Thallium Trinitrate Mediated Oxidation of 3-Alkenols: Ring Contraction vs Cyclization

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Abstract: The reaction of a series of six-membered ring 3-alkenols with thallium trinitrate (TTN) in three different experimental conditions was studied. Either cyclization products or ring contraction products were obtained, depending on the structure of the substrate as well as the nature of the solvent. The reaction of a seven-membered ring 3-alkenol with TTN led to the ring contraction product exclusively.

Introduction

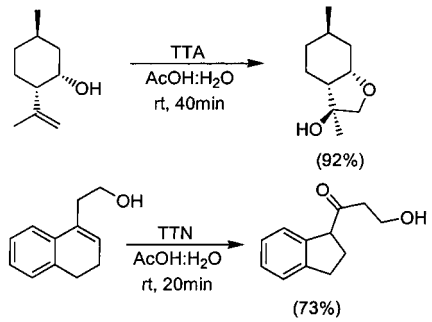
Thallium(III) salts can promote a number of different reactions in organic substrates.[1] Among the most useful transformations mediated by these salts are the ring contraction of cyclic olefins and the cyclofunctionalization of unsaturated alcohols.

Although the ring contraction of simple substrates, such as cyclohexene[2,3] and cycloheptene,[4] is a well-known reaction, its application to more complex olefins is less common than might be expected.[5]

Concerning the thallium(III)-promoted cyclization of unsaturated alcohols, the works developed by Mihailovic et al.[6] and Bartlett et al.[7] should be mentioned. The former studied the cyclization of some 4-, 5-, and 6-alkenols, using thallium triacetate (TTA), and carefully discussed the influence of different solvents in the course of the reaction. Bartlett et al. reported a number of examples of TTN- and TTA-mediated cyclization of 4-alkenols and elucidated several aspects of this reaction. Nevertheless, the only 3-alkenol studied by them gave rise to a complex mixture of products.

In a previous paper,[8] we described the reaction of the monoterpenes isopulegol and neoisopulegol with TTA and TTN, using aqueous AcOH as solvent. This reaction furnished the cyclization products in very good yields. Recently,[9] we observed that homoallylic alcohols bearing an endocyclic double bond react with TTN to afford ring contraction products, instead of the expected cyclic ethers. In Scheme 1 are shown two representative examples of these reactions.

Scheme 1



On the basis of these results, it is possible to suppose that 3-alkenols containing an endocyclic double bond would undergo ring contraction preferentially to cyclization. However, Kocovsky et al.[10,11] reported a different behavior for some steroidal 3-alkenols, which underwent a fragmentation reaction, instead of ring contraction and/or cyclization, when treated with TTN in dioxane.

Taking into account the different results mentioned above, we decided to investigate the behavior of other cyclic 3-alkenols toward TTN, under different experimental conditions, to better understand the influence of the substrate structure, as well as of the solvent, in the course of the reaction.

Results and Discussion

The 3-alkenols **4a**−**f** were prepared from the corresponding cyclohexanones, using classical methodologies,[12] as outlined in Scheme 2.

The first set of reactions with TTN was carried out using 50% aqueous AcOH as solvent. Under these conditions, the alkenols **4a** and **4b** had furnished the corresponding cyclopentane derivatives **5a** and **5b**, respectively, as previously communicated by us[13] (Table 1, entries 1 and 3). However, the reaction of **4c** under the same conditions led to a mixture of the ring contraction product **5c** and the cyclic ether **6c**, isolated in poor yields, while **4d** afforded the cyclic ether **6d** as the only identified product (Table 1, entries 5 and 7). The alkenols **4e** and **4f** led to an untractable mixture of products.

NMR and GC analysis of the crude products of the TTN oxidation performed in aqueous AcOH indicated the formation of diastereomeric glycol derivatives as the main products of the reaction. It is noteworthy that the substrates **4a** and **4b**, which afforded the ring contraction products in reasonable yields, differ from **4c**−**f** only by

(1) For reviews, see: (a) McKillop, A.; Taylor, E. C. In *Comprehensive Organometallic Chemistry*; Pergamon Press: New York, 1982; Vol. 7, p 465. (b) Ferraz, H. M. C.; Silva, L. F., Jr.; Vieira, T. de O. *Synthesis* **1999**, 2001.

(2) Kabbe, H.-J. *Ann.* **1962**, *656*, 204.

(3) McKillop, A.; Hunt, J. D.; Kienzle, F.; Bigham, E.; Taylor, E. C. *J. Am. Chem. Soc.* **1973**, *95*, 3635.

(4) Abley, P.; Byrd, J. E.; Halpern, J. *J. Am. Chem. Soc.* **1973**, *95*, 2591.

(5) For a review concerning thallium(III) salt mediated ring contraction, see: Ferraz, H. M. C.; Silva, L. F., Jr. *Quím. Nova* **2000**, *23*, 216.

(6) Mihailovic, M. Lj.; Vukicevic, R.; Konstantinovic, S.; Milosavljevic, S.; Schroth, G. *Liebigs Ann. Chem.* **1992**, 305.

(7) Michael, J. P.; Ting, P. C.; Bartlett, P. A. *J. Org. Chem.* **1985**, *50*, 2416.

(8) Ferraz, H. M. C., Ribeiro, C. M. R.; Grazini, M. V. A.; Brocksom, T. J.; Brocksom, U. *Tetrahedron Lett.* **1994**, *35*, 1497.

(9) Ferraz, H. M. C.; Silva, L. F., Jr. *Tetrahedron* **2001**, *57*, 9939.

(10) Kocovsky, P.; Pour, M. *J. Org. Chem.* **1990**, *55*, 5580.

(11) Kocovsky, P.; Baines, R. S. *J. Org. Chem.* **1994**, *59*, 5439.

(12) For references concerning the preparation of compounds outlined in Scheme 2, see the Supporting Information.

(13) Ferraz, H. M. C.; Santos, A. P.; Silva, L. F., Jr.; Vieira, T. de O. *Synth. Commun.* **2000**, *30*, 751.

10.1021/jo011178m CCC: $22.00
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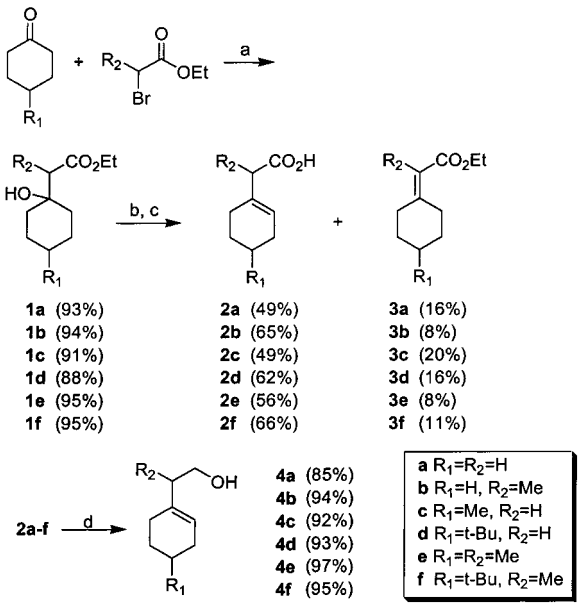
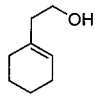
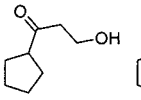
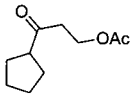
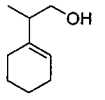
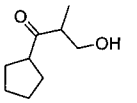
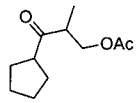
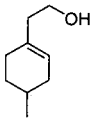
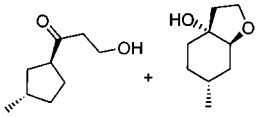
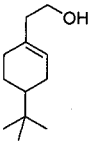
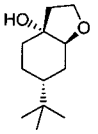
Scheme 2[a]



[a] Reagents and Conditions: (a) Zn, benzene, reflux then 10% aqueous H_2SO_4; (b) $SOCl_2$, Py, Et_2O, rt; (c) 10% aqueous NaOH, EtOH, 30 °C; (d) $LiAlH_4$, THF, rt.

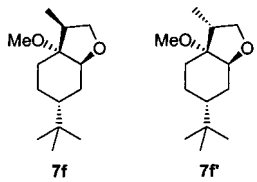
Table 1. Reaction of 3-alkenols 4a−d with TTN

Entry	Substrate	Conditions	Products (yield)
1[a]	 4a	50% aq. AcOH r.t., 15 min	 5a (71%)  5a' (10%)
2	4a	MeOH 0°C, 1 min	5a (62%)
3[a]	 4b	50% aq. AcOH r.t., 15 min	 5b (68%)  5b' (11%)
4	4b	MeOH 0°C, 1 min	5b (77%)
5	 4c	50% aq. AcOH r.t., 15 min	 5c (20%) 6c (9%)
6	4c	MeOH 0°C, 3 min	5c (32%)
7	 4d	50% aq. AcOH r.t., 15 min	 6d (22%)
8	4d	MeOH 0°C, 5 min	complex mixture

[a] Reference 13.

the absence of the alkyl group at the ring. The 1,3-trans relationship of the substituents of **5c** was tentatively assigned by NMR analysis and comparison with data of similar structures.[14,15]

The next set of reactions was performed in methanol, since this solvent has proved to be efficient for the ring contraction of a series of 1,2-dihydronaphthalenes.[16] The consumption of the starting materials occurred almost instantaneously, at 0 °C, but the results were very similar to those observed when the solvent was aqueous AcOH. Thus, the alkenols **4a** and **4b** afforded the ring contraction products in moderate yields, while **4c** led to the cyclopentane derivative **5c** in poor yield, along with a mixture of glycolic products (Table 1, entries 2, 4, and 6). The substrates **4d**−**f** furnished complex mixtures of products, mainly glycolic derivatives. In the mixture obtained from **4f** were detected the β-methoxy cyclic ethers **7f** and **7f′**, which could be isolated in 6% yield (4:1 ratio, respectively).



7f **7f'**

These results indicate that the formation of glycolic derivatives is the preferential process when the reaction is carried out in MeOH. Moreover, only the substrates **4a** and **4b**, without substituents in the ring, were able to undergo selectively the ring contraction reaction.

The alkenols **4a** and **4b** were then treated with TTN in 35% aqueous $HClO_4$ at room temperature.[17] In contrast to the favorable results obtained using aqueous AcOH and MeOH, both reactions led to a complex mixture of products, from which no identifiable material could be isolated. Somewhat surprisingly, the substrates **4c**−**f** underwent a smooth cyclization reaction with a high degree of stereocontrol (Table 2). The β-hydroxy cyclic ethers **6c**−**f** thus obtained exhibit cis-fused rings and cis-relationships between the hydroxyl group and the alkyl substituent at the carbocyclic moiety.

The diastereoisomers **6e**/**6e′** and **6f**/**6f′** were obtained in 5:1 and 7:3 ratios, respectively, as deduced by GC and NMR analysis of the crude products. These isomers were separated by flash chromatography and duly characterized. A suitable crystal of the minor isomer **6e′** could be obtained and was submitted to crystallographic analysis, which corroborated the previously assigned structure. The relative configurations of **6f** and **6f′** was proposed by comparison of the ^1H and ^{13}C NMR data with those of **6e** and **6e′**, respectively.

We also investigated the behavior of the seven-membered ring alkenol **8**[18] toward TTN oxidation, under the three experimental conditions already mentioned. Using 35% aqueous $HClO_4$, a complex mixture of products was obtained, similar to **4a** and **4b**. When the reaction was run in aqueous AcOH or MeOH, the expected six-membered ring contraction product **9** was

(14) Ferraz, H. M. C.; Silva, L. F., Jr. *Tetrahedron Lett.* **1997**, *38*, 1899.

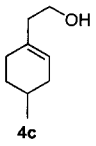
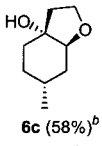
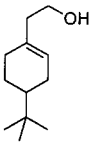
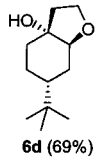
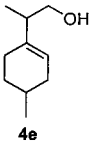
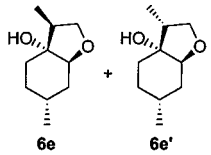
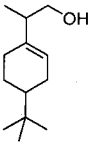
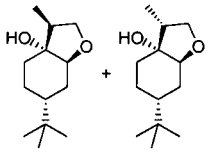
(15) Hoberg, H.; Ballesteros, A.; Sigan, A.; Jegat, C.; Milchereit, A. *Synthesis* **1991**, 395.

(16) Ferraz, H. M. C.; Silva, L. F., Jr.; Vieira, T. O. *Tetrahedron* **2001**, *57*, 1709.

(17) For examples of TTN-promoted oxidations performed in aqueous $HClO_4$, see: (a) Wiberg, K. B.; Koch, W. *Tetrahedron Lett.* **1966**, 1779. (b) Byrd, J. E.; Halpern, J. *J. Am. Chem. Soc.* **1973**, *95*, 2586. (c) Corey, E. J.; Snider, B. S. *J. Org. Chem.* **1974**, *39*, 256.

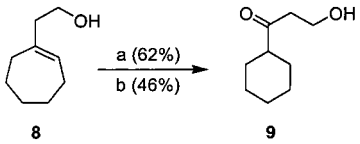
(18) The alkenol **8** was prepared from cycloheptanone, according to the sequence of reactions shown in Scheme 2.

Table 2. Reaction of 3-alkenols 4c−f with TTN in 35% Aqueous $HClO_4$

Entry	Substrate	Products (Yield)[a]
1		
	4c	6c (58%)[b]
2		
	4d	6d (69%)
3		
	4e	6e + 6e' (75%, 5:1)[c]
4		
	4f	6f + 6f' (75%, 7:3)[c]

[a] Isolated yields. [b] A small amount of **5c** (ca. 5%) was detected in the NMR spectra. [c] Ratio determined by GC and ^1H NMR.

Scheme 3[a]



[a] Reagents and conditions: (a) 1.2TTN, 50% aqueous AcOH, rt, 8 min; (b) 1.0 TTN, MeOH, 0 °C, 2 min.

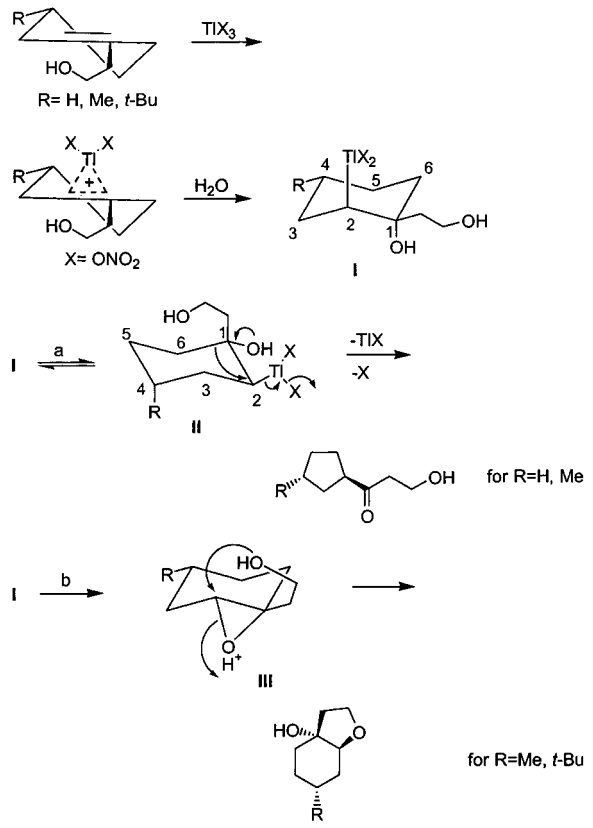
obtained in 62% and 46% isolated yield, respectively (Scheme 3).

A possible explanation for the different behavior of the 3-alkenols **4a**,**b** and **4c**−**f** toward TTN-promoted oxidation is depicted in Scheme 4. Due to the required antiperiplanarity between the C1−C6 bond and the C2−Tl bond for the contraction to occur, the oxythallated adduct **I** must equilibrate to its conformer **II** before the rearrangement step. Such an equilibration (pathway a) is easily achieved when R is hydrogen, but is not favored when R is a bulky group. Thus, for these latter groups, the glycolic derivatives (using aqueous AcOH or MeOH as solvent) or the cyclic ethers (using aqueous $HClO_4$) become the main products of the reaction. To explain the stereochemistry observed for the cyclic ethers, the cyclization of **I** must involve the participation of the oxonium ion **III** (pathway b). Such a kind of intermediate was already postulated by McKillop et al. for the ring contraction of cyclohexanone.[19]

Conclusion

From the results herein discussed, it can be concluded that the presence of substituents (*tert*-butyl or, at a least extension, methyl) in the cyclohexene ring of the 3-alkenols precludes the oxidative rearrangement to the

Scheme 4



corresponding cyclopentane derivatives. For these substrates, the alternative cyclization reaction becomes the preferable pathway, providing the solvent is non-nucleophilic. Otherwise, a conventional electrophilic addition to the double bond takes place, and the glycolic derivatives are the major components of the reactional mixture.

Experimental Section

General Methods. Thallium trinitrate[20] was used as received. Other known compounds used in this research were also purchased from standard chemical suppliers and were dried and/or purified by usual methods. Column chromatography was performed using silica gel (230−400 mesh). TLC analyses were performed with silica gel plates using vanilline or *p*-anisaldehyde solution for visualization.

General Procedure A. Reaction of 3-Alkenols with TTN in 50% Aqueous AcOH. To a stirred solution of the 3-alkenol (1.00 mmol) in 50% aqueous AcOH (3 mL) was added $TTN{\cdot}3H_2O$ (1.20 mmol), which promptly dissolved. The mixture was stirred at room temperature for the time indicated in Table 1, and saturated aqueous $NaHCO_3$ was added dropwise. The aqueous phase was extracted with ethyl acetate (three times), the combined organic phases were washed with brine (twice) and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure.

3-Hydroxy-1-(*trans*-3-methylcyclopentyl)propan-1-one (5c) and 6α-Methyl-7aαH-hexahydrobenzofuran-3aα-ol (6c). The crude product was purified by flash chromatography (CH_2Cl_2/AcOEt 9:1 as eluent) to afford **5c** and **6c** in 20% and 9% yield, respectively. **5c**: colorless oil; IR (film) 3425 and 1705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.98 (d, J = 6.4 Hz, 3H), 1.10−1.50 (m, 2H), 1.75−2.03 (m, 5H), 2.70 (t, J = 5.4 Hz, 2H), 2.90−3.10 (m, 1H), 3.85 (t, J = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2, 28.5, 34.2, 34.9, 36.5, 43.2, 51.1, 58.0, 214.0; MS *m*/*z* 156

(19) McKillop, A.; Hunt, J. D.; Taylor, E. C. *J. Org. Chem.* **1972**, *37*, 3381.

(20) WARNING! Thallium salts are toxic and must be handled with care.

(11, M^+). **6c**: colorless oil; IR (film) 3410 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (d, J = 6.7 Hz, 3H), 1.14−1.20 (m, 1H), 1.31 (ddd, J = 3.6, 11.5, 14.8 Hz, 1H), 1.49−1.71 (m, 4H, OH), 1.85−2.04 (m, 3H), 3.63 (t, J = 3.3, 3.3 Hz, 1H), 3.87 (dd, J = 8.8, 17 Hz, 1H), 3.98 (ddd, J = 4.0, 8.8, 10 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 26.2, 29.8, 34.0, 34.4, 39.9, 64.9, 75.1, 80.2; MS m/z 156 (20, M^+); HRMS calcd for $C_9H_{16}O_2$ 156.1150, found 156.0699.

6α-*tert*-Butyl-7aα*H*-hexahydrobenzofuran-3aα-ol (6d). The crude product was purified by flash chromatography (CH_2Cl_2/AcOEt 9:1 as eluent) to afford **6d** in 22% yield. **6d**: white solid; mp = 81.2−82.0 °C. Analytical samples of **6d** were obtained by recrystallization in dry hexanes: IR (KBr) 3320 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (s, 9H), 1.18−1.43 (m, 3H), 1.55−1.82 (m, 4H), 1.87−2.07 (m, 3H), 3.68 (br s, 1H), 3.83−4.02 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 26.8, 27.4, 32.0, 34.8, 40.2, 40.9, 65.0, 75.0, 80.7; MS m/z 198 (6.0, M^+). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.28; H,-10.88.

1-Cyclohexyl-3-hydroxypropan-1-one (9). The crude product was purified by flash chromatography (gradient elution, 10−60% AcOEt in hexanes) affording **9** in 62% yield. **9**: colorless oil; IR (film) 3410 and 1703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.18−1.41 (m, 5H), 1.65−1.89 (m, 5H), 2.30−2.38 (m, 1H), 2.58 (br s, OH), 2.69 (t, J = 5.4 Hz, 2H), 3.84 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 25.9, 28.4, 42.2, 51.2, 58.0, 214.9; MS m/z 156 (11, M^+); HRMS calcd for $C_9H_{16}O_2$ 156.1150, found 156.1152.

General Procedure B. Reaction of 3-Alkenols with TTN in MeOH. To a stirred solution of the 3-alkenol (1.00 mmol) in MeOH (6 mL) at 0 °C was added TTN·$3H_2O$ (1.00 mmol), which promptly dissolved. The mixture was stirred for the time indicated in Table 1, and an abundant precipitation was observed. The resulting suspension was filtered through a silica gel pad (70−230 mesh, ca. 10 cm), using CH_2Cl_2 as eluent. The filtrate was then washed with water followed by brine (twice) and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure.

1-Cyclopentyl-3-hydroxypropan-1-one (5a).[13] The crude product was purified by flash chromatography (gradient elution, 10−50% AcOEt in hexanes) to afford **5a** in 62% yield. (**5a**): colorless oil; ^1H NMR (300 MHz, $CDCl_3$) δ 1.52−1.89 (m, 8H), 2.46 (br s, OH), 2.72 (t, J = 5.4 Hz, 2H), 2.88 (quintet, J = 7.5 Hz, 1H), 3.85 (t, J = 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.0, 28.8, 43.4, 51.9, 58.0, 214.0.

1-Cyclopentyl-3-hydroxy-2-methylpropan-1-one (5b).[13] The crude product was purified by flash chromatography (gradient elution, 20−50% AcOEt in hexanes) to afford **5b** in 77% yield. **5b**: colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 1.13 (d, J = 7.2 Hz, 3H), 1.56−1.90 (m, 8H), 2.35 (br s, OH), 2.79−3.07 (m, 2H), 3.64 (dd, J = 4.5 e 11.0 Hz, 1H), 3.76 (dd, J = 7.2 e 11.0 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.4, 26.0, 26.1, 28.5, 29.7, 47.3, 50.2, 64.5, 217.7.

General Procedure C. Reaction of 3-Alkenols with TTN in 35% Aqueous $HClO_4$. To a stirred solution of the 3-alkenol (1.00 mmol) in 35% aqueous $HClO_4$ (3 mL) was added TTN·$3H_2O$ (1.20 mmol), which promptly dissolved. The mixture was stirred for 15 min at room temperature, and water was added. The aqueous phase was extracted with CH_2Cl_2 (three times), the combined organic phases were washed with brine (twice) and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure.

3β,6α-Dimethyl-7aα*H*-hexahydrobenzofuran-3aα-ol (6e) and 3α,6α-Dimethyl-7aα*H*-hexahydrobenzofuran-3aα-ol (6e′). The crude product was purified by flash chromatography (gradient elution 0−40% AcOEt in hexanes) to afford a 5:1 mixture (by GC and ^1H NMR) of **6e** and **6e′**, respectively, in 75% yield. Analytical samples of diastereoisomers **6e** and **6e′** were obtained performing a second flash chromatography (gradient elution, 0−35% AcOEt in hexanes) followed by recrystallization in dry hexanes. **6e**: white solid; mp = 57.1−57.2 °C; IR (KBr) 3394 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.90 (d, J = 6.6 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H), 1.15 (ddd, J = 4.2, 12.3, 24.7 Hz, 1H), 1.27 (ddd, J = 3.3, 12.0, 14.7 Hz, 1H), 1.44−1.64 (m, 4H, OH), 1.87 (dq, J = 2.3, 14.7 Hz, 1H), 2.27−2.32 (m, 1H), 3.40 (dd, J = 8.5, 10.2 Hz, 1H), 3.69 (br s, 1H), 4.08 (t, J = 8.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.4, 22.0, 26.4, 28.4, 29.4, 34.7, 44.2, 71.9, 75.0, 81.3; MS m/z 170 (4.1, M^+). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.39; H, 10.33. **6e′**: white solid; mp = 54.8−55.6 °C; IR (KBr) 3394 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (d, J = 6.7 Hz, 3H), 1.00 (d, J = 7.2 Hz, 3H), 1.17−1.35 (m, 2H), 1.46−1.51 (m, 1H), 1.59−1.73 (m, 3H, OH), 1.83−1.88 (m, 1H), 1.99−2.06 (m, 1H), 3.50 (dd, J = 4.5, 8.8 Hz, 1H), 3.67 (t, J = 3.6 Hz, 1H), 4.14 (dd, J = 7.7, 8.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 21.5, 26.3, 29.7, 34.5, 34.8, 41.2, 76.1, 76.7, 78.2; MS m/z 170 (3.9, M^+). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.36; H, 10.33.

3β-Methyl-6α-*tert*-butyl-7aα*H*-hexahydrobenzofuran-3aα-ol (6f) and 3α-Methyl-6α-*tert*-butyl-7aα*H*-hexahydrobenzofuran-3aα-ol (6f′). The crude product was purified by flash chromatography (gradient elution 0−50% AcOEt in hexanes) to afford a 7:3 mixture (by GC and ^1H NMR) of **6f** and **6f′**, respectively, in 75% yield. Analytical samples of diastereoisomers **6f** and **6f′** were obtained by performing a second flash chromatography (gradient elution, 0−40% AcOEt in hexanes) followed by recrystallization in dry hexanes. **6f**: white solid; mp = 102.5−103.2 °C; IR (KBr) 3378 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.87 (s, 9H), 0.93 (d, J = 6.9 Hz, 3H), 1.17−1.66 (m, 6H, OH), 1.94 (dq, J = 2.6, 14.1 Hz, 1H), 2.26−2.33 (m, 1H), 3.41 (dd, J = 8.5 and 10.1 Hz, 1H), 3.76 (br s, 1H), 4.09 (t, J = 8.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.5, 21.8, 27.3, 27.4, 29.1, 32.0, 41.3, 44.2, 71.9, 75.1, 81.8; MS m/z 212 (13, M^+). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.35; H, 11.05. **6f′**: white solid; mp = 93.8−94.2 °C; IR (KBr) 3378 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.86 (s, 9H), 1.01 (d, J = 7.2 Hz, 3H), 1.24−1.37 (m, 3H, OH), 1.54−1.70 (m, 3H), 1.95−2.00 (m, 2H), 3.49 (dd, J = 4.1, 8.9 Hz, 1H), 3.70 (br s, 1H), 4.15 (dd, J = 7.5, 8.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 22.3, 26.9, 27.3, 32.1, 36.2, 40.8, 41.8, 73.8, 75.9, 78.5; MS m/z 212 (17, M^+). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.44; H, 11.09.

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Supporting Information Available: Experimental procedures and structural data for all compounds not described within the text. Representative NMR spectra of **5b**, **9**, and **6e**, **6e′** (including X-ray crystallographic data of **6e′**). This material is available free of charge via the Internet at http://pubs.acs.org.

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