Silver-Catalyzed Cyclization of Acetylenic Alcohols: Synthesis of Functionalized 2-Methylene-oxolanes

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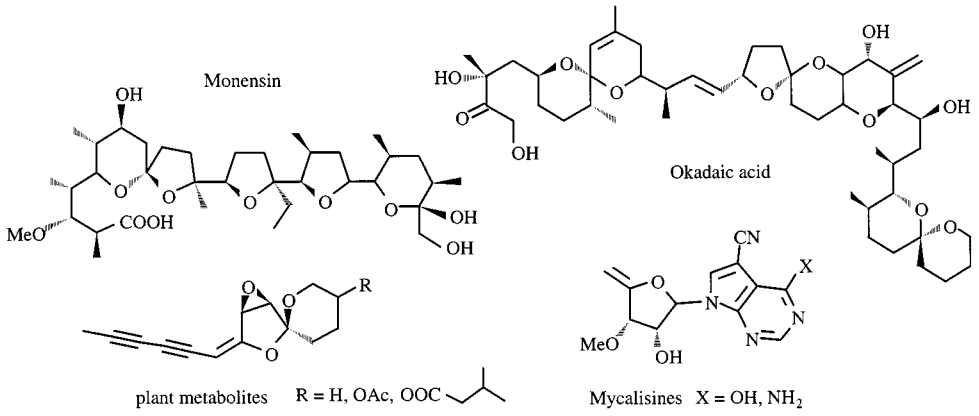
Silver salts which have a basic counter-ion are efficient catalysts for the regiospecific intramolecular addition of various acetylenic alcohols. Silver carbonate in aromatic solvent proved to be the best catalyst. Alkynols in which the two reacting parts of the molecule are relatively close together in space required only catalytic amounts of silver ion, while others cyclize readily with stoichiometric quantities. This heterocyclization reaction provides a mild and convenient access to 2-methylene-oxolanes or oxanes.

Introduction

The presence of oxolane or oxane motifs in a wide variety of natural products has attracted the attention of synthetic chemists in the last decades, and led to the development of various methods for the synthesis of such oxygenated heterocycles, especially in a stereodefined way.[1]

Most of the biologically active natural products which contain oxacycles are actually highly oxygenated compounds, e. g. ionophore antibiotics[2] such as monensin, marine toxins[3] such as okadaic acid, and plant metabolites[4] or antiproliferative compounds such as mycalysines[5] (Scheme 1). Therefore convenient and stereocontrolled access to oxolane or oxane heterocycles bearing other functions, especially oxygenated groups, is now the next challenge in this area.

In an effort to develop new methods for the synthesis of polyoxygenated heterocycles,[6] we have examined the intramolecular cyclization of acetylenic epoxy alcohols using electrophilic salts as catalysts (Scheme 2). Heterocyclization through intramolecular addition of a nucleophile to a π-system is a well-known process.[1,7] Far less studied than cyclization of ethylenic alcohols, only a few examples of cyclization of acetylenic alcohols have been described. Salts of mercury[8–9] or palladium[10] have been reported to be effective catalysts for these electrophilic intramolecular additions. Given the ease of access to epoxy alcohols, especially in an enantioselective way,[11–13] epoxy-substituted acetylenic alcohols would be an interesting class of compounds for electrophilic cyclization.



Scheme 1

With the simplest members of this family of compounds, *i. e.* the 2,3-epoxypent-4-ynols **1**, both 5-*exo*-dig or 6-*endo*-dig cyclizations would be allowed according to the Baldwin rules (Scheme 2).[14] Whatever the cyclization mode, the enol ether function created in the cyclization would serve as a handle for further elaboration.[15–16] In these compounds, the epoxy group would also be a useful tool for

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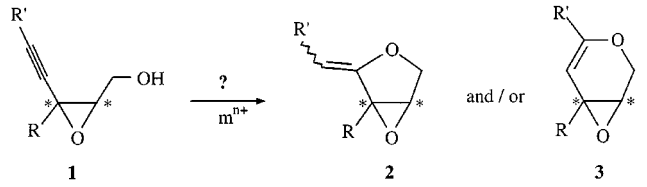
functional group transformations.[12,17] Moreover, the epoxy group could be seen as a source of chirality, enabling diastereoselective modifications at the adjacent double bond.[18]



Scheme 2

Results and Discussion

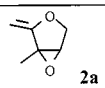
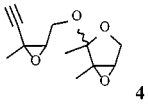
As our purpose was to apply electrophilic intramolecular addition to functionalized acetylenic alcohols, we first looked for suitable, mild conditions under which the cyclization could proceed, tolerating functional groups and especially the presence of an epoxy group. This screening was performed on the (*Z*)-2,3-epoxy-3-methylpent-4-ynol **1a** (R' = H, R = Me in Scheme 2), readily prepared from the commercially available (*Z*)-3-methylpent-2-en-4-ynol by *m*-CPBA epoxidation.

This acetylenic epoxy alcohol **1a** (R' = H, R = Me, Scheme 2) was submitted to various reaction conditions, the results of which are summarized in Table 1.

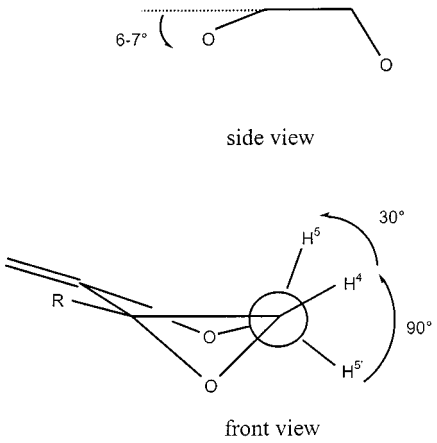
When applied to **1a**, the known mild method using palladium dichloride complexes[10] gave a single product but the conversion was too low to be useful for synthetic applications (Table 1, entry 1). The isolated product was shown to be an isomer of the starting material, by mass spectrometry and elemental analysis. The IR spectrum revealed the absence of both hydroxyl and ethynyl groups, suggesting the formation of a cyclization product. ^{13}C NMR confirmed the presence of an enol ether with characteristic signals at $\delta = 160.00$ and 84.97. ^1H NMR proved the exocyclic nature of this enol ether double bond with two doublets at $\delta = 4.47$ and 4.22 showing a small coupling constant (2.1 Hz). These data can only be ascribed to the product **2a** resulting from a 5-*exo*-dig cyclization.

The ^1H NMR spectrum of this product exhibited a particular coupling pattern, which proved to be general for all systems having the oxirane–oxolane moiety. In the 3,4-epoxy-3-methyl-2-methylene-oxolane **2a**, the epoxide proton (H4, Scheme 3) exhibited a very small coupling (1 Hz) with only one of the two adjacent protons (H5–H5', Scheme 3). Taking into account the fact that electronegative substituents result in smaller coupling constants, especially effective in antiperiplanar arrangements,[19] the Karplus

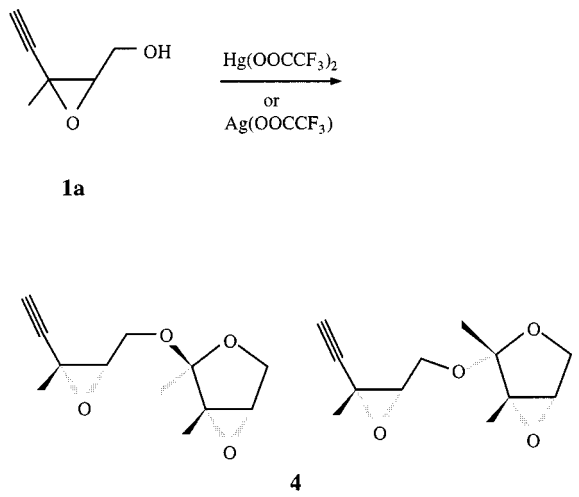
Table 1. Catalyst screening

	Catalyst	Equiv.	Solvent	Temp.	Time	Yield[a]	Product
1	$PdCl_2(PhCN)_2$	0.05	Et_2O	20 °C	2 d	15%[b]	 **2a**
2	$Pd(OOCCF_3)_2$	0.1	THF	20 °C	2 d	traces	**2a**
3	$HgCl_2 - NEt_3$	1–4	CH_2Cl_2	20 °C	6 h	47%[c]	**2a**
4	$Hg(OOCCF_3)_2$	0.1	CH_2Cl_2	20 °C	1 h	84%[c]	 **4**
5	$AgNO_3$	1	PhH	20 °C	2 d	0%[d]	-
6	$AgBF_4$	1	PhH	20 °C	2 min	0%[e]	-
7	$AgBF_4$	0.1	Et_2O	20 °C	5 h	0%[e]	-
8	AgOAc	1	PhH	80 °C	30 min	79%	**2a**
9	AgOAc	0.1	PhH	80 °C	1 h	89%	**2a**
10	Ag_2O	1	PhH	80 °C	30 min	85%	**2a**
11	Ag_2O	0.1	PhH	80 °C	1 h	89%	**2a**
12	Ag_2CO_3	1	PhH	20 °C	16 h	90%	**2a**
13	Ag_2CO_3	1	PhH	80 °C	1 h	91%	**2a**
14	Ag_2CO_3	0.1	PhH	20 °C	2 d	97%	**2a**
15	Ag_2CO_3	0.1	PhH	80 °C	1 h	99%	**2a**
16	$AgOOCCF_3$	1	PhH	20 °C	12 h	95%	**4**
17	$AgOOCCF_3$	0.1	PhH	20 °C	16 h	35%	**4**

[a] Yields refer to isolated, chromatographically pure compounds. – [b] Only 20% of the starting material was converted. The yield (taking into account the conversion) was therefore 72%. – [c] A complete conversion was observed, but degradation occurred. – [d] No conversion of the starting material. – [e] Extensive decomposition.



Scheme 3



Scheme 4

equation indicated from this coupling pattern a quasi-orthogonal arrangement of the two rings, with the oxolane oxygen end lying out of the plane toward the oxirane moiety (Scheme 3). This spatial arrangement has been confirmed by ab initio calculations.[18a]

When a more electrophilic salt of palladium was used (e.g. trifluoroacetate), the conversion was surprisingly even lower, and only traces of the cyclization product **2a** were detected (Table 1, entry 2).

The Schwartz protocol[8] for intramolecular electrophilic addition, i.e. stoichiometric amount of mercuric chloride in the presence of triethylamine, allowed for the complete consumption of **1a** within 6 hours. However a collection of products was formed from which **2a** was the major product isolated (Table 1, entry 3). A more electrophilic mercuric salt gave as expected a faster reaction, but under these conditions, a single but different product was formed (Table 1, entry 4). Surprisingly, IR analysis of this new product revealed the presence of a terminal acetylene, but the absence of an hydroxyl group. The mass spectrum indicated a mass which was twice that of the starting material, but this mass peak was very weak. The base peak corresponded to the mass of the starting material. This feature indicated that this new product was a dimer that could easily be cleaved back to the starting material or an isomer. The doubling of most of the signals in the ^{13}C NMR spectrum also revealed that this compound was actually a mixture of diastereoisomers. Correspondingly, the ^{1}H NMR spectrum was quite complex, especially in $CDCl_3$. Fortunately in C_6D_6 each set of signals appeared almost independently, revealing four AB systems: two doublets of doublets (δ = 3.95 and 3.79, 3.89 and 3.77) and two doublets in half of the doublet (δ = 3.69 and 3.65) and in the other half of the doublet, is a doublet of doublet (δ = 3.47 and 3.45) showing a very small constant (J = 1.1 Hz) to two signals at δ = 2.99 and 2.95. The latter corresponded to the characteristic pattern of the epoxy–oxolane moiety. Two others sets of signals (dd) at δ = 2.90 and 2.88 indicated the presence of an acetylenic epoxide. Further 2D NMR experiments finally confirmed the structure of **4a** as a mixture of diastereomeric self-adducts (Scheme 4).

The acetylenic epoxy alcohol **1a** was also treated with the silver salts which are useful catalysts for the cyclization of allenic alcohols.[20] Silver nitrate proved to be ineffective, even after prolonged time and with amounts of catalyst up to 1 equivalent (Table 1, entry 5). On the contrary, silver tetrafluoroborate was too reactive and led to extensive degradation of **1a** within seconds, regardless of the conditions, and even in the presence of basic solvent able to reduce $AgBF_4$ electrophilicity (Table 1, entries 6–7).

Silver acetate, silver oxide and silver carbonate exhibited the same behavior, giving the cyclization product **2a** in good to excellent yields (Table 1, entries 8, 10, 12). These silver salts have a basic counter-ion and proved to act as true catalysts since 10 mol-% could convert all the starting material into the exocyclic enol ether **2a**, (Table 1, entries 9, 11, 14). Silver carbonate proved to be the best catalyst, giving the cyclization product **2a**, without any decomposition, in almost quantitative yields (Table 1, entry 12–15). Raising the temperature dramatically increased the reaction rate (Table 1, entries 12 vs. 13, 14 vs. 15).

As in the case of the mercuric trifluoroacetate, the more electrophilic trifluoroacetate salt of silver gave a mixture of diastereoisomeric self-adducts **4a**, in good to moderate yields, depending on the amount of catalyst used (Table 1, entries 16–17).

To extend the scope of this new reaction, the nature of the solvent in which the reaction can proceed was also investigated. We submitted our acetylenic oxirane model **1a** to the most efficient catalyst, silver carbonate, in various solvents. The following results, listed in Table 2, were obtained. Surprisingly, it turned out that the cyclization proceeded in any solvent we tried.

From the results obtained, two classes of solvents can be distinguished. Aprotic solvents allowed for a very clean reaction, resulting in high yields (Table 2, entries 1–5). As expected, protic solvents cause some degradation (Table 2, entries 6–7), probably by reacting with the sensitive 3,4-epoxy-2-methylene-oxolane formed. However, no adduct

Table 2. Cyclization of **1a** in various solvents using Ag_2CO_3 as catalyst

Catalyst equiv.	Solvent	Temp.	Time	Conversion	Yield[a]	Product
1 Ag_2CO_3 0.1	PhMe	110 °C	0.2 h	100%	98%	**2a**
2 Ag_2CO_3 0.1	PhH	80 °C	1 h	100%	99%	**2a**
3 Ag_2CO_3 0.1	THF	66 °C	2 h	100%	90%	**2a**
4 Ag_2CO_3 0.1	CH_2Cl_2	38 °C	4.5 h	100%	95%	**2a**
5 Ag_2CO_3 0.1	Et_2O	35 °C	24 h	41%	39%[b]	**2a**
6 Ag_2CO_3 0.2	MeOH	20 °C	24 h	100%	84%[c]	**2a**
7 Ag_2CO_3 0.1	H_2O	20 °C	24 h	100%	70%[c]	**2a**

[a] Yields refer to isolated, chromatographically pure compounds. – [b] 95% Yield taking into account the conversion. – [c] Several unidentified side-products were detected.

could be unambiguously detected among the degradation products in these conditions.[21]

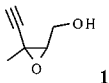
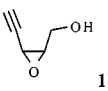
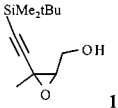
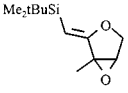
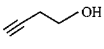
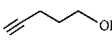
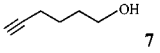
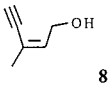
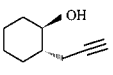
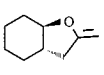
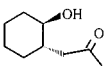
Except in the case of diethyl ether, it seems from these data that the reaction rate is only dependent on the temperature: the higher the reaction temperature, the faster the reaction completion. However, any conclusions have to be taken with care since the reaction is essentially heterogeneous.

In order to evaluate the possibilities and the limitations of this cyclization, other acetylenic epoxy alcohols as well as various acetylenic alcohols were also reacted with silver carbonate in aromatic solvents. These results are collected in Table 3.

2,3-Epoxypent-4-ynols, substituted or not at the propargylic position, i.e. **1a** or **1b**, were readily converted into the expected 3,4-epoxy-2-methylene-oxolanes **2a**, **2b** in quantitative yields with our standard conditions (Table 3, entries 1, 2). The substitution seems not to influence the cyclization reaction. However, the substitution at the acetylenic end of the molecule dramatically affects the cyclization rate. Under the same conditions, the silyl-substituted derivative **1c** remained unchanged (Table 3, entry 3). Since traces of the expected product were nevertheless detected, more forcing conditions were used. With excess silver carbonate in refluxing toluene, the cyclization product **2c** was isolated in an excellent yield as a single isomer (Table 3, entry 4).

The chemical shift of the vinylic proton in the ^1H NMR spectrum of **2c** ($\delta = 4.45$) allowed for the assignment of the stereochemistry of the exocyclic double bond as *Z*. Further NOE experiments confirmed this assignment with an interaction (7%) between the vinylic proton and the allylic methyl group.

Table 3. Cyclization of acetylenic alcohols assisted by silver carbonate in benzene

	Acetylenic alcohol	Catalyst	Equiv.	Solvent	Temp.	Time	Yield[a]	Product
1	 **1a**	Ag_2CO_3	0.1	PhH	80 °C	1 h	99%	 **2a**
2	 **1b**	Ag_2CO_3	0.1	PhH	80 °C	1 h	90%[b]	 **2b**
3	 **1c**	Ag_2CO_3	0.1	PhH	80 °C	16 h	Traces[c]	 **2c**
4	**1c**	Ag_2CO_3	2	PhMe	110 °C	10 h	95%	**2c**
5	 **5**	Ag_2CO_3	0.1	PhH	80 °C	16 h	0%[c]	-
6	 **6**	Ag_2CO_3	0.1	PhH	80 °C	6 h	traces	 **10**
7	**6**	Ag_2CO_3	1	C_6D_6	80 °C	6 h	90%	**10**
8	 **7**	Ag_2CO_3	0.1	C_6D_6	80 °C	6 h	traces	 **11**
9	**7**	Ag_2CO_3	1	C_6D_6	80 °C	6 h	90%	**11**
10	 **8**	Ag_2CO_3	1	C_6D_6	20 °C	2 h	95%[d]	 **12**
11	 **9**	Ag_2CO_3	1	C_6D_6	80 °C	6 h	95%[d]	 **13**
12	**9**	Ag_2CO_3	1	PhH	80 °C	5 h	74%[e]	 **14**

[a] Yields refer to isolated, chromatographically pure compounds. – [b] Quantitative as judged from TLC or NMR analysis but the yield was lowered by the volatility of the product. – [c] The starting alcohol was recovered. – [d] Yield estimated by NMR. – [e] Yield obtained after aqueous acid treatment; several unidentified by-products were also formed.

By comparison, linear acetylenic alcohols were treated with silver carbonate in refluxing benzene. As expected from our precedent results, 3-butynol (**5**), which should cyclize only through a 5-*endo*-dig process, did not react even in the presence of excess silver carbonate (Table 1, entry 5). Its homologues, 4-pentynol (**6**) and 5-hexynol (**7**), were almost unaffected under our standard conditions (Table 1, entries 6, 8). However, in the presence of stoichiometric amounts of silver carbonate, the cyclization occurred readily and the expected 2-methylene-oxolane and oxane **10**, **11** were formed (Table 1, entries 7, 9). As already described,[22] these known products were very unstable and decomposed rapidly.

The difference in reactivity towards silver carbonate between the linear acetylenic alcohols and their epoxy analogues suggested that the epoxy group activated the adjacent triple bond in a certain manner toward electrophilic addition. By setting in an appropriate position the two reacting ends of the molecule, i.e. the acetylene and the hydroxyl group, the *cis* stereochemistry of the epoxide might also favored the cyclization. In order to test this assumption, two other acetylenic alcohols were submitted to silver-mediated cyclization. Although neither alcohol contained an epoxy group, both compounds exhibit a spatial arrangement in which the acetylenic part and the hydroxyl group are close to each other.

The *Z*-enynol **8**, precursor of the epoxide **1a**, was readily cyclized in the presence of a catalytic amount of silver salt. Under these standard conditions, the cyclization rate observed for this enynol **8** was comparable to the rate obtained with the corresponding epoxide **1a** (Table 3, entry 10 vs 1). Although the extreme sensitivity of the obtained heterocycle **12** precluded its isolation, it could nevertheless be kept for a couple of hours in a benzene matrix. Running the reaction in deuterated benzene allowed for monitoring and direct identification of **12** by NMR.

Nucleophilic opening of the epoxy group of epoxycyclohexane with propargylmagnesium bromide[23] provided the *trans*-2-propargyl cyclohexanol (**9**). This acetylenic alcohol could also be cyclized in our standard conditions, although at a lower rate than the epoxide **1a** and the enynol **8** (Table 3, entry 11 vs 10, 1). As before, the cyclization product **13** was too unstable to be isolated and it was also identified by NMR after reaction in deuterated benzene. However, in this case, mild acid hydrolysis yielded the corresponding hydroxy ketone **14** in good overall yield (Table 3, entry 12).

As with other metal-catalyzed electrophilic additions,[8–10] silver π-coordination is likely to occur,[24] activating the triple bond toward nucleophilic addition. However, unlike other processes,[8–10] the results presented here with silver as catalyst showed the importance of the proximity of the two reacting part of the molecule, i.e. the internal nucleophile and the electrophilic π complex, for an efficient cyclization. Indeed, the results presented here clearly showed two classes of acetylenic alcohols: those having a spatial arrangement which may favor the cyclization required only catalytic amounts of catalyst, while the others required at least stoichiometric amounts of silver ion to be converted in a reasonable time into α-methylene-oxolanes or oxanes. Therefore, in the cyclizations described here, the entropic activation of the starting acetylenic alcohol seems to facilitate the cyclization.

Conclusion

In this work, we have shown that silver salts which have a basic counter-ion are efficient catalysts for the intramolecular electrophilic addition of various acetylenic alcohols. Silver carbonate in aromatic solvent proved to be the best set of conditions for this new cyclization.

The structure of the acetylenic part seems to be critical to the rate of cyclization. From the results obtained, it seems that only alkynes in which the two reacting parts of the molecule are relatively close together in space cyclize rapidly.

The method described here offers a new access to exocyclic enol ethers. Some of the α-methylene heterocycles so obtained are highly functionalized compounds, which could be further manipulated. For example, this novel method allows for a mild, efficient and rapid access to a new family of compounds, the 3,4-epoxy-2-methylene-oxolanes. Their reactivity is now actively studied in our group.[16,18]

Experimental Section

General: ^{1}H and ^{13}C NMR: 250 MHz and 62 MHz, respectively, on a Bruker AC-250 spectrometer. For ^{1}H NMR, $CDCl_3$ or C_6D_6 as solvent, TMS as internal standard; for ^{13}C NMR, $CDCl_3$: δ = 77.00 or C_6D_6: δ = 128.00. – IR spectra: Spectrafile IR™ Plus MIDAC spectrophotometer. – MS: Jeol D300 (70 eV) mass spectrometer. – Melting points were uncorrected. – Column chromatography: Merck silica gel (0.040–0.063 mesh). – TLC-analysis: MERCK Art 5554 DC Alufolien Kieselgel 60 PF_{254} with detection by UV-absorption (254 nm). THF was distilled from Na/benzophenone; C_6H_6, CH_2Cl_2 were distilled from CaH_2. Yields were on isolated products.

Starting Materials: Preparation of the Acetylenic Alcohols 1a–c, 5–9

***cis*-2,3-Epoxy-3-methylpent-4-ynol (1a):** To a cold (0°) solution of the commercial 3-methylpent-2-en-4-yn-2-ol (7 g, 72.9 mmol, 1 equiv.) in dichloromethane (200 mL), was successively added sodium bicarbonate (12.9 g, 121 mmol, 1.5 equiv.) and a solution of *m*-CPBA (22.7 g, 103.8 mmol, 1.4 equiv.). The suspension was vigorously stirred until the disappearance of the starting enynol. The resulting white slurry was then filtered and the solvent evaporated. The white solid was purified by flash-chromatography (PE/EA = 70:30). – M.p. 40 °C. – IR (film): $\tilde{\nu}$ = 3350, 3290, 2120, 1440, 1280, 1080, 1050, 1045 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 1.60 (3 H, s), 2.3 (OH, br. s), 2.4 (1 H, s), 3.1 (1 H, t, *J* = 5), 3.8 (1 H, dd, *J* = 5, 2 Hz), 3.9 (1 H, dd, *J* = 5, 2 Hz). – ^{13}C NMR ($CDCl_3$): δ = 23.07 (q), 61.60 (s), 62.23 (t), 63.93 (d), 73.28 (d), 80.96 (s). – MS; *m*/*z* (%): 114 [M^+ + 2] (100). – $C_6H_8O_2$ (112): calcd. C 64.20, H 7.19; found C 64.25, H 7.19.

***cis*-2,3-Epoxypent-4-ynol (1b):** The same procedure as above was used, starting from pent-2-en-4-ynol. – Colourless oil. – IR (thin film): $\tilde{\nu}$ = 3350, 3270, 2110, 1040, 985, 895, 805 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 2.41 (1 H, d, *J* = 2 Hz), 2.94 (OH, br. s), 3.25 (1 H, ddd, *J* = 6.2, 4.5, 4.4 Hz), 3.49 (1 H, dd, *J* = 4.5, 2.0 Hz), 3.78 (1 H, dd, *J* = 12.5, 6.2 Hz), 3.89 (1 H, dd, *J* = 12.5, 4.4 Hz). – ^{13}C NMR ($CDCl_3$): δ = 43.95 (d), 57.21 (d), 61.83 (t), 74.48 (d), 77.95 (s). – MS; *m*/*z* (%): 98 $[M]^+$, (100). – $C_5H_6O_2$ (98): calcd. C 61.21, H 6.15; found C 61.25, H 6.30.

***cis*-5-*tert*-Butyldimethylsilyl-2,3-epoxy-3-methylpent-4-ynol (1c):** To a solution of the commercial (*Z*)-3-methylpent-2-en-4-ynol (5 mL, 48 mmol, 1 equiv.) and hexamethyldisilazane (11.1 mL, 52.8 mmol, 1.1 equiv.) in dichloromethane (50 mL), was added trimethylsilyl chloride (0.376 mL, 4.8 mmol, 0.1 equiv.).[25] After 2 h, the white precipitate which rapidly formed was filtered off. Solvent evaporation left a colorless oil pure enough to be used directly in the subsequent step. To a cold (–70°) solution of the (*Z*)-3-methyl-1-trimethylsilyloxypent-2-en-4-yne thus obtained (7.3 g, 48 mmol, 1 equiv.) in THF (50 mL), was slowly added a solution of *n*-butyllithium (43.4 mmol, 1 equiv.). After warming up to –20°C within 45 min and then cooling at –70°C, a solution of *tert*-butyldimethylsilyl chloride (47.7 mmol, 1.1 equiv.) in THF (5 mL) was added dropwise. After warming up to room temperature, hydrolysis and ether extraction, a yellow oil was obtained (9.27 g). This oil was then taken up in methanol (20 mL) and a solution of citric acid (2.7 g, 13 mmol, 0.3 equiv.) in methanol (10 mL) was added. After 15 min, the mixture was concentrated, then diluted with water and extracted with ether. Solvent evaporation yielded a yellow oil which was purified by chromatography (PE/EA 80:20), yield 80%. To a cold (0°) solution of the (*Z*)-5-*tert*-butyldimethylsilyl-3-methylpent-2-en-4-ynol thus obtained (14.8 g, 70.7 mmol, 1 equiv.) in dichloromethane (100 mL), was successively added sodium bicarbonate (10.4 g, 99 mmol, 1.4 equiv.) and a dichloromethane solution (100 mL) of *m*-CPBA (20.6 g, 99 mmol, 1.4 equiv.). The suspension was vigorously stirred until the disappearance of the starting enynol. The resulting white slurry was then filtered and the solvent evaporated. The white solid was purified by flash-chromatography (PE/EA, 70:30). – White solid. – M.p. 55°C. – IR (thin film): $\tilde{\nu}$ = 3400, 2165, 1250, 1055, 1045, 1015, 840, 775 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.10 (6 H, s), 0.95 (9 H, s), 1.65 (3 H, s), 3.10 (1 H, t, *J* = 5 Hz), 3.8 (1 H, dd, *J* = 5, 2 Hz), 3.9 (1 H, dd, *J* = 5, 2 Hz). – ^{13}C NMR ($CDCl_3$): δ = –4.8 (q), 16.45 (s), 23.25 (q), 26.04 (q), 51.91 (s), 62.59 (t), 64.29 (d), 88.52 (s), 103.09 (s). – MS; *m*/*z* (%): 226 $[M^+]$ (0.1), 151 (40), 139 (100), 112 (28), 100 (60), 85(43), 76 (100). – $C_{12}H_{22}O_2Si$ (226): calcd. C 63.66, H 9.79; found C 63.40, H 9.79.

***trans*-Propargyl-2-cyclohexanol (9):** This acetylenic alcohol was prepared according to a known procedure,[23] by addition of propargylmagnesium bromide to epoxycyclohexane. – IR (thin film): $\tilde{\nu}$ = 3540, 3295, 2100, 1440, 1420, 1250, 1055, 1030 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 1.05–1.25 (4 H, m), 1.29–1.42 (1 H, m), 1.58–1.7 (2 H, m), 1.78–1.82(1 H, m), 1.83–1.92 (1 H, m), 1.90 (1 H, t, *J* = 2 Hz), 2.23 (1 H, ddd *J* = 16, 7, 2 Hz), 2.35 (1 H, ddd, *J* = 16, 4, 2 Hz), 3.29 (1 H, td, *J* = 9, 4 Hz). – ^{13}C NMR ($CDCl_3$): δ = 21.80 (t), 24.98 (t), 25.49 (t), 30.32 (t), 35.38 (t), 43.99 (d), 69.75 (d), 73.39 (d), 83.11 (s).

Formation of the Dimer 4: The same product can be obtained by treatment of the acetylenic alcohol **1a** with either silver or mercuric trifluoroacetate (see Table 1): To a stirred solution of the acetylenic alcohol **1a** (163 mg, 1.45 mmol 1 equiv.) in benzene (2 mL/mmol), was added at room temperature silver trifluoroacetate (0.1 equiv. or 1 equiv. see Table 1). The mixture was stirred overnight. The heterogeneous mixture, which gradually turned from yellow to brownish, was filtered over Celite and the resulting solution concentrated in vacuo. The crude product was usually chromatographically pure.

To a stirred solution of the acetylenic alcohol **1a** (340 mg, 3 mmol 1 equiv.) in dichloromethane (5 mL/mmol), was added at room temperature mercuric trifluoroacetate (0.1 equiv.). The resulting homogeneous mixture was stirred until TLC (PE/EA, 80:20) showed the disappearance of the starting acetylenic alcohol (1 h). The mixture, which gradually turned greenish-gray, was filtered over Celite and the resulting solution concentrated in vacuo. The crude product was usually chromatographically pure. Silica gel chromatography led to some decomposition of the product. – Colourless oil. – IR (thin film): $\tilde{\nu}$ = 3265, 2120, 1455, 1440, 1340, 1180, 1135, 1075, 1030 cm^{-1}. – ^1H NMR (C_6D_6): δ = 1.31 (3 H, s), 1.42 and 1.43 (3 H, s), 1.45 (3 H, s), 1.65 and 1.66 (1 H, s), 2.88 and 2.90 (1 H, 2dd, *J* = 5.8, 4.5 Hz), 2.95 and 2.99 (1 H, 2d, *J* = 1.0 Hz), 3.45 and 3.47 (part of 2AB, 2dd, *J* = 10.0, 1.0 Hz), 3.65 and 3.69 (part of 2 AB, 2d, *J* = 10.0 Hz), 3.77 and 3.89 (AB, dd, *J* = 11.0, 5.8 Hz), 3.79 and 3.95 (AB, dd, *J* = 11.0, 4.5 Hz). – ^{13}C NMR ($CDCl_3$): δ = 11.71 (q), 16.28 (q), 22.98 (q), 51.04 (s), 51.18 (s), 60.80 (d), 60.85 (d), 61.41 (t), 62.61 (d), 62.61 (d), 65.79 (t), 65.84 (t), 72.79 (d), 72.84 (d), 79.01(s), 105.47 (s), 105.62 (s). – MS; *m*/*z* (intensity): 227 $[M^+ + 3]$ (0.2), 209 (1), 113 (100), 69 (42), 55 (60). – $C_{12}H_{16}O_4$ (224): calcd. C 63.55, H 7.24; found C 63.49; H 7.27.

General Procedure for the Silver-Catalyzed Cyclization of Acetylenic Alcohols: To a stirred solution of acetylenic alcohol (1 equiv.) in benzene (1 mL/mmol), was added at room temperature silver carbonate (0.1 equiv. or 1.2 equiv. see Table 3 for details). The mixture was heated at reflux until TLC (PE/EA, 90:10) showed the disappearance of the starting acetylenic alcohol (see Table 3). The heterogeneous mixture, which gradually turned from yellow to brown then black, was filtered over Celite or a small pad of silica and the resulting solution concentrated in vacuo. The crude product was usually chromatographically pure. The α-methylene heterocycles thus obtained proved to be very sensitive even at low (freezer) temperatures. Nevertheless the 3,4-epoxy-2-methyleneoxolanes **2a–c** could be kept for weeks in a freezer (–20°C). Special glassware treatment are even required with nonepoxidic compounds.[22] The sensitivity precluded the measurement of some spectroscopic data and some elemental analysis.

3,4-Epoxy-3-methyl-2-methyleneoxolane (2a): Colourless oil. – IR (thin film): $\tilde{\nu}$ = 1680, 1655, 1455, 1380, 1360, 1300, 1150, 1100, 1055, 970, 930, 890, 850 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 1.59 (3 H, s), 3.83 (1 H, d, *J* = 0.9 Hz), 3.95 (1 H, dd, *J* = 10.5, 0.9 Hz), 4.09 (1 H, d, *J* = 10.5 Hz), 4.21 (1 H, d, *J* = 2.1 Hz), 4.46 (1 H, d, *J* = 2.1 Hz). – ^{13}C NMR ($CDCl_3$) δ = 13.38 (q), 61.52 (s), 62.71 (d), 68.86 (t), 84.97 (t), 160.03 (s). – MS; *m*/*z* (%): 112 $[M]^+$ (100), 69 (45), 53 (40). – $C_6H_8O_2$ (112): calcd. C 63.55, H 7.24; found C 63.47, H 7.29.

3,4-Epoxy-2-methyleneoxolane (2b): Colourless oil. – IR (thin film): $\tilde{\nu}$ = 1680, 1660, 1355, 1290, 1230, 1055, 980, 925, 890, 850 cm^{-1}. – ^1H NMR (C_6D_6): δ = 3.15 (1 H, dd, *J* = 2.9, 1.1 Hz), 3.28 (1 H, dd, *J* = 10.6, 1.1 Hz), 3.35 (1 H, d, *J* = 2.9 Hz), 3.75 (1 H, d, *J* = 10.6 Hz), 4.17 (1 H, d, *J* = 1.5 Hz), 4.52 (1 H, d, *J* = 1.5 Hz). – ^{13}C NMR (C_6D_6): δ = 55.49 (s), 57.02 (d), 70.19 (t), 86.81 (t), 159.10 (s). – MS; *m*/*z* (%): 98 $[M]^+$ (100). – $C_5H_6O_2$ (98): calcd. C 61.21, H 6.15; found C 61.29, H 6.33.

(*Z*)-2-*tert*-Butyldimethylsilylmethylene-3,4-epoxyoxolane (2c): Colourless oil. – IR (thin film): $\tilde{\nu}$ = 1640, 1465, 1290, 1250, 1070, 1005,

860 cm^{-1}. – ^1H NMR (C_6D_6): δ = 0.35 (6 H, s), 1.10 (9 H, s), 1.30 (3 H, s), 3.03 (1 H, d, *J* = 1.2 Hz), 3.27 (1 H, dd, *J* = 10.5, 1.2 Hz), 3.76 (1 H, d, *J* = 10.5 Hz), 4.55 (1 H, s). – ^{13}C NMR (C_6D_6): δ = – 4.55 (q), 13.44 (q), 17.18 (s), 26.76 (q), 61.38 (s), 61.91 (d), 68.44 (t), 91.14 (d), 167.20 (s). – MS; *m/z* (%): 226 [M^+] (0.1). – $C_{12}H_{22}O_2Si$ (226): calcd. C 63.66, H 9.79; found C 63.45, H 9.50.

2-Methyleneoxolane (10):[22] Colourless oil. – IR (C_6D_6): ν̃ = 1665. – ^1H NMR (C_6D_6): δ = 1.5 (2 H, br. qu, *J* = 6.5), 2.2 (2 H, br. t, *J* = 6.5), 3.7 (2 H, br. t, *J* = 6.5), 3.9 (1 H, br. s), 4.5 (1 H, br. s).

2-Methyleneoxane (11):[22] Colourless oil. – IR (C_6D_6): ν̃ = 1650. – ^1H NMR (C_6D_6) *δ*: 1.3–1.7 (4 H, m), 1.9–2.1 (2 H, m), 3.5–3.6 (2 H, m), 4.25 (1 H, br. s), 4.75 (1 H, br. s).

3-Methyl-2-methylene-3-oxolene (12): Colourless oil. – IR (C_6D_6): ν̃ = 1645, 1625, 1355, 1240, 1215, 1135, 1060, 850, 780, 735, 700. – ^1H NMR (C_6D_6): δ = 2.25 (3 H, ddd, *J* = 1.8, 1.7, 1.5), 4.67 (1 H, dq, *J* = 1.7, 1.5), 5.09 and 5.12 (2 H, AB, *J* = 3.9, 2.0), 5.22 (1 H, dq, *J* = 1.8, 1.7), 5.32–5.39 (1 H, m). – ^{13}C NMR (C_6D_6): δ 11.57 (q), 75.34 (t), 77.14 (t), 129.08 (d), 134.03 (s), 167.97 (s).

2-Methylene-1-oxabicyclo[4,3]nonane (13): Colourless oil. – IR (C_6D_6): ν̃ = 1675, 1650, 1440, 1230, 1080, 1040, 940, 860, 835 cm^{-1}. – ^1H NMR (C_6D_6): δ = 1.0–1.9 (8 H, m), 2.0–2.6 (3 H, m), 3.4 (1 H, br t, *J* = 10 Hz), 3.86 (1 H, br s), 3.76 (1 H, d, *J* = 10.5 Hz), 4.25 (1 H, br s).

***trans* 1-(2-Hydroxycyclohexyl)propan-2-one (14):** Colourless oil. IR (neat): ν̃ = 3400, 1695, 1440, 1350, 1160, 1030. – ^1H NMR ($CDCl_3$): δ = 0.95–1.30 (4 H, m), 1.60–1.87 (4 H, m), 1.90–2.05 (1 H, m), 2.18 (3 H, s), 2.28 (1 H, dd, *J* = 15.9, 6.2 Hz), 2.4 (OH), 2.80 (1 H, dd, *J* = 15.9, 5.7 Hz), 3.13 (1 H, dt, *J* = 11.4, 4.5 Hz). – ^{13}C NMR ($CDCl_3$): δ = 25.04 (t), 25.58 (t), 30.60 (q), 31.91 (t), 36.13 (t), 41.61 (d), 48. 42 (t), 75.21 (d), 210.51 (s). – $C_9H_{16}O_2$ (156): calcd. C 69.23, H 10.26; found C 69.45, H 10.50.

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