1): IR 1740, 1640 cm^{-1}; ^{1}H NMR δ 3.32 (1 H, m), 2.90 (4 H, m), 2.55 (1 H, m), 2.37 (3 H, s), 1.98 (1 H, m), 1.87 (1 H, ddd, J = 1.7, 6.4, 12.8 Hz), 1.26 (3 H, s); ^{13}C NMR δ 216.18, 188.48, 162.11, 132.61, 63.44, 39.97, 33.40, 32.07, 23.04, 20.54, 11.31; MS m/e 210, 182, 167, 135, 120; exact mass calcd for $C_{11}H_{14}O_2S$ 210.0701, found 210.0715.

7,7a-Dihydro-7a-methyl-1,5(6*H*)-indenedione (4m) was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (2:1): IR 1738, 1673 cm^{-1}; ^{1}H NMR δ 5.96 (1 H, d, J = 2.0 Hz), 2.93 (1 H, m), 2.76 (2 H, m), 2.47 (3 H, m), 2.10 (1 H, ddd, J = 2.0, 4.8, 13.6 Hz), 1.84 (1 H, m) 1.31 (3 H, s); ^{13}C NMR δ 216.42, 198.03, 169.67, 123.78, 48.60, 35.78, 32.78, 29.08, 26.73, 20.48; MS m/e 164, 136, 122, 107, 93, 79; exact mass calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0834.

7,7a-Dihydro-7a-((ethoxycarbonyl)propyl)-1,5(6*H*)-indenedione (4n) was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (2:1): IR 1728, 1665 cm^{-1}; ^{1}H NMR 5.86 (1 H, d, J = 1.4 Hz), 4.00 (2 H, q, J = 7.1 Hz), 2.91 (1 H, m), 2.68 (2 H, m), 2.39 (3 H, m), 2.19 (3 H, m), 1.58 (5 H, m), 1.14 (3 H, t, J = 7.1 Hz); ^{13}C NMR δ 215.43, 197.83, 172.43, 169.49, 123.97, 60.21, 51.87, 35.55, 33.49, 32.64, 32.39, 26.60, 25.85, 19.40, 13.98; MS m/e 264, 219, 200, 163, 135; exact mass calcd for $C_{15}H_{20}O_4$ 264.1376, found 264.1376.

4-Acetyl-3,6,7,7a-tetrahydro-7a-methyl-1(2*H*)-indenone (18) was isolated by flash chromatography on silica gel

eluting with hexanes/ethyl acetate (2:1): IR 1742, 1684, 1655, 1624 cm^{-1}; ^1H NMR δ 3.06 (1 H, m), 2.83 (1 H, m), 2.60 (1 H, ddd, J = 2.6, 10.8, 19.4 Hz), 2.28 (2 H, m), 2.16 (3 H, s), 2.13 (1 H, m), 1.72 (3 H, m), 1.26 (1 H, m), 1.12 (3 H, s); ^{13}C NMR δ 218.70, 201.23, 152.09, 131.46, 49.41, 35.62, 28.92, 27.31, 26.34, 26.21, 23.67, 18.00; MS m/e 192, 177, 164, 150, 135, 107; exact mass calcd for $C_{12}H_{16}O_2$ 192.1150, found 192.1156. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.98; H, 8.38. Found: C, 75.05; H, 8.30.

4-Acetyl-3,5,5a,6-tetrahydro-7,7-dimethylcyclopenta[*c*]-pentalen-1(2*H*)-one (19a) was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (3:1): IR 1738, 1682, 1661, 1232 cm^{-1}; ^1H NMR δ 3.13 (1 H, m), 2.87 (3 H, m), 2.60 (1 H, dt, J = 3.6, 16.7 Hz), 2.42, (1 H, m), 2.28 (3 H, s), 2.00 (1 H, dd, J = 8.6, 12.9 Hz), 1.70 (2 H, m), 1.44 (1 H, dd, J = 5.9, 12.9 Hz), 1.24 (1 H, s), 1.04 (6 H, d, J = 6.7 Hz); ^{13}C NMR δ 213.19, 196.11, 160.78, 133.77, 76.64, 50.44, 49.89, 43.61, 41.97, 39.86, 39.64, 29.32, 28.41, 27.83, 23.72; MS m/e 232, 205, 190, 175, 147, 134; exact mass calcd for $C_{15}H_{20}O_2$ 232.1442, found 232.1444.

4-Acetyl-3,5,5a,6,7,8-hexahydrocyclopenta[*c*]pentalen-1(2*H*)-one (21) was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (4:1): IR 1738, 1686, 1659 cm^{-1}; ^1H NMR δ 3.15 (2 H, m), 2.81 (2 H, m), 2.77 (1 H, m), 2.45 (2 H, m), 2.25 (3 H, s), 1.95 (1 H, m), 1.79 (2 H, m), 1.62 (3 H, m); ^{13}C NMR δ 216.04, 196.01, 160.80, 135.23, 75.28, 43.71, 42.35, 40.70, 38.82, 34.68, 29.61, 25.66, 24.20; MS m/e 204, 162, 147, 134, 119, 105; exact mass calcd for $C_{13}H_{16}O_2$ 204.1159, found 204.1149.

3-Acetyl-2,3b,4,7,7a,8a-hexahydro-8a-methyl-cyclopent[*a*]inden-8(1*H*)-one ((3bα,7aα,8aβ) and (3bα,7aα,8aα)-29) was purified by flash chromatography on silica gel eluting with hexanes/ethyl acetate (2:1), and the diastereomers were separated by preparative HPLC using hexanes/ethyl acetate (3:1). Faster eluting isomer: IR 1740, 1682, 1624 cm^{-1}; ^1H NMR δ 5.71 (2 H, m), 2.92 (1 H, m), 2.77 (3 H, m), 2.38 (2 H, m), 2.25 (3 H, m), 2.16 (2 H, m), 1.92 (2 H, m), 1.16 (3 H, s); ^{13}C NMR δ 217.65, 197.31, 162.73, 133.00, 127.56, 125.39, 62.99, 55.94, 38.73, 34.85, 34.36, 30.22, 30.16, 26.59, 20.32; MS m/e 230, 188, 148, 134; exact mass calcd for $C_{15}H_{18}O_2$ 230.1302, found 230. 1307. Slower eluting isomer: IR 1740, 1653, 1636 cm^{-1}; ^1H NMR δ 5.76 (2 H, m), 2.81 (3 H, m), 2.54 (3 H, m), 2.34 (3 H, m), 2.02 (1 H, m), 1.88 (3 H, m), 1.27 (3 H, s); ^{13}C NMR δ 218.92, 196.10, 166.35, 136.36, 126.17, 125.13, 61.28, 51.12, 36.95, 34.10, 32.81, 29.41, 24.66, 21.74, 21.04; MS m/e 230, 188, 148, 134; exact mass calcd for $C_{15}H_{18}O_2$ 230.1302, found 230. 1307.

5-Acetyl-1,2,3,3a,4,6,7,8-octahydro-9*H*-cyclopent[*c*]inden-9-one (31) was isolated by flash chromatography on silica gel eluting with hexanes/ethyl acetate (2:1): IR 1711, 1678, 1663 cm^{-1}; ^1H NMR δ 3.46 (1 H, dt, J = 4.4, 15.1 Hz), 3.17 (1 H, m), 2.89 (1 H, m), 2.52 (1 H, m), 2.32 (2 H, m), 2.19 (3 H, s), 2.06 (2 H, m), 1.94 (1 H, m), 1.84 (1 H, m), 1.56 (5 H, m); ^{13}C NMR δ 211.06, 198.34, 155.25, 133.42, 75.41, 40.54, 39.25, 39.15, 38.82, 35.17, 30.37, 25.53, 25.27, 23.34; MS m/e 218, 203, 176, 148, 133, 119, 105, 91; exact mass calcd for $C_{14}H_{18}O_2$ 218.1306, found 218.1289.

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Supplementary Material Available: Copies of ^1H NMR spectra of all ketals and ^1H and ^{13}C NMR spectra of all annulative products (51 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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