Rearrangements of Linear Triquinanes to the Angular Isomers

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Warming substituted linear triquinanes in *t*-BuOK/*t*-BuOH resulted in their isomerization to the corresponding angularly fused isomers in good yield (59−84%). An alternate route employs a base-catalyzed intramolecular Michael addition of bicyclo[6.3.0]undecenediones, a class of compounds found to be readily available from 1-alkenylbicyclo[3.2.0]hepten-7-ones via a "one-pot" sequence of reactions. This method is complementary to the isomerization reaction since it provides access to angular triquinanes not readily available from their linear isomers.

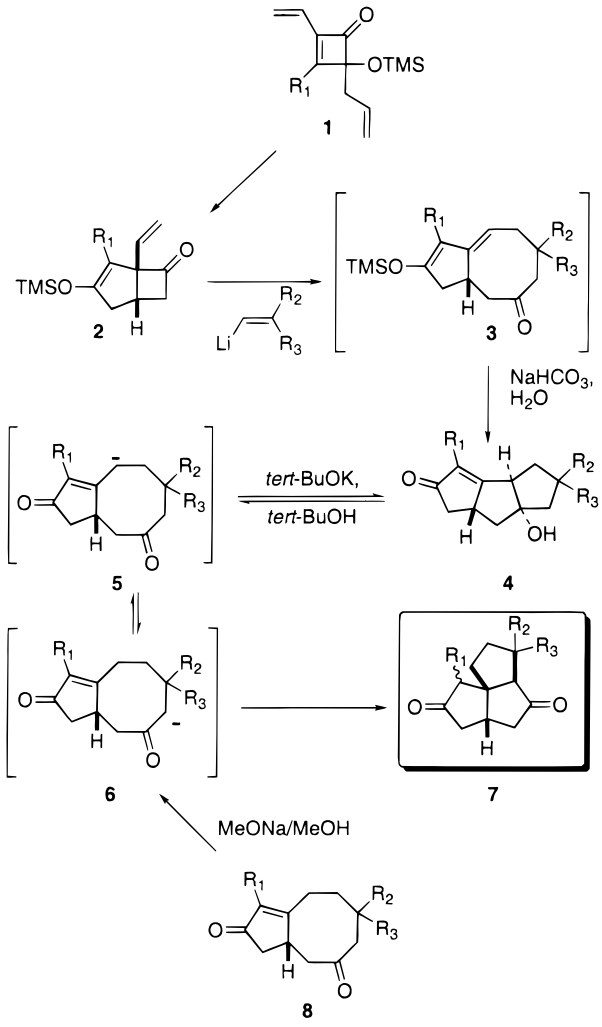
Introduction

Reported here are the details of new methodology applicable for the general synthesis of highly substituted angularly fused polyquinanes **7** (Scheme 1). Two related generalized methods starting with squaric acid-derived 4-allylcyclobutenones **1** are presented. One involves a base-catalyzed isomerization of readily available linear triquinanes **4**, which are obtained from a tandem oxy-Cope ring expansion of 1-alkenylbicyclo[3.2.0]hepten-7-ones **2** to the intermediate bicyclo[6.3.0]undecenones **3** followed by transannular ring closure upon aqueous workup.[2,3] Subsequent treatment of these with potassium *tert*-butoxide in *tert*-butyl alcohol induces their rearrangement to the angular isomers **7**, a transformation envisaged to involve formation and equilibration of the enolates **5** and **6** followed by an intramolecular Michael addition of the enolate ion in **6** to the cyclopentenone moiety. The second related method employs a new "one-pot" synthesis of bicyclo[6.3.0]undecenediones **8** from **1** and their conversion to the angular triquinanes upon treatment with sodium methoxide in methanol, a reaction that also proceeds via the enolate **6**.[4]

Results and Discussion

Preparation of 1-Alkenylbicyclo[3.2.0]hepten-7-ones. The 1-alkenylbicyclo[3.2.0]hepten-7-ones needed for these studies were prepared from cyclobutenedione monoketals **9a**,**b** or cyclobutenediones **9c**,**d** (Scheme 2).[5−8] Addition of an allyl Grignard reagent to **9a**,**b** or to the more electrophilic carbonyl of **9c**,**d** followed by acid hydrolysis gave 4-allylcyclobutenones **10a**−**f**.[9] The lower yield of **10d**,**e**,**f**, as compared to **10a**,**b**,**c** is due to the fact that they originate from **9c**,**d**, and here the allylation reaction suffers some diaddition. For example, the diol resulting from treatment of **9d** with 2-methyl-2-prope-

Scheme 1



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(2) For reviews, see: (a) Mehta, G. *Chem. Rev.* **1997**, *97*, 671. (b) Paquette, L. A.; Doherty, A. M. Polyquinane Chemistry. *Reactivity and Structure Concepts in Organic Chemistry*; Springer-Verlag: New York, 1987; Vol. 26.

(3) For a preliminary account of this work, see: MacDougall, J. M.; Moore, H. W. *J. Org. Chem.* **1997**, *62*, 4712.

(4) For reviews on cyclooctanoids, see: Petasis, N. A.; Patane, M. A. *Tetrahedron* **1992**, *48*, 5757.

(5) (a) Santora, V. J.; Moore, H. W. *J. Am. Chem. Soc.* **1995**, *117*, 8486. (b) MacDougall, J. M.; Santora, V. J.; Verma, S. K.; Turnbull, P.; Hernandez, C. R.; Moore, H. W. *J. Org. Chem.* **1998**, *63*, 6905.

(6) Liu, H.; Gayo, L.; Sullivan, R. W.; Choi, Y. H.; Moore, H. W. *J. Org. Chem.* **1994**, *59*, 3284.

(7) Xu, S. L.; Yerxa, B.; Sullivan, R. W.; Moore, H. W. *Tetrahedron Lett.* **1991**, *32*, 1129.

(8) The ring expansion chemistry of cyclobutenones has been reviewed: Moore, H. W.; Yerxa, B. R. *Adv. Strain Org. Chem.* **1995**, *4*, 81−162.

(9) (a) Xu, S. L. Moore, H. W. *J. Org. Chem.* **1989**, *54*, 6018. (b) Xia, H.; Xu, S. L.; Moore, H. W. *J. Org. Chem.* **1991**, *56*, 6094.

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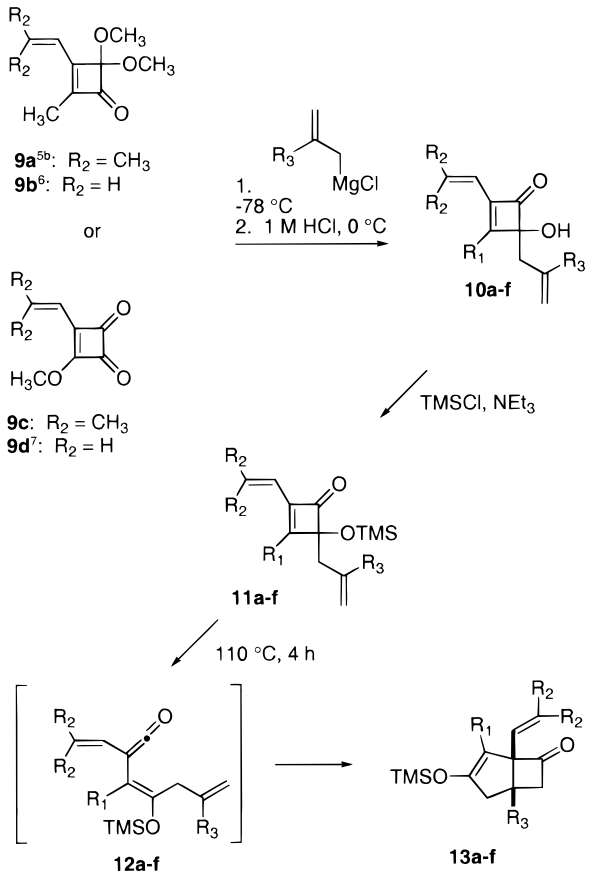
Scheme 2[a]



	R1	R2	R3	%10	%11	%13
a	Me	H	Me	92	97	97
b*	Me	Me	H	93	94	98
c*	Me	H	H	75	81	98
d	OMe	H	Me	37	78	98
e	OMe	H	H	37**	82	97
f	OMe	Me	H	39	86	92

* ref 5b
** ref 9a

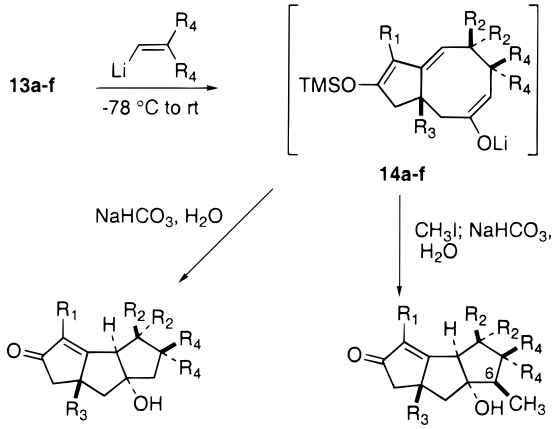
[a] One asterisk indicates ref 5b. Two asterisks indicate ref 9a.

nylmagnesium bromide was isolated in 21% yield along with the monoadduct **10d** in 37% yield.

Trimethylsilyl protection of the hydroxyl group in **10a**−**f** gave **11a**−**f**, which were directly thermolyzed (toluene, 110 °C).[5,9] This results in their electrocyclic ring opening to the intermediate vinylketenes **12a**−**f** and subsequent intramolecular [2+2] cycloaddition to provide 1-alkenylbicyclo[3.2.0]hepten-7-ones **13a**−**f** in high yield.[10] Interestingly, ^{1}H NMR analysis of the crude reaction mixtures obtained upon treatment of **10a**,**d** with TMSCl and NEt_3 and aqueous bicarbonate workup indicated the presence of trace amounts of the corresponding 1-ethenylbicyclo[3.2.0]hepten-7-ones **13a**,**d**, suggesting that the barrier to rearrangement of **11** to **13** is reduced by the presence of the methyl group (R_3 = Me) on the 4-allyl side chain. Such a result is anticipated if the intramolecular [2+2] cycloaddition of the vinylketene **12** is rate limiting and involves some polar or diradical character in the transition state.

(10) For a review of intramolecular ketene/alkene cycloadditions see: Snider, B. B. *Chem. Rev.* **1989**, *88*, 793.

Scheme 3[a]



	R1	R2	R3	R4	% Yield
15a	Me	H	Me	H	73
15b*	Me	Me	H	H	69
15c*	Me	H	H	H	67
15d	OMe	H	Me	H	67
15e	OMe	H	H	H	66
15f	OMe	Me	H	H	72
15g	Me	H	Me	Me	41
15h*	Me	H	H	Me	67
16a*	Me	H	H	H	62
16b	Me	H	Me	H	59
16c	OMe	H	Me	H	57
16d	OMe	H	H	H	57

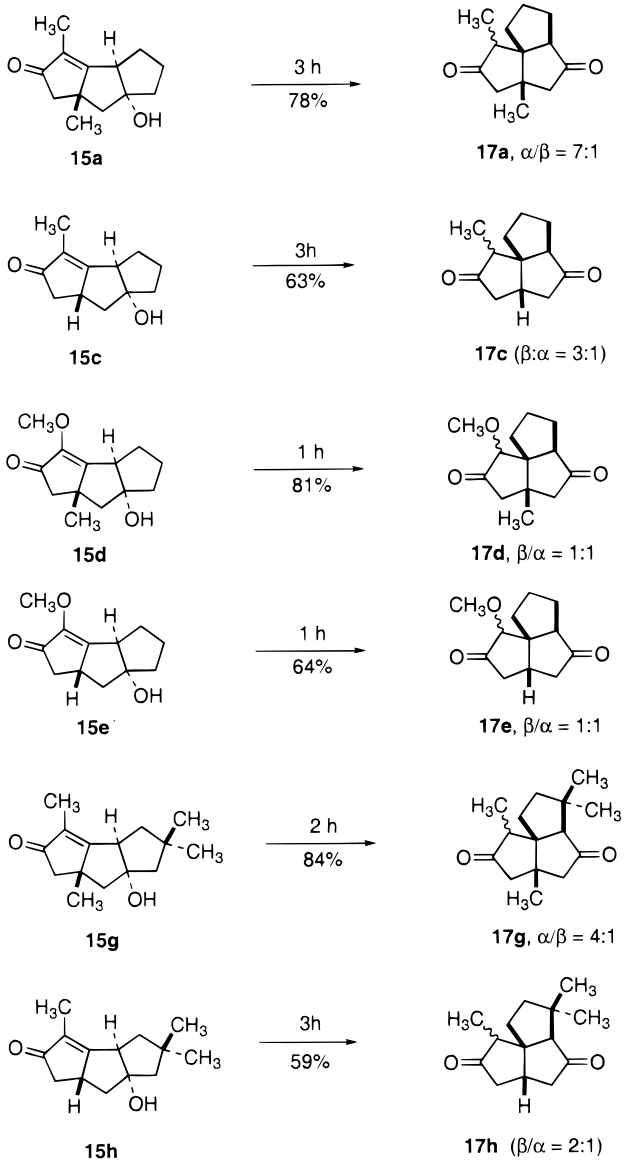
[a] The asterisk indicates ref 5b.

Preparation of the Linear Triquinanes. Treatment of **13a**−**f** with an alkenyllithium reagent induced an oxy-Cope rearrangement, thus leading to the intermediate enolates **14a**−**f** (Scheme 3).[5] Workup of the reaction using aqueous sodium bicarbonate resulted in enolate protonation followed by desilylation and concomitant transannular ring closure to give the linear triquinanes **15a**−**h**. Alternatively, treatment of **14c**−**f** with methyl iodide followed by aqueous bicarbonate gave the 6-methyl derivatives **16a**−**d** along with minor amounts of the C_6 epimers.

Rearrangements of Linear to Angular Triquinanes. Treatment of the linear triquinanes **15a**,**c**,**d**,**e**,**g**,**h** with potassium *tert*-butoxide in warm (35 °C) *tert*-butyl alcohol caused their rearrangement to the respective angular isomers **17a**,**c**,**d**,**e**,**g**,**h** in yields ranging from 59% to 84% (Scheme 4). Under analogous conditions **16a**,**b**,**d** gave, respectively, **18a**,**b**,**d** in 82−84% (Scheme 5). It is of interest to note that any equilibration greatly favors the angular isomers since the reactions were terminated (20 min to 3 h) when the starting linear triquinanes could not be detected by TLC and/or ^{1}H NMR analyses of the crude reaction mixtures.

Structure assignments of the angular triquinanes are based upon their characteristic spectral properties as well as a single-crystal X-ray structure of the major diastereomer of **18a**. The ^{13}C NMR spectra of all angular triquinanes display two downfield carbonyl absorptions (δ 213−222) and no alkene carbon absorptions. The ^{1}H NMR spectra of compounds **18a**,**b** and **17a**,**c**,**g**,**h** show a characteristic doublet for the C-1 methyl group at δ 1.05−1.00 (J = 7 Hz). The spectra of **17d**, **17e**, and **18d** display a downfield methine proton at δ 3.65−3.60 (d, ^4J = 1−2

Scheme 4[a]



[a] Conditions: *t*-BuOH/*t*-BuOK, 35 °C.

Hz). In most instances the stereochemistry at position 1 of the angular triquinanes was determined by 1D NOE studies.

The following points concerning these rearrangements warrant further discussion: (1) The relatively rapid rearrangements of compounds **16a**,**b**,**d** indicate that the $C_{6\beta}$ methyl group facilitates the rearrangement. This is postulated to result from steric acceleration accompanying the release of unfavorable nonbonding interaction between the C_6 methyl group and the C_7 methylene group during the retroaldol fragmentation step. (2) A π-donating methoxyl group on the enone double bond of the starting linear triquinane has little effect on the efficiency or rate of the rearrangement as indicated by comparing the reaction time of, for example, **16a** with **16d**, both of which take approximately 20 min for completion and give >80% yield of the corresponding angular triquinane. Thus, the Michael addition step is kinetically fast compared to the retroaldol step. (3) The rearrangement of **16b** to **18b** is particularly noteworthy, since this product, bearing angular methyl groups at C_{3a} and C_{5a}, may serve as a valuable advanced intermediate in natural product

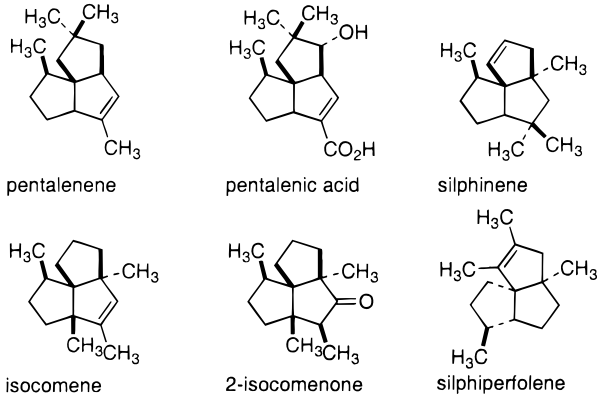
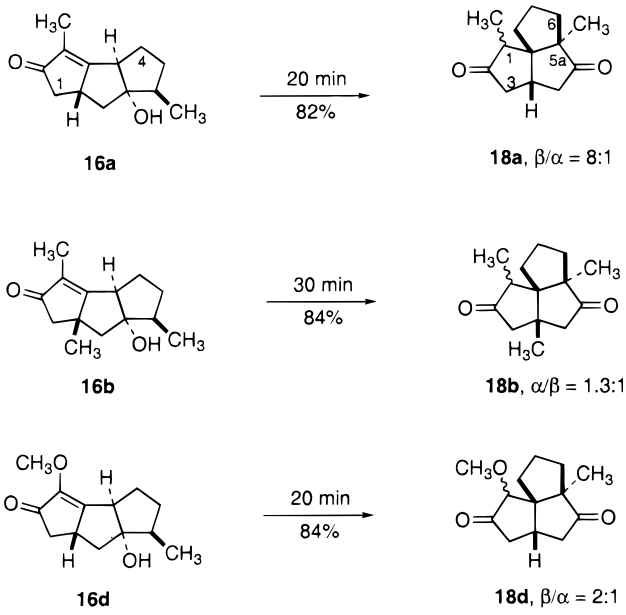


Figure 1. Examples of naturally occurring angular triquinanes.

Scheme 5[a]

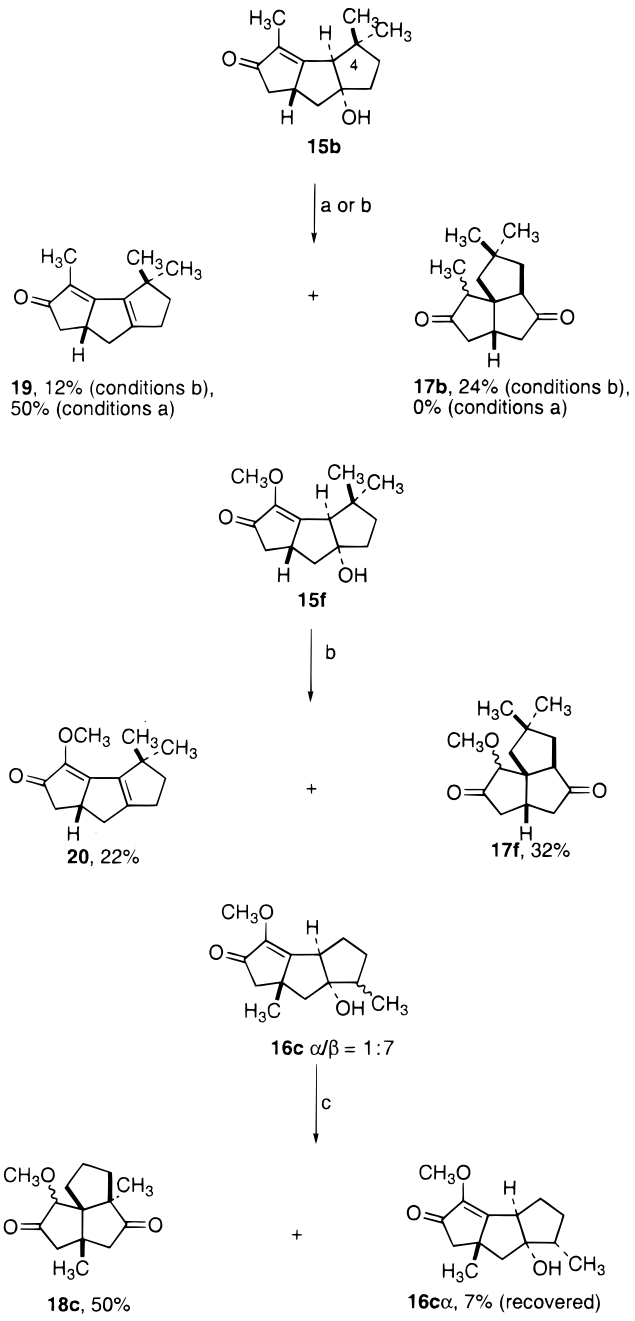


[a] Conditions: *t*-BuOH/*t*-BuOK, 35 °C.

syntheses., e.g., isocomene[2] (Figure 1). (4) In the absence of a C_{3a} angular methyl group, the major angular triquinane diastereomers possess a β-oriented C_1 group, while the presence of a C_{3a} methyl group results in a preference for the C_1 α-diastereomer. For examples, compare **17a** to **17c** and **17g** to **17h**. Additionally, a severe steric interaction apparently exists between an α-disposed C_1 group and the C_{5a} methyl group. This results in a preference for the β-diastereomer for those cases even when position 3a is unsubstituted. This is supported by a comparison of the observed diastereoselectivities in, for example, the rearrangements of **16a** to **18a** and **15a** to **17a**. The former gives predominantly the β-isomer, and the latter leads mainly to the α-isomer.

A limitation to the above rearrangement was encountered for those linear triquinanes bearing geminal dimethyl substitution at position 4. For example, treatment of **15b** under the conditions employed above (*t*-BuOK/*t*-BuOH, 35 °C) gave the dehydrated linear triquinane **19** in 50% yield as the only isolable product (Scheme 6). Under more forcing conditions (KOH, H_2O, THF, 120 °C), the angular isomer **17b** was realized, but in poor yield; e.g., **19** was obtained in 12% yield and **17b** in only 24% yield. Analogously, subjecting **15f** to these vigorous

Scheme 6[a]

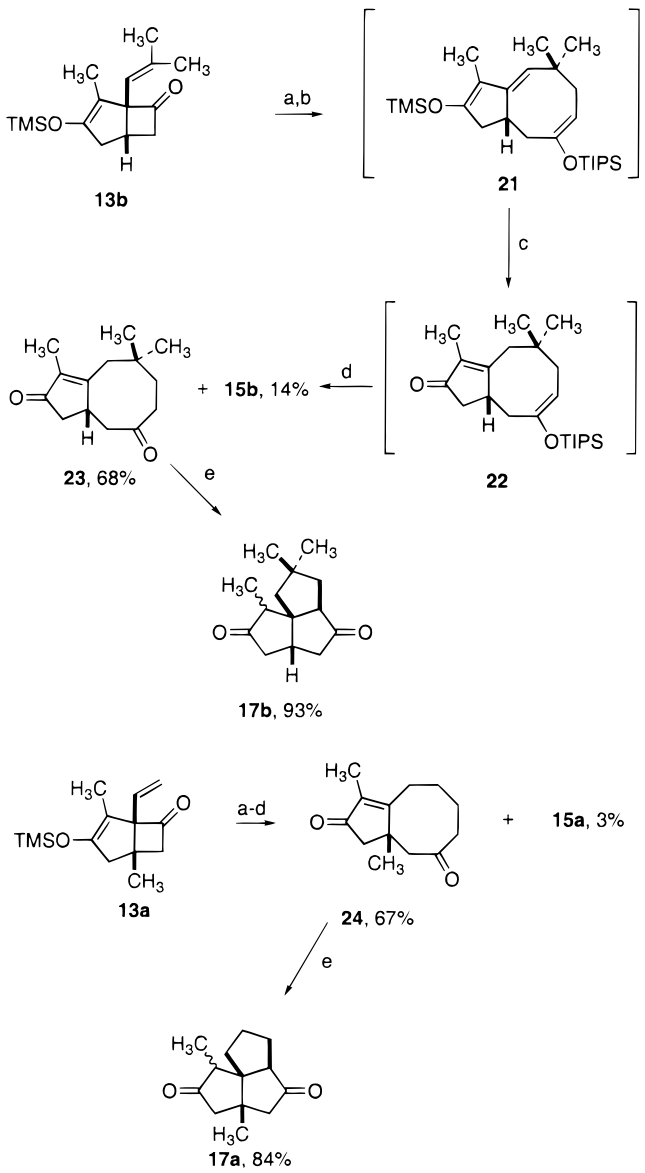


[a] Conditions: (a) *t*-BuOK, *t*-BuOH, reflux; (b) KOH, H_2O, THF, 120 °C; (c) *t*-BuOK, *t*-BuOH, 35 °C.

conditions gave the dehydrated linear triquinane **20** in 22% yield and the angular triquinanes **17f** in 32%. The failure of **15b** and **15f** to efficiently rearrange to their angular isomers is likely due to unfavorable van der Waals interactions between the 4,4-dimethyl groups and the 3-methyl or 3-methoxy substituents that manifest themselves during the retroaldol step. That it is due to unfavorable interactions during the Michael addition step was ruled out by experiments outlined subsequently.

Still another limitation is reflected by the observation that linear triquinanes bearing a *β*-methyl group at position 6 readily rearrange to the corresponding angular isomers while the α-epimers do not. For example, when a 1:7 mixture of, respectively, α- and *β*-epimers of **16c** was treated with potassium *tert*-butoxide in *tert*-butyl alcohol, a 50% isolated yield of the angular triquinane

Scheme 7[a]



[a] Conditions: (a) $LiCH{=}CH_2$, −78 °C to rt; (b) TIPSOTf; (c) K_2CO_3, CH_3OH, 0 °C to rt; (d) TBAF, H_2O; (e) MeONa/MeOH, reflux, 2 h.

18c was obtained along with 7% of the unreacted α-epimer **16c**α (Scheme 6). The reason for this selectivity is not well understood but may simply reflect a steric protection of the C-6a hydroxyl group by the adjacent C-6 *β*-methyl group.

The poor yield encountered for the rearrangement of linear triquinanes bearing a *gem*-dimethyl group at position 4 (e.g., **15d**,**f**) was disappointing since the resulting angular triquinanes would be valuable synthetic intermediates in natural product syntheses; e.g., such a substitution pattern is found in pentalenene and pentalenic acid (Figure 1). Fortunately, this limitation was circumvented by the experiments outlined below. Specifically, triquinane **17b** could be obtained in high yield (>93%) from the intramolecular Michael addition reaction of bicyclo[6.3.0]undecenedione **23** upon treatment with MeONa/MeOH (Scheme 7).

For the above transformation to be synthetically viable, it was necessary to develop a good synthetic route to bicyclo[6.3.0]undecenediones such as **23**. This presented

a challenge since, as noted above, simply treating **13b** with vinyllithium followed by an aqueous $NaHCO_3$ quench gave the linear triquinane **15b** (69%). When an acidic quench was employed, **23** was obtained but only as a minor product. It was, however, reasoned that **23** might be obtained from the bis(silyl enol ether) **21**, a compound in which the two enol ether moieties are differentiated. The TMS enol ether might be selectively deprotected to give **22**, a compound that could not undergo the transannular ring closure to the triquinane. Subsequent desilylation of **22** would then lead to the desired **23**. *This was accomplished in a one-pot sequence of reactions as outlined below.*

Treatment of 1-(2-methylpropenyl)bicyclo[3.2.0]hepten-7-one **13b** with vinyllithium followed by a triisopropylsilyl triflate (TIPSOTf) quench gave the bis(silyl enol ether) **21**, which was not isolated but treated directly with potassium carbonate in methanol to give **22** via selective removal of the TMS group.[11] A final quench of the reaction mixture with tri-*n*-butylammonium fluoride (TBAF) and an aqueous workup gave cyclooctanoid **23** in 68% overall yield from **13b** along with a 14% yield of the linear triquinane **15b**. The formation of intermediates **21** and **22** was supported by spectral analysis of aliquots taken over the course of the transformations. For example, key absorptions in the ^{1}H NMR spectrum of **21** were observed for the silyl enol ether protons at δ 4.73 (s) and δ 4.87 (t, J = 9.5 Hz).

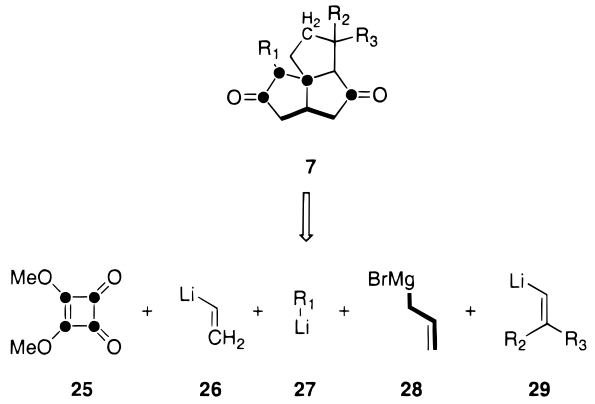
In a similar manner **24** was prepared in 67% overall yield from **13a**. This cyclooctanoid, like **23**, was observed to undergo facile transannular Michael cyclization to the corresponding angular triquinane **17a** (84%) upon heating with sodium methoxide in methanol.

It is noteworthy that the preparation of the angular triquinane **17b** from **23** carries both synthetic and mechanistic importance. For example, preparation of **22** documents an efficient one-pot procedure for the synthesis of bicyclo[6.3.0]undecenones from readily available 1-alkenylbicyclo[3.2.0]hepten-7-ones. In addition, the efficiency of the ring closure of **23** to **17b** reveals that the problematic step in the isomerization of the 4,4-dimethyl-substituted linear triquinane **15b** to its angular isomer **17b** rests in the retroaldol step and not in the transannular Michael addition step.

Conclusions

In conclusion we note the following significant points. (1) Of the numerous known methods for the construction of the triquinane ring system, none are amenable to the regiospecific synthesis of both angular and linear derivatives from a common starting material.[2] In contrast, the method outlined here documents a general approach for the regiospecific synthesis of functionalized angularly fused triquinanes from their linear counterparts and further displays the rich synthetic potential of cyclobutenone derivatives as valuable precursors to a variety of highly condensed ring systems. (2) The method is highly convergent and efficient and starts with readily available reagents. As an illustration, the generalized triquinane **7** translates to dimethylsquarate **25** and the organometallic reagents **26**−**29** (Scheme 8). (3) The value of cyclobutenone-derived 1-alkenylbicyclo[3.2.0]hepten-7-ones was further realized by the discovery of an efficient synthesis of bicyclo[6.3.0]undecenediones, a class of compounds that also serve as precursors to angular triquinanes.[12] (4) The method outlined here is particularly valuable for the synthesis of highly functionalized angular triquinanes. Selected naturally occurring examples are provided in Figure 1.

Scheme 8



Experimental Section

General Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, in $CDCl_3$ unless specified otherwise. All other general experimental information is provided in ref 5b.

3-Methoxy-4-(2-methyl)-1-propenyl-3-cyclobutene-1,2-dione (9c). 1-Bromo-2-methyl-1-propene (1.87 mL, 18.3 mmol) was added to a −78 °C THF (100 mL) solution of *t*-BuLi (21.5 mL, 36.5 mmol), and after 30 min the colorless solution was transferred to a −78 °C THF (200 mL) solution of dimethylsquarate (2.00 g, 14.1 mmol) over 30 min. Trifluoroacetic anhydride (4.4 mL, 31.0 mmol) was added after 10 min, followed by water after an additional 10 min. The yellow mixture was warmed to rt and extracted with ether. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. Chromatography (2:1 hexanes/EtOAc) provided **9c** (1.4 g, 60%) as a yellow solid: mp, 48−49 °C; ^{1}H NMR δ 6.01 (m, 1H), 4.43 (s, 3H), 2.20 (d, J = 0.5 Hz, 3H), 1.99 (d, J = 1.0 Hz, 3H); ^{13}C NMR δ 193.1, 192.5, 191.9, 176.5, 155.8, 112.5, 61.1, 27.5, 22.7; IR ($CHCl_3$, cm^{-1}) 1786, 1744; HRMS (EI) calcd for $C_9H_{10}O_3$ (M^+) 166.0630, obsd 166.0631.

2-Ethenyl-4-hydroxy-3-methyl-4-(2-methyl-2-propenyl)-2-cyclobuten-1-one (10a). The Grignard reagent was formed by the dropwise addition of an ether (260 mL) solution of 3-chloro-2-methylpropene (25.9 mL, 262 mmol) to magnesium ribbon (5.5 g, 227 mmol) over 25 min. The Grignard reagent was then added over 20 min to a −78 °C solution of **9b** (1.62 g, 9.63 mmol) in THF (300 mL) until the green-yellow color of the solution had dissipated. This required 150 mL of the Grignard solution. Water (100 mL) was added, and the cooling bath was removed. The mixture was extracted with ether, washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude ketal intermediate was dissolved in THF (100 mL), cooled to 0 °C, and treated with HCl (1 M aqueous, 0.5 mL). After 40 min, $NaHCO_3$ (saturated aqueous, 50 mL) was added, and the mixture was extracted with EtOAc, washed with brine, dried (Na_2SO_4), filtered, and concentrated. Chromatography (2:1 hexanes/EtOAc) gave **10a** (1.57 g, 92%) as a white crystalline solid: mp 46−47 °C; ^{1}H NMR δ 6.18 (dd, J = 17.6, 11.1 Hz, 1H), 5.98 (d, J = 17.6 Hz, 1H), 5.49 (d, J = 11.1 Hz, 1H), 4.93 (s, 1H), 4.85 (s, 1H), 3.09 (m, 1H), 2.59 (d, J = 13.8

(11) Hurst, G. T.; McInnes, A. G. *Can. J. Chem.* **1965**, *43*, 2004.

(12) For recent syntheses of the bicyclo[6.3.0]undecane ring system, see: (a) Castro, J.; Moyano, A.; Pericas, Riera, A. *J. Org. Chem.* **1998**, *63*, 3346; (b) Snapper, M. L.; Tallarico, J. T.; Randall, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 1478. (c) Furstner, A.; Langemann, K. *J. Org. Chem.* **1996**, *61*, 8746.

Hz, 1H), 2.46 (d, J = 13.8 Hz, 1H), 2.17 (s, 3H), 1.79 (s, 3H); ^{13}C NMR δ 193.2, 175.1, 146.1, 140.8, 123.8, 122.9, 115.9, 92.3, 42.1, 23.1, 11.0; IR (film, cm^{-1}) 3410, 3076, 1760, 1748, 1651, 1612, 1582; HRMS (EI) calcd for $C_{11}H_{14}O_2$ (M^+) 178.0994, obsd 178.0992.

2-Ethenyl-3-methyl-4-(2-methyl-2-propenyl)-4-[(trimethylsilyl)oxy]-2-cyclobuten-1-one (11a). To a THF (50 mL) solution of **10a** (1.57 g, 8.81 mmol) were added NEt_3 (8.4 mL, 60.2 mmol) and TMSCl (7.4 mL, 58.3 mmol). A white precipitate of NEt_3·HCl formed immediately. After 7 d the yellow-white mixture was poured onto CH_2Cl_2 (80 mL) and $NaHCO_3$ (40 mL). The aqueous layer was extracted with additional CH_2Cl_2, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The residue was immediately chromatographed (Florisil, 4:1 hexanes/EtOAc) to provide **11a** (2.13 g, 97%) as a yellow oil: ^{1}H NMR δ 6.16 (dd, J = 18.0, 11.0 Hz, 1H), 5.97 (dd, J = 18.0, 1.0 Hz, 1H), 5.46 (dd, J = 11.0, 1.0 Hz, 1H), 4.79 (s, 1H), 4.72 (s, 1H), 2.51 (d, J = 13.8 Hz, 1H), 2.45 (d, J = 13.8 Hz, 1H), 2.15 (s, 3H), 1.70 (s, 3H), 0.09 (s, 9H); ^{13}C NMR δ 193.3, 176.6, 145.4, 141.3, 123.3, 123.0, 115.0, 95.3, 43.5, 23.5, 11.6, 1.2 (3C); IR (film, cm^{-1}) 3096, 3076, 1760, 1654; HRMS (isobutane CI) calcd for $C_{14}H_{22}SiO_2$ (M^+) 250.1389, obsd 250.1393.

Representative Procedure for the Rearrangement of 4-Allylcyclobutenones to Bicyclo[3.2.0]heptenones. 1-Ethenyl-2-methyl-3-[(trimethylsilyl)oxy]bicyclo[3.2.0]hept-2-en-7-one (13a). A toluene (430 mL) solution of **11a** (2.13 g, 8.52 mmol) was heated at reflux for 5 h, cooled to rt and concentrated to provide **13a** (2.1 g, 97%) as a yellow oil: ^{1}H NMR δ 5.57 (dd, J = 17.5, 10.7 Hz, 1H), 5.35 (dd, J = 17.5, 1.6 Hz, 1H), 5.25 (dd, J = 10.7, 1.6 Hz, 1H), 3.04 (d, J = 17.7 Hz, 1H), 2.76 (d, J = 17.7 Hz, 1H), 2.54 (dq, J = 15.9, 2.4 Hz, 1H), 2.43 (d, J = 15.9 Hz, 1H), 1.46 (br s, 3H), 1.17 (s, 3H), 0.21 (s, 9H); ^{13}C NMR δ 208.3, 148.7, 132.3, 118.1, 113.4, 81.9, 57.7, 47.0, 35.8, 21.9, 9.4, 0.60 (3C); IR (film, cm^{-1}) 1770, 1672; HRMS (isobutane CI) calcd for $C_{14}H_{22}SiO_2$ (M^+) 250.1389, obsd 250.1394.

Representative Procedure for the Oxy-Cope Rearrangement of 1-Alkenylbicyclo[3.2.0]hepten-7-ones to Linear Triquinanes. 1,3bα,4,5,6,6a,7,7a*β*-Octahydro-6aα-hydroxy-3-methoxy-1*H*-cyclopenta[*a*]pentalen-2-one (15e). A −78 °C THF (20 mL) solution of **13e** (144 mg, 0.57 mmol) was treated with vinyllithium (0.57 mL, 0.68 mmol), and after 45 min the cooling bath was removed. After an additional 1.5 h $NaHCO_3$ (saturated aqueous,10 mL) was added, and the mixture was stirred for 10 min. The mixture was extracted with ether, washed with brine, dried (Na_2SO_4), filtered, and concentrated. Chromatography (1:1 hexanes/EtOAc) provided **15e** (78 mg, 66%) as a white solid: mp, 91−92 °C; ^{1}H NMR δ 3.83 (s, 3H), 3.17 (t, J = 8.5 Hz, 1H), 2.86−2.81 (m, 1H), 2.56−2.50 (br s overlapping dd, J = 18.5, 6.0 Hz, 2H), 2.33−2.28 (m overlapping dd, J = 12.0, 7.0 Hz, 2H), 2.05 (dd, J = 18.5, 2.0 Hz, 1H), 1.99−1.95 (m, 1H), 1.85−1.76 (m, 2H), 1.70−1.64 (m, 1H), 1.54−1.46 (m, 1H), 1.33 (t, J = 12.0 Hz, 1H); ^{13}C NMR δ 202.8, 155.2, 148.6, 93.0, 57.8, 52.4, 45.9, 42.3, 39.2, 38.4, 34.4, 26.7; IR (film, cm^{-1}) 3422, 1702, 1654, 1648; HRMS (isobutane CI) calcd for $C_{12}H_{16}O_3$ 208.1099 (M^+), obsd 208.1095.

Representative Procedure for the Rearrangement of Linear Triquinanes to Their Angular Isomers. 1,3,3a*β*,4,-5aα,6,7,8-Octahydro-1α-methyl-1*H*-cyclopenta[*c*]pentalene-2,5-dione (18cα) and 1,3,3a*β*,4,5aα,6,7,8-Octahydro-1*β*-methyl-1*H*-cyclopenta[*c*]pentalene-2,5-dione (18c*β*). To a 35 °C *t*-BuOH (4.1 mL) solution of **15c** (79 mg, 0.41 mmol) was added *t*-BuOK (127 mg, 1.13 mmol) in a single portion. After 3 h, NH_4Cl (saturated aqueous, 5 mL) and water (5 mL) were added, and the mixture was extracted with ether. The separated organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. Chromatography (1:1 hexanes/EtOAc) provided **18c** (49.4 mg, 63%) as white needles that consisted of a 2.9:1 mixture of diastereomers: ^{1}H NMR δ 2.77 (dd, J = 18.5, 10.0 Hz, 1H), 2.70 (dd, J = 16.5, 8.0 Hz, 1H), 2.64−2.56 (m, 2H), 2.52−2.40 (m, 4H), 2.36 (q, J = 7.0 Hz, 1H), 2.32−2.22 (m, 3H), 2.17 (d, J = 8.0 Hz, 1H), 2.06−1.99 (m, 1H), 1.97−1.84 (m, 4H), 1.82−1.66 (m, 5H), 1.61−1.54 (m, 1H), 1.49−1.36 (m, 2H), 1.04 (overlapping doublets, J = 7.0 Hz, 6H); ^{13}C NMR δ 221.5, 220.1, 218.5, 217.5, 58.8, 58.6, 58.0, 54.1, 52.9, 49.7, 45.4, 44.9, 44.3, 41.6, 39.7, 38.1, 32.5, 32.0, 29.6, 26.3, 25.8, 9.5, 9.3 (the quaternary carbon of the minor diastereomer was not observed); IR (film, cm^{-1}) 1731; HRMS (EI) calcd for $C_{12}H_{16}O_2$ (M^+) 192.1150, obsd 192.1150. An analytical sample of the major diastereomer, **18c*β***, was obtained as fine white needles by recrystallization from hexanes: mp, 84−85 °C; ^{1}H NMR δ 2.81 (ddd, J = 16.7, 10.0, 1.5 Hz, 1H), 2.73 (dd, J = 16.7, 8.0 Hz, 1H), 2.54 (dd, J = 18.5, 7.5 Hz, 1H), 2.39 (dq, J = 7.0, 1.5 Hz, 1H), 2.33 (d, J = 18.5 Hz, 1H), 2.20 (d, J = 8.0 Hz, 1H), 2.09−2.05 (m, 1H), 2.02−1.92 (m, 2H), 1.86−1.74 (m, 3H), 1.53−1.45 (m, 1H), 1.08 (d, J = 7.0 Hz, 3H); ^{13}C NMR δ 221.6, 217.7, 58.9, 54.2, 53.0, 45.0, 44.4, 39.9, 38.2, 32.6, 26.4, 9.4.

(±)-3,3a*β*,4,6,7,8,9-Heptahydro-1,8,8-trimethyl-2*H*-cyclopentacyclooctene-2,5-dione (23). Vinyllithium (1.3 mL, 1.03 mmol) was added to a −78 °C THF (20 mL) solution of **13b** (249 mg, 0.94 mmol), and after 30 min the solution was warmed to rt. TIPSOTf (0.27 mL, 1.03 mmol) was added after an additional 30 min. After 1.5 h, the mixture was cooled to 0 °C, and K_2CO_3 in MeOH (10 mL of a 0 °C saturated solution prepared from 138 mg of K_2CO_3 and 31 mL of anhydrous MeOH) was added. The mixture was warmed to rt over 18 h. TBAF (0.9 mL, 1.0 mmol) was added, and after 45 min the mixture was poured onto brine (20 mL) and water (10 mL), and the separated aqueous layer was extracted with ether. The combined organics were washed with brine, dried (Na_2SO_4), filtered, and concentrated. Chromatography (3:1 to 2:1 hexanes/EtOAc) provided **23** (119 mg, 68%) as a white solid (mp, 89−90 °C), followed by **15b** (29 mg, 14%). Spectral data for **15b** were identical to those cited in the literature.[5b] Spectral data for **23** follows: ^{1}H NMR δ 3.06−3.04 (m, 1H), 2.76−2.66 (m, 2H), 2.63−2.53 (m, 2H), 2.44 (d, J = 13.9 Hz, 1H), 2.39 (ddd, J = 16.3, 6.8, 2.8 Hz, 1H), 2.07 (dd, J = 18.7, 2.8 Hz, 1H), 2.00−1.94 (m, 2H), 1.73 (d, J = 2.0 Hz, 3H), 1.57 (dd, J = 15.1, 6.4 Hz, 1H), 1.07 (s, 3H), 1.03 (s, 3H); ^{13}C NMR δ 213.9, 207.5, 171.0, 140.8, 43.8, 43.6, 41.8, 41.4, 40.8, 37.5, 36.0, 31.4, 28.7, 10.0; IR (film) 1695, 1634 cm^{-1}; HRMS (isobutane CI) calcd for $C_{14}H_{20}O_2$ 220.1463, obsd 220.1462.

Preparation of 17b from 23. To a MeOH (anhydrous, 27 mL) solution of **23** (119 mg, 0.54 mmol) was added NaOMe (146 mg, 2.7 mmol) in a single portion. The solution was heated at reflux for 2 h. Workup according to the procedure described for **18c** and chromatography (3:1 hexanes/EtOAc) and concentration provided **17b** (111 mg, 93%, 2:1 mixture of diastereomers) as a yellow-green oil. The spectral data for these diastereomers were identical to those reported above.

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Supporting Information Available: ^{13}C NMR spectral data for all new compounds and characterization data for compounds **10d**,**f**, **11a**,**e**,**f**, **13d**−**f**, **15a**,**d**−**g**, **16b**−**d**, **17a**−**h**, **18a**−**d**, **19**, **20**, **23**, and **24**. This material is available free of charge via the Internet at http://pubs.acs.org.

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