# Synthesis of Hepialone and Related Dihydro-γ-pyrones by Various (3+3) Methods[‡]

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*Dedicated to Professor Richard Neidlein on the occasion of his 70th birthday*

**Keywords:** Oxiranes / Cyclizations / Alkynes / Pheromones / Natural products

Four routes towards the synthesis of the natural dihydropyrans **1**, i.e. from chiral oxiranes **9** as $C_2O$ building blocks and sulfur-substituted allyl (**14**) or propargyl (**10**, **11**) anions as $C_3$ fragments, have been investigated. The resulting $C_5O$ derivatives **4**, **8** could be cyclized after generation of a carbonyl group by oxidation (**6**, **7**) or hydrolysis (**8**). Here, the Pummerer reaction of **6** turned out to be only moderately efficient, whereas the hydroxylation of sulfone **7b** allowed smooth access to dihydropyran **1b**. Cyclization of bis(homoallyl) alcohol **13** was achieved by acid catalysis, but attempts to introduce a methyl group at C-2 of dihydropyran **12** did not meet with success.

## Introduction

The chiral 2,6-dialkyl-substituted 2,3-dihydropyran-4-one (+)-hepialone (**1a**) and the analogous oxacycle **1b** have been isolated from *Hepialus hecta L.* and *Hepialus californicus Bdv.* as male moth sex pheromones.[1] Because of their occurrence in nature and their simple structures, these compounds have already been the targets of several synthetic studies.[2] Generally, the construction of the ring system has been achieved starting from chiral 5-hydroxy-substituted 1,3-diketones by formation of the cyclic hemiacetals and subsequent elimination of the hydroxy group.[2a,2c−2i] Recently, we have developed novel routes to di- or tetrahydropyrans based on (3+3) methods employing oxiranes and lithiated methoxy sulfides[3] or carbanions of hetero-substituted alkynes as building blocks.[4] Here, oxiranes are particularly useful building blocks as they are readily available in optically active form, opening up avenues into natural product synthesis.[5] Moreover, it appeared feasible to modify our methods to allow the generation of a carbonyl group, thus making the title compounds available. Indeed, a retrosynthetic analysis (Scheme 1) revealed several options for generation and use of the carbonyl functionality. In routes A (Scheme 1), the final cyclization corresponds to an intramolecular Michael-type addition of a hydroxy group to an ynone **2** ($R^3$ = H); there is some precedent for 6-*endo*-dig ring-closure reactions[6] and also specifically for Michael additions to ynones.[7] The carbonyl group is envisaged as being generated from **6** or **7** by sulfur methodology involving oxidation reactions (route $A_1$) or by thioacetal hydrolysis in the case of **8** (route $A_2$). Alkynes **4** should be accessible from oxiranes **9** and functionalized alkynes **10**, **11** with complete control of regioselectivity.[4,8] Alternatively, the cyclization step may precede carbonyl generation (route B) if the cyclization is controlled by an electron-donating alkyloxy group.[3] This approach should allow introduction of the ring substituent $R^2$ as the final step.

## The Pummerer Route (Route $A_1$: 4 → 6 → 2 → 1)

It is well established that a carbonyl function can be formed from the corresponding sulfoxide by the Pummerer reaction.[9]

The required phenylthio-substituted bis(homopropargylic) alcohols **4** were readily obtained by ring-opening of oxiranes **9** with lithiated propargyl sulfides **10** in good yield as 1:1 diastereomeric mixtures (Scheme 2). Protection of the hydroxy group in **4a** by acetylation to give **5** and subsequent monooxidation of the sulfide unit with *m*-chloroperbenzoic acid in dichloromethane yielded the functionalized sulfoxide **6** (Scheme 2). This sulfoxide was then treated with an excess of trifluoroacetic anhydride, a particularly efficient promoter of the Pummerer reaction,[10] resulting in the intermediate generation of O,S-acetal **15**. This was easily hydrolyzed under basic conditions (Scheme 2).[11] At the same time, acetyl cleavage occurred, liberating the hydroxy function and allowing Michael-type addition to the ynone unit of **2a** ($R^3$ = H) to give target compound **1a**. Unfortunately, however, this domino process was accompanied by complex reaction pathways and purification of the product **1a** was complicated by its sensitivity. Thus, product **1a** was isolated only in poor yield (6%) and the Pummerer route was not investigated further.

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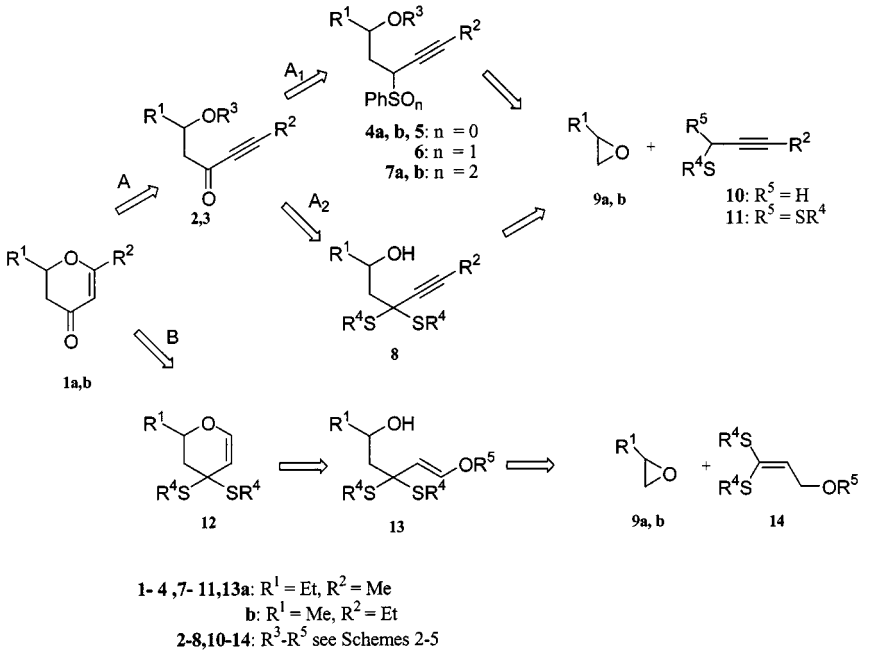
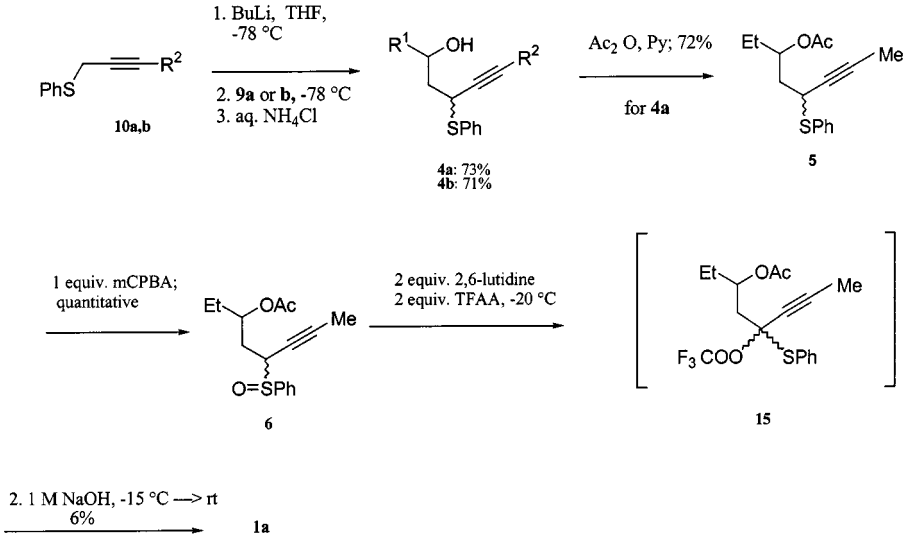



Scheme 1




Scheme 2

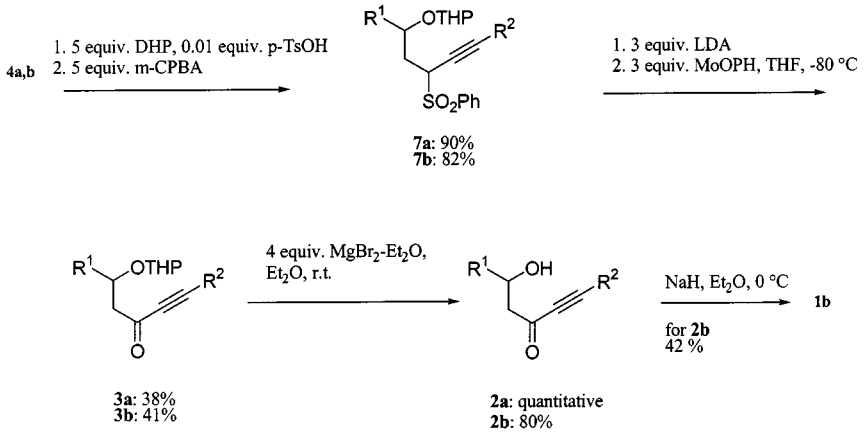
## The Sulfone Hydroxylation Route (Route $A_1$: 4 → 7 → 2 → 1)

Another possible means of achieving the conversion of alkynyl sulfides **4** to ynones **2** was offered by hydroxylation of the corresponding sulfones **7** using the molybdenum peroxide reagent $MoO_5$/pyridine/HMPA (MoOPH).[12]

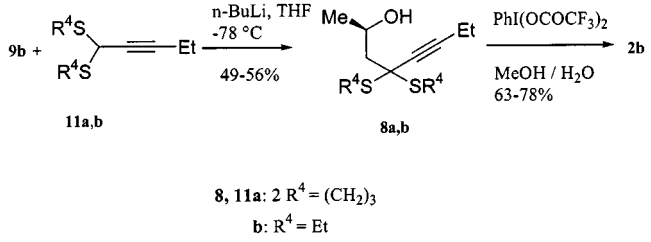
Prior to oxidation of the sulfide unit, the alcohol function in **4** was protected as a THP acetal by acid-catalyzed reaction with dihydropyran (Scheme 3). Subsequent oxidation of the crude acetals with *m*-chloroperbenzoic acid furnished sulfones **7** in excellent yields as mixtures of diastereomers. Oxidation of the sulfone unit was accomplished by deprotonation with LDA and addition of the MoOPH reagent, which led, after aqueous work-up, to the α,β-unsaturated alkynones **3**. Even though an excess of MoOPH was employed, the hydroxylation did not go to completion and some unchanged sulfone **7** was recovered. The synthesis was continued by hydrolysis of the THP protecting group under mildly acidic conditions using magnesium bromide in diethyl ether.[13] As shown for **1b**, the final regioselective cyclization to the six-membered oxacycle **1** could be realized by treatment with sodium hydride at 0 °C (Scheme 3).

## The Thioacetal Route (Route $A_2$: 11 → 8 → 2 → 1)

Rather than employing an oxidation step, in this synthetic sequence the carbonyl unit is present from the beginning in the masked form of a thioacetal, i.e. **11**. The sulfur functionality allowed smooth deprotonation and regioselec-




Scheme 3

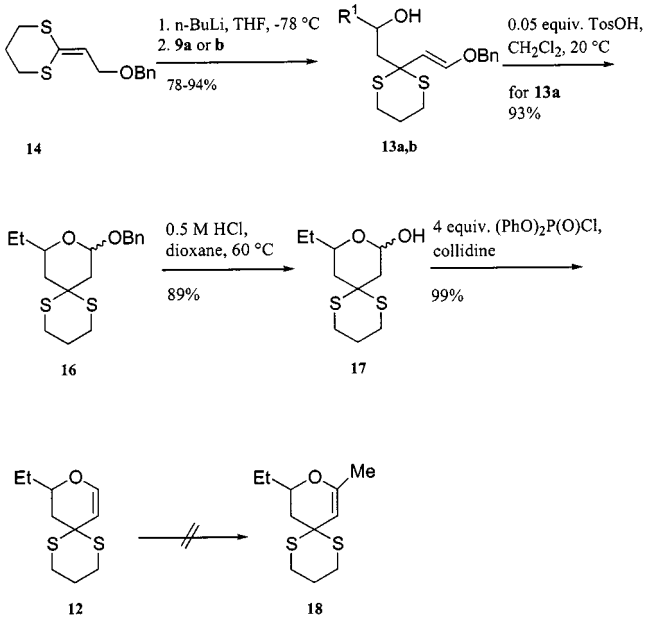



Scheme 4

tive ring-opening of oxirane **9a** to give alkynols **8a**,**b** (Scheme 4). The carbonyl group was liberated by hydrolysis using Stork's hypervalent iodine reagent,[14] which tolerates both triple bonds and hydroxy groups. Thus, in our hands, the formation of by-products was reduced in comparison to procedures using NBS[15] or mercury(II) chloride. The final cyclization was again achieved through the use of sodium hydride (Scheme 3).

## Introduction of $R^2$ as the Final Step (Route $B_2$: 13 → 12 → 1)

While the acid-induced cyclization of bis(homoallyl) alcohols normally yields tetrahydrofurans,[16] a terminal alkyloxy substituent changes the regioselectivity of the cyclization such that it leads to formation of tetrahydropyrans.[3] The requirement of introducing a masked carbonyl group from the beginning led to the $C_3$ building block **14** as a reaction partner for oxiranes **9a**,**b** (Scheme 5). In fact, lithiated **14** underwent a smooth and regioselective reaction with **9a**,**b** to give bis(homoallyl) alcohols **13a**,**b** in good yields. It is noteworthy that the γ-directing effect of the alkyloxy group[17] and the α-directing effect of the sulfur unit[16,18] work together such that C−C bond formation occurs specifically at the sulfur-substituted terminus in **14**. As shown for **13a**, the benzyloxy group then controls the regioselectivity of the acid-catalyzed cyclization step to exclusively afford the pyran derivative **16** (Scheme 5). After liberation of the hemiacetal, diphenylphosphorochloridate[19] turned out to be an extremely efficient reagent for the dehydration of **17** to give dihydropyran **12**. It had been anticipated that strategies for introducing a methyl group at C-2 of glycals such as **12** by deprotonation with *tert*-butyllithium and subsequent alkylation[20] might be applicable to the generation of dihydropyran **18**. However, despite testing a broad range of reaction conditions, deprotonation could not be achieved.




Scheme 5

In summary, the synthesis via sulfone **6** (route $A_1$) and that involving hydrolysis of thioacetals **8** (route $A_2$) have turned out to be the most convenient routes to 2,6-disubstituted dihydropyrans **1**. However, for 2-unsubstituted derivatives, route B involving bis(homoallyl) alcohols **13** offers an attractive alternative.

## Experimental Section

**General:** NMR: Bruker DPX 200 (200 MHz); solvent $CDCl_3$ unless noted otherwise; coupling constants *J* are given in Hz. − IR: Pye Unicam SP3-200; Bruker Vector 22 FT-IR. − Elemental analyses: Institut für Pharmazeutische Chemie, TU Braunschweig. − Column chromatography: Merck silica gel (70−230 mesh), petroleum ether (PE) of boiling range 60−70 °C, and ethyl acetate (EA) were

used. − Reactions for which general procedures are given were performed on a 2−5-mmol scale.

### $C_3$ Building Blocks

**2-(2-Benzyloxyethylidene)-1,3-dithiane (14):** A solution of 2-trimethylsilyl-1,3-dithiane (4.23 g, 22 mmol) in dry THF (50 mL) was cooled to −78 °C and a solution of *n*BuLi in hexane (16.5 mL of a 1.6 M solution, 26.4 mmol) was added dropwise. The mixture was allowed to warm to 0 °C over a period of 3 h and stirred for 10 min. It was then cooled to −78 °C once more, whereupon benzyloxyacetaldehyde (4.96 g, 33 mmol) was slowly added. The reaction mixture was allowed to warm to room temperature overnight and then stirred for a further 8 h. It was subsequently poured into a mixture of water and PE (1:1) and the biphasic mixture was vigorously stirred for 10 min. After separation of the phases, the organic layer was washed with water (5 ×), dried ($MgSO_4$), and concentrated in vacuo. The residue was subjected to kugelrohr distillation (b.p. 79 °C/0.01 mbar) to yield 5.29 g (95%) of **14**. − IR (film): $\tilde{\nu}$ = 2913, 2853, 1565, 1421, 1353, 1105, 1087, 1071, 738, 698 $cm^{-1}$. − $^1H$ NMR: δ = 1.99−2.15 (m, 2 H, $SCH_2CH_2$), 2.75−2.90 (m, 4 H, $SCH_2CH_2$), 4.11 (d, *J* = 6.5, 2 H, $CH_2OBn$), 4.44 (s, 2 H, $OCH_2Ph$), 5.98 (t, *J* = 6.5, 1 H, SC=CH), 7.21−7.30 (m, 5 H, arom. CH). − $^{13}C$ NMR (50 MHz): δ = 24.6 ($SCH_2CH_2$), 29.6, 29.1 ($SCH_2CH_2$), 66.6 ($CH_2OBn$), 72.3 ($PhCH_2O$), 126.9 (SC=*C*H), 127.6, 127.8, 128.3 (arom. CH), 132.0 (arom. C), 138.2 (SC). − $C_{13}H_{16}OS$ (220.3): calcd. C 61.72, H 6.53; found C 61.86, H 6.39.

### Ring-Opening of Oxiranes 9 by Carbanions

**Lithiation of 10, 11, and 14 and Reaction with Oxiranes 9. − General Procedure:** A solution of **10a**,**b**, **11a**,**b**, or **14** (1.2 equiv.) in dry THF (4 mL/mmol) was cooled to −78 °C. Then, 1.1 equiv. of *n*BuLi (1.6 M solution in *n*-hexane) was slowly added and the resulting mixture was stirred for 2.5 h. At −78 °C, epoxide **9a** or **9b** was added and the mixture was either kept at this temperature or allowed to warm to −60 °C. The progress of the reaction was monitored by TLC and after complete consumption of the starting material the cold solution was hydrolyzed by the addition of aqueous $NH_4Cl$ and diethyl ether (1:1). The aqueous phase was extracted three times with diethyl ether, the combined organic layers were washed twice with brine, dried ($MgSO_4$), and concentrated in vacuo. The resulting crude product, **4**, **8**, or **13**, was purified by column chromatography.

**5-(Phenylthio)oct-6-yn-3-ol (4a):** Prepared by reaction of **10a**[21] with ethyloxirane (**9a**). Column chromatography (PE/EA, 15:1) gave 2 diastereomers (1:1*) as a pale-yellow oil (73%). − IR (film): $\tilde{\nu}$ = 3369, 3058, 2963, 2919, 2237, 1583, 1439, 1116, 1025, 739, 691 $cm^{-1}$. − $^1H$ NMR: δ = 0.93, 0.94* (each t, *J* = 7.2, 3 H, $CH_3CH_2$), 1.49 (br. q, *J* = 7.2, 4 H, $CH_3CH_2$, $CH_3CH_2$*), 1.77−1.89 (m, 5 H, $CH_2$, OH, $CH_2$*), 1.81, 1.82* (each d, *J* = 2.4, 3 H, $CH_3$−C≡), 2.15* (d, *J* = 4.0, 1 H, OH), 3.86 (m, 2 H, CHOH, CHOH*), 3.96, 4.08* (each tq, *J* = 7.2, 2.4, 1 H, CHSPh), 7.3, 7.5 ($m_c$, 10 H, arom. CH, CH*). − $^{13}C$ NMR (50 MHz): δ = 3.6, 3.7* ($CH_3$−C≡), 9.7, 9.8* ($CH_3CH_2$), 30.0, 30.4* ($CH_3CH_2$), 35.8*, 36.3 (CHSPh), 41.9, 42.3* ($CH_2CS$), 71.0, 71.0* (CHOH), 78.1, 78.9*, 81.0*, 81.1 (C≡C), 127.4*, 127.6, 128.7, 128.7*, 132.3*, 132.7 (arom. CH), 133.7, 134.0* (arom. C). − $C_{14}H_{18}OS$ (234.4): calcd. C 71.75, H 7.74, S 13.68; found C 71.57, H 7.61, S 13.59.

**(2*R*)-4-(Phenylthio)oct-5-yn-2-ol (4b):** Prepared by reaction of **10b**[22] with (+)-(*R*)-methyloxirane (**9b**). Column chromatography (PE/EA, 15:1) gave 2 diastereomers (1:1) as a pale-yellow oil (71%). − IR (film): $\tilde{\nu}$ = 3365, 3059, 2971, 2935, 2235, 1583, 1479, 1439, 1375, 1319, 1126, 1069, 1025, 742, 691 $cm^{-1}$. − $^1H$ NMR: δ = 1.08 (t, *J* = 7.6, 6 H, $CH_3CH_2$, $CH_3CH_2$*), 1.19, 1.22* (each d, *J* = 6.0, 3 H, $CH_3CH$), 1.85 (m, 5 H, $CH_2$, OH, $CH_2$*), 2.18 (br. q, *J* = 7.6, 4 H, $CH_2C$≡, $CH_2C$≡*), 2.30* (m, 1 H, OH), 3.90−4.20 (m, 4 H, CHOH, CHSPh, CHOH*, CHSPh*), 7.2−7.5 (m, 10 H, arom. CH, CH*). − $^{13}C$ NMR (50 MHz): δ = 12.5, 12.5* ($CH_2C$≡), 13.7, 13.8* ($CH_3$), 23.2, 23.7* ($CH_3$), 36.0, 36.5* (CHSPh), 44.0, 44.3* ($CH_2$), 66.0, 66.3 (CHOH), 78.3, 78.8*, 87.2, 87.3* (C≡C), 127.5, 127.7, 128.7, 128.7, 132.8, 133.1 (arom. CH), 133.5, 133.8* (arom. C). − $C_{14}H_{18}OS$ (234.4): calcd. C 71.75, H 7.74, S 13.68; found C 71.77, H 7.36, S 13.72.

**(2*R*)-1-(2-But-1-ynyl-1,3-dithian-2-yl)propan-2-ol (8a):** Prepared by reaction of (+)-**9b** with **11a**.[23] Column chromatography gave a clear oil (56%). − IR (film): $\tilde{\nu}$ = 3449, 2972, 2934, 2906, 2361, 2233, 1455, 1422, 1373, 1275, 1172, 1128, 1089, 1064, 935, 906, 867, 779, 729 $cm^{-1}$. − $^1H$ NMR ($C_6D_6$): δ = 0.86 (t, *J* = 7.4, 3 H, $CH_2CH_3$), 1.16 (d, 3 H, *J* = 6.3, $CH_3$), 1.47−1.64 (m, 2 H, $SCH_2CH_2$), 1.91 (q, *J* = 7.4, 2 H, $CH_2CH_3$), 2.14 (dd, *J* = 14.2, 2.2, 1 H, $CH_2CHOH$), 2.35 (dd, *J* = 14.2, 8.6, 1 H, $CH_2CHOH$), 2.97 (s, 1 H, OH), 2.24−2.43, 3.01−3.19 (m, 4 H, $SCH_2CH_2$), 4.65 (ddq, *J* = 8.6, 6.3, 2.2, 1 H, CHOH). − $^{13}C$ NMR ($C_6D_6$): δ = 12.6 ($CH_2CH_3$), 14.0 ($CH_2CH_3$), 23.7 ($CH_3$), 25.7 ($SCH_2CH_2$), 28.4, 28.7 ($SCH_2CH_2$), 45.1 (CS), 51.0 ($CH_2CHOH$), 65.2 (CHOH), 79.8 (*C*CS), 90.1 (*C*$CH_2CH_3$). − $C_{11}H_{18}OS_2$ (230.4): calcd. C 57.34, H 8.01, S 27.92; found C 57.35, H 7.87, S 27.84. − $[\alpha]_D^{25}$ = 0.6 (*c* = 1.04, $CHCl_3$).

**(2*R*)-4,4-Bis(ethylthio)oct-5-yn-2-ol (8b):** Prepared by reaction of (+)-**9b** with **11b**.[24] Column chromatography gave a clear oil (49%). − IR (film): $\tilde{\nu}$ = 3472, 2972, 2930, 2874, 2234, 1451, 1401, 1374, 1317, 1265, 1173, 1130, 1089, 1054, 931, 782 $cm^{-1}$. − $^1H$ NMR ($C_6D_6$): δ = 0.82 (t, *J* = 7.5, 3 H, $CH_2CH_3$), 1.10 (t, *J* = 7.5, 3 H, $SCH_2CH_3$), 1.13 (t, *J* = 7.5, 3 H, $SCH_2CH_3$), 1.22 (d, *J* = 6.3, 3 H, $CH_3$), 1.85 (q, *J* = 7.5, 2 H, $CH_2CH_3$), 2.09 (dd, *J* = 14.5, 2.0, 1 H, $CH_2CHOH$), 2.28 (dd, *J* = 14.5, 8.5, 1 H, $CH_2CHOH$), 2.74 (q, *J* = 7.5, 2 H, $SCH_2CH_3$), 2.76 (q, *J* = 7.5, 2 H, $SCH_2CH_3$), 3.50 (s, 1 H, OH), 4.64 (ddq, *J* = 8.5, 6.3, 2.0, 1 H, CHOH). − $^{13}C$ NMR ($C_6D_6$): δ = 12.6 ($CH_2CH_3$), 13.7 ($CH_2CH_3$), 13.8, 13.9 ($SCH_2CH_3$), 23.7 ($CH_3$), 25.5, 25.6 ($SCH_2CH_3$), 50.7 ($CH_2CHOH$), 53.7 [*C*$(SEt)_2$], 66.0 (CHOH), 79.2 [*C*C$(SEt)_2$], 90.3 (*C*$CH_2CH_3$). − $C_{12}H_{22}OS_2$ (246.4): calcd. C 58.49, H 9.00, S 26.02; found C 58.05, H 9.06, S 26.02. − $[\alpha]_D^{25}$ = 28.1 (*c* = 1.11, $CHCl_3$).

**1-[2-(2-Benzyloxyvinyl)-1,3-dithian-2-yl]butan-2-ol (13a):** Prepared by reaction of **9a** with **14** at −78 °C (12 h). Column chromatography (PE/EA, 8:1) gave two diastereomers (9.4:1*) as clear oils (85%, 9%*). − First diastereomer: IR (film): $\tilde{\nu}$ = 3446, 3032, 2930, 1640, 1456, 1421, 1382, 1175, 1129, 740, 699 $cm^{-1}$. − $^1H$ NMR ($C_6D_6$): δ = 0.98 (t, *J* = 7.5, 3 H, $CH_3$), 1.27−1.70 (m, 4 H, $SCH_2CH_2$, $CH_2CH_3$), 2.04 (dd, *J* = 14.6, 1.6, 1 H, $SCCH_2$), 2.34 (dd, *J* = 14.6, 8.8, 1 H, $SCCH_2$), 2.34−2.54 (m, 4 H, $SCH_2CH_2$), 2.83 (d, *J* = 2.8, 1 H, OH), 3.95−4.13. (m, 1 H, CHOH), 4.48 (s, 2 H, $OCH_2Ph$), 5.21 (d, *J* = 12.5, 1 H, CH=CHOBn), 6.99 (d, *J* = 12.5, 1 H, CH=CHOBn), 7.09−7.29 (m, 5 H, arom. CH). − $^{13}C$ NMR ($C_6D_6$): δ = 10.1 ($CH_3$), 25.1 ($SCH_2CH_2$), 27.2, 27.5 ($SCH_2CH_2$), 31.1 ($CH_2CH_3$), 49.7 ($SCCH_2$), 51.4 (CS), 70.0 (CHOH), 71.7 ($OCH_2Ph$), 109.8 (CH=CHOBn), 127.7, 128.0, 128.6 (arom. CH), 137.2 (arom. C), 151.4 (CH=CHOBn). − $C_{17}H_{24}O_2S_2$ (324.5): calcd. C 62.92, H 7.45, S 19.76; found C 62.85, H 7.55, S 19.42. − Second diastereomer: IR (film): $\tilde{\nu}$ = 3443, 2961, 2931, 1737, 1655, 1455, 1421, 1373, 1244, 1169, 1118, 1048, 758, 702 $cm^{-1}$. − $^1H$ NMR ($C_6D_6$): δ = 0.91 (t, *J* = 7.6, 3 H, $CH_3$), 1.31−1.56 (m, 4 H, $SCH_2CH_2$, $CH_2CH_3$), 1.97 (dd, *J* = 14.4, 1.6, 1 H, $SCCH_2$), 2.17 (dd, *J* = 14.4, 3.1, 1 H, $SCCH_2$), 2.28−2.40 (m, 4 H, $SCH_2CH_2$), 2.71 (d, *J* = 6.5, 1 H, OH), 3.96 (m, 1 H, CHOH),

4.42 (s, 2 H, OC$H_2$Ph), 6.04 (d, $J$ = 8.3, 1 H, C$H$=CHOBn), 7.07 (d, $J$ = 8.3, 1 H, CH=C$H$OBn), 7.10−7.18 (m, 5 H, arom. CH). − $^{13}$C NMR ($C_6D_6$): δ = 10.1 ($CH_3$), 25.0 (SC$H_2$C$H_2$), 27.2, 27.5 (S$C$H$_2$CH$_2$), 31.0 ($C$H$_2$CH$_3$), 49.6 (SC$C$H$_2$), 51.3 (CS), 71.7 (OC$H_2$Ph), 79.8 (CHOH), 109.8 (C$H$=CHOBn), 126.5, 128.9, 130.9 (arom. CH), 138.2 (arom. C), 151.4 (CH=C$H$OBn). − $C_{17}H_{24}O_2S_2$ (324.5): calcd. C 62.92, H 7.45, S 19.76; found C 62.89, H 6.82, S 19.56.

**1-[2-(2-Benzyloxyvinyl)-1,3-dithian-2-yl]propan-2-ol (13b):** Prepared by reaction of **9b** with **14** at −78 °C (12 h). Column chromatography (PE/EA, 5:1) gave a clear oil (78%). − IR (film): ṽ = 3449, 2964, 2929, 2905, 1655, 1639, 1497, 1454, 1422, 1373, 1316, 1276, 1246, 1175, 1130, 935, 809, 739, 699 cm$^{-1}$. − $^1$H NMR ($C_6D_6$): δ = 1.13 (d, $J$ = 6.3, 3 H, $CH_3$), 1.37−1.58 (m, 2 H, SCH$_2$C$H_2$), 1.93 (dd, $J$ = 14.7, 1.9, 1 H, $CH_2$), 2.31 (dd, $J$ = 14.7, 8.5, 1 H, C$H_2$), 2.39−2.48 (m, 4 H, SC$H_2$CH$_2$), 2.83 (s, 1 H, OH), 4.24 (ddq, $J$ = 8.5, 6.3, 1.9, 1 H, C$H$OH), 4.42 (s, 2 H, OC$H_2$Ph), 5.14 and 6.94 (each d, $J$ = 12.6, 1 H, C$H$=C$H$OBn), 7.09−7.21 (m, 5 H, arom. CH). − $^{13}$C NMR ($C_6D_6$): δ = 24.1 ($CH_3$), 25.0, 27.2, 27.4 (S$C$H$_2$CH$_2$, SCH$_2$$C$H$_2$), 51.2 ($C$H$_2$CS), 51.3 (CS), 65.1 (CHOH), 71.6 (OC$H_2$Ph), 128.6, 128.0, 127.7 (arom. CH), 109.7 (C$H$=CHOBn), 137.2 (arom. C), 151.4 (CH=C$H$OBn). − $C_{16}H_{22}O_2S_2$ (310.5): calcd. C 61.90, H 7.15, S 20.66; found C 61.87, H 7.14, S 20.66.

**Route $A_1$ (Pummerer Reaction)**

**6-Acetoxy-4-(phenylsulfinyl)oct-2-yne (6):** To a solution of **4a** (468 mg, 2 mmol) in pyridine (35 mL) was added acetic anhydride (9.4 mL, 100 mmol) and the mixture was stirred overnight. The pyridine was then removed by azeotropic distillation with toluene and the residual mixture was taken up in $CH_2Cl_2$. The resulting solution was washed with aqueous $NH_4Cl$ solution and water. After drying ($Na_2SO_4$), the solvent was removed in vacuo and the crude product was purified by column chromatography (PE/EA, 10:1) to give *6-acetoxy-4-(phenylthio)oct-2-yne* (**5**) as a colorless oil [398 mg, 72%, 2 diastereomers (1:1*)]. − IR (film): ṽ = 3059, 2969, 2920, 2239, 1738, 1439, 1372, 1024, 746, 692 cm$^{-1}$. − $^1$H NMR: δ = 0.86, 0.87* (each t, $J$ = 7.4, 3 H, C$H_3$CH$_2$), 1.59, 1.60* (each quint, $J$ = 7.4, 2 H, C$H_2$CH$_3$), 1.80*, 1.82 (each d, $J$ = 2.0, 3 H, $CH_3$), 1.90 (m, 4 H, $CH_2$, $CH_2$*), 2.02, 2.04* (each s, 3 H, COC$H_3$), 3.76, 3.81* (each dq, $J$ = 9.2, 2.0, 1 H, CHSPh), 5.08 (m, 2 H, CHOAc, CHOAc*), 7.3, 7.5 (m, 10 H, arom. CH, CH*). − $^{13}$C NMR (50 MHz): δ = 3.7, 3.7 ($CH_3$), 9.2, 9.2 ($C$H$_3$CH$_2$), 21.2, 21.2 (CO$C$H$_3$), 26.8, 27.2 ($C$H$_2$CH$_3$), 35.5, 36.0 (CHSPh), 39.1, 39.6 ($CH_2$), 73.0, 73.3 (CHOAc), 77.5, 78.4, 80.6, 81.1 (C≡C), 127.5, 127.7, 128.7, 128.7, 132.5, 133.1 (arom. CH), 133.7, 133.9 (arom. C), 170.6, 170.6 (C=O). − $C_{16}H_{20}O_2S$ (276.4): calcd. C 69.53, H 7.29, S 11.60; found C 69.68, H 7.12, S 11.64. − The intermediate **5** (276 mg, 1.0 mmol) was dissolved in $CH_2Cl_2$ (10 mL) and a solution of *m*-chloroperbenzoic acid (247 mg, stabilized by the presence of 30% $H_2O$, 1.0 mmol) in $CH_2Cl_2$ (3 mL) was added at −20 °C. After 2 h at −20 °C, the resulting reaction mixture was washed with water and brine, dried ($Na_2SO_4$), and concentrated in vacuo. The resulting product, **6** [290 mg, 99%, mixture of four diastereomers (1:1:1:1)], was found to be sufficiently pure for direct use in the next step. − IR (film): ṽ = 3060, 2970, 2880, 2235, 1736, 1444, 1373, 1241, 1085, 1050, 1025, 751, 691 cm$^{-1}$. − $^1$H NMR: δ = 0.85, 0.89, 0.90, 0.94 (each t, $J$ = 7.2, 3 H, $CH_3$), 1.56−1.70 (m, 8 H, C$H_2$CH$_3$), 1.79, 1.80, 1.80, 1.81 (each s, 3 H, C$H_3$C≡), 2.03, 2.04, 2.05, 2.06 (each s, 3 H, COC$H_3$), 2.09−2.30 (m, 4 H, $CH_2$), 2.63 (ddd, $J$ = 15.0, 7.0, 4.8, 1 H, $CH_2$), 2.84 (m, 2 H, $CH_2CH_2$), 3.06 (ddd, $J$ = 15.2, 9.2, 8.0, 1 H, $CH_2$), 3.38−3.66 (m, 4 H, C$H$SOPh), 4.90−5.12 (m, 4 H, CHOAc), 7.6−7.7 (m, 20 H, arom. H).

**(±)-2-Ethyl-6-methyl-2,3-dihydropyran-4-one (1a):** **6** (146 mg, 0.5 mmol) was dissolved in dry MeCN (3 mL) and 2,6-lutidine (107 mg, 1.0 mmol) was added. A solution of trifluoroacetic anhydride (210 mg, 1.0 mmol) in MeCN (4 mL) was then slowly added at −20 °C. After 1 h, the resulting mixture was treated with 1 M aqueous NaOH solution (1 mL), initially at −15 °C, but then the temperature was allowed to rise to 20 °C over a period of 3 h. TLC showed the presence of several products. The mixture was diluted with $Et_2O$ and the organic layer was washed several times with aq. $NH_4Cl$ solution and brine, dried ($Na_2SO_4$), and concentrated. Column chromatography (PE/EA, 20:1 → 10:1) of the residue gave 8.5 mg (6%) of **1a** as a colorless liquid. Spectroscopic data were as given in ref.[1c]

**Route $A_1$ (Sulfone Hydroxylation)**

**Acetalization and Oxidation of 4a,b to give *O*-Protected Sulfones 7a,b:** At room temperature, alkynol **4a** or **4b** (1 equiv.) was dissolved in $CH_2Cl_2$ (4 mL/mmol) and 3,4-dihydro-2*H*-pyran (5 equiv.) as well as *p*TosOH (0.01 equiv.) were added. The mixture was stirred for 1 h, then washed with $H_2O$, aqueous $NaHCO_3$ solution, and brine, and finally concentrated in vacuo. The THP derivatives thus obtained were used without further purification. − A solution of the crude sulfide (1 equiv.) in $CH_2Cl_2$ (10 mL/mmol) was treated with *m*-CPBA (70% in $H_2O$, 2.5 equiv.) at 0 °C. The stirred mixture was allowed to warm to room temperature over a period of 2 h. It was then washed as described above, dried ($Na_2SO_4$), and the solvent was evaporated. The residue was purified by flash chromatography (PE/EA, 10:1).

**4-Phenylsulfonyl-6-(tetrahydropyran-2-yloxy)oct-2-yne (7a):** Colorless viscous oil (4 diastereomers, 1:1:1:1); 90% yield based on **4a**. − IR (film): ṽ = 3066, 2940, 2877, 2247, 1447, 1320, 1151, 1084, 734, 689 cm$^{-1}$. − $^1$H NMR: δ = 0.86, 0.88, 0.90, 0.94 (each t, $J$ = 7.6, 3 H, $CH_3$), 1.46−1.76 [m, 32 H, C$H_2$CH$_3$, C$H_2$(THP)], 1.78, 1.79, 1.79, 1.81 (each d, $J$ = 2.2, 3 H, C$H_3$C≡), 1.90−2.26 (m, 8 H, $CH_2$), 3.46 [m, 4 H, $CH_2$O(THP)], 3.86 [m, 4 H, $CH_2$O(THP); 4 H, CHO(THP); 2 H, CHSO$_2$Ph], 4.22 (m, 1 H, CHSO$_2$Ph), 4.31 (dq, $J$ = 11.6, 2.4, 1 H, CHSO$_2$Ph), 4.62 (m, 4 H, OCHO), 7.5−7.7 (m, 12 H, arom. H), 7.9−9.0 (m, 8 H, arom. H). − $^{13}$C NMR: δ = 3.68, 3.70, 3.72, 3.72 (C$H_3$C≡), 8.7, 9.1, 9.2, 9.6 ($CH_3$), 19.6, 19.7, 20.1, 25.2, 25.3, 25.3, 25.4, 30.8, 30.9, 31.0, 31.0 [$CH_2$(THP)], 26.2, 26.3, 27.2, 28.5 (C$H_2$CH$_3$), 31.9, 33.0, 33.8, 34.2 ($CH_2$), 55.7, 55.8, 56.9, 57.0 (C$H$SO$_2$Ph), 62.5, 62.7, 62.8, 63.2 [$CH_2$O(THP)], 71.2, 71.6, 71.9, 72.2 (C≡C), 73.3, 74.9, 76.3, 77.2 [CHO(THP)], 84.1, 84.5, 84.6, 85.1 (C≡C), 96.1, 97.3, 98.7, 100.1 (OCHO), 128.6, 128.7, 128.7, 129.4, 133.7, 133.9 (arom. CH), 136.8, 136.9, 137.0, 137.1 (arom. C). − $C_{19}H_{26}O_4S$ (350.5): calcd. C 65.11, H 7.47, S 9.15; found C 64.89, H 7.31, S 8.96.

**(7*R*)-5-Phenylsulfonyl-7-(tetrahydropyran-2-yloxy)oct-3-yne (7b):** Colorless viscous oil (4 diastereomers); 82% yield based on (2*R*)-**4b**. − IR (film): ṽ = 3066, 2940, 2877, 2242, 1448, 1321, 1151, 1084, 1023, 735, 690 cm$^{-1}$. − $^1$H NMR: δ = 1.03, 1.04, 1.05, 1.06 (each t, $J$ = 7.6, 3 H, C$H_3$CH$_2$), 1.16 (d, $J$ = 6.4, 6 H, 2 × $CH_3$), 1.25, 1.29 (each d, $J$ = 6.4, 6 H, 2 × $CH_3$), 1.45−1.60 [m, 20 H, $CH_2$(THP)], 1.60−1.80 [m, 4 H, $CH_2$(THP), 8 H, $CH_2$], 2.08−2.22 (m, 8 H, C$H_2$CH$_3$), 3.49 [m, 4 H, $CH_2$O(THP)], 3.75−4.12 [m, 4 H, $CH_2$O(THP); 4 H, CHOTHP; 3 H, CHSO$_2$Ph], 4.28 (dq, $J$ = 11.6, 2.4, 1 H, CHSO$_2$Ph), 4.58−4.76 (m, 4 H, OCHO), 7.5−7.7 (m, 12 H, arom. H), 7.9−8.0 (m, 8 H, arom. H). − $^{13}$C NMR: δ = 12.4 (C$H_2$CH$_3$), 13.2, 13.2, 13.3, 13.4, 18.9, 19.1, 19.1, 19.2 ($CH_3$, C$H_3$CH$_2$), 19.6, 19.8, 19.8, 19.8, 25.3, 30.7, 30.9, 31.0, 31.0

[$CH_2$(THP)], 36.3, 36.5, 36.5, 36.5 ($CH_2$), 56.0, 56.3, 56.8, 56.9 ($CHSO_2Ph$), 62.0, 62.5, 62.7, 62.8 [$CH_2O$(THP)], 66.8, 69.7, 71.1, 72.9 (CHOTHP), 71.4, 71.6, 72.0, 72.2, 90.1, 90.4, 90.5, 90.8 (C≡C), 94.0, 96.3, 98.4, 100.5 (OCHO), 128.6, 128.7, 129.6, 129.7, 129.8, 133.7, 133.8, 133.9 (arom. CH), 136.7, 136.8, 136.8, 136.9 (arom. C). − $C_{19}H_{26}O_4S$ (350.5): calcd. C 65.11, H 7.47, S 9.15; found C 65.50, H 7.29, S 9.35.

**Hydroxylation of Sulfones 7a,b To Give Alkynones 3a,b:** Sulfone **7a** or **7b** (1 equiv.) was dissolved in THF (30 mL/mmol) and the solution was cooled to −80 °C. Then, 3 equiv. of LDA in THF (prepared from 3.6 equiv. of HN*i*$Pr_2$ and 3 equiv. of *n*BuLi) were slowly added and the mixture was stirred for 10 min. With the temperature maintained at −80 °C, $MoO_5$/pyridine/HMPT reagent[12a] (3 equiv.) in THF (6 mL/mmol) was added dropwise. After stirring for 1 h, the intermediate formed was hydrolyzed by the addition of saturated aqueous $Na_2SO_3$ solution (10 mL/mmol) to the cold reaction mixture. After separation of the phases, the organic phase was washed with $H_2O$ and brine, dried ($Na_2SO_4$), and concentrated in vacuo at 30 °C. The crude product was purified by chromatography to afford **3** along with some unchanged **7**. The products proved to be too unstable for elemental analysis.

**6-(Tetrahydropyran-2-yloxy)oct-2-yn-4-one (3a):** Colorless oil (2 diastereomers, 1:1*); yield 38% (corrected for 10% of recovered **7a**). − IR (film): $\tilde{\nu}$ = 2940, 2877, 2219, 1673, 1600, 1440, 1260, 1118, 1024 $cm^{-1}$. − $^1H$ NMR: δ = 0.91, 0.95* (each t, *J* = 7.4, 3 H, $CH_3$), 1.5−1.7 [m, 16 H, $CH_2$(THP), C*H*$_2$CH$_3$, $CH_2$(THP)*, C*H*$_2$CH$_3$*], 2.02 (s, 6 H, C*H*$_3$C≡, $CH_3$C≡*), 2.62 (dd, *J* = 15.6, 5.4, 2 H, $CH_2$, $CH_2$*), 2.78 (dd, *J* = 15.6, 7.4, 1 H, $CH_2$), 2.96 (dd, *J* = 15.6, 7.0, 1 H, $CH_2$*), 3.48, 3.88 [each m, 2 H, $CH_2O$(THP)], 4.16 [m, 2 H, CHO(THP), CHO(THP)*], 4.68 (m, 2 H, OCHO, OCHO*). − $^{13}C$ NMR: δ = 4.1, 4.1* (*C*H$_3$C≡), 9.3, 9.7* ($CH_3$), 19.7, 19.8*, 25.3, 25.4*, 30.9, 31.0* [$CH_2$(THP)], 26.8, 28.5* (*C*H$_2$CH$_3$), 49.9, 51.0* ($CH_2$), 62.5, 62.8* [$CH_2O$(THP)], 74.2, 74.9* (CHOTHP), 80.6, 80.6*, 89.3, 90.0* (C≡C), 98.1, 98.8* (OCHO), 186.1, 186.3* (C=O).

**(2*R*)-2-(Tetrahydropyran-2-yloxy)oct-5-yn-4-one (3b):** Colorless oil (2 diastereomers, 1:1*); yield 41% (corrected for 32% of recovered **7b**). − IR (film): $\tilde{\nu}$ = 2941, 2873, 2211, 1675, 1455, 1375, 1132, 1076, 1022, 995 $cm^{-1}$. − $^1H$ NMR: δ = 1.19, 1.30 (each d, *J* = 6.4, 3 H, $CH_3$), 1.20 (t, *J* = 7.6, 6 H, C*H*$_3$CH$_2$, C*H*$_3$CH$_2$*), 1.45−1.60 [m, 12 H, $CH_2$(THP), $CH_2$(THP)*], 2.37 (q, *J* = 7.6, 4 H, C*H*$_2$CH$_3$, C*H*$_2$CH$_3$*), 2.57 (dd, *J* = 16.0, 5.4, 1 H, $CH_2$), 2.60 (dd, *J* = 15.8, 5.8, 1 H, $CH_2$*), 2.83 (dd, *J* = 16.0, 7.6, 1 H, $CH_2$), 2.94 (dd, *J* = 15.8, 7.2, 1 H, $CH_2$*), 3.48, 3.88 [each m, 2 H, $CH_2O$(THP), $CH_2O$(THP)*], 4.34 [m, 2 H, CHO(THP), CHO(THP)*], 4.71 (m, 2 H, OCHO, OCHO*). − $^{13}C$ NMR: δ = 12.6, 12.6* (*C*H$_2$CH$_3$), 12.7, 12.7*, 19.6, 22.0* ($CH_3$, *C*H$_3$CH$_2$), 19.4*, 19.8, 25.4, 25.4*, 30.9, 30.9* [$CH_2$(THP)], 52.7, 53.2* ($CH_2$), 62.2*, 62.8 [$CH_2O$(THP)], 80.5, 80.6*, 95.5*, 95.7 (C≡C), 96.0*, 99.4 (OCHO), 185.9, 185.9* (C=O).

**Deprotection of Ynones 3a,b to give Alcohols 2a,b:** Ynone **3a** or **3b** (1 equiv.) was dissolved in diethyl ether (20 mL/mmol) and stirred with $MgBr_2 \cdot OEt_2$ (4 equiv.) at room temperature for 1 h. Work-up was performed as described above for the synthesis of **3a**,**b**. In the final purification step, column chromatography using *n*-pentane/diethyl ether (1.5:1) gave pure **2b**; **2a** was obtained in sufficiently pure form from the reaction mixture.

**6-Hydroxyoct-2-yn-4-one (2a):** Colorless oil, quantitative yield. − IR (film): $\tilde{\nu}$ = 3413, 2963, 2220, 1671, 1443, 1413 $cm^{-1}$. − $^1H$ NMR: δ = 0.93 (t, *J* = 7.4, 3 H, $CH_3$), 1.50 (m, 3 H, C*H*$_2$CH$_3$, OH), 2.01 (s, 3 H, $CH_3$C≡), 2.62 (dd, *J* = 17.0, 8.0, 1 H, $CH_2$), 2.74 (dd, *J* = 17, 0, 4.0, 1 H, $CH_2$), 4.00 (m, 1 H, CHOH).

**(2*R*)-2-Hydroxyoct-5-yne-4-one (2b):** Colorless oil, 80% yield; $[\alpha]_D^{23}$ = −60 (*c* = 1, *n*-pentane). − IR (film): $\tilde{\nu}$ = 3415, 2971, 2940, 2211, 1671, 1458, 1376, 1317, 1172, 1118, 1076 $cm^{-1}$. − $^1H$ NMR: δ = 1.21 (t, *J* = 7.6, 3 H, C*H*$_3$CH$_2$), 1.21 (d, *J* = 6.4, 3 H, $CH_3$), 1.50 (br. s, 1 H, OH), 2.39 (q, *J* = 7.6, 2 H, C*H*$_2$CH$_3$), 2.67 (dd, *J* = 17.6, 7.2, 1 H, $CH_2$), 2.76 (dd, *J* = 17.6, 4.6, 1 H, $CH_2$), 4.30 (m, 1 H, C*H*OH). − $^{13}C$ NMR: δ = 12.6 (*C*H$_2$CH$_3$), 12.7, 22.2 ($CH_3$), 53.6 ($CH_2$), 63.8 (CHOH), 80.2, 96.6 (C≡C), 187.7 (C=O).

**Cyclization of 2b To Give (6*R*)-6-Ethyl-2-methyl-2,3-dihydro-4*H*-pyran-4-one (1b):** At 0 °C, NaH (50% in mineral oil, 1 equiv.) was added in small portions to a solution of **2b** (1 equiv.) in diethyl ether (20 mL/mmol). The mixture was stirred for 1 h, then washed with water and dried ($Na_2SO_4$). The resulting mixture was carefully concentrated at 30 °C. The crude product was purified by column chromatography (*n*-pentane/diethyl ether, 2:1) on neutral alumina to give a colorless oil (42%); the specific optical rotation of the product was found to be identical to that reported in ref.[2b] − IR (film): $\tilde{\nu}$ = 2965, 2900, 1716, 1670, 1606, 1458, 1262, 1120, 1077, 867 $cm^{-1}$. − $^1H$ NMR: δ = 1.09 (t, *J* = 7.4, 3 H, C*H*$_3$CH$_2$), 1.48 (d, *J* = 6.4, 3 H, $CH_3$), 2.24 (q, *J* = 7.4, 2 H, $CH_2CH_3$), 2.34 (dd, *J* = 16.0, 11.2, 1 H, $CH_2$), 2.41 (dd, *J* = 16.0, 6.2, 1 H, $CH_2$), 4.46 (ddd, *J* = 11.1, 6.3, 6.2, 1 H, CHO), 5.30 (s, 1 H, HC=C).

**Route $A_2$ (Thioacetal Hydrolysis)**

**(2*R*)-2-Hydroxyoct-5-yn-4-one (2b):** To a solution of **8a** or **8b** (1 equiv.) in a mixture of MeOH and water (9:1, 1 mL/mmol), [bis(trifluoroacetoxy)iodo]benzene (1.5 equiv.) was added in small portions at room temperature and the mixture was stirred until TLC showed complete conversion of the ketone (20 min). It was then hydrolyzed with aqueous $NaHCO_3$ solution, extracted five times with diethyl ether, and the combined extracts were dried ($MgSO_4$) and concentrated. Column chromatography (*n*-pentane/$Et_2O$, 1.5:1) of the residue afforded 63% (from **8a**) and 78% (from **8b**) of **2b** as a colorless oil; $[\alpha]_D^{27}$ = −59.0° (*c* = 1.1, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3432, 2977, 2941, 2211, 1671, 1459, 1377, 1318, 1247, 1173, 1120, 1083, 1056, 1010, 945, 773 $cm^{-1}$. − $^1H$ NMR ($C_6D_6$): δ = 0.72 (t, 3 H, *J* = 7.5, $CH_2$C*H*$_3$), 0.96 (d, 3 H, *J* = 6.3, $CH_3$), 1.74 (q, 2 H, *J* = 7.5, C*H*$_2$CH$_3$), 2.28 (dd, 1 H, *J* = 17.0, 3.8, C*H*$_2$CHOH), 2.47 (dd, 1 H, *J* = 17.0, 8.4, C*H*$_2$CHOH), 4.13 (ddq, 1 H, *J* = 8.4, 6.3, 3.8, C*H*OH). − $^{13}C$ NMR ($C_6D_6$): δ = 12.4, 12.6 ($CH_2$*C*H$_3$), 22.6 (*C*H$_3$), 54.2 (*C*H$_2$CHOH), 63.8 (CHOH), 81.0 (*C*CH$_2$CH$_3$), 94.9 (*C*C=O), 186.7 (C=O).

**Route B (Pyran Elaboration)**

**8-Benzyloxy-10-ethyl-9-oxa-1,5-dithiaspiro[5.5]undecane (16):** To a solution of bis(homoallylic) alcohol **13a** (1 equiv.) in dichloromethane (7 mL/mmol) was added *p*TosOH (0.05 equiv.) and the mixture was stirred at room temperature for 1 h. After complete conversion, the mixture was diluted with diethyl ether, washed with aqueous $NaHCO_3$ solution and twice with brine, and then dried ($MgSO_4$). The solvent was evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column (PE/EA, 50:1) to give two diastereomers (1:0.3*). − $^1H$ NMR ($C_6D_6$): δ = 0.90 (t, 3 H, *J* = 7.4, $CH_3$), 0.93 (t, 3 H, *J* = 7.0, $CH_3$*), 1.19−1.79 (m, 12 H, 7-H*, 11-H*, C*H*$_2$CH$_3$, C*H*$_2$CH$_3$*, SCH$_2$C*H*$_2$, SCH$_2$C*H*$_2$*), 2.06 (dd, 1 H, *J* = 13.5, 9.3, 7-H), 2.09 (dd, 1 H, *J* = 13.5, 2.0, 11-H), 2.46 (dd, 1 H, *J* = 13.5, 7.4, 11-H), 1.90−2.62 (m, 8 H, SC*H*$_2$CH$_2$, SC*H*$_2$CH$_2$*), 2.71 (ddd, 1 H, *J* = 13.5, 2.0, 7-H), 3.80 (dddd, 1 H, *J* = 11.1, 7.4, 5.0, 2.0, 10-H), 4.15 (dddd, 1 H, *J* = 10.8, 7.8, 4.5, 1.7, 10-H*), 4.31 (d, 1 H, *J* = 12.5, PhC*H*$_2$O*),

4.47 (d, 1 H, $J$ = 12.0, PhC$H_2$O), 4.77 (d, 1 H, $J$ = 12.5, PhC$H_2$O*), 4.79 (d, 1 H, $J$ = 3.0, 8-H*), 4.98 (d, 1 H, $J$ = 12.0, PhC$H_2$O), 5.05 (dd, 1 H, $J$ = 9.3, 2.0, 8-H) 7.01−7.48 (m, 10 H, arom. CH, CH*). − $^{13}$C NMR ($C_6D_6$): δ = 10.1 ($CH_3$*), 10.2 ($CH_3$), 25.5 ($CH_2CH_3$*), 25.7 ($CH_2CH_3$), 25.9, 28.7 (S$CH_2CH_2$), 25.8 (SC$H_2$C$H_2$), 26.2 (SC$H_2$C$H_2$*), 26.4, 28.5 (S$CH_2CH_2$*), 42.0 (C-7*), 42.7 (C-11*), 43.1 (C-7), 43.3 (C-11), 46.5 (C-6*), 48.2 (C-6), 67.3 (C-10*), 68.8 (Ph$CH_2$O*), 70.3 (Ph$CH_2$O), 72.1 (C-10), 96.4 (C-8*), 98.2 (C-8), 127.0, 127.2, 128.2 (arom. CH*), 127.3, 127.7, 128.2 (arom. CH), 138.8 (arom. C), 139.1 (arom. C*). − $C_{17}H_{24}O_2S_2$ (324.5): calcd. C 62.92, H 7.45, S 19.76; found C 62.92, H 7.41, S 19.61.

**10-Ethyl-9-oxa-1,5-dithiaspiro[5.5]undecan-8-ol (17):** To a solution of oxacycle **16** (1 equiv.) in dioxane (3 mL/mmol) was added 0.5 M hydrochloric acid (3 mL/mmol). The mixture was stirred at 60 °C for 12 h and then hydrolyzed by the addition of a mixture of aqueous $NaHCO_3$ solution and $CH_2Cl_2$. The aqueous phase was washed five times with $CH_2Cl_2$. The combined organic layers were washed three times with aqueous $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated in vacuo, and the residue was purified by column chromatography (PE/EA, 5:1) to give two diastereomers (1:0.3*) as a colorless solid (m.p. 89 °C) in 89% yield. − IR (film): $\tilde{\nu}$ = 3397, 2933, 1424, 1376, 1338, 1279, 1240, 1200, 1115, 1081, 1063, 980, 930, 908, 887, 872 cm$^{-1}$. − $^1$H NMR ($C_6D_6$): δ = 0.88 (t, 6 H, $CH_3$, $CH_3$*), 1.15−1.93 (m, 12 H, SC$H_2$C$H_2$, C$H_2$C$H_3$, 5-H*, 5-H), 1.95−2.78 (m, 12 H, SC$H_2$C$H_2$, SC$H_2$C$H_2$*, 3-H, 3-H*), 3.65−3.92 (m, 1 H, 6-H), 4.08−4.25 (m, 1 H, 6-H*), 4.40 (s, 1 H, OH), 5.13−5.42 (m, 2 H, 2-H, 2-H*). − $^{13}$C NMR ($C_6D_6$): δ = 9.8 ($CH_2CH_3$*), 10.0 ($CH_2CH_3$), 25.2 ($CH_2CH_3$*), 25.7 ($CH_2CH_3$), 25.9 (SC$H_2$C$H_2$), 26.1 (SC$H_2$C$H_2$*), 28.7 (S$CH_2CH_2$), 28.9 (S$CH_2CH_2$*), 40.0 (C-5*), 42.9 (C-5), 43.6 (C-3*), 44.5 (C-3), 46.2 (C-4*), 48.1 (C-4), 72.4 (C-6*), 72.4 (C-6), 92.5 (C-2*), 93.3 (C-2). − $C_{10}H_{18}O_2S_2$ (234.4): calcd. C 51.24, H 7.74, S 27.36; found C 51.49, H 7.50, S 25.44.

**10-Ethyl-9-oxa-1,5-dithiaspiro[5.5]-7-undecene (12):** To a solution of **17** in dry collidine (20 mL/mmol) was added diphenyl dichlorophosphate (4 equiv.). The resulting mixture was stirred at room temperature for 48 h. The progress of the reaction was monitored by TLC (PE/EA, 5:1) and, after complete consumption of the starting material, the solution was hydrolyzed by the addition of aqueous $NH_4Cl$, ice, and $CH_2Cl_2$. The aqueous phase was extracted five times with $CH_2Cl_2$ and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product thus obtained was purified by column chromatography on silica gel (PE/EA, 8:1) to give **12** in 99% yield. − IR (film): $\tilde{\nu}$ = 2963, 2932, 1631, 1423, 1244, 1042, 931, 888, 767, 750 cm$^{-1}$. − $^1$H NMR ($C_6D_6$): δ = 0.90 (t, 3 H, $J$ = 7.5, $CH_3$), 1.25−1.68 (m, 4 H, SC$H_2$C$H_2$, C$H_2$C$H_3$), 1.86 (dd, 1 H, $J$ = 13.7, 11.0, 5-H), 2.06−2.30 (m, 2 H, SC$H_2$C$H_2$), 2.46 (dd, 1 H, $J$ = 13.7, 3.0, 5-H), 2.30−2.59 (m, 2 H, SC$H_2$C$H_2$), 4.03 (dddd, 1 H, $J$ = 11.0, 7.5, 5.3, 1.8, 6-H), 4.83 (dd, 1 H, $J$ = 6.0, 2.3, 3-H), 6.18 (d, 1 H, $J$ = 6.0, 2-H). − $^{13}$C NMR ($C_6D_6$): δ = 9.6 ($CH_2CH_3$), 24.8 ($CH_2CH_3$), 26.7 (SC$H_2$C$H_2$), 27.2, 27.9 (S$CH_2CH_2$), 42.0 (C-5), 45.1 (C-4), 74.6 (C-6), 104.6 (C-3), 146.4 (C-2). − $C_{10}H_{16}OS_2$ (216.4): calcd. C 55.51, H 7.45, S 29.64; found C 55.36, H 7.44, S 29.23.

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