Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 947–955

TETRAHEDRON: *ASYMMETRY*

Asymmetric synthesis of α-acetylenic epoxides

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Received 5 February 1999; accepted 3 March 1999

Abstract

Chiral α-acetylenic oxiranes were easily synthesized from readily available propargylic esters by a four-step sequence involving the stereoselective reduction of α′-alkynyl β-keto sulfoxides with DIBAH (*de* 66–78%) and DIBAH/$ZnBr_2$ (*de* 78–88%), followed by further reduction of the resulting hydroxy sulfoxides into the corresponding sulfenyl derivatives and final epoxy ring closure via sulfonium salt.

1. Introduction

Chiral α-acetylenic epoxides may serve as versatile building blocks for the preparation of chiral α-functionalized alkyne units, which are present in natural products exhibiting interesting biological activity.[1] They can undergo carbonylation catalyzed by Pd,[2] silver assisted heterocyclization,[3] regio- and stereoselective nucleophilic ring opening[4] and selective deprotonation with *n*-BuLi followed by the capture of the formed anions by various electrophiles.[5] In addition, they have been transformed into chiral allenes.[6] Moreover, other interesting reactions on racemic alkynyl epoxides, which could be used on enantiomerically pure substrates, have also been reported.[6b,7] Despite this wide usefulness, the asymmetric synthesis of these compounds has received little attention. Only two strategies, involving the chiral epoxidation of racemic enynes and the alkynylation of chiral epoxides have been reported so far. The most widely used method involves the Sharpless asymmetric epoxidation[8] of the corresponding enynols, which is highly efficient (*ee* >95%) when applied to (*E*)-3-alkynyl-2-propen-1-ols,[4,6a] less satisfactory (*ee* ~60%) with trisubstituted allylic alcohols[2,3] and cannot be used to prepare terminal propargylic epoxides. On the other hand, the preparation of a chiral epoxy monoester by enzymatic

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0957-4166/99/$ - see front matter
PII: S0957-4166(99)00079-8

resolution[9] and its transformation into ethynyl oxiranes by a multi-step route[10] has been reported as an alternative to the Sharpless methodology.

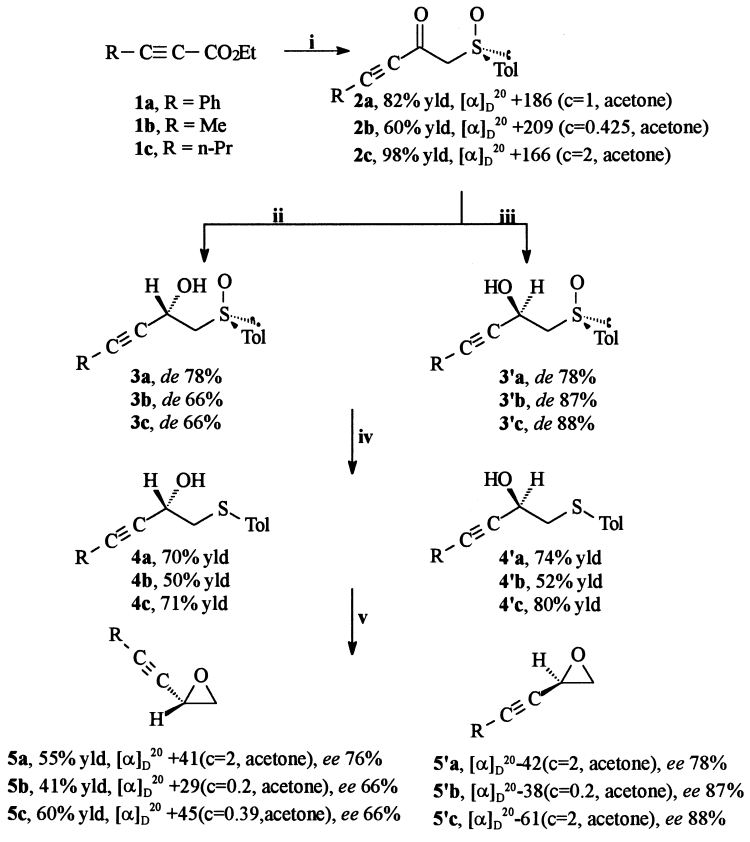
The formation of the oxirane ring by intramolecular Williamson syntheses starting from propargylic alcohols was used to prepare racemic epoxides[7a,11] but, to our knowledge, it had not been applied to synthesize enantiomerically enriched substrates.[12] This strategy had allowed the preparation of enantiomerically pure epoxyalkanes according to sequences involving highly stereoselective reduction[13] or hydrocyanation[14] of chiral β-keto sulfoxides as the key step to form the alcohol in the appropriate configuration. The stereoselective reduction of β-keto sulfoxides with DIBAH and DIBAH/ZnX_2 has been widely used in the asymmetric synthesis of secondary alcohols because of the good yields and high *de*s (ranging from 85 to >95%) possible.[15] The absence of any report concerning the use of this methodology in the synthesis of chiral propargylic alcohols was therefore surprising. These facts prompted us to investigate the behavior of α′-alkynyl β-keto sulfoxides as starting products for the optically active epoxyalkynes. In this paper, we report a new method for the asymmetric synthesis of these compounds starting from readily available propargylic esters based on the DIBAH reduction of α′-acetylenic β-keto sulfoxides and further closure to the oxirane ring from the resulting β-hydroxy sulfoxides.

2. Results and discussion

The overall synthetic sequence is depicted in Scheme 1. The starting α-acetylenic esters **1** were easily obtained by ethoxycarbonylation of commercial alkynes following conventional procedures.[16] The conditions needed to achieve the synthesis of the alkynyl keto sulfoxides **2** was the first problem we had to solve. The reaction of compound **1** with (*R*)-(+)-methyl *p*-tolyl sulfoxide and LDA at −78°C, according to the procedure reported by Solladié for saturated esters,[17] yielded complex reaction mixtures, where 1,4-addition products were predominant. Starting from alkenyl keto sulfoxides Solladié had been able to avoid the formation of these products by increasing the reaction temperature,[18] but it was unsuccessful with our substrates. In order to obtain good yields of compound **2** and to avoid the formation of several by-products, it was necessary to invert the order of the addition of reagents (methyl sulfinyl carbanion must be added dropwise to a solution of the acetylenic ester, see Experimental). Having established this, the desired process was straightforward and no detectable competitive 1,4-addition was observed.

The reduction of β-keto sulfoxides **2** (**a**–**c**) with DIBAL[13,19] at −78°C gives the β-hydroxy sulfoxides as a mixture of diastereoisomers **3** and **3′** (**a**–**c**), the first being the major isomer. Diastereoisomeric ratios of the resulting sulfinyl carbinols were determined on the crude products by 300 MHz ^{1}H NMR (Scheme 1). Although the yields of crude **3**+**3′** mixtures were almost quantitative, these products suffer extensive degradation when purified by silica gel chromatography and thus, only ^{1}H NMR data of compounds **3** and **3′** could be obtained from the spectra of the crude reaction products. Therefore, we tried the next step, the reduction of the sulfinyl group, on the crude product **3**+**3′**. Several reducing agents were studied (BF_3–Et_2O/NaI,[20] $MeSiCl_3$/NaI[21]), but satisfactory results were only obtained with $TiCl_3$ in EtOH at room temperature[22] thus yielding the corresponding β-sulfenyl propargyl alcohols **4a**–**4c**. Finally, the reaction of the sulfenyl derivatives **4** with trimethyloxonium tetrafluoroborate in anhydrous CH_2Cl_2 followed by aqueous K_2CO_3 (one-pot procedure)[13,14] afforded the optically active α-acetylenic epoxides **5a**–**5c**.

The enantiomeric excesses of the final epoxides **5** (see Scheme 1) were determined by ^{1}H NMR spectroscopy using Eu(hfc)$_3$ as a chiral shift reagent. The required racemic epoxides were prepared from (±)-methyl *p*-tolyl sulfoxide. As we can see, the *ee*s determined for oxiranes (66–76%) are almost

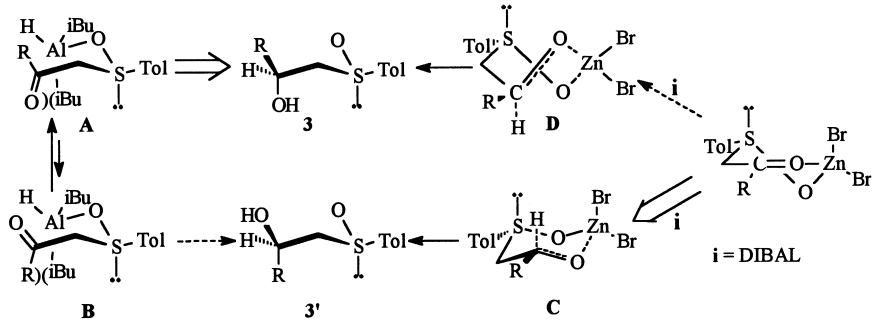


Scheme 1. Key: (i) (*R*)-*p*-Td-SO-Me (2 equiv.), LDA (2 equiv.), THF, −78°C, 3 h; (ii) DIBAL, THF, −78°C, 1 h; (iii) $ZnBr_2$, DIBAL, THF, −23°C, 0.5 h; (iv) $TiCl_3$, EtOH, rt, 15 min; (v) 1.Me_3OBF_4, CH_2Cl_2 rt, 3 h; 2. K_2CO_3 (2 equiv.), H_2O, rt, 30 h

identical to the *de*s corresponding to their starting hydroxy sulfoxides, which provides evidence that cyclization occurs in a completely stereoselective manner. Configurational assignment of the obtained diastereoisomers was made from their ^{1}H NMR parameters (see Experimental), taking into account the well known behavior of the diastereomeric β-hydroxy sulfoxides,[23] which agrees with the predictions made on the basis of the stereochemical course proposed for these reactions.[24]

The obtained diastereomeric excesses deserve some comment, because they are clearly lower than those observed for other R-CO-CH_2-SOTol with R=alkyl or aryl (*de* ≥90%). These differences are not unexpected from the stereochemical model proposed to explain the DIBAH reduction of β-keto sulfoxides[24] that involves the association of the reagent as a step prior to the intramolecular hydride transfer. This model suggests that the stereoselectivity must be related to the relative stability of the transition states (**A**>**B**), which in turn will be dependent on the different magnitude of their *i*-Bu/O and *i*-Bu/R 1,3-parallel interactions (see Scheme 2). Therefore, the lower *de* observed in reduction of alkynyl derivatives **2** with respect to those from alkyl or aryl keto sulfoxides must be considered as a consequence of the smaller size of the alkynyl groups. Similar considerations would explain that the formation of **2a** (R=Ph–C≡C) was more stereoselective (*de* 78%) than that of **2b** (R=Me–C≡C) and **2c** (R=*n*-Pr–C≡C) (*de* 66%).

At this point we decided to investigate the reactions of compound **2** with DIBAH/$ZnBr_2$, the stereoselectivity of which is usually less dependent on steric effects. In the presence of the Lewis acid, DIBAH also afforded mixtures of hydroxy sulfoxides **3** and **3′**, but the second isomer is now the major product.



Scheme 2.

This is the result of a chelation of $ZnBr_2$ to both oxygen atoms at the substrates prior to the attack of the reagent. The approach of DIBAH from the upper face yielding **C** (Scheme 2) would be favored by stereoelectronic factors (interactions of Al with the lone electron pair at sulfur) and steric strain (chair-like *TS* **C** is more stable than twist-like *TS* **D**).[24] Stereoselectivity must be slightly dependent on the size of the R group since it adopts a pseudoequatorial arrangement in both *TS*s.

The search for the best conditions to transform **2**(**a**–**c**) into **3′**(**a**–**c**) with DIBAH/$ZnBr_2$ required extensive experimentation. Reaction temperature and the DIBAH/substrate/Lewis acid ratio were critical to obtain hydroxy sulfoxides with high enantiomeric excess. The optimal conditions we found involved the use of a 3:1:1 ratio at −23°C (see Experimental) and yielded the results depicted in Scheme 1. The use of 3 equiv. of DIBAH was required to achieve complete transformation of the starting products while a higher proportion of Lewis acid increased the amount of hydroxy thioether (obtained as by-product in these reactions). Lower stereoselectivity was observed by decreasing the reaction temperatures.[25] As expected, the observed *de*s (see Scheme 1) are higher than those obtained with DIBAL, mainly in the case of **2b** and **2c** (88% *de*).[26] Compounds **3′**(**a**–**c**) were reduced to give **4′**(**a**–**c**) and subsequently converted into the epoxides **5′**(**a**–**c**) following the same methodology used for **3**(**a**–**c**) (see above). The enantiomeric excess of **5′** (78–88% by ^{1}H NMR) was clearly higher than that of **5**.

In summary, we have shown that (*R*)- and (*S*)-α-acetylenic oxiranes can easily be synthesized in high enantiomeric excesses from the readily available propargylic esters by a three-step sequence. The first step involves the formation of β-keto sulfoxides **2** by reaction of compound **1** with (+)-Me-SOTol/LDA. The stereoselective reduction of compound **2** with DIBAH or DIBAH/$ZnBr_2$ (more efficient) yielded the hydroxy sulfoxides **3** and **3′**, respectively, which were transformed into their corresponding thioethers **4** and **4′** by treatment of the crude products with $TiCl_3$. The last step yielding **5** and **5′** involves epoxy ring closure by *S*-methylation of the thioethers with Me_3OBF_4 and subsequent reaction of the resulting sulfonium salts with K_2CO_3.

3. Experimental

3.1. General methods

Melting points were determined in a Culatti melting point apparatus. All moisture sensitive reactions were performed in flame-dried glassware equipped with rubber septa under a positive pressure of argon and monitored by TLC. Solvents were dried according to literature procedures. Optical rotations were measured on a Jasco DIP-360 digital polarimeter at 20°C (concentration in g/100 ml). The IR spectra were recorded on a Nicolet-5SX spectrophotometer. The ^{1}H and ^{13}C NMR spectra were obtained either

on Varian Gemini-200 or Unity-300 spectrometers at room temperature on deuteriochloroform using TMS as an internal standard. Mass spectra were measured on a Jeol AX-505 mass spectrometer at 70 eV and 190°C.

3.2. Preparation of β-keto sulfoxides **2**

A solution of (*R*)-(+)-methyl *p*-tolyl sulfoxide (16 mmol) in 25 ml of THF was added dropwise to a solution of LDA (16.5 mmol) in 25 ml of THF at −78°C. The mixture was stirred at −78°C for 1 h and added dropwise via a cannula into a solution of α-acetylenic ester **1** (8 mmol) in 50 ml of THF cooled at −78°C. After 3 h at −78°C, the reaction mixture was decomposed with 100 ml of saturated ammonium chloride solution and 100 ml of Et_2O. The organic layer was separated and the aqueous solution was extracted with EtOAc (3×25 ml). The combined organic extracts were washed with brine, dried and evaporated. The residue was purified by silica gel column chromatography eluting with hexane:EtOAc 50:50.

3.2.1. (R)-4-Phenyl-1-(p-tolylsulfinyl)-3-butyn-2-one **2a**

White crystals, mp 63°C (hexane–Et_2O), 82% yield; $[\alpha]_D$ +186 (c=1, acetone); IR (film) ν_{max}: 2923, 2203, 1911, 1659, 1595, 1491, 1443, 1398 and 1287 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.37 (s, 3H), 3.99 and 4.20 (AB system, J=13.5 Hz, 2H), 7.31–7.64 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.4, 70.8, 87.9, 95.0, 119.1, 124.3, 128.7, 130.1, 131.4, 133.3, 139.5, 142.5, 176.9; EIMS m/z 282 (4%, M^+), 192 (10), 145 (15), 139 (100), 137 (96), 115 (73), 91 (38), 89 (35), 65 (39), 63 (28).

3.2.2. (R)-1-(p-Tolylsulfinyl)-3-pentyn-2-one **2b**

Oil, 60% yield; $[\alpha]_D$ +209 (c=0.425, acetone); IR (film) ν_{max}: 2919, 2243, 2213, 1688, 1596, 1494, 1443, 1400 and 1250 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 2.03 (s, 3H), 2.42 (s, 3H), 3.83 and 4.05 (AB system, J=13.5 Hz, 2H), 7.34 and 7.58 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 4.3, 21.5, 70.9, 80.2, 95.0, 124.3, 130.1, 139.6, 142.4, 177.3; EIMS m/z 220 (46%, M^+), 139 (100), 137 (24), 91 (20), 67 (13), 65 (12).

3.2.3. (R)-1-(p-Tolylsulfinyl)-3-heptyn-2-one **2c**

Oil, 98% yield; $[\alpha]_D$ +166 (c=2, acetone); IR (film) ν_{max}: 2966, 2933, 2206, 1668, 1274 and 1241 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.00 (t, J=7.4 Hz, 3H), 1.59 (sextuplet, J=7.3 Hz, 2H), 2.34 (t, J=7 Hz, 2H), 2.42 (s, 3H), 3.84 and 4.07 (AB system, J=13.6 Hz, 2H), 7.33 and 7.58 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 13.4, 21.0, 21.4, 21.5, 71.1, 81.0, 99.1, 124.3, 130.1, 139.7, 142.3, 177.2; EIMS m/z 248 (4%, M^+), 220 (5), 139 (100), 137 (9), 111 (16), 91 (10).

3.3. Preparation of β-hydroxy sulfides **4**

3.3.1. Reduction with DIBAH

To a solution of compound **2** (1 mmol) in 30 ml of THF at −78°C a 1.5 M solution of DIBAH in toluene (5 mmol) was added dropwise. After 1 h the reaction was shown to be complete and the excess of DIBAH was decomposed by adding 1 ml of MeOH. The solvents were removed under vacuum and the residue was treated with 25 ml of saturated aqueous ammonium chloride solution and 25 ml of Et_2O. The organic phase was separated and the aqueous phase was extracted with Et_2O (3×15 ml). The combined organic extracts were washed with brine, dried and evaporated to yield a mixture of **3**+**3′** with the former being the major compound (see Scheme 1).

*3.3.2. (3*S,R$_S$*)-4-Phenyl-1-(*p-*tolylsulfinyl)-3-butyn-2-ol* ***3a***

^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.41 (s, 3H), 3.11 (dd, J=13.5 and 2.1 Hz, 1H), 3.29 (dd, J=13.5 and 9.0 Hz, 1H), 4.80 (sa, 1H), 5.18 (dd, J=9.0 and 2.1 Hz, 1H), 7.20–7.60 (m, 9H).

*3.3.3. (3*S,R$_S$*)-1-(*p-*Tolylsulfinyl)-3-pentyn-2-ol* ***3b***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.84 (d, J=2.0 Hz, 3H), 2.43 (s, 3H), 2.93 (dd, J=13.4 and 2.6 Hz, 1H), 3.18 (dd, J=13.4 and 8.6 Hz, 1H), 4.17 (da, 1H), 4.89 (m, 1H), 7.35 and 7.54 (AA′BB′ system, 4H).

*3.3.4. (3*S,R$_S$*)-1-(*p-*Tolylsulfinyl)-3-heptyn-2-ol* ***3c***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.96 (t, J=7.3 Hz, 3H), 1.51 (sextuplet, J=7.2 Hz, 2H), 2.18 (td, J=7.0 and 2.0 Hz, 2H), 2.43 (s, 3H), 2.96 (dd, J=13.4 and 2.7 Hz, 1H), 3.17 (dd, J=13.4 and 8.7 Hz, 1H), 4.12 (da, 1H), 4.89 (m, 1H), 7.35 and 7.54 (AA′BB′ system, 4H).

3.3.5. Reduction with DIBAH/$ZnBr_2$

A solution of compound **2** (1 mmol) in 4 ml of THF was added to a solution of $ZnBr_2$ (1 mmol) in 4 ml of THF at 0°C under argon. The resulting solution was stirred at 0°C for 1 h and cooled to −23°C. Then, a 1.5 M solution of DIBAH in toluene (3 mmol) was added dropwise. The reaction was stirred at −23°C for 0.5 h and then 1 ml of MeOH was added. The solvents were removed under vacuum and the residue was treated with 25 ml of saturated aqueous ammonium chloride solution and 25 ml of Et_2O. The organic phase was separated and the aqueous phase was extracted with Et_2O (3×15 ml). The combined organic extracts were washed with brine, dried and evaporated to yield a mixture of **3**+**3′** with the latter being the major compound (see Scheme 1).

*3.3.6. (3*R,R$_S$*)-4-Phenyl-1-(*p-*tolylsulfinyl)-3-butyn-2-ol* ***3′a***

^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.41 (s, 3H), 3.14 (dd, J=12.9 and 4.5 Hz, 1H), 3.38 (dd, J=12.9 and 8.4 Hz, 1H), 5.18 (dd, J=8.4 and 4.5 Hz, 1H), 7.22–7.62 (m, 9H). The OH signal was not observed.

*3.3.7. (3*R,R$_S$*)-1-(*p-*Tolylsulfinyl)-3-pentyn-2-ol* ***3′b***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.84 (d, J=2.0 Hz, 3H), 2.43 (s, 3H), 3.00 (dd, J=13.2 and 4.6 Hz, 1H), 3.23 (dd, J=13.2 and 8.0 Hz, 1H), 4.89 (m, 1H) 7.35 and 7.54 (AA′BB′ system, 4H). The OH signal was not observed.

*3.3.8. (3*R,R$_S$*)-1-(*p-*Tolylsulfinyl)-3-heptyn-2-ol* ***3′c***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.95 (t, J=7.3 Hz, 3H), 1.51 (sextuplet, J=7.2 Hz, 2H), 2.19 (td, J=7.0 and 1.9 Hz, 2H), 2.42 (s, 3H), 3.00 (dd, J=13.0 and 4.7 Hz, 1H), 3.26 (dd, J=13.0 and 8.2 Hz, 1H), 4.90 (m, 1H), 7.37 and 7.58 (AA′BB′ system, 4H). The OH signal was not observed.

3.4. Reduction of crude hydroxy sulfoxides

To a solution of the crude mixture of **3**+**3′** in 5 ml of EtOH, a 15% hydrochloric acid solution of $TiCl_3$ (2 equiv.) was added at room temperature. After 15 min, 10 ml of water was added and the mixture was extracted with CH_2Cl_2 (3×10 ml). The combined organic extracts were washed with brine, dried and concentrated. The residue was purified by silica gel column chromatography eluting with hexane:EtOAc 80:20.

3.4.1. (S)-4-Phenyl-1-(p-tolylsulfenyl)-3-butyn-2-ol ***4a***

Pale yellow crystals, mp 43–45°C, 70% yield; $[\alpha]_D$ −142 (c=2, acetone); IR (KBr) ν_{max}: 3456, 1490 and 1059 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 2.31 (s, 3H), 2.71 (d, J=5.2 Hz, 1H), 3.28 (ddd, J=13.8, 7.4 and 4.8 Hz, 2H), 4.63 (ddd, J=7.4, 5.2 and 4.8 Hz, 1H), 7.05–7.45 (m, 9H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 21.0, 43.1, 61.1, 85.7, 88.8, 122.6, 128.2, 128.5, 129.9, 130.8, 131.3, 131.7, 137.3; EIMS m/z 268 (100%, M^+), 253 (7), 235 (10), 138 (92), 137 (80), 131 (41), 124 (11), 103 (13), 91 (23), 77 (15). Starting from the crude reaction obtained from the reduction of compound **2a** with $ZnBr_2$/DIBAH, compound **4′a** was obtained in 74% yield, $[\alpha]_D$ 146 (c=2, acetone).

3.4.2. (S)-1-(p-Tolylsulfenyl)-3-pentyn-2-ol ***4b***

Oil, 50% yield; $[\alpha]_D$ −62 (c=0.59, acetone); IR (film) ν_{max}: 3409, 2920, 1493 and 1023 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.81 (d, J=2.1 Hz, 3H), 2.32 (s, 3H), 2.55 (d, J=4.5 Hz, 1H), 3.15 (ddd, J=13.8, 7.8 and 4.5 Hz, 2H), 4.37 (m, 1H), 7.11 and 7.33 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 3.5, 21.0, 43.3, 60.8, 78.4, 82.2, 124.0, 129.8, 131.1, 137.1; EIMS m/z 206 (70%, M^+), 191 (5), 173 (9), 138 (42), 137 (100), 123 (11), 105 (8), 91 (34), 77 (10). Starting from the crude reaction obtained by reduction of compound **2b** with $ZnBr_2$/DIBAH, compound **4′b** was obtained in 52% yield, $[\alpha]_D$ 84 (c=0.59, acetone).

3.4.3. (S)-1-(p-Tolylsulfenyl)-3-heptyn-2-ol ***4c***

Oil, 71% yield; $[\alpha]_D$ −66 (c=0.82, acetone); IR (film) ν_{max}: 3385, 2963, 2931, 2871, 2231, 1493 and 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.96 (t, J=7.2 Hz, 3H), 1.49 (sextuplet, J=7.5 Hz, 2H) 2.15 (td, J=7.2 and 2.1 Hz, 2H), 2.32 (s, 3H), 2.56 (d, J=4.8 Hz, 1H), 3.16 (ddd, J=13.8, 7.5 and 4.5 Hz, 2H), 4.40 (m, 1H), 7.10 and 7.33 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.4, 20.7, 21.0, 21.9, 43.4, 60.8, 79.4, 86.5, 124.0, 129.8, 131.1, 137.1; EIMS m/z 234 (35%, M^+), 206 (9), 190 (8), 138 (82), 137 (100), 124 (23), 114 (13), 91 (35), 77 (11). Starting from the crude reaction obtained by the reduction of compound **2c** with $ZnBr_2$/DIBAH, compound **4′c** was obtained in 80% yield, $[\alpha]_D$ 92 (c=0.82, acetone).

3.5. Preparation of α-acetylenic epoxides ***5***

Trimethyloxonium tetrafluoroborate (1.1 mmol) was added to a solution of hydroxy sulfide derivative **4** (1 mmol) in 5 ml of CH_2Cl_2. The mixture was stirred at room temperature for 3 h and then a solution of K_2CO_3 (2 mmol) in 3 ml of water was added. The resulting mixture was vigorously stirred for 30 h. The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (3×3 ml). The combined organic layers were washed with brine, dried and concentrated at ordinary pressure.

3.5.1. (S)-1-Phenyl-3,4-epoxy-1-butyne ***5a***

The title compound was obtained from compound **4a**. The residue was purified by silica gel chromatography eluting with hexane:EtOAc 95:5 to give compound **5a**. Oil, 55% yield; *ee*=76%; $[\alpha]_D$ +41 (c=2, acetone); IR (film) ν_{max}: 2926, 2230, 1491 and 1096 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 3.01 (d, J=3.3 Hz, 2H), 3.59 (t, J=3.3 Hz, 1H), 7.29–7.50 (m, 5H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 40.2, 49.1, 83.4, 85.7, 121.9, 128.3, 128.8, 131.9; EIMS m/z 144 (22%, M^+), 115 (45), 114 (100), 113 (15), 88 (12), 63 (10). Similar treatment of compound **4′a** gave compound **5′a**; *ee*=78%; $[\alpha]_D$ −42 (c=2, acetone).

3.5.2. (S)-4,5-Epoxy-2-pentyne ***5b***

The title compound was obtained from compound **4b**. The residue was purified by silica gel chromatography eluting with pentane:CH_2Cl_2 75:25; oil, 41% yield (the rather low yield of compound **5b** is due to its high volatility); *ee*=66%; $[\alpha]_D$ +29 (c=0.2, acetone); IR (film) ν_{max}: 2920, 2248, 1494, 1377 and 1093 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.84 (d, J=1.8 Hz, 3H), 2.86 (ddd, J=6.0, 3.9 and 3.0 Hz, 2H), 3.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 3.6, 40.1, 48.7, 76.0, 80.2; EIMS m/z 82 (9%, M^+), 81 (7), 54 (46), 52 (100), 51 (61). Similar treatment of compound **4′b** gave compound **5′b**; *ee*=87%; $[\alpha]_D$ −38 (c=0.2, acetone).

3.5.3. (S)-1,2-Epoxy-3-heptyne ***5c***

The title compound was obtained from compound **4c**. The residue was purified by silica gel chromatography eluting with hexane:EtOAc 98:2; oil, 60% yield; *ee*=66%; $[\alpha]_D$ +45 (c=0.39, acetone); IR (film) ν_{max}: 2965, 2243, 1462 and 1378 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.98 (t, J=7.2 Hz, 3H), 1.53 (sextuplet, J=7.2 Hz, 2H), 2.18 (dt, J=7.2 and 1.8 Hz, 2H), 2.86 (ddd, J=6.0, 4.2 and 2.7 Hz, 2H), 3.35 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.4, 20.7, 21.8, 40.1, 48.8, 77.0, 84.5; EIMS m/z 110 (5%, M^+), 95 (15), 82 (31), 79 (100), 65 (36), 52 (34). Similar treatment of compound **4′c** gave compound **5′c**; *ee*=88%; $[\alpha]_D$ −61 (c=2, acetone).

Acknowledgements

We thank R. Patiño, M. I. Chávez, R. Gaviño, B. Quiroz, J. Pérez and L. Velasco for their technical assistance and Consejo Nacional de Ciencia y Tecnología (CONACYT-México) for partial financial support (Project 26375-E).

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25. A similar unexpected effect had been previously observed in the Diels–Alder reaction of 2-*p*-tolylsulfinyl naphthoquinones with cyclopentadiene catalyzed by $ZnBr_2$ (Carreño, C.; García Ruano, J. L.; Urbano, A. *J. Org. Chem*. **1992**, *57*, 6870). It seems that decreasing the temperature below −20°C makes the chelation difficult and lower stereoselective cycloadditions are observed.
26. These values are only slightly lower than those usually observed for alkyl keto sulfoxides, which could be attributed to the fact that the extended conjugation of compounds **2** decreases the ability of the carbonyl to become chelated.