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Chemo- and enantioselective catalytic addition of propargyl chloride to aldehydes promoted by [Cr(Salen)] complexes

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Abstract—We describe a full account of our study concerning the [Cr(Salen)]-catalysed addition of propargyl halides to aldehydes. Such a procedure allows the synthesis of enantiomerically enriched homopropargyl alcohols in satisfactory yields with enantiomeric excesses (e.e.s) up to 56%. The excellent chemoselectivity for homopropargyl versus homoallenyl alcohol, represents a peculiar characteristic our process in comparison to other chromium-mediated propargylation reactions. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

The reactions of allenyl and propargyl organometallic reagents with carbonyl compounds provide useful synthetic intermediates.[1] Nevertheless, the metallotropic rearrangement between propargyl and allenyl species results in poor chemoselectivity and a mixture of compounds is often obtained.† In recent years, pertinent synthetic strategies for the introduction of propargyl or allenyl groups into carbonyl compounds have been described.[2] In such procedures, the regiochemical selectivity was elegantly tuned towards either acetylenic or allenyl products. A highly enantioselective propargylation reaction of aldehydes with alkynes was recently reported by Carreira using stoichiometric chiral auxiliaries.[3] Moreover, a number of catalytic additions of allenyl tin reagents to aldehydes, mediated by BINOL–Ti(IV) complexes and Et_2BS^iPr as a synergystic reagent, have been published.[4] In the chromium-mediated Nozaki–Hiyama–Kishi reactions, organochromium reagents were employed in promoting the addition of allenyl and propargyl halides to aldehydes with variable success.[5] Herein we report the catalytic enantioselective propargylation of aldehydes promoted by chiral [Cr(Salen)] complex (Salen: (*R*,*R*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine, **1**, Fig. 1). The Schiff-base ligands were observed to play a decisive role in controlling the regioselectivity of the reaction.

2. Results and discussion

Chiral Schiff-bases have become increasingly important in modern organic and inorganic chemistry.[5] In particular, the metallo-Salen complexes have found several interesting applications in asymmetric catalysis.[6] An important characteristic of such a class of compounds is the facile access to a large variety of structurally related Schiff-bases which allows fine tuning of the stereoelectronic properties of the ligand. In earlier studies, we have described the first enantioselective version of the Nozaki–Hiyama reactions promoted by a catalytic amount (10 mol%) of [Cr(Salen)] complex.[7] Allyl, crotyl and α-halo substituted crotyl halides were successfully coupled to aliphatic and aromatic aldehydes in a highly stereoselective fashion using this methodology (Scheme 1).

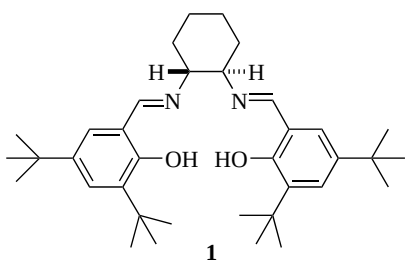

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Figure 1. (*R*,*R*)-Salen.

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† Normally, propargyl and allenyl metal compounds furnish allenyl and propargylic adducts, respectively via an S_E2' type addition to carbonyls.

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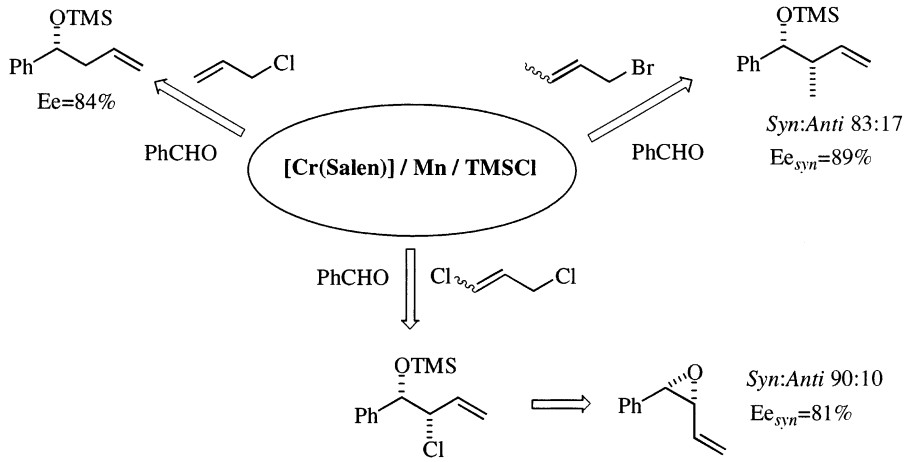


Scheme 1. The catalytic redox system [Cr(Salen)]/Mn/TMSCl] in the stereocontrolled coupling of reactive organohalides to carbonyl compounds.

These chromium-mediated redox reactions are based on two crucial features previously presented by Fürstner:[8] (a) the use of Mn powder (50 mesh) as the stoichiometric reductant and (b) the use of Me_3SiCl as the scavenger. Normally, the addition of propargyl bromide to carbonyl compounds mediated by a stoichiometric amount of $CrCl_2$, affords the allenyl product **4** in moderate yields, due to the low reactivity of the chromium organometallic species involved. However, we were delighted to find that by applying our redox protocol to the addition of propargyl chloride to the benzaldehyde, the regioselectivity was workable and the desired homopropargyl alcohol was isolated in a satisfactory yield of 50% and 56% e.e. (Scheme 2).

The absolute configuration of the predominant enantiomer (*R*)-**3a** was established by comparison of the specific rotation value with the reported data.[9] It is noteworthy that the facial selection observed in the [Cr(Salen)]-mediated addition of propargyl chloride follows the general behaviour seen with other chiral and achiral allylhalides. Our initial efforts to optimise the yield and stereoselectivity of the reactions were directed towards the screening of structurally correlated Schiff-bases **5**–**12** as ligands (Fig. 2).

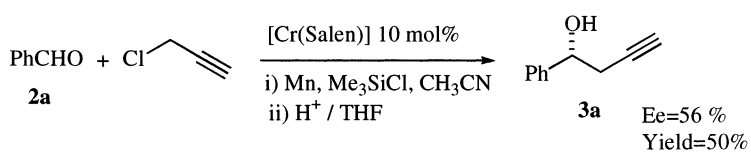
Although the regioselectivity (acetylene versus allene compound) was preserved in almost all cases, the e.e. was not improved. The results obtained are summarised in Table 1.

Interestingly, the enantioselectivities observed with Schiff-bases **5**–**12** (Table 1) indicate that the presence of bulky substituents at C(3)-C(3′) and C(5)-C(5′) in the aromatic rings of the Salen ligand **1** are of great importance in the enantiofacial descrimination step.[10] The presence of bulky substituents at C(3)-C(3′) in the C_2-symmetric Schiff-bases **5**, **6**, **7**, **10**, **11** are also crucial to stereoinduction. The results obtained with the chiral ligand **9** are noteworthy, because the introduction of bromine at the C(5)-C(5′) positions switches the facial selection of the reaction (Table 1, entry 5). Although we do not have any explanation for this finding, the result clearly shows that slight modification of the Schiff-base structure can significantly modify the geometry of the resulting metal complex.[11]

Since the Salen **1** was the ligand of choice, different aromatic and aliphatic aldehydes were tested in the asymmetric propargylation in the presence of 10 mol% of catalytic complex. The chiral organometallic chromium reagent reacted smoothly only with aromatic aldehydes giving the acetylenic alcohol in satisfactory yields (Table 2).‡

Aliphatic aldehydes were found to be less reactive and in only a few cases was the desired product isolated (Table 2, entry 9). However, side products from pinacol coupling or reduction of the carbonyl substrates were also detected in variable amounts, depending on the

‡ No allenyl alcohol was detected in the crude mixture (GC, ^{1}H NMR assay).



Scheme 2. The [Cr(Salen)]-mediated addition of propargyl chloride to the benzaldehyde.

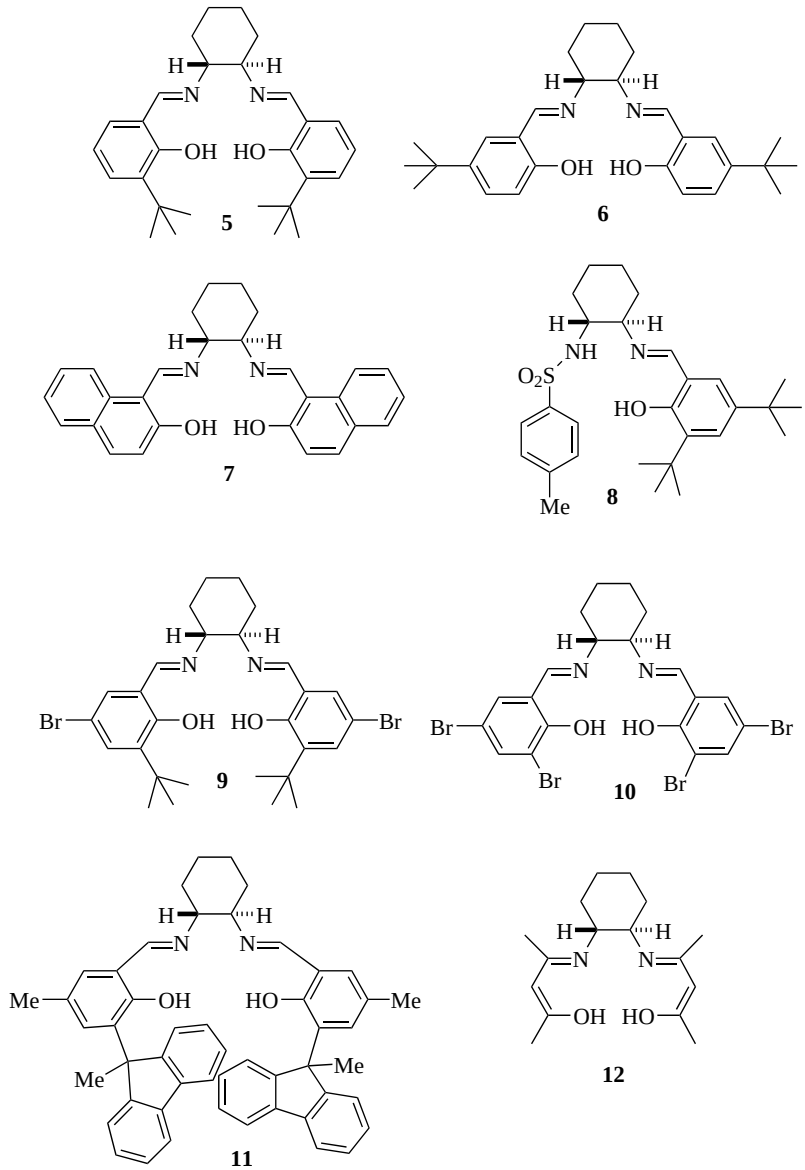


Figure 2. Schiff-bases tested as ligands in the addition of propargyl chloride to PhCHO.

nature of the aldehydes. In general aromatic aldehydes substituted with strong ED-groups furnished a considerable amount of unwanted pinacol coupling.[12]

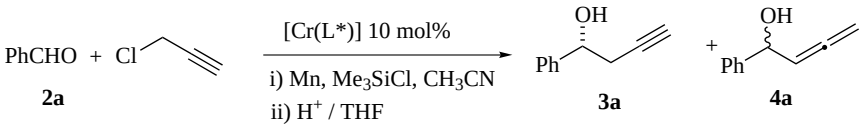
The same strategy was also applied to stereogenic halides, however 3-bromo-but-1-yne **16** reacted with PhCHO giving a 1:1 mixture of the *syn* and *anti* diastereoisomers **17** with low enantioselectivity (e.e.$_{syn}$ <10%, Scheme 3).[13]

To date, the factors that govern the regioselectivity are still unclear. However, the employment of Schiff-bases as chiral ligands appears to be beneficial to regiocontrol in the reaction. In fact, supposing that the allenyl and propargyl organochromium species exist in dynamic equilibrium, the regiochemistry observed could be explained assuming that the [Cr(Salen)allenyl] complexes **A** is more reactive that the [Cr(Salen)propargyl] **B**. On the other hand, our catalytic system appears mechanistically quite complex, and a subtle role played by weak Lewis acids (i.e. MnX_2, [Cr(Salen)X]) in driving the aggregation state towards a stereo-effective dimeric catalytically active species has been proposed.[14] A working model for this catalytic propargylation reaction is represented in Fig. 3.

3. Conclusion

In summary we have presented the results of our work on the addition of propargyl halides to aldehydes mediated by catalytic amounts of [Cr(Salen)] complex. Moderate yields and enantioselectivities were obtained in the addition of propargyl chloride to aromatic aldehydes. For the first time a selective propargylating reagent based on commercially available propargyl chloride was

Table 1. Results of the asymmetric propargylation of PhCHO in the presence of several [Cr(L*)] complexes as catalysts[a]



Entry	L*	Isomer ratio[b] **3a**:**4a**	E.e. of **3a** (%)[c]	Config.
1	**5**	95:5	44	*R*
2	**6**	>99:1	0	–
3	**7**	>99:1	31	*R*
4	**8**	>99:1	27	*R*
5	**9**	99:1	15	*S*
6	**10**	91:9	17	*R*
7	**11**	>99:1	11	*R*
8	**12**	99:1	15	*R*

[a] Reactions were carried out following the general procedure (see Section 4). The catalytic complexes were always obtained in situ as described for [Cr/**1**].
[b] The isomer ratio was estimated by GC and ^{1}H NMR analysis.
[c] Determined by chiral GC analysis (Megadex-5 column) on the *O*-silyloxy product.

Table 2. Asymmetric propargylation of aldehydes in the presence of [Cr(Salen)] complex as the catalyst[a]

Entry	RCHO **2**	Yield (%)[b] **3**	E.e. (%)[d] **3**
1	C_6H_5CHO **2a**	50 **3a**	56
2	2F-C_6H_4CHO **2b**	36 **3b**	35
3	4F-C_6H_4CHO **2c**	45 **3c**	56
4	4^{t}Bu-C_6H_4CHO **2d**	30 **3d**	45
5	4^{i}Pr-C_6H_4CHO **2e**	32 **3e**	43
6	4MeO-C_6H_4CHO **2f**	40 **3f**	28
7	4Br-C_6H_4CHO **2g**	36[c] **3g**	22
8	4CF_3-C_6H_4CHO **2h**	20 **3h**	27
9	$C_6H_5CH_2CH_2CHO$ **2i**	21 **3i**	15

[a] Reactions carried out following the general procedure (see Section 4).
[b] Isolated yields after chromatography.
[c] Allenyl compound (10%) was isolated. The % e.e. of the allenyl adduct was evaluated as 60% by chiral CG analysis (Megadex-5 column). The absolute configuration of the compound was not established.
[d] The e.e. of the product was evaluated by chiral GC analysis (Megadex-5 column).

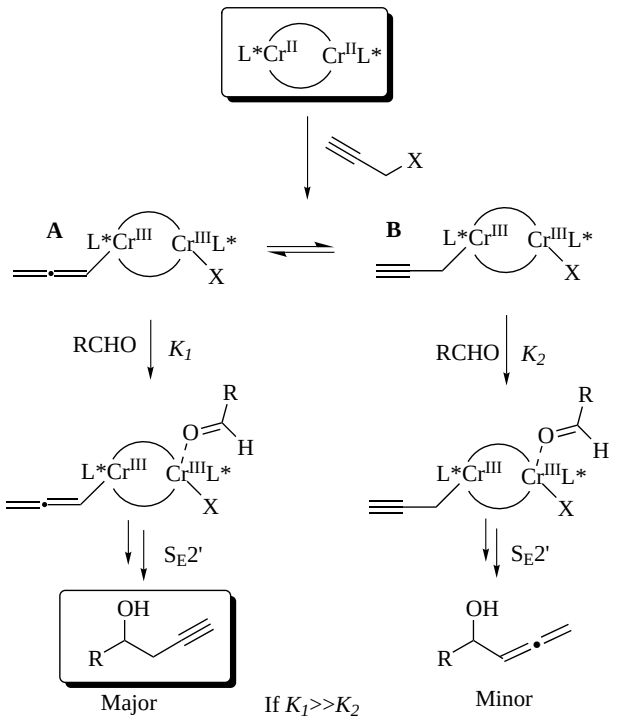
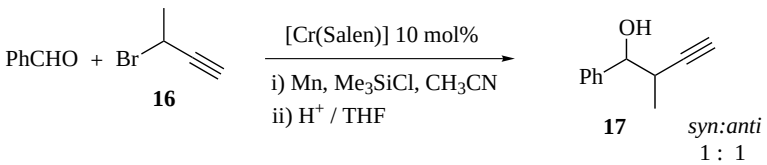


Figure 3. A tentative explanation for the high regioselectivity of the [Cr(Salen)]-catalysed propargylation.

described. These results support the general applicability of the [Cr(Salen)] catalyst in the stereocontrolled coupling of reactive organo halides to carbonyl compounds. Studies towards the use of the chromium Salen catalytic system in Reformatsky and intramolecular coupling reactions are currently under investigation in our laboratory.



Scheme 3. Catalytic addition of stereogenic propargyl bromide **16** to PhCHO mediated by [Cr(Salen)] catalyst.

4. Experimental

^{1}H NMR spectra were recorded on Varian 200 (200 MHz) and Varian 300 (300 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ 7.27 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian 200 (50 MHz) and Varian 300 (75 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (deuterochloroform: δ 77.0 ppm). Mass spectra were performed at an ionising voltage of 70 eV. Chromatographic purification was done with 240–400 mesh silica gel. Analytical gas chromatography (GC) was performed on a Hewlett–Packard HP 6890 gas chromatograph with a flame-ionisation detector and split mode capillary injection system, using a Crosslinked 5% PH ME Siloxane (30 m) column or a Megadex-5 chiral (25 m) column (flow rate 15 mL/min, method: 50°C for 2 min, ramp @ 10°C/min to 250°C for 15 min). Analytical high-performance liquid chromatography (HPLC) was performed on an HP 1090 liquid chromatograph equipped with a variable wavelength UV detector (deuterium lamp 190–600 nm), using a Daicel Chiralcel™ OD column (0.46 cm I.D.×25 cm) (Daicel Inc.). HPLC grade *iso*-propanol and *n*-hexane were used as the eluting solvents. Elemental analyses were carried out by using an EACE 1110 CHNOS analyser. All reactions were carried out under a nitrogen atmosphere in flame-dried glassware using standard inert techniques for introducing reagents and solvents. All the aldehydes were distilled prior to use. All the other commercially available reagents were used as received. Anhydrous CH_3CN were purchased from the Fluka Co. Manganese powder (50 mesh) was purchased from Aldrich Co. and used as received. Different batches of 50 mesh manganese gave reproducible results. The chiral Schiff-bases **5**–**12** were synthesised following known procedures.[15]

4.1. General procedure for the enantioselective addition of propargyl chloride to aldehydes

In a round-bottomed flask containing anhydrous CH_3CN (2 mL), manganese (55 mg, 1 mmol) and anhydrous $CrCl_3$ (8 mg, 0.05 mmol) were added. The mixture was left without stirring for about 10 min (the violet colour of the $CrCl_3$ disappeared),[§] then the mixture was vigorously stirred until the formation of a green–white solid took place. Salen **1** (27 mg, 0.05 mmol) was added followed by anhydrous Et_3N (14 μL, 0.1 mmol). The resulting maroon solution was stirred for a further 1 h and propargyl chloride (72 μL, 1 mmol) was added. The mixture was stirred for 1 h then the aldehyde **2a**–**2i** (0.5 mmol) and TMSCl (95 μL, 0.75 mmol) were added. The mixture was stirred at room temperature until the aldehyde disappeared (reaction time ca. 32–48 h). Then quenched with a saturated solution of $NaHCO_3$ (10 mL) and filtered on Celite. The solvent was evaporated under reduced pressure and the residue was extracted with Et_2O (3×8 mL). The combined organic extract was evaporated under reduced pressure and the resulting brown oil was dissolved in 2N HCl/THF 1:4 (2 mL). The mixture was stirred until desilylation of the propargylic alcohol was complete by TLC. The reaction was diluted with AcOEt (10 mL) and THF was removed under reduced pressure. The mixture was extracted with AcOEt (3×5 mL) and the organic phases were collected, dried over Na_2SO_4, and evaporated under reduced pressure. Finally the crude oil was purified by flash chromatography.

[§] The addition of TMSCl (5 mol% referred to aldehyde) usually shortens the reduction time of the Cr(III) to Cr(II).

4.2. (*R*)-1-Phenyl-3-butyn-1-ol 3a

Yield: 37 mg (50%) (pale yellow oil). The separation of enantiomers was performed by chiral GC analysis: isothermal 120°C, $t_r(R) = 19.91$ min, $t_r(S) = 22.51$ min (e.e. = 56%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.98 (1H, t, $J = 2.6$ Hz), 2.30 (1H, d, $J = 3.3$ Hz), 2.57 (2H, dd, $J_1 = 2.6$ Hz, $J_2 = 6.6$ Hz), 4.79 (1H, m), 7.16–7.30 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.35, 70.92, 72.26, 80.65, 125.70, 127.93, 128.42, 142.39. IR (neat): 3403, 3310, 2912, 2110, 1454, 751, 698 cm^{-1}. MS (EI, 70 ev): *m*/*z* 51, 77, 79, 107, 115. Anal. calcd for $C_{10}H_{10}O$ (146.19): C, 82.16; H, 6.89. Found: C, 82.02; H, 6.84%. $[\alpha]_D^{20} = +26.0$ (*c* 2.5, $CHCl_3$).

4.3. (*R*)-1-(2-Fluorophenyl)-3-butyn-1-ol 3b

Yield: 30 mg (36%) (pale yellow oil). Separation of enantiomers was performed by chiral GC analysis: isothermal 115°C, $t_r(R) = 22.88$ min, $t_r(S)$-- = 26.55 min (e.e. = 35%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.89–2.24 (1H, m), 2.46 (1H, d, $J = 4.5$ Hz), 2.62–2.80 (2H, m), 5.22 (1H, br), 7.05 (1H, t, $J = 8.7$ Hz), 7.18 (1H, t, $J = 6.6$ Hz), 7.30–7.40 (1H, m), 7.55 (1H, t, $J = 6.0$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 29.60, 66.44, 71.17, 80.17, 115.06 (d, $J = 21.5$ Hz), 124.30, 127.20, 129.25, 129.42, 160.91. IR (neat): 3403, 3310, 2926, 2137, 1620, 1487, 1261, 1109, 1016, 798, 758 cm^{-1}. MS (EI, 70 ev): *m*/*z* 51, 77, 97, 125. Anal. calcd for $C_{10}H_9FO$ (164.18): C, 73.16; H, 5.53. Found: C, 73.01; H, 5.48%. $[\alpha]_D^{20} = +9.8$ (*c* 0.5, $CHCl_3$).

4.4. (*R*)-1-(4-Fluorophenyl)-3-butyn-1-ol 3c

Yield: 37 mg (45%) (pale yellow oil). Separation of enantiomers by chiral GC analysis: isothermal 140°C, $t_r(R) = 38.17$ min, $t_r(S)$-- = 39.95 min (e.e. = 56%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.10 (1H, t, $J = 2.6$ Hz), 2.38 (1H, br), 2.63 (2H, dd, $J_1 = 2.6$ Hz, $J_2 = 6.2$ Hz), 4.88 (1H, t, $J = 6.3$ Hz), 7.06 (2H, t, $J = 8.8$ Hz), 7.34-7.42 (2H, dd, $J_1 = 5.3$ Hz, $J_2 = 8.8$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.56, 71.20, 71.66, 80.31, 115.26 (d, $J = 21.3$ Hz), 127.33, 138.07, 161.65. IR (neat): 3423, 3290, 2912, 2217, 1600, 1500, 1208, 1043, 1016, 877, 830 cm^{-1}. MS (EI, 70 ev): *m*/*z* 51, 77, 97, 125. Anal. calcd for $C_{10}H_9FO$ (164.18): C, 73.16; H, 5.53. Found: C, 73.09; H, 5.48%. $[\alpha]_D^{20} = +20.3$ (*c* 0.7, $CHCl_3$).

4.5. (*R*)-1-(4-*tert*-Butylphenyl)-3-butyn-1-ol 3d

Yield: 30 mg (30%) (pale yellow oil). Separation of enantiomers was performed by chiral GC analysis: program 110°C for 10 min then 2°C/min to 120°C, $t_r(R)=$ 28.49 min, $t_r(S)-=32.58$ min (e.e. = 45%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.31 (9H, s), 2.08 (1H, t, $J=2.7$ Hz), 2.36 (1H, d, $J=3.6$ Hz), 2.63 (2H, dd, $J_1=2.7$ Hz, $J_2=6.3$ Hz), 4.80–4.85 (1H, m), 7.30–7.41 (4H, m); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.21, 31.29, 34.50, 70.78, 72.10, 80.92, 125.34, 125.45, 139.47, 150.89. IR (neat): 3423, 3290, 2217, 1918, 1527, 1460, 1268, 1038, 835, 669 cm^{-1}. MS (EI, 70 ev): *m*/*z* 57, 91, 148, 163. Anal. calcd for $C_{14}H_{18}O$ (202.29): C, 83.12; H, 8.97. Found: C, 83.03; H, 8.89%. $[\alpha]_D^{20}=+12.1$ (*c* 0.59, $CHCl_3$).

4.6. (*R*)-1-(4-*iso*-Propylphenyl)-3-butyn-1-ol 3e

Yield: 30 mg (32%) (pale yellow oil). Separation of enantiomers was performed by chiral GC analysis: isothermal 140°C, $t_r(R)=21.68$ min, $t_r(S)-=23.42$ min (e.e. = 43%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.24 (3H, d, $J=6.9$ Hz), 1.26 (3H, d, $J=6.9$ Hz), 2.09 (1H, t, $J=2.6$ Hz), 2.38 (1H, brs), 2.65 (2H, dd, $J_1=2.6$ Hz, $J_2=6.4$ Hz), 2.92 (1H, sept, $J=8.1$ Hz), 4.87 (1H, t, $J=6.3$ Hz), 7.10–7.40 (4H, AB, $J_1=8.1$ Hz, $J_2=17.0$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.99, 29.35, 33.85, 70.83, 72.22, 80.87, 125.67, 126.48, 139.76, 148.63. IR (neat): 3238, 3952, 2925, 2210, 1049, 1500, 1009, 837 cm^{-1}. MS (EI, 70 ev): *m*/*z* 51, 77, 79, 91, 107, 133, 149, 188. Anal. calcd for $C_{13}H_{16}O$ (188.27): C, 82.94; H, 8.57. Found: C, 82.89; H, 8.50%. $[\alpha]_D^{20}=+5.0$ (*c* 1, $CHCl_3$).

4.7. (*R*)-1-(4-Methoxyphenyl)-3-butyn-1-ol 3f

Yield: 35 mg (40%) (pale yellow oil). Separation of enantiomers was performed by chiral GC analysis: isothermal 140°C, $t_r(R)=25.61$ min, $t_r(S)-=28.71$ min (e.e. = 28%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.05 (1H, t, $J=2.7$ Hz), 2.35 (1H, d, $J=2.4$ Hz), 2.60–2.63 (2H, m), 3.79 (3H, s), 4.83–4.90 (1H, m), 6.87 (2H, d, $J=8.7$ Hz), 7.30 (2H, d, $J=8.7$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 29.63, 55.63, 71.09, 72.23, 80.50, 114.08, 114.67, 125.27, 127.25, 130.19, 143.48. IR (neat): 3443, 3290, 2959, 2919, 2833, 2110, 1600, 1507, 1242, 1169, 1029, 804 cm^{-1}. MS (EI, 70 ev): *m*/*z* 51, 65, 77, 94, 109, 137, 171. Anal. calcd for $C_{11}H_{12}O_2$ (176.21): C, 74.98; H, 6.86. Found: C, 74.90; H, 6.81%. $[\alpha]_D^{20}=+11.0$ (*c* 1, $CHCl_3$)

4.8. (*R*)-1-(4-Bromophenyl)-3-butyn-1-ol 3g

Yield: 41 mg (36%) (pale yellow oil). Separation of enantiomers was performed by chiral GC analysis: program 120°C for 10 min then 2°C/min to 180°C, $t_r(R)=$ 33.43 min, $t_r(S)-=34.71$ min (e.e. = 22%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.09 (1H, t, $J=2.7$ Hz), 2.45 (1H, d, $J=2.6$ Hz), 2.62 (2H, dd, $J_1=2.6$ Hz, $J_2=6.0$ Hz), 4.80–4.90 (1H, m), 7.28 (2H, d, $J=8.0$ Hz), 7.50 (2H, $J=8.0$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.73, 71.61, 71.90, 80.36, 122.01, 127.70, 131.76, 141.57. IR (neat): 3338, 3297, 2912, 1951, 1586, 1487, 1071, 1009, 824, 837, cm^{-1}. MS (EI, 70 ev): *m*/*z* 51, 65, 77, 91, 117, 127, 156, 206, 208. Anal. calcd for $C_{10}H_9BrO$ (225.08): C, 53.56; H, 4.03. Found: C, 53.49; H, 4.01%. $[\alpha]_D^{20}=$ –0.59 (*c* 0.68, $CHCl_3$).

4.9. (*R*)-1-[4-(Trifluoromethyl)phenyl]-3-butyn-1-ol 3h

Yield: 21 mg (20%) (pale yellow oil). Separation of enantiomers was performed by chiral GC analysis: isothermal 140°C, $t_r(R)=8.19$ min, $t_r(S)-=9.92$ min (e.e. = 27%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.11 (1H, t, $J=2.8$ Hz), 2.45 (1H, d, $J=2.6$ Hz), 2.58–2.70 (2H, m), 4.86–4.96, (1H, m), 7.40 (2H, d, $J=7.07$ Hz), 7.48 (2H, d, $J=7.0$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.73, 65.87, 71.59, 78.65, 94.80, 125.37, 126.03, 126.27, 144.21. IR (neat): 3330, 3932, 2839, 2369, 1613, 1328, 1122, 1062, 844, 791 cm^{-1}. MS (EI, 70 ev): *m*/*z* 51, 77, 127, 145, 175, 213. Anal. calcd for $C_{11}H_9F_3O$ (214.18): C, 53.56; H, 4.03. Found: C, 53.48; H, 4.01%. $[\alpha]_D^{20}=$ +5.0 (*c* 1, $CHCl_3$).

4.10. (*R*)-1-Phenyl-5-esyn-3-ol 3i

Yield: 18 mg (21%) (pale yellow oil). Separation of enantiomers was performed by chiral GC analysis: program 130°C for 10 min then 1.5°C/min to 160°C, $t_r(R)=20.33$ min, $t_r(S)-=20.57$ min (e.e. = 15%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.18–1.27 (2H, m), 1.82–1.93 (1H, m), 2.07 (1H, t, $J=2.6$ Hz), 2.18 (1H, s), 2.37–3.45 (2H, m), 2.71–2.80 (1H, m), 3.73–3.86 (1H, m), 7.21–7.31 (5H, m); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 27.47, 31.69, 31.86, 37.75, 69.06, 71.00, 76.17, 80.59, 125.90, 128.40, 128.42, 141.58. IR (neat): 3397, 3296, 3018, 2391, 2853, 2103, 1453, 1056, 746, 700 cm^{-1}. MS (EI, 70 ev): *m*/*z* 65, 91, 117. Anal. calcd for $C_{12}H_{14}O$ (174.24): C, 82.72; H, 8.10. Found: C, 82.70; H, 8.05%. $[\alpha]_D^{20}=+3.5$ (*c* 0.56, $CHCl_3$).

4.11. 1-Phenyl-2-methyl-3-butyn-1-ol 17

Yield: 26 mg (32%) (pale yellow oil). Mixture of diastereoisomers (1:1). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.11 (3H, d, $J=6.9$ Hz), 2.13 (1H, d, $J=2.4$ Hz), 2.18–2.23 (1H, m), 2.72–2.90 (1H, m), 4.73–4.79 (1H, m), 7.18–7.42 (5H, m); [*second disatereoisomer*: 1.14 (3H, d, $J=6.8$ Hz), 4.51–4.56 (m, 1H)]. MS (EI, 70 ev): *m*/*z* 51, 75, 107, 118, 159.

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