134. An Enantioselective Approach to the Taxanes: Direct Access to Functionalized *cis*-Tricyclo[9.3.1.$0^{3,8}$]pentadecanes *via* α-Hydroxy Ketone and *Wagner-Meerwein* Rearrangements[1])

by **Leo A. Paquette***, **Steven W. Elmore**[2]), **Keith D. Combrink**, and **Eugene R. Hickey**

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210, USA

and **Robin D. Rogers**[3])

Department of Chemistry, Northern Illinois University, DeKalb, Illinois 60115, USA

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The feasibility of the titled reactions for the rapid, enantioselective synthesis of *cis*-tricyclo[9.3.1.$0^{3,8}$]pentadecane precursors to taxusin and taxol has been examined. The catalysts most well suited to inducing the appropriate 1,2-shifts have been identified. To a great extent, the rearrangement products are formed as a direct consequence of appropriate structural features (kinetic phenomenon) and strain minimization (thermodynamic driving force). Complementary MM2 calculations of the global minimum in each series provided indications that were completely in line with the experimental observations. Sophisticated NMR studies and X-ray crystallographic determinations were coordinated to remove any ambiguity of product structure and solid-state conformation.

Introduction. – The two-step sequence involving 1,2-addition of optically enriched cerate **2** to enantiomerically homogeneous **1** [1] and subsequent anionic oxy-*Cope* rearrangement of carbinol **3** holds considerable synthetic promise (*Scheme 1*). Most notably, the [3,3] sigmatropic process proceeds exclusively *via* the *endo*-chair transition state [2] to deliver (*E*)-*cis*-ketone **4** in good yield after *in situ* methylation [3]. Further, the β-oriented TBSO (= (*t*-Bu)Me_2SiO) substituent contributes thermodynamically to preferred adoption by **4** of the ground-state 'carbonyl down' conformation. The union of **1** with the enantiomeric cerate **5** serves to provide access to **6**. Here the (*S*)-carbinol configuration causes the 'carbonyl up' atropisomer to be more stable [3]. Consequently, sterically controlled access to the ketone functionality in **4** and **6** should, practically speaking, be diastereospecific in opposite directions.

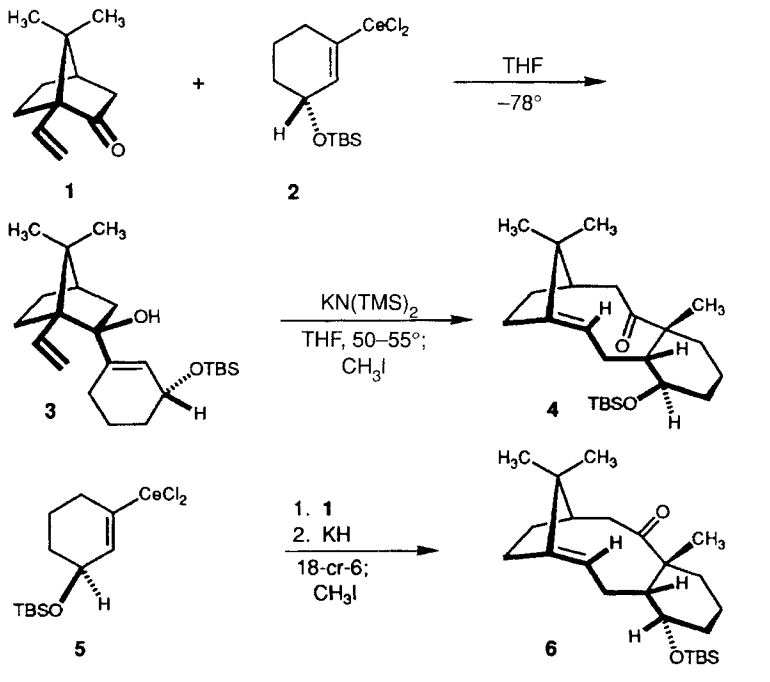
Now, that the topological aspects of these processes have been elucidated [3], an investigation of possible 1,2-migration of the C_1 bridge to arrive at functionalized tricyclo[9.3.1.$0^{3,8}$]pentadecanes has been initiated. This ring system is at the core of the taxane diterpenes, intensive study of which is being spurred on in recent years by the promising chemotherapeutic properties of taxol (**7**) [4]. The special significance of the present approach (preliminary communication: [5]) resides in its brevity, enantiospecificity, and ability to control the oxidation level of bridgehead carbon C(1) as

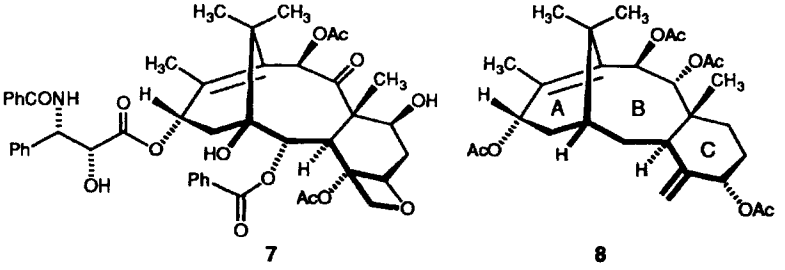
[1]) Originally presented in a lecture at the meeting celebrating the 100th Anniversary of the Geneva Conference: 'Organic Chemistry: Its Language and Its State of the Art', Geneva, April 22–24, 1992.

[2]) Chemistry Department Fellow, 1988–1989; National Needs Fellow, 1991–1992.

[3]) Author to whom inquiries should be directed regarding the X-ray crystallographic analyses.

Scheme 1

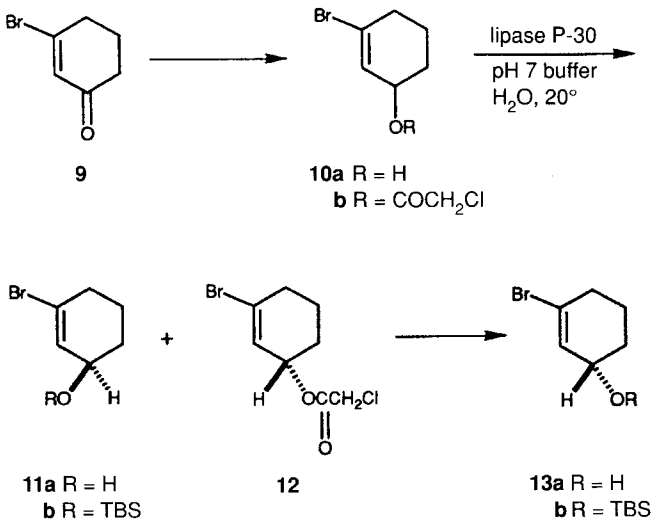




required of complementary approaches to **7** and taxusin (**8**) (isolation and characterization: [7]; synthesis of the unnatural (–)-enantiomer: [8]). While the present report details the feasibility of accomplishing these goals, the accompanying paper addresses those issues surrounding construction of the conformationally distinctive *trans*-B/C-fused congeners [8].

Results and Discussion. – *Improved Preparation of* **2** *and* **5**. Earlier, 3-bromocyclohex-2-enone (**9**) had been converted to the (*R*)- and (*S*)-carbinols by separate reaction with freshly prepared complexes of $LiAlH_4$ with DARVON and NOVRAD alcohols, respectively [3]. Although these reductions are conveniently performed and reasonably efficient,

Scheme 2

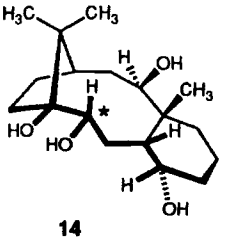


the maximum attainable levels of enantiomeric excess are 60%, and more often approach 50%. To improve on this situation, racemic **10a** was transformed into its chloroacetate **10b**, and the latter was subjected to hydrolysis with lipase P-30 [9] [10] (*Scheme 2*). This substrate underwent selective hydrolysis very rapidly in the presence of this enzyme. When reaction was allowed to proceed to 45% completion in H_2O at 20°, (*R*)-carbinol **11a** (80% ee) was obtained alongside (*S*)-chloroacetate **12** (79% ee) in an overall yield of 96%.

Following chromatographic separation and the saponification of **12** to **13a**, the (*tert*-butyl)dimethylsilyl ethers **11b** and **13b** were prepared as before, metalated, and admixed with anhydrous $CeCl_3$ to generate quantities of **2** and **5** 30% more enantiomerically enriched than heretofore.

Computational Analysis of Stereoalignment and Thermodynamic Issues Associated with Bridge Migration. The principal objective of this study was to determine the suitability of two rearrangements for transforming derivatives of **4** and **6** into *cis*-tricyclo[9.3.1.$0^{3,8}$]-pentadecanes. The literature dealing with base-induced pinacol-type eliminations of 1,2-glycol monotosylates [11] indicates that the stereoselectivity of the *Wagner-Meerwein* shift is dictated entirely by stereoalignment factors. The pathway that is followed involves expulsion of the tosylate group by that C–C bond oriented antiperiplanar to the site of C–O heterolysis.

Fig. 1, a shows a computer drawing of the global minimum of tetrol **14** as derived computationally through use of *Allinger*'s MM2 force field [12]. The structure is interesting not only because all three secondary OH groups are seen to be oriented equatorially in order to relieve nonbonded strain, but because the hypothetical leaving group at the asterisked C-atom is locked into a *trans*-relationship with the apical quaternary C-atom. The expectation, therefore, is that isomerization of a suitably activated derivative would proceed along the reaction trajectory involving 1,2-shift of this particular C-atom to give **15**.



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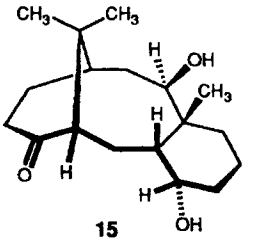

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The fact that **14** features no drastic structural distortions is reflected in the calculated E_S and E_T values of 49.4 and 67.8 kcal/mol, respectively. Analogous computational scrutiny of **15** (*Fig. 1, b*) indicates that contraction of the central ring has little effect on the overall strain energy (now 49.9 kcal/mol), but results in a favorable reduction (by 3.6

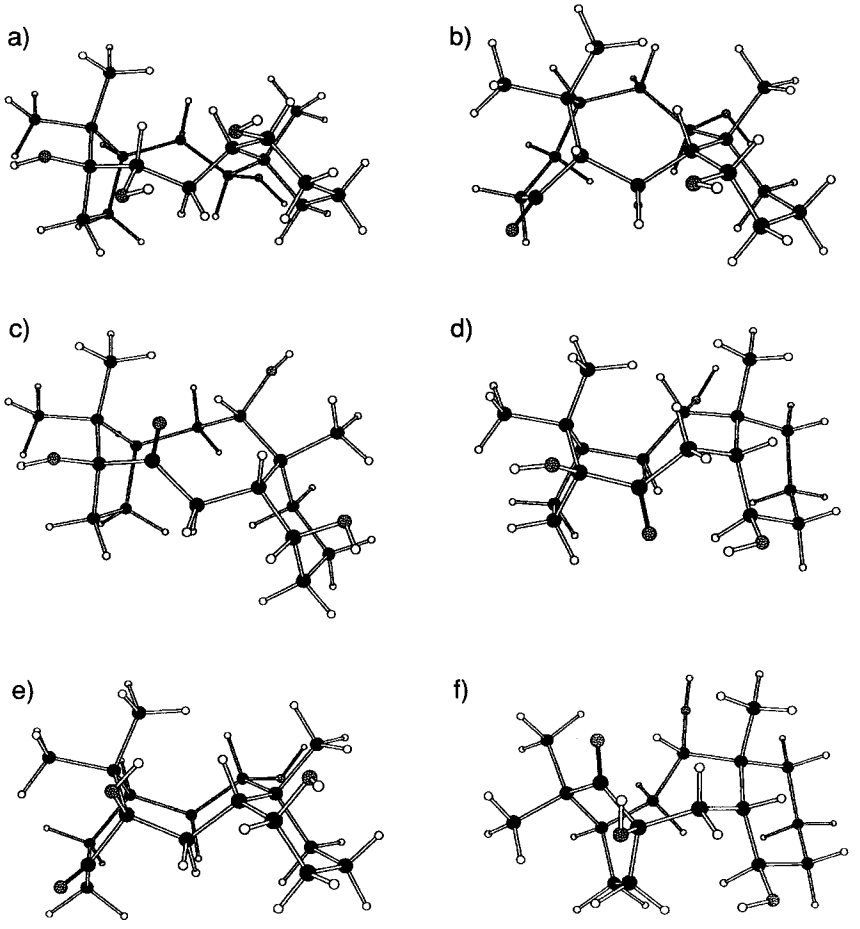
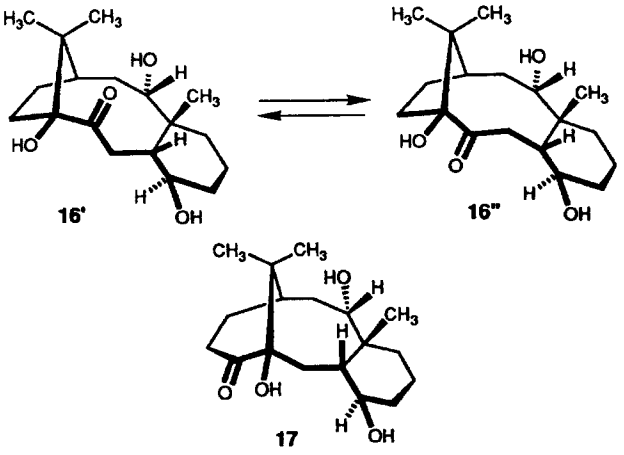


Fig. 1. *Global-minimum-energy conformations of:* a) **14**, b) **15**, c) **16′**, d) **16″**, e) **17**, *and* f) **19** *as determined by molecular mechanics calculations* (Chem-3D output)

kcal/mol) of the total strain energy. These considerations also lead to the prediction that rearrangements of molecules related to **14** should proceed as desired to generate ketones structurally akin to **15**.

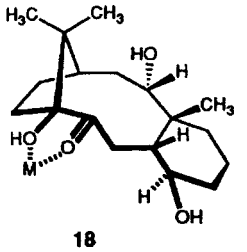
Bridgehead ketols are known for their ability to isomerize under cationic, anionic, or neutral conditions [11] [13]. Since these reactions are presumably mediated by a bridged intermediate or transition state [14], stereoelectronic factors necessarily play a decisive role. Computational assessment of the idealized geometry of ketone **16** revealed that two rather different ground-state conformations reside in close energetic proximity. The numerical estimates indicate **16′** (*Fig. 1, c*; $E_S = 54.3$ kcal/mol; $E_T = 70.0$ kcal/mol) to be only modestly more stable than **16″** (*Fig. 1, d*; $E_S = 55.2$ kcal/mol; $E_T = 70.9$ kcal/mol). Two critical regions of the molecule are affected by the conformational changes. In **16′**, the C ring is chair-like with resultant axial projection of its OH group. The torsion angles introduced by this arrangement force the C=O group residing in the nine-membered ring to orient its O-atom upward. In contrast, adoption by ring C of an equatorial disposition for its OH group provides for a chair geometry concomitant with downward flexing of the carbonyl O-atom.



The possibility that these two conformers could be in rapid equilibrium does not of itself cause concern about the projected isomerization to **17**, since the C–C bond to the quaternary methano C-atom is uniquely aligned with the carbonyl π cloud in either case.

Since the α-ketol rearrangement is an equilibrium reaction, thermodynamics plays an obvious key role in determining the direction in which bond reorganization will prefer to proceed. For this reason, we have also located the minimum-energy conformation of **17** (*Fig. 1, e*) and found it to be lower than those of either **16′** or **16″**. In fact, the E_S (50.3 kcal/mol) and E_T parameters (66.1 kcal/mol) for **17** provide solid indication that such tricyclic pentadecanones might well be favored end products.

Would this prediction be contraindicated if the catalyst involved in triggering the rearrangement held the two neighboring O-atoms coplanar as in **18**? This realignment significantly improves the status of the ethano bridge as a possible migrator. Were this to



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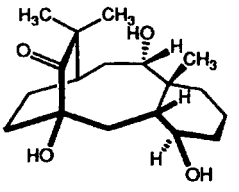

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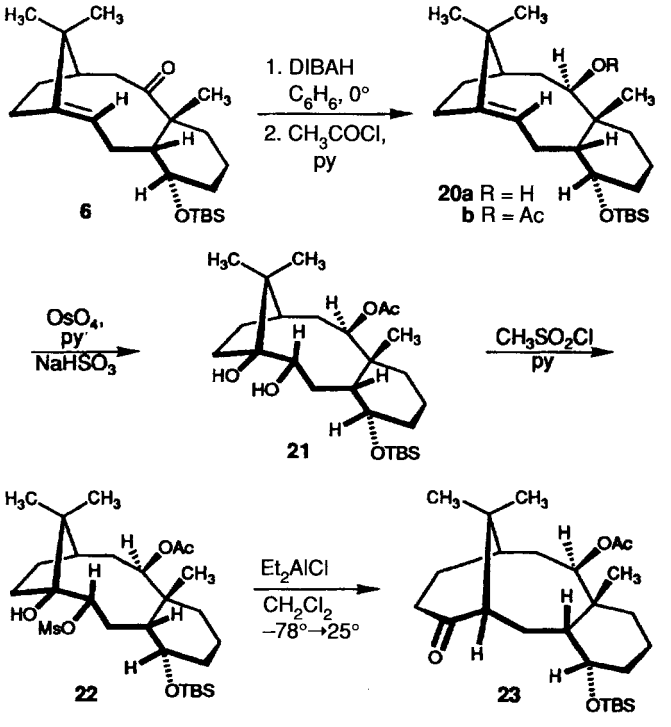
occur, **19** would be formed (*Fig. 1,f*). MM2 calculations place the E_S (50.8 kcal/mol) and E_T values (67.4 kcal/mol) of **19** decidedly below those of **16′** and **16″**, and modestly above those of **17**. The indication is, therefore, that **17** should persist as the thermodynamic product under fully reversible conditions.

Implementation of the Wagner-Meerwein *Rearrangement.* Ketones such as **4** and **6** possess a sterically hindered C=O group in close transannular proximity to the C=C bond. As a consequence, exposure of **6** to $LiAlH_4$ does not eventuate in 1,2-hydride addition, but to slow transannular reduction with formation of a tertiary alcohol [15]. To circumvent this unwanted reaction and achieve stereocontrolled conversion to **20a**, recourse was made to diisobutylaluminum hydride (DIBAH) *in benzene solution* at 0° (*Scheme 3*). In this medium, the DIBAH reagent does not coordinate to the solvent. Its

Scheme 3



effective size remains relatively small, and reduction proceeds effectively (76% of **20a**). Attempts to substitute THF failed to achieve any reaction, since complexation involving this solvent enhances the bulkiness of the reducing agent beyond useful limits. The configuration of the carbinol C-atom in **20a** was initially inferred from the absence of an NOE effect between the *syn*-apical Me group and the C*H*(OH) proton. Conclusive corroboration was achieved somewhat later, when X-ray data for **23** became available.

The *cis*-dihydroxylation of **20b** proceeds slowly in pyridine at room temperature with complete diastereofacial control to deliver **21** after decomposition of the osmate ester with $NaHSO_3$. The availability of **21** permitted conversion to monomesylate **22**. This intermediate proved unsuited to chromatography on silica gel or *Biosil*® and slowly decomposed simply on standing at 25° for 12–15 h. Storage, when necessary, was, therefore, best achieved by freezing benzene solutions at −20°. The instability of **22** may be partly responsible for the modest-yield conversion to **23** (45%). Of the various catalysts screened for their ability to promote the *Wagner-Meerwein* rearrangement, diethylaluminum chloride emerged as the most suitable. After 12 h in CH_2Cl_2 at −78° to 25°, **23** was isolated chromatographically as the only isomerized ketone. Also produced in small amounts was a mixture of aldehydes whose identities were not sought.

To establish beyond doubt the absolute configuration of **23**, a single-crystal X-ray analysis was undertaken. The ORTEP diagram resulting from this study (*Fig. 2*) disclosed further that both six-membered rings prefer to adopt chair conformations.

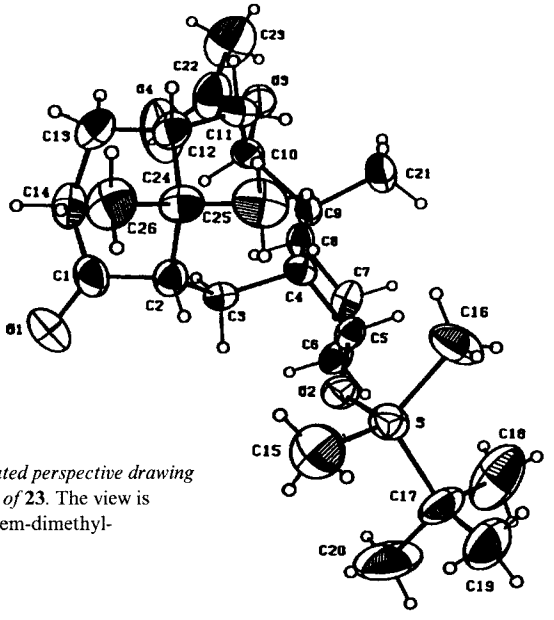
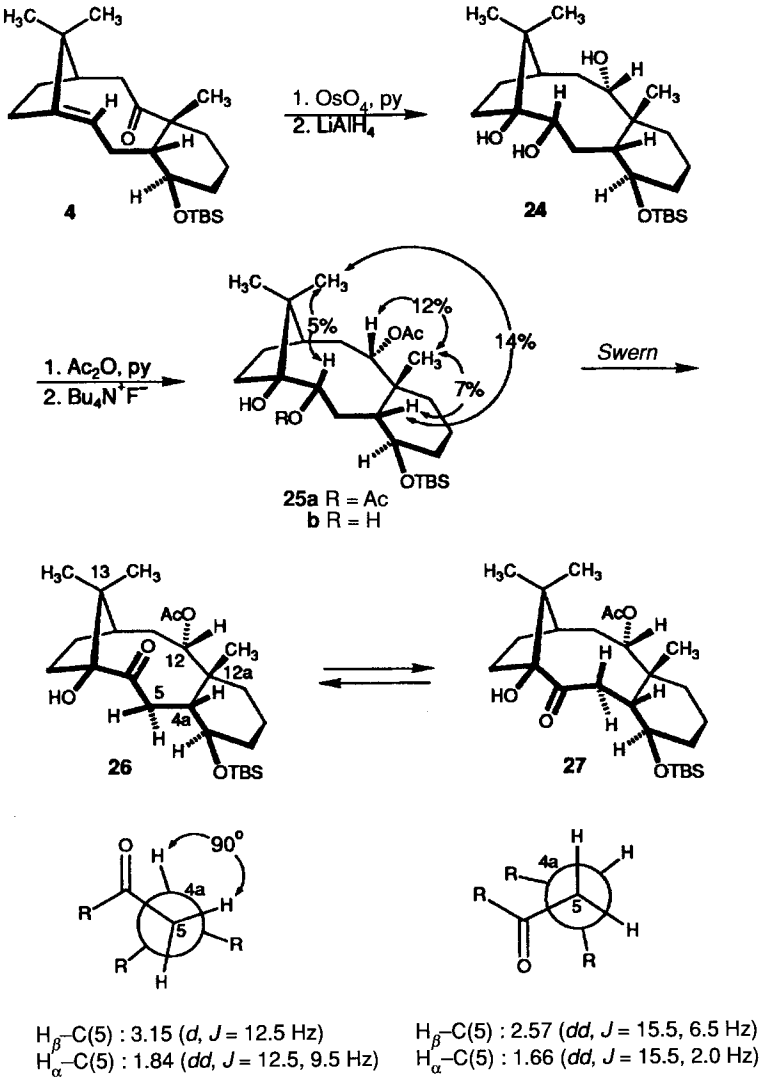


Fig. 2. *Computer-generated perspective drawing of the final X-ray model of* **23**. The view is from above the apical gem-dimethyl-substituted C-atom.

The α-Ketol Protocol for Bridgehead Hydroxylation. In our hands, it has not proven possible to effect direct hydride addition to ketone **4** in order to generate the unsaturated α-carbinol. The transannular process cannot be properly circumvented. Saturation of the central C=C bond of these systems is known to be accompanied by an increase in

Scheme 4



conformational mobility, unless a cycloaddition is involved. For example, epoxide derivatives give evidence of high conformational rigidity [3]. The osmate ester of **4**, formed by reaction with OsO_4 in pyridine, appears to be equally inflexible, since direct $LiAlH_4$ reduction of this intermediate leads efficiently and exclusively to triol **24** (91%, *Scheme 4*). Interestingly, diol **25b** was the sole product obtained following treatment of diacetate **25a** with tetrabutylammonium fluoride (TBAF) in THF at room temperature for 12 h. The reductive deacylation presumably occurs *via* vicinal α-OH-assisted nucleophilic attack by F^- ion. This process occurs considerably faster than desilylation, which

can be accomplished by heating **25b** with TBAF in THF for an additional 48 h [16]. NOE studies performed on **25b** at 300 MHz served to confirm the configurational assignments; the key interactions are indicated in the formula.

The selective deprotection that makes **25b** conveniently available was used to advantage. Oxidation under *Swern* conditions led to an inseparable mixture of the α-ketol conformers **26** and **27**. Identification of the two constituents was achieved by means of a series of NMR experiments. Thus, a presaturation-delay sequence allowed detection of chemical exchange (or cosaturation) between the *CH*(OAc) protons in the major (*d* at 4.90 ppm) and minor (*m* at 5.10 ppm) acetates. A rapid dynamic equilibrium on the NMR time scale is, therefore, necessarily operative. The lack of H_β–C(4) coupling to H–C(4a) in the more prevalent conformer requires a 90° dihedral angle that can be achieved only with the 'carbonyl up' arrangement present in **26** (see *Scheme 4*). Appropriately, the same protons interact strongly in **27** as required of the considerably smaller dihedral angle involved. NOE studies served to provide insight into the spatial arrangement in the rear sector of ring B. In particular, the observed interaction of H–C(12) with the Me groups at C(12) and C(13) can only be satisfied by a pseudoequatorial AcO substituent.

A chemical consequence of α-AcO configuration at C(12) surfaced, when attempts were made to bring about the α-ketol rearrangement under basic conditions. Treatment of the 4:1 mixture with *t*-BuOK in refluxing *t*-BuOH proceeded smoothly to deliver a single product (89% isolated) during 8 h. AcOH was lost to give *trans*-fused cyclobutane **29a** as confirmed by X-ray diffraction analysis of the suitably crystalline 3,5-dinitrobenzoate derivative **29c** (*Fig. 3*). This remarkable ring closure, which can be effected equally

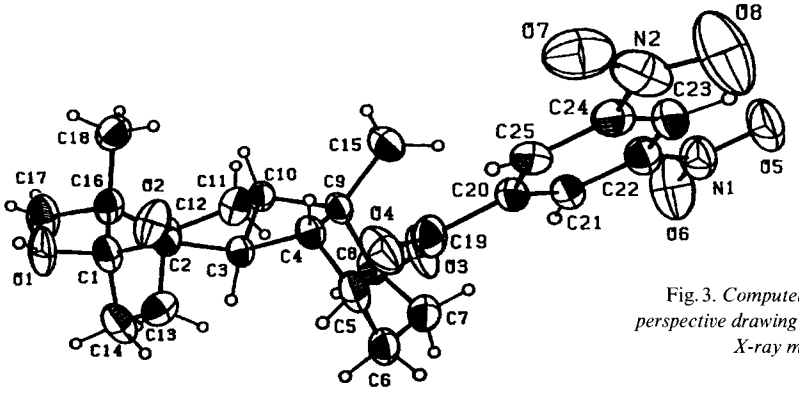
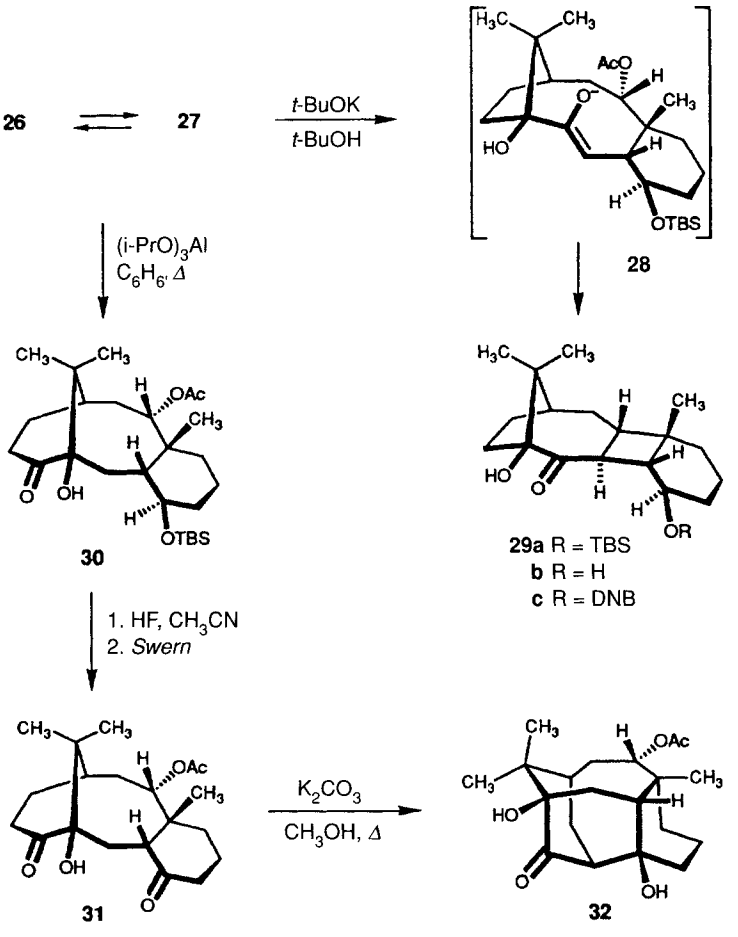


Fig. 3. *Computer-generated perspective drawing of the final X-ray model of* **29c**

well with TBAF in THF at room temperature, requires that the (*Z*)-enolate be formed first (*Scheme 5*). The reactive centers in this intermediate are felicitously aligned for facile intramolecular S_N2 displacement of acetate ion.

At this point, attention was turned to *Lewis* acidic catalysis of the desired α-ketol rearrangement. Heating **26**/**27** in $CDCl_3$ at 60° in an NMR tube for 2 days brought about no detectable change. Stirring with Et_2AlCl in benzene at 25° was likewise ineffective. Success was achieved, however, upon heating the ketols with 3 equiv. of $(i\text{-PrO})_3Al$ in refluxing benzene overnight. In the presence of this catalyst, isomerization was efficient

Scheme 5



(90%) and afforded tricyclopentadecanone **30** as a 9:1 mixture of dynamic conformational isomers. Knowledge of the precise stereoalignment within these α-ketols was not sought. However, to remove any ambiguity, **30** was converted to the more highly crystalline diketone **31** for X-ray structure determination (*Fig. 4*). This compound, which exists as a single conformational species at room temperature, is capable of sufficient coiling to undergo rapid intramolecular aldol reaction when heated with K_2CO_3 in MeOH. The conversion to **32** has given every indication of being irreversible. Indeed, significant levels of nonbonded steric interaction are relieved when advancing from **31** to **32**.

Conclusion. – The success realized in arriving at optically pure **23** and **30** in 7 and 8 steps, respectively, from **1** has established the viability of the *Wagner-Meerwein* and α-ketol rearrangements for delivering functionalized *cis*-tricyclo[9.3.1.$0^{3,8}$]pentadecanes. The nature of the substituent at C(1) rests directly on the level of oxidation of the

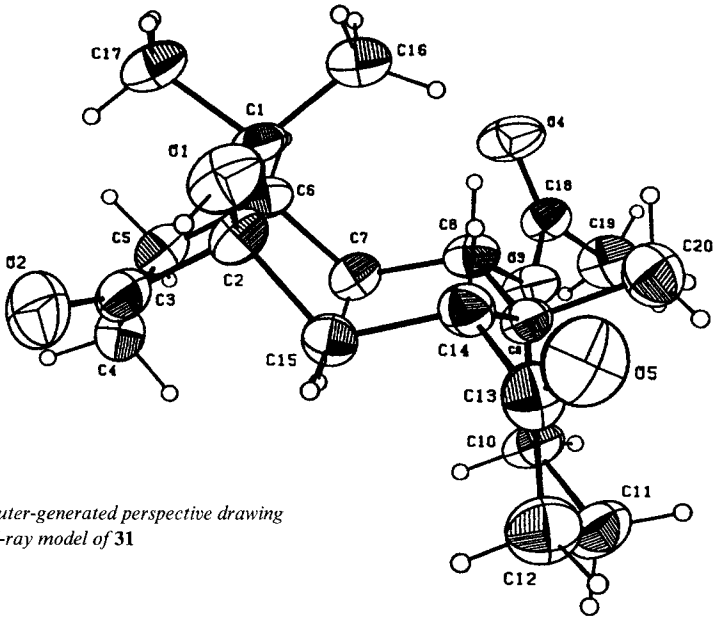


Fig. 4. *Computer-generated perspective drawing of the final X-ray model of* **31**

immediate rearrangement precursors and can be easily controlled. As a result, the tactics outlined here could serve as the basis of enantiospecific syntheses of taxol (**7**) and taxusin (**8**). There exists the need to demonstrate crossover to the *trans*-B/C series, and this accomplishment is described in the ensuing paper [8]. More advanced pursuit of **7** and **8** is in progress and will be reported in due course.

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Experimental Part

General. M.p.: uncorrected. The column chromatographic separations were performed with *Woelm* silica gel (230–400 mesh). Solvents were reagent grade and in most cases dried prior to use. The purity of all compounds was shown to be $\geq 95\%$ by TLC and high-field ^{1}H-NMR analyses. ^{1}H-NMR spectra: at 300 MHz. ^{13}C-NMR spectra: at 75 MHz. High-resolution and fast-atom-bombardment MS: obtained by *Dick Weisenberger* and *David Chang* of The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

3-Bromocyclohex-2-enyl Chloroacetate (**10b**). A cold (0°), magnetically stirred soln. of **10a** [17] (5.19 g, 29.5 mmol) and Et_3N (4.70 ml, 62 mmol) in dry CH_2Cl_2 (150 ml) was blanketed with N_2 and treated dropwise with $ClCH_2COCl$ (6.66 g, 59 mmol) during 30 min. After an additional 30 min at this temp., the mixture was poured onto crushed ice (200 ml) and the phases were separated. The aq. layer was extracted with CH_2Cl_2 (2 × 50 ml) and the combined org. solns. were washed with H_2O (2 × 50 ml) and brine (2 × 50 ml) prior to drying. Solvent evaporation left a black oil that was purified by column chromatography (elution with 4% AcOEt in petroleum ether): 6.43 g (87%) of racemic **10b**. IR (neat): 1750. ^{1}H-NMR ($CDCl_3$): 6.15 (*m*, 1 H); 5.29 (*m*, 1 H); 4.03 (*s*, 2 H); 2.56–2.42 (*m*, 2 H); 1.92–1.68 (series of *m*, 4 H). ^{13}C-NMR ($CDCl_3$): 166.4; 130.1; 126.0; 70.5; 40.8; 34.8; 26.5; 20.0. MS: M^+ calc.: 251.9750, observed: 251.9726.

Lipase-Promoted Hydrolysis of **10b**. Into a 250-ml flask was placed 100 ml of a 9:1 mixture of H_2O and commercial pH 7.0 buffer, 4.70 g (18.6 mmol) of **10b**, and 3 ml of THF to improve solubility. A 30-ml syringe was charged with 16.8 ml of 0.5M NaOH soln. (8.4 mmol) and fastened to a syringe pump that was interfaced with a pH controller. The pH of the mixture was adjusted to 7.5. *Lipase* (0.05 g) was now introduced and the syringe needle inserted into the flask. With the pH controller set at 7.4 and the syringe flow rate at 0.78 ml/min, the kinetic resolution was allowed to proceed. The base was fully consumed after 90 min, at which point the mixture was extracted with Et_2O (6 × 50 ml) and the combined org. layers were washed with brine (3 × 20 ml) and dried. Solvent evaporation and chromatography of the residue (elution with 10% AcOEt in petroleum ether) gave 1.41 g (43%) of *(R)-3-Bromocyclohex-2-enol* (**11a**) and 2.47 g (53%) of (*S*)-chloroacetate **12**.

Alcohol **11a** was determined to have $[\alpha]_D^{21} = +31.7$ ($c = 2.8$, $CHCl_3$) corresponding to 80.1% ee (*Mosher*-ester analysis). Conversion of this material to **11b** as described in [3] gave product exhibiting $[\alpha]_D^{21} = +29.8$ ($c = 3.5$, $CHCl_3$).

A 6.52-g (25.9 mmol) sample of **12** was dissolved in MeOH (100 ml) and treated with 50 ml of 1N NaOH soln. Hydrolysis was complete in less than 5 min. The mixture was diluted sequentially with brine and AcOEt until immiscible layers were formed. The aq. phase was extracted with AcOEt (3 × 75 ml) and the combined org. layers were washed with H_2O (2 × 20 ml) and brine (2 × 20 ml) prior to drying. Concentration and chromatography (elution with 20% AcOEt in petroleum ether) afforded 4.51 g (99%) of **13a**. $[\alpha]_D^{25} = -32.4$ ($c = 1.5$, $CHCl_3$).

*(1S,4aR,5R,7R,10E,12aR)-1-[(*tert*-Butyl)dimethylsilyloxy]-1,2,3,4,4a,5a,6,7,8,9,12,12a-dodecahydro-4a,13,13-trimethyl-7,10-methanobenzocyclodecen-5-ol* (**20a**). A soln. of **6** [3] (120 mg, 0.308 mmol) in cold (0°), dry benzene (20 ml) was treated with DIBAH (0.37 ml of 1.0M in hexanes, 0.37 mmol). After 1 h, the ice-bath was removed, an additional 0.20 ml of DIBAH was introduced, and stirring was continued for 2 h. The mixture was treated with sat. sodium potassium tartrate soln. (20 ml) and stirred overnight. The aq. layer was separated and extracted with Et_2O (3 × 20 ml). The combined org. solns. were washed with H_2O (20 ml) and sat. brine (20 ml) prior to drying and evaporation. Chromatography of the residue (elution with 8% AcOEt in petroleum ether) gave 92.0 mg (76%) of **20a** as a white solid. M.p. 119–121°. IR ($CHCl_3$): 3610, 3418. ^{1}H-NMR ($CDCl_3$): 4.87 (*d*, $J = 11.3$, 1 H); 3.87 (*dt*, $J = 11.8, 4.3$, 1 H); 3.13 (*d*, $J = 6.1$, 1 H); 2.47 (*dd*, $J = 13.1, 2.9$, 1 H); 2.23–2.14 (*m*, 2 H); 2.01–1.79 (*m*, 2 H); 1.79–1.75 (*m*, 1 H); 1.65 (*dd*, $J = 5.8, 8.5$, 1 H); 1.60–1.17 (*m*, 7 H); 1.14 (*s*, 3 H); 1.05 (*s*, 3 H); 1.14–0.94 (*m*, 3 H); 0.90 (*s*, 9 H); 0.88 (*s*, 3 H); 0.07 (*s*, 3 H); 0.06 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 141.6; 125.4; 75.9; 70.4; 54.9; 46.7; 42.8; 42.6; 31.8; 31.2; 30.6; 26.1; 25.9; 25.0; 23.0; 21.8; 20.5; 20.3; 18.1; 16.2; –4.5; –4.7. MS: M^+ calc.: 392.3110; observed: 392.3106. Anal. calc. for $C_{24}H_{44}O_2Si$: C 73.41, H 11.29; found: C 73.48, H 11.21.

*(1S,4aR,5R,7R,10E,12aR)-1-[(*tert*-Butyl)dimethylsilyloxy]-1,2,3,4,4a,5,6,7,8,9,12,12a-dodecahydro-4a,13,13-trimethyl-7,10-methanobenzocyclodecen-5-yl Acetate* (**20b**). A soln. of **20a** (133 mg, 0.339 mmol) in CH_2Cl_2 (20 ml) at 0° was treated with pyridine (0.82 ml, 1.02 mmol) and AcCl (36 µl, 0.51 mmol). The mixture was stirred for 15 h, poured into H_2O (20 ml), and diluted with Et_2O (20 ml). The separated aq. layer was extracted with Et_2O (3 × 20 ml), and the combined org. layers were dried and concentrated. Chromatography of the residue (elution with 3% AcOEt in petroleum ether) gave **20b** (120 mg, 82%) as a white solid. M.p. 138–139.5° (from Et_2O). IR ($CHCl_3$): 1728. ^{1}H-NMR ($CDCl_3$): 4.86 (*d*, $J = 11.2$, 1 H); 4.75 (*d*, $J = 5.3$, 1 H); 3.82 (*dt*, $J = 4.3, 11.7$, 1 H); 2.56–2.46 (*m*, 2 H); 2.18–2.03 (*m*, 2 H); 2.01 (*s*, 3 H); 2.00–1.83 (*m*, 2 H); 1.60–1.42 (*m*, 4 H); 1.41–1.14 (*m*, 5 H); 1.12 (*s*, 3 H); 1.05 (*s*, 3 H); 0.91 (*s*, 3 H); 0.89 (*s*, 9 H); 1.02–0.87 (*m*, 1 H); 0.06 (*s*, 3 H); 0.05 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 170.6; 141.8; 125.5; 79.2; 70.1; 55.4; 47.1; 43.4; 43.3; 31.1; 30.5; 29.2; 25.8; 25.7; 24.7; 23.1; 22.1; 21.5; 20.6; 20.3; 18.1; 16.9; –4.5; –4.7. MS: $[M^+ - AcOH]^+$ calc. 374.3005; observed: 374.2981. Anal. calc. for $C_{26}H_{46}O_3Si$: C 71.83, H 10.66; found: C 71.82, H 10.64.

*(1S,4aR,4R,10S,11S,12R)-1-[(*tert*-Butyl)dimethylsilyloxy]perhydro-10,11-dihydroxy-4a,13,13-trimethyl-7,10-methanobenzocyclodecene-5-yl Acetate* (**21**). Acetate **20b** (751 mg, 1.73 mmol) dissolved in pyridine (5 ml) was treated with a soln. of OsO_4 (0.5 g, 1.9 mmol) in pyridine (5 ml) and stirred at 25° for 4 d. Additional OsO_4 (25 mg) was introduced, and the mixture was heated at 40° for 12 h. The osmate ester was hydrolyzed with 10% $NaHSO_3$ soln. (10 ml) at 40° for 24 h. Additional $NaHSO_3$ soln. (20 ml) was added, and the mixture was stirred at 40–50° for 24 h, filtered through *Celite*, and concentrated. Chromatography of the residue (elution with 10% AcOEt in petroleum ether) gave **21** (317.6 mg, 24%) as a white solid. M.p. 172–174°. $[\alpha]_D^{19} = -5.26$ ($c = 0.76$, $CHCl_3$). IR ($CHCl_3$): 3610, 3510, 1722. ^{1}H-NMR ($CDCl_3$): 5.08 (*d*, $J = 6.3$, 1 H); 4.07 (*dt*, $J = 4.06, 10.5$, 1 H); 3.64 (*d*, $J = 7.8$, 1 H); 2.34–2.18 (*m*, 3 H); 2.13–2.02 (*m*, 3 H); 1.98 (*s*, 3 H); 1.81–1.65 (*m*, 1 H); 1.62–1.39 (*m*, 8 H); 1.39–1.12 (*m*, 3 H); 1.11 (*s*, 3 H); 1.05 (*s*, 3 H); 0.99 (*s*, 3 H); 0.90 (*s*, 9 H); 0.07 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$): 170.5; 85.9; 77.2; 76.9; 70.5; 47.9; 44.4; 42.9; 41.4; 32.4; 31.9; 30.4; 29.5; 29.3; 27.9; 25.9; 21.8; 21.3; 20.0; 19.4; 18.2; 16.9; –4.69; –4.71. MS: M^+ calc. 468.3271; observed: 468.3360. Anal. calc. for $C_{26}H_{48}O_5Si$: C 66.62, H 10.32; found: C 66.75, H 10.33.

In a separate experiment, the osmate ester was isolated in 81% yield, when the $NaHSO_3$ hydrolysis was stopped after 6 h at 25°. ^{1}H-NMR ($CDCl_3$): 8.78 (*d*, *J* = 5.1, 4 H); 7.78 (*tt*, *J* = 5.1, 1.5, 2 H); 7.41 (*t*, *J* = 6.7, 4 H); 5.32 (*m*, 1 H); 4.33 (*d*, *J* = 9.4, 1 H); 4.04 (*dt*, *J* = 7.1, 9.8, 1 H); 2.59 (*dd*, *J* = 4.3, 9.7, 1 H); 2.55–2.41 (*m*, 1 H); 2.32–2.02 (*m*, 4 H); 1.99 (*s*, 3 H); 1.90–1.70 (*m*, 2 H); 1.60–1.26 (*m*, 8 H); 1.24 (*s*, 3 H); 1.16 (*s*, 3 H); 1.06 (*s*, 3 H); 1.01 (*s*, 9 H); 0.09 (*s*, 3 H); 0.06 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 170.2; 149.7 (2C); 139.5; 124.7 (2C); 99.8; 94.9; 76.9; 70.0; 48.2; 46.4; 43.4; 41.7; 32.5; 30.5; 29.9; 29.4; 29.2; 28.1; 26.0; 22.3; 21.3; 20.5; 19.9; 18.1; 16.5; –4.5; –4.8.

*(1*S*,4a*R*,4*R*,10*S*,11*S*,12*R*)-1-[(*tert*-Butyl)dimethylsilyloxy]perhydro-10-hydroxy-11-(methanesulfonyloxy)-4a,13,13-trimethyl-7,10-methanobenzocyclodecene-5-yl Acetate* (**22**). A soln. of **21** (110.5 mg, 0.236 mmol) in pyridine (3 ml) was treated with MsCl (110 µl, 1.42 mmol), stirred overnight at r.t., diluted with CH_2Cl_2 (50 ml), and washed with H_2O (10 ml), 0.1N HCl (4 × 20 ml), sat. $CuSO_4$ soln. (2 × 20 ml), H_2O (10 ml), and brine (10 ml). The org. phase was dried and evaporated to give 122 mg (95%) of **22**. Due to its instability, **22** was used directly without further purification. ^{1}H-NMR (300 MHz, C_6D_6): 5.22 (*d*, *J* = 5.4, 1 H); 4.93 (*dd*, *J* = 10.1, 1.1, 1 H); 4.04 (*m*, 1 H); 2.70 (*s*, 3 H); 2.47–2.20 (*m*, 2 H); 2.20–1.70 (series of *m*, 9 H); 1.68 (*s*, 3 H); 1.54–1.16 (*m*, 6 H); 1.16 (*s*, 3 H); 1.11 (*s*, 3 H); 0.97 (*s*, 9 H); 0.94 (*s*, 3 H); 0.15 (*s*, 3 H); 0.14 (*s*, 3 H). ^{13}C-NMR (75 MHz, C_6D_6): 169.6; 91.4; 85.7; 75.7; 71.2; 51.5; 49.2; 46.0; 41.9; 41.6; 39.2; 34.2; 33.0; 30.6; 29.0; 27.6; 26.5; 22.8; 20.8; 20.2; 19.8; 19.0; 16.6; –4.5.

*(4*S*,4a*R*,6*S*,10*R*,12*R*,12a*R*)-4-[(*tert*-Butyl)dimethylsilyloxy]perhydro-12a,13,13-trimethyl-7-oxo-6,10-methano-1*H*-benzocyclodecen-12-yl Acetate* (**23**). A cold (–78°), magnetically stirred soln. of unpurified **22** (122 mg, 0.223 mmol) in CH_2Cl_2 (10 ml) was treated with diethylaluminum chloride (1.11 ml of 1.0M in hexane, 1.11 mmol) and allowed to warm slowly to 25° during 12 h. The mixture was diluted with Et_2O (50 ml) and washed with H_2O (20 ml). The separated aq. phase was extracted with Et_2O (2 × 50 ml), and the combined org. solns. were washed with brine, dried, and concentrated. The residue was chromatographed (elution with 10% AcOEt in petroleum ether) to give **23** (45.6 mg, 46%) and a mixture of unidentified aldehydes (9 mg).

Data of **23**: white solid. M.p. 162–165° (from AcOEt/hexane). $[\alpha]_D^{21} = +40.9$ (*c* = 0.45, $CHCl_3$). IR ($CHCl_3$): 1718, 169. ^{1}H-NMR ($CDCl_3$): 5.08 (*d*, *J* = 8.4, 1 H); 3.90 (*dt*, *J* = 11.7, 4.6, 1 H); 3.18–3.05 (*m*, 1 H); 2.39 (*td*, *J* = 15.9, 8.5, 1 H); 2.30–2.18 (*m*, 5 H); 2.08–1.98 (*m*, 2 H); 2.04 (*s*, 3 H); 1.68 (*t*, *J* = 7.1, 1 H); 1.55–1.30 (*m*, 4 H); 1.30–1.18 (*m*, 3 H); 1.26 (*s*, 3 H); 1.07 (*s*, 3 H); 0.94 (*s*, 3 H); 0.89 (*s*, 9 H); 0.04 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$): 214.7; 170.4; 78.1; 69.5; 56.7; 41.5; 40.8; 39.0; 38.3; 34.4 (2C); 33.8; 29.6; 29.5; 28.2; 25.8; 24.3; 22.9; 21.3; 20.1; 18.0; 16.7; –4.5; –4.9. MS: $[M - CH_3]^+$ calc.: 435.2930; observed: 435.2953. Anal. calc. for $C_{26}H_{46}O_4Si$: C 69.29, H 10.29; found: C 69.24, H 10.35.

X-Ray Data Collection, Structure Determination, and Refinement for **23**. A transparent single crystal of **23** was mounted on a pin and transferred to the goniometer. The space group was determined to be the acentric $P2_12_12_1$ from the systematic absences. A summary of data collection parameters is given in the *Table*.

Table. *Crystal Data and Summary of Intensity Data Collection and Structure Refinement*

	23	**29c**	**31**
Formula	$C_{26}H_{46}O_4Si$	$C_{25}H_{30}N_2O_8$	$C_{20}H_{30}O_5$
Color/shape	colorless/parallelepiped	colorless/parallelepiped	colorless/parallelepiped
Formula wt.	450.74	486.52	350.46
Space group	$P2_22_12_1$	$P2_12_12_1$	$P2_1$
Temp. [°C]	18	18	18
Cell constants[a])			
a [Å]	10.664(5)	6.764(3)	7.434(8)
b [Å]	12.458(6)	18.324(6)	9.738(7)
c [Å]	20.090(8)	19.252(5)	13.093(9)
β [deg]			104.45(9)
Cell vol. [Å^3]	2669.0	2386	917.8
Formula units/unit cell	4	4	2
D_{calc} [g cm^{-3}]	1.12	1.35	1.27
μ_{calc} [cm^{-1}]	1.19	1.09	0.96
Diffractometer/scan	*Enraf-Nonius CAD-4/*$\omega - 2\theta$	*Enraf-Nonius CAD-4/*$\omega - 2\theta$	*Enraf-Nonius CAD-4/*$\omega - 2\theta$
Radiation, graphite monochromator	MoK_α (λ = 0.71073)	MoK_α (λ = 0.71073)	MoK_α (λ = 0.71073)

Table (cont.)

	23	**29c**	**31**
Max. crystal dimensions [mm]	0.25 × 0.30 × 0.45	0.20 × 0.23 × 0.30	0.15 × 0.18 × 0.45
Scan width	$0.80 + 0.35 \tan\theta$	$0.80 + 0.35 \tan\theta$	$0.80 + 0.35 \tan\theta$
Standard reflections	354, $\bar{3}5\bar{4}$, 456, $\bar{4}5\bar{6}$, 451, $\bar{4}5\bar{1}$	400; 060; 006	$2\bar{1}\bar{7}$, $3\bar{1}\bar{6}$, $3\bar{1}\bar{6}$, $1\bar{4}\bar{5}$, $3\bar{4}\bar{4}$, $\bar{1}4\bar{3}$, $2\bar{1}\bar{6}$
Decay of standards	± 2%	± 1%	± 2%
Reflections measured	2683	2430	1846
2θ range [deg]	$2 \leqslant 2\theta \leqslant 50$	$2 \leqslant 2\theta \leqslant 50$	$2 \leqslant 2\theta \leqslant 50$
Range of h, k, l	+12, +14, +24	+8, +21, +22	+8, +11, ±15
Reflections observed [$F_0 \geq 5\sigma(F_0)$][b])	1726	1389	1114
Computer programs[c])	SHELX [18]	SHELX [18]	SHELX [18]
Structure solution	SHELXS [20]	SHELXS [20]	SHELXS [20]
No. of parameters varied	307	325	237
Weights	$[\sigma(F_0)^2 + 0.00004\ F_0^2]^{-1}$	$[\sigma(F_0)^2 + 0.00004\ F_0^2]^{-1}$	$[\sigma(F_0)^2 + 0.0008\ F_0^2]^{-1}$
GOF	2.99	2.76	1.58
$R = \Sigma\|\|F_0\| - \|F_c\|\|\Sigma\|F_0\|$	0.058	0.056	0.056
R_w	0.059	0.060	0.071
R inverse configuration	0.059	0.058	0.056
Largest feature final diff. map	$0.9\,e^{-1}$ Å^{-3} near Si	$0.2\,e^{-1}$ Å^{-3}	$0.2\,e^{-1}$ Å^{-3}

[a]) Least-squares refinement of $((\sin\theta)/\lambda)^2$ values for 25 reflections $\theta > 20°$ (for **23**), $> 16°$ (for **29c**), and $> 10°$ (for **31**).

[b]) Corrections: *Lorentz* polarization.

[c]) Neutral scattering factors and anomalous dispersion corrections from [19].

Least-squares refinement with isotropic thermal parameters led to $R = 0.120$. The geometrically constrained H-atoms were placed in calculated positions 0.95 Å from the bonded C-atom and allowed to ride on that atom with B fixed at 5.5 Å^2. The Me H-atoms were included as a rigid group with rotational freedom at the bonded C-atom (C–H = 0.95 Å, B = 5.5 Å^2). The absolute configuration was determined from the attachment of the Si group with known configuration. Refinement of non-H-atoms with anisotropic temp. factors led to the final values of $R = 0.058$ and $R_w = 0.059$.

*(1*R*,4a*R*,5*S*,7*R*,10*S*,11*S*,12a*R*)-1-[(*tert*-Butyl)dimethylsilyloxy]perhydro-4a,13,13-trimethyl-7,10-methanobenzocyclodecene-5,10,11-triol* (**24**). Into a soln. of **4** (766 mg, 1.96 mmol) in dry pyridine (25 ml) was syringed 15.0 ml of a 0.157M soln. of OsO_4 in pyridine (2.36 mmol). The resulting black soln. was stirred magnetically under N_2 for 6 h, when TLC indicated **4** to be completely consumed. Following removal of pyridine at 0.1 Torr and 25°, the black residue was dissolved in anh. THF (45 ml), treated with $LiAlH_4$ (745 mg, 19.6 mmol), and stirred at r.t. for 24 h. Water was carefully introduced, the mixture was filtered through *Celite*, and the filtrate was washed with H_2O and brine. The aq. washing was extracted with AcOEt, and the combined org. solns. were dried and concentrated. Chromatographic purification of the tan solid (elution with 5% EtOH/45% hexane/50% AcOEt) afforded **24** (760 mg, 91%) as a fluffy white solid. M.p. 155–158°. $[\alpha]_D^{20} = +3.5$ (c = 2.4, $CHCl_3$). IR ($CHCl_3$): 3620, 3540. ^{1}H-NMR ($CDCl_3$): 3.80 (*d*, J = 1.8, 1 H); 3.58 (*m*, 1 H); 3.42 (*d*, J = 8.4, 1 H); 2.97 (*m*, 1 H); 2.78 (*d*, J = 1.4, 1 H); 2.48 (*dd*, J = 8.8, 15.7, 2 H); 2.3–2.14 (series of *m*, 3 H); 2.01–1.13 (series of *m*, 11 H); 1.13 (*s*, 3 H); 1.07 (*s*, 6 H); 1.05–0.90 (*m*, 1 H); 0.87 (*s*, 9 H); 0.04 (*s*, 3 H); 0.03 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 87.8; 85.2; 76.6; 71.2; 48.4; 47.6; 44.0; 40.2; 33.4; 32.0; 30.1; 29.9; 28.4; 27.2; 26.4; 25.7; 21.6; 19.4; 17.8; 16.3; −4.9; −5.0. FAB-MS: $[M - 1]^+$ calc.: 427.43; observed: 427.15.

*(1*R*,4a*R*,5*S*,7*R*,10*S*,11*S*,12a*R*)-1-[(*tert*-Butyl)dimethylsilyloxy]perhydro-10-hydroxy-4a,13,13-trimethyl-7,10-methanobenzocyclodecene-5,11-diyl Diacetate* (**25a**). To a magnetically stirred soln. of **24** (223 mg, 0.523 mmol) and several crystals of 4-(dimethylamino)pyridine in dry pyridine (10 ml) was added *via* syringe under N_2 5 ml of Ac_2O. The mixture was stirred at r.t. for 12 h, diluted with AcOEt (50 ml), and washed sequentially with H_2O, 1M HCl, sat. $NaHCO_3$ soln., and brine. The org. phase was dried and evaporated to leave a clear residual oil that was purified by chromatography (elution with 10% AcOEt in petroleum ether). There was isolated 229 mg (85%)

of **25a** as a white foam. M.p. 58–61°. $[\alpha]_D^{20} = +29.6$ ($c = 1.5$, $CHCl_3$). IR ($CHCl_3$): 3600, 1730. ^{1}H-NMR ($CDCl_3$): 4.78 (*d*, $J = 8.1$, 1 H); 4.71 (*d*, $J = 9.0$, 1 H); 4.08 (*m*, 1 H); 2.50–2.10 (series of *m*, 6 H); 2.05 (*s*, 3 H); 2.04 (*s*, 3 H); 2.0–1.6 (series of *m*, 6 H); 1.45 (*m*, 2 H); 1.30–1.21 (*m*, 2 H); 1.20 (*s*, 3 H); 1.18 (*s*, 3 H); 1.06 (*s*, 3 H); 0.99 (*m*, 1 H); 0.86 (*s*, 9 H); 0.09 (*s*, 3 H); 0.04 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 170.4; 169.9; 85.7; 84.4; 80.2; 69.9; 48.1; 48.0; 43.0; 40.4; 34.0; 32.4; 30.3; 29.5; 27.9; 26.3; 25.7; 25.2; 21.7; 21.4; 21.3; 19.5; 17.7; 15.9; −5.1; −5.2. FAB-MS: $[M + 1]^+$ calc.: 511.78; observed: 511.33. Anal. calc. for $C_{28}H_{50}O_6Si$: C 65.84, H 9.87; found: C 65.54, H 9.90.

*(1*R*,4a*R*,5*S*,7*R*,10*S*,11*S*,12a*R*)-1-[(*tert*-Butyl)dimethylsilyloxy]perhydro-10,11-dihydroxy-4a,13,13-trimethyl-7,10-methanobenzocyclodecen-5-yl Acetate* (**25b**). A N_2-blanketed, magnetically stirred soln. of **25a** (225 mg, 0.439 mmol) was treated with 2.3 ml of 1M $Bu_4N^+F^-$ in THF (2.30 mmol) and stirred overnight. AcOEt and H_2O were added, the layers were separated, and the org. phase was washed wit H_2O and brine then dried. Chromatographic purification of the residue (elution with 20% AcOEt in petroleum ether) furnished 188 mg (91%) of **25b** as a white solid. M.p. 150–152°. $[\alpha]_D^{20} = +14.4$ ($c = 3.9$, $CHCl_3$). IR ($CHCl_3$): 3620, 3540, 1725. ^{1}H-NMR ($CDCl_3$): 4.78 (*d*, $J = 8.4$, 1 H); 3.82 (br. *s*, 1 H); 3.45 (*d*, $J = 8.3$, 1 H); 2.89 (br. *s*, 1 H); 2.43–2.10 (series of *m*, 6 H); 2.03 (*s*, 3 H); 2.10–0.70 (series of *m*, 13 H); 1.18 (*s*, 3 H); 1.14 (*s*, 3 H); 1.06 (*s*, 3 H); 0.86 (*s*, 9 H); 0.03 (*s*, 3 H); 0.02 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 170.1; 87.6; 84.4; 76.5; 71.1; 47.8; 47.5; 43.8; 40.6; 33.4; 31.7; 30.8; 29.5; 28.2; 26.3; 25.7; 25.2; 21.3 (2C); 19.3; 17.8; 16.0; −4.9; −5.1. FAB-MS: $[M + 1]^+$ calc.: 469.43; observed: 469.36. Anal. calc. for $C_{26}H_{50}O_5Si$: C 66.62, H 10.32; found: C 66.62, H 10.29.

*(4*S*,4a*R*,6*S*,10*R*,12*R*,12a*R*)-4-[(*tert*-Butyl)dimethylsilyloxy]perhydro-7-hydroxy-12a,13,13-trimethyl-6-oxo-7,10-methano-2*H*-benzocyclodecen-12-yl Acetate* (**26** ⇄ **27**). N_2-blanketed DMSO (0.25 ml, 3.50 mmol) was treated dropwise with oxalyl chloride (0.15 ml, 1.75 mmol) in CH_2Cl_2 (3 ml) while being stirred at −78°. A soln. of **25b** (410 mg, 0.875 mmol) in CH_2Cl_2 (8 ml) was next introduced, and the resulting cloudy soln. was stirred at −78° for 15 min. After the addition of Et_3N (0.732 ml, 5.25 mmol), the mixture was stirred for 40 min, quenched with H_2O, and separated into layers. The org. phase was washed with H_2O and brine, dried, and concentrated. Chromatography of the residue (elution with 10% AcOEt in petroleum ether) provided 343 mg (84%) of α-ketol as a white solid. M.p. 140–142°. $[\alpha]_D^{20} = +11.2$ ($c = 2.3$, $CHCl_3$). IR ($CHCl_3$): 3450, 1725, 1680. ^{1}H-NMR ($CDCl_3$): 4.90 (*d*, $J = 8.6$, 1 H); 4.25 (*d*, $J = 1.5$, 1 H); 4.11 (*s*, 1 H); 3.13 (*d*, $J = 12.0$, 1 H); 2.60 (*m*, 2 H); 2.45–2.15 (series of *m*, 4 H); 2.10 (*s*, 3 H); 2.05–1.25 (series of *m*, 11 H); 1.22 (*s*, 3 H); 1.10 (*s*, 3 H); 0.94 (*s*, 3 H); 0.86 (*s*, 9 H); 0.05 (*s*, 3 H); 0.00 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 215.2; 169.9; 90.1; 84.1; 71.1; 50.2; 46.6; 42.6; 41.2; 34.5; 33.3; 31.6; 29.9; 27.9; 26.7; 25.7; 24.7; 21.7; 21.4; 20.1; 17.8; 15.6; −5.0; −5.2. FAB-MS: $[M + 1]^+$ calc.: 467.42; observed: 467.41. Anal. calc. for $C_{26}H_{48}O_5Si$: C 66.91, H 9.93; found: C 66.51, H 9.81.

*(4*R*,4a*R*,4b*S*,6*S*,9*R*,10a*S*,10b*S*)-4-[(*tert*-Butyl)dimethylsilyloxy]perhydro-6-hydroxy-10b,11,11-trimethyl-6,9-methanobenzo[3,4]cyclobuta[1,2]cycloocten-5(2*H*)-one* (**29a**). A soln. of **26** ⇄ **27** (113 mg, 0.242 mmol) in dry *t*-BuOH (10 ml) was blanketed with N_2, treated with 1.54 ml of 0.118M *t*-BuOK in the same solvent (0.182 mmol), and refluxed overnight. The mixture was diluted with H_2O, and the org. phase was washed with H_2O and brine prior to drying. Concentration gave a crude oil that was chromatographed (elution with 10% AcOEt in petroleum ether) to give 91 mg (89%) of **29a** as colorless needles. M.p. 88–91° (from Et_2O/hexane). $[\alpha]_D^{21} = +58.4$ ($c = 1.9$, $CHCl_3$). IR ($CHCl_3$): 3460, 1690. ^{1}H-NMR ($CDCl_3$): 3.92 (*s*, 1 H); 3.77 (*d*, $J = 1.9$, 1 H); 2.87 (*dd*, $J = 11.9$, 10.5, 1 H); 2.50 (*m*, 1 H); 2.12 (*m*, 1 H); 2.05 (*d*, $J = 9.7$, 1 H); 2.01–1.70 (series of *m*, 4 H); 1.70–1.43 (series of *m*, 4 H); 1.40–1.20 (series of *m*, 4 H); 1.12 (*s*, 3 H); 1.08 (*s*, 3 H); 0.90 (*s*, 9 H); 0.88 (*s*, 3 H); 0.11 (*s*, 3 H); 0.04 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 212.7; 89.3; 66.5; 46.9; 45.1; 44.8; 43.1; 42.0; 37.5; 32.7; 31.0; 29.6; 28.5; 27.9; 27.8; 27.7; 25.7; 19.4; 17.9; 14.8; −4.9; −5.1. FAB-MS: $[M + 1]^+$ calc.: 407.29; observed: 407.31. Anal. calc. for $C_{24}H_{42}O_3Si$: C 70.89, H 10.41; found: C 70.63, H 10.32.

*(4*R*,4a*R*,4b*S*,6*S*,6*R*,10a*S*,10b*S*)-Perhydro-4,6-dihydroxy-10b,11,11-trimethyl-6,9-methanobenzo[3,4]cyclobuta[1,2]cycloocten-5(2*H*)-one* (**29b**). Into a soln. of **29a** (49 mg, 0.115 mmol) was syringed, under N_2, 0.23 ml of 1M $Bu_4N^+F^-$ in THF (0.231 mmol). The mixture was heated in a 55° oil bath overnight and partitioned between AcOEt and H_2O. The org. layer was washed with H_2O and brine, while the aq. layer was extracted with AcOEt. The combined org. phases were dried and concentrated, and the residue was purified by chromatography (elution with 50% AcOEt in petroleum ether) to give 35 mg (98%) of **29b** as a white solid. M.p. 181–183°. $[\alpha]_D^{21} = +74.1$ ($c = 3.5$, $CHCl_3$). IR ($CHCl_3$): 3605, 3460, 1690. ^{1}H-NMR ($CDCl_3$): 3.89 (*s*, 1 H); 3.84 (*d*, $J = 1.7$, 1 H); 2.91 (*dd*, $J = 12.1$, 10.2, 1 H); 2.50 (*m*, 1 H); 2.25–1.31 (series of *m*, 15 H); 1.15 (*s*, 3 H); 1.08 (*s*, 3 H); 0.88 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 212.50; 89.3; 66.5; 46.9; 45.1; 44.6; 43.1; 42.0; 37.4; 32.6; 30.3; 29.5; 28.5; 27.9; 27.8; 27.6; 19.4; 14.7.

The 3,5-dinitrobenzoate **29c** was prepared conventionally and obtained as a colorless crystalline solid. M.p. 163–166° (from Et_2O/hexane), suitable for X-ray crystallographic analysis.

X-Ray Data Collection, Structure Determination, and Refinement for **29c**. A transparent single crystal of **29c** was mounted on a pin and transferred to the goniometer. The space group was determined to be the acentric $P2_12_12_1$ from the systematic absences. A summary of data collection parameters is given in the *Table*.

Least-squares refinement with isotropic thermal parameters led to $R = 0.138$. The geometrically constrained H-atoms were placed in calculated positions 0.95 Å from the bonded C-atom and allowed to ride on that atom with B fixed at 5.5 Å^2. The Me H-atoms were included as a rigid group with rotational freedom at the bonded C-atom (C–H = 0.95 Å, $B = 5.5$ Å^2). The remaining H-atom was located from a difference *Fourier* map and included with fixed contributions ($b = 5.5$ Å^2). Absolute configuration was controlled by the use of optically pure starting materials. Refinement of non-H-atoms with anisotropic temp. factors led to the final values of $R = 0.056$ and $R_w = 0.060$.

*(4*R*,4a*R*,6*R*,10*R*,12*S*,12a*R*)-4-[(*tert*-Butyl)dimethylsilyloxy]perhydro-6-hydroxy-12a,13,13-trimethyl-7-oxo-6,10-methano-1*H*-benzocyclodecen-12-yl Acetate* (**30**). A soln. of **26** ⇄ **27** (280 mg, 0.060 mmol) in benzene (25 ml) was treated with (i-PrO)$_3$Al' (368 mg, 1.80 mmol) and heated at reflux under N_2 for 8 h. The cooled mixture was diluted with H_2O (10 ml) and the separated org. phase was washed with H_2O, 1N HCl, and brine, while the aq. washings were extracted twice with AcOEt. The combined org. solns. were dried and concentrated to leave a residue that was purified by chromatography (elution with 15% AcOEt in petroleum ether). A total of 237 mg (85%) of **30** was isolated as a white solid. M.p. 117–119°. $[\alpha]_D^{21} = +56.9$ ($c = 2.7$, $CHCl_3$). IR ($CHCl_3$): 3500, 1705. ^{1}H-NMR ($CDCl_3$): 5.51 (*d*, $J = 10.0$, 1 H); 3.55 (*d*, $J = 1.3$, 1 H); 3.52 (*s*, 1 H); 2.82–2.60 (*m*, 1 H); 2.45–2.27 (*m*, 4 H); 2.15–1.90 (*m*, 2 H); 1.94 (*s*, 3 H); 1.75 (*m*, 1 H); 1.59 (*m*, 1 H); 1.52–0.95 (series of *m*, 7 H); 1.29 (*s*, 3 H); 1.24 (*s*, 3 H); 0.79 (*s*, 9 H); 0.75 (*s*, 3 H); –0.02 (*s*, 3 H); –0.06 (*s*, 3 H). FAB-MS: $[M + 1]^+$ calc.: 467.42; observed: 467.41. Anal. calc. for $C_{26}H_{46}O_5Si$: C 66.91, H 9.93; found: C 66.64, H 9.90.

*(4a*R*,6*R*,10*R*,12*S*,12a*R*)-Perhydro-6-hydroxy-12a,13,13-trimethyl-4,7-dioxo-1*H*,4a*H*-6,10-methanobenzocyclodecen-12-yl Acetate* (**31**). α-Ketol **30** (235 mg, 0.504 mmol) was dissolved in 25 ml of a 95:5 mixture of CH_3CN and 48% HF soln., stirred at r.t. for 3 h, and diluted with H_2O (20 ml) and CH_2Cl_2 (20 ml). The org. phase was washed with H_2O and brine, and the aq. washings were extracted with CH_2Cl_2. The combined org. solns. were dried and concentrated to leave a white solid foam that was passed through a small plug of silica gel: 175 mg (99%) of alcohol as a white solid. M.p. 169–171°. $[\alpha]_D^{21} = +121.2$ ($c = 3.8$, $CHCl_3$). IR ($CHCl_3$): 3600, 3470, 1705. ^{1}H-NMR ($CDCl_3$): 5.52 (*d*, $J = 9.9$, 1 H); 3.69 (br. *s*, 1 H); 3.66 (*s*, 1 H); 2.84–2.70 (*m*, 1 H); 2.61–2.35 (series of *m*, 4 H); 2.26–2.02 (*m*, 2 H); 2.05 (*s*, 3 H); 1.90–1.20 (series of *m*, 7 H); 1.41 (*s*, 3 H); 1.37 (*s*, 3 H); 0.99 (*d*, $J = 16.1, 7.0$, 1 H); 0.91 (*m*, 1 H); 0.86 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 214.3; 170.8; 81.7; 78.6; 77.0; 43.5; 41.1; 40.7; 40.1; 38.6; 37.3; 32.4; 28.9; 27.4; 26.9; 25.3; 24.3; 24.1; 21.3; 16.1. FAB-MS: $[M + 1]^+$ calc.: 353.23; observed: 353.33. Anal. calc. for $C_{20}H_{32}O_5 \cdot CH_3COOC_2H_5$: C 65.43, H 9.15; found: C 65.69, H 9.16.

A cold (–78°) soln. of DMSO (29 µl, 0.409 mmol) in CH_2Cl_2 (4 ml) was treated dropwise with a soln. of oxalyl chloride (18 µl, 0.204 mmol) in CH_2Cl_2 (3 ml) and subsequently a soln. of the preceding product (36 mg, 0.102 mmol) in CH_2Cl_2 (5 ml). After an added 15 min of stirring, Et_3N (85 µl, 0.613 mmol) was introduced *via* syringe, the mixture was warmed to r.t., and stirred at this temp. for 2 h. H_2O (5 ml) was introduced, and the separated org. phase was washed with H_2O and brine. The washings were extracted with CH_2Cl_2, and the combined org. solns. were dried and concentrated. Chromatography of the residue (elution with 50% AcOEt in petroleum ether) afforded 28 mg (78%) of **31** as a highly crystalline white solid. M.p. 198–200°. $[\alpha]_D^{21} = +96.7$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): 3490, 1705. ^{1}H-NMR ($CDCl_3$): 5.52 (*d*, $J = 9.4$, 1 H); 3.62 (*s*, 1 H); 3.12 (*d*, $J = 8.6$, 1 H); 2.78 (*m*, 1 H); 2.64 (*dd*, $J = 15.8, 8.8$, 1 H); 2.59–2.35 (*m*, 2 H); 2.30–2.08 (*m*, 3 H); 2.06 (*s*, 3 H); 2.05–1.90 (*m*, 2 H); 1.85–1.70 (*m*, 3 H); 1.52–1.46 (*m*, 1 H); 1.39 (*s*, 3 H); 1.30–1.15 (*m*, 2 H); 1.01 (*s*, 3 H); 0.87 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 213.1; 211.7; 170.4; 80.8; 76.6; 52.4; 43.7; 41.8; 39.9; 39.1; 36.9; 36.7; 32.3; 29.3; 27.5; 25.2; 24.1; 22.9; 21.2; 20.7. FAB-MS: $[M + 1]^+$ calc.: 351.21; observed: 351.14.

X-Ray Data Collection, Structure Determination, and Refinement for **31**. A transparent single crystal of **31** was mounted on a pin and transferred to the goniometer. The space group was determined to be either the centric $P2_1/m$ or acentric $P2_1$ from the systematic absences. Statistical tests indicated that the space group was acentric, and the subsequent soln. and successful refinement of the structure was carried out in the acentric space group $P2_1$. A summary of data collection parameters is given in the *Table*.

Least-squares refinement with isotropic thermal parameters led to $R = 0.121$. The geometrically constrained H-atoms were placed in calculated positions 0.95 Å from the bonded C-atom and allowed to ride on that atom with B fixed at 5.5 Å^2. The Me H-atoms were included as a rigid group with rotational freedom at the bonded C-atom (C–H = 0.95 Å, $B = 5.5$ Å^2). H–C(1)(O(1)) was located from a difference *Fourier* map and included with fixed contributions ($B = 5.5$ Å^2). Absolute conformation was known from the systematic scheme employed. Refinement of non-H-atoms with anisotropic temp. factors led to the final values of $R = 0.056$ and $R_w = 0.071$.

*(1*R*,4a*R*,5*S*,7*R*,10a*R*,13*S*)-Perhydro-4a,9,13-trihydroxy-1,8,8-trimethyl-11-oxo-1,7-ethano-5,9-methanobenzocycloocten-13-yl Acetate* (**32**). Ketone **31** (30 mg, 0.086 mmol) was dissolved in MeOH (10 ml) containing 5 drops of THF (to improve solubility). Anh., granular K_2CO_3 (30 mg, 0.214 mmol) was introduced, and the mixture was stirred at r.t. for 2.5 h then diluted with H_2O and AcOEt. Following the predescribed workup, the residue was

purified by chromatography (elution with 2% EtOH/48% AcOEt/50% hexanes) to give 22 mg (72%) of **32** as a white solid. M.p. 205–207°. $[\alpha]_D^{21} = +7.2$ ($c = 0.23$, $CHCl_3$). IR ($CHCl_3$): 3680, 3580, 1720. ^{1}H-NMR ($CDCl_3$): 5.45 (*dd*, $J = 12.3, 5.1$, 1 H); 3.75 (*s*, 1 H); 2.55 (*d*, $J = 15.3$, 1 H); 2.49–2.40 (*m*, 2 H); 2.20–2.10 (*m*, 2 H); 2.05 (*s*, 3 H); 2.06–1.92 (*m*, 2 H); 1.90–1.75 (*m*, 2 H); 1.74–1.65 (*m*, 4 H); 1.56 (*s*, 1 H); 1.51 (*s*, 1 H); 1.41–1.23 (*m*, 1 H); 1.36 (*s*, 3 H); 1.03 (*s*, 3 H); 0.93 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 216.6; 170.4; 80.6; 78.6; 74.4; 57.8; 46.7; 46.6; 40.5; 38.8; 37.7; 35.8; 34.2; 31.9; 31.0; 28.0; 21.1; 20.3; 19.5. FAB-MS: $[M + 1]^+$ calc.: 351.21; observed: 351.19.

Supplementary Material. Tables of final fractional coordinates, bond distances, bond angles, and thermal parameters for **23**, **29c**, and **31**, as well as the final atomic coordinates for the six compounds displayed in *Fig. 1*.

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