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Enantioselective Oxidation of Aromatic Ketones by Molecular Oxygen, Catalyzed by Chiral Monoaza-Crown Ethers.

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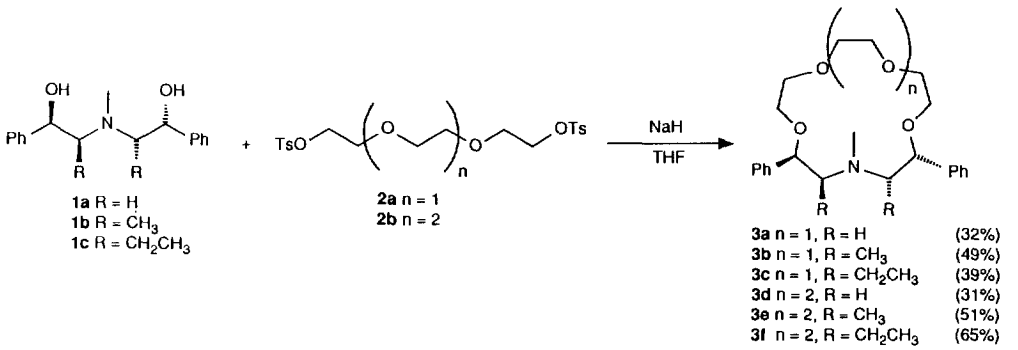
Abstract: Chiral monoaza-15-crown-5 ethers **3a-c** and monoaza-18-crown-6 ethers **3d-f** have been synthesized from optically active diethanolamines in moderate to good yields. One of these crown ethers, i.e. **3a**, proved to be both an efficient and a selective phase transfer catalyst in the asymmetric oxidation of aromatic ketones by molecular oxygen. Yields of the oxidation reaction were high and enantiomeric excesses of up to 72% could be obtained. To account for the remarkable differences in asymmetric induction between the crown ethers tested, a model for the structure of the transition state was proposed.

INTRODUCTION

Synthesis of optically active tertiary α-hydroxy ketones from achiral or racemic precursors, using a suitable chiral catalyst, continues to be an exciting challenge for chemists. Such a structural unit is present in many biologically active compounds, such as the anthracycline antitumor antibiotics[1] and the homoisoflavanone eucomol.[2] Chiral tertiary α-hydroxy ketones have recently been prepared by addition of Grignard reagents to α-keto ketals,[3] oxidation of ketone enolates by oxaziridines,[4] and dihydroxylation of enol ethers.[5] One of the more attractive methods to synthesize optically active α-hydroxy ketones is the oxidation of ketone enolates in a two phase system by molecular oxygen, because only catalytic amounts of a chiral phase transfer catalyst are needed and cheap chemicals are used. Surprisingly, only a few examples of this type of asymmetric oxidation have been described,[6-8] despite the fact that high ee's (up to 79%) were obtained when cinchona alkaloids were employed as the chiral catalysts.[6]

Recently, we have prepared a series of chiral diethanolamines with two, three, and four stereogenic centers in the diethanolamine backbone.[9,10] The reaction pathway followed allowed systematic variation of the substituents. We now report the conversion of diethanolamines **1a-c** into chiral aza-15-



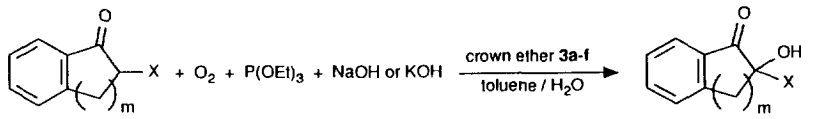
Scheme I: *Synthesis of chiral aza-crown ethers.*

crown-5 ethers **3a-c** and 18-crown-6 ethers **3d-f**. These crown ethers have been applied as chiral catalysts in the enantioselective oxidation of aromatic ketones by molecular oxygen, even though discouraging results have been reported in literature when crown ethers were used to catalyze this reaction.[7]

RESULTS AND DISCUSSION

Optically active diethanolamines **1a-c**, prepared from chiral TBDMS protected cyanohydrins,[9,10] were converted in one step into chiral aza-crown ethers **3a-f** in acceptable yields *via* a cyclization reaction with tri- and tetraethylene glycol ditosylate (**2a,b**)[11] under high dilution conditions (Scheme I). Yields were higher for crown ethers having substituents α to nitrogen, which is probably due to the decreased nucleophilicity of nitrogen in these compounds. It has previously been shown that racemization does not occur during this cyclization reaction.[9]

The enantioselective oxidation of 2-methyl-1-tetralone (**4a**) by molecular oxygen was chosen to determine the efficiency of crown ethers **3a-f** as chiral phase transfer catalysts (Scheme II). First, in a toluene-water two phase system, **4a** was deprotonated by a complex of 15-crown-5 **3a-c** and NaOH, or 18-

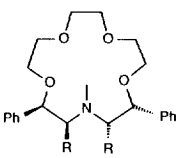
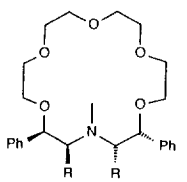


4a m = 1, X = CH_3
4b m = 1, X = CH_2CH_3
4c m = 2, X = CH_3
4d m = 2, X = CH_2CH_3
4e m = 2, X = $CH_2CH{=}CH_2$
4f m = 2, X = $CH_2C{\equiv}CH$
4g m = 1, X = H
4h m = 2, X = $COCH_3$

5a-h

Scheme II: *Enantioselective oxidation of aromatic ketones by molecular oxygen.*

Table 1: *Enantioselective Oxidation of Ketone **4a** by Molecular Oxygen, Catalyzed by Chiral Crown Ethers **3a-f**.*[a]

Crown ether	R	no	Time (h)	Conv (%)	Yield[b] (%)	ee[c] (%)	Config[d]
none	-	-	72	< 5%	-	-	-
	H	**3a**	24	100	93	52	R
	CH_3	**3b**	48	100	85	2	S
	C_2H_5	**3c**	72	33	85	6	S
	H	**3d**	24	100	91	6	R
	CH_3	**3e**	72	61	94	2	S
	C_2H_5	**3f**	72	40	75	3	S

a) **4a**:**3a-f** = 10:1. The reaction mixture was allowed to warm from -20 °C to +6 °C in 24 hours and was stirred at this temperature for the rest of the reaction time. b) Isolated yields, based upon the amount of converted starting material. c) Determined by HPLC-analysis, using a CHIRALCEL OD column (flow: 0.7 mL/min; eluent: 2-propanol/hexane = 1/99). d) Determined by the sign of the optical rotation.[5]

crown-6 **3d-f** and KOH. Then, the chiral enolate-crown ether complex, that was formed, reacted with molecular oxygen as present in air to give the α-keto peroxide anion, which was reduced *in situ* by triethyl phosphite. α-Hydroxy ketone **5a** was obtained in good yield.

As shown in Table 1, crown ethers **3a-f** do all catalyze the oxidation reaction. However, the reaction rate decreased with increasing size of the substituents R, α to nitrogen, in the crown ethers. This can be caused either by the increased lipophilicity of the crown ether, retarding the rate of complexation of the metal hydroxide, or by the increased steric demand of the crown ether, delaying the deprotonation of **4a** and hindering the attack of the enolate complex by oxygen. Although asymmetric induction was poor when crown ethers **3b-f** were applied, use of the structurally related crown ether **3a**, having only two stereogenic centers, as the catalyst resulted in formation of **5a** with an enantiomeric excess of 52%. Apparently, the extra alkyl substituents present in **3b,c,e,f**, compared to **3a**, have an unfavorable impact not only on the reaction rate, but also on the selectivity of the reaction.

Next, the asymmetric oxidations of several other aromatic ketones by oxygen, using crown

Table 2: *Asymmetric Oxidation of Ketones* ***4a-h*** *by Molecular Oxygen, Catalyzed by Crown Ether* ***3a****.*[a]

Ketone no	X	m	Yield[b] (%)	ee[c] (%)	$[\alpha]_D^{20}$ (c=1,$CHCl_3$)	Config[d]
4a	CH_3	1	93	52	+20	R
4b	CH_2CH_3	1	83	43	+37	R
4c	CH_3	2	89	66	+8	R
4d	CH_2CH_3	2	95	67	+13	R
4e	$CH_2CH{=}CH_2$	2	89	72	+4	S
4f	$CH_2C{\equiv}CH$	2	80[e]	71	+20	S
4g	H	1	0[f]	-	-	-
4h	$COCH_3$	2	0[g]	-	-	-

a) See Table 1 footnote a. b) Isolated yields. c) Determined by HPLC-analysis. d) Determined by the sign of the optical rotation. **5a**, ref. 5; **5c**, ref. 4; **5d**, ref. 6. The absolute configurations of **5b,e,f** were tentatively assigned by analogy. Due to the priority rules **5e,f** were assigned (*S*). e) Based upon converted starting material. Conversion 82%. f) Only polymeric material was isolated. g) The starting material was recovered.

ether **3a** as the phase transfer catalyst, were investigated. All reactions were carried out under the following conditions: while stirred vigorously, air was bubbled through the reaction mixture for 24 hours, in which time the reaction mixture was allowed to warm from -20 °C to +6 °C. As evident from the results summarized in Table 2, indanone derivatives **4a,b** were oxidized less selectively than tetralone derivatives **4c-f**. The nature of the substituent X at the carbon atom α to the ketone function in **4c-f** does not seem to have any major impact on the stereoselectivity of the reaction. Although the relatively acidic acetylenic proton in ketone **4f** decreases the rate of the reaction, it does not affect the selectivity. Oxidation of **4g** (X = H) did not yield the corresponding α-hydroxy ketone, but only polymeric material. The presence of two hydrogen atoms α to the ketone function makes this substrate prone to other sequential reactions. When 2-acetyl-1-tetralone (**4h**) was subjected to the reaction conditions used for the oxidation, only starting material was isolated. The anion of **4h** appears to be too stable to react with oxygen. Thus, ketones, that can form stabilized anions, or have more than one α-hydrogen atoms, can not be oxidized to their corresponding α-hydroxy ketones by this method.

For the oxidation reaction to occur with the observed selectivity, an enolate-crown ether complex needs to be formed, in which only the *re*-phase of the enolate is available for reaction. To this effect, at least three sites of interaction between the enolate and the crown ether have to exist. In an

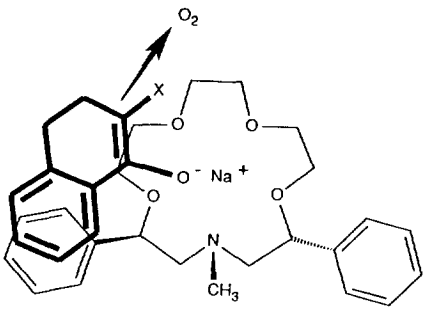


Figure 1: *Model for the transition state of the stereoselctive oxidation of aromatic ketones.*

attempt to explain the results obtained, a model for the transition state, depicted in Figure 1, was proposed. In this model the structure of the complex is governed by i) ionic attraction of the enolate and the sodium cation, bound in the crown ether ring, by ii) π-π interaction of the aromatic rings in the crown ether and in the enolate, and by iii) steric repulsion of the enolate and the methyl substituent at nitrogen in the crown ether. This last interaction forces the substituent at nitrogen to be *syn*-oriented with respect to the enolate. Johnson *et al.*[12] have previously shown that in complexes of aza-15-crown-5 ethers and alkylammonium salts the substituent at nitrogen is indeed only *syn*-oriented, whereas this substituent was shown to be both *syn*- and *anti*-oriented in complexes of alkylammonium salts and monoaza-18-crown-6 ethers. This can explain the dramatic decrease in stereoselectivity, when **3d**, instead of **3a**, was used as the catalyst. The unfavorable effect of the alkyl substituents R in crown ethers **3b,c,e,f** on the selectivity of the oxidation reaction is probably due to the fact that these substituents sterically repel the aromatic ring of the enolate, thereby disturbing the π-π interaction. In the proposed model (Figure 1) the substituent X in the enolate is positioned on the outside of the complex, so the size of this substituent is not expected to have a major influence on the selectivity of the reaction. This was indeed observed.

In conclusion it can be said that crown ether **3a** has shown to be a selective phase transfer catalyst in the enantioselective oxidation of aromatic ketones to their corresponding tertiary α-hydroxy ketones by molecular oxygen. Structurally related crown ethers **3b-f**, on the other hand, hardly induced any selectivity at all. This remarkable difference was ascribed to subtle changes in steric and electronic interactions in the crown ether-enolate complex.

EXPERIMENTAL

^{1}H NMR and ^{13}C NMR samples were measured in $CDCl_3$ with TMS as internal standard for ^{1}H NMR and $CDCl_3$ as internal standard for ^{13}C NMR. Enantiomeric excesses were determined by HPLC-analysis, using

a CHIRALCEL OD column (eluent: **5a,b,f**: 2-propanol/hexane = 1/99, **5c,d,e**: 2-propanol/hexane = 0.25/99.75; flow: **5a**: 0.7 mL/min, **5b-f**: 1 mL/min; UV-detection: 254 nm).

Commercially available chemicals were used, with the exception of **1a-c**[9,10] and **2a,b**,[11] which were synthesized by known methods. Ketones **4b,d,e,f** were prepared in moderate yields by alkylation of the enolate of 1-indanone or 1-tetralone, respectively. THF was freshly distilled from $LiAlH_4$ prior to use.

(3*R*,14*R*)-1-Aza-1-methyl-4,7,10,13-tetraoxa-3,14-diphenylcyclopentadecane (3a)

To a suspension of 1.40 g (34 mmol) of NaH (60% suspension in mineral oil, washed twice with petroleum ether 40-60) in 50 mL of anhydrous THF was added dropwise a solution of 2.30 g (8.5 mmol) of **1a** in 100 mL of THF. The mixture was stirred for 1 hour at room temperature and was refluxed for 1 hour, successively. At 0 °C, 3.90 g (8.5 mmol) of **2a** in 50 mL of THF was added. After stirring at 0 °C for 30 minutes and at room temperature for 1 hour, the reaction mixture was refluxed for 40 hours. The reaction was quenched by the addition 2 mL of water, after which the solvent was evaporated *in vacuo*. The crude product was dissolved in 50 mL of CH_2Cl_2 and was washed with 100 mL of water. The water layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were dried on $MgSO_4$ and concentrated *in vacuo*. After purification by flash column chromatography (eluent: Et_3N/CH_2Cl_2/petroleum ether 40-60 = 3/19/78) 1.07 g (32%) of **3a** was obtained.

$[\alpha]_D^{20}$ -124 (c=1, $CHCl_3$).

^1H NMR: δ (ppm) 7.31 (m, 10H, Ph), 4.72 (dd, 2H, J = 3.8 Hz, J = 8.2 Hz, CHO), 3.66 (m, 12H, OCH_2), 3.07 (dd, 2H, J = 8.2 Hz, J = 13.4 Hz, CH_2N), 2.43 (dd, 2H, J = 3.8 Hz, J = 13.4 Hz, CH_2N), 2.28 (s, 3H, NCH_3).

^{13}C NMR: δ (ppm) 141.4, 128.3, 127.4, 126.8 (Ph), 79.9 (CHO), 70.8, 70.6, 67.9 (CH_2O), 64.5 (CH_2N), 45.1 (NCH_3).

MS (CI): m/z 386 ($M+H^+$, 100%).

Anal. Calcd. for $C_{23}H_{31}NO_4$: C, 71.66; H, 8.10; N, 3.63. Found: C, 71.64; H, 8.17; N, 3.63.

(2*S*,3*R*,14*R*,15*S*)-1-Aza-1,2,15-trimethyl-4,7,10,13-tetraoxa-3,14-diphenylcyclopentadecane (3b)

Prepared as described for **3a**, with **1b** and **2a** as the starting materials. The product was purified by flash column chromatography (eluent: Et_3N/CH_2Cl_2/petroleum ether 40/60 = 3/10/87).

Yield: 49%, $[\alpha]_D^{20}$ -82 (c=1, $CHCl_3$), de > 95% (^1H NMR).

^1H NMR: δ (ppm) 7.31 (m, 10H, Ph), 4.88 (d, 2H, J = 3.1 Hz, CHO), 3.49-3.85 (m, 12H, CH_2O), 3.10 (dq, 2H, J = 3.1 Hz, J = 6.7 Hz, CHN), 2.19 (s, 3H, NCH_3), 0.97 (d, 6H, J = 6.7 Hz, CH_3).

^{13}C NMR: δ (ppm) 141.8, 127.6, 127.4, 126.5 (Ph), 84.7 (CHO), 71.4, 70.7, 67.2 (CH_2O), 61.1 (CHN), 36.7 (NCH_3), 10.7 (CH_3).

MS (CI): m/z 414 ($M+H^+$, 100%).

Anal. Calcd. for $C_{25}H_{35}NO_4$: C, 72.61; H, 8.53; N, 3.39. Found: C, 72.35; H, 8.71; N, 3.47.

(2*S*,3*R*,14*R*,15*S*)-1-Aza-2,15-diethyl-1-methyl-4,7,10,13-tetraoxa-3,14-diphenylcyclopentadecane (3c)

Prepared as described for **3a**, with **1c** and **2a** as the starting materials. The product was purified by flash column chromatography (eluent: Et_3N/CH_2Cl_2/petroleum ether 40-60 = 3/10/87).

Yield: 39%, $[\alpha]_D^{20}$ -52 (c=1, $CHCl_3$), de > 95% (^1H NMR).

^1H NMR: δ (ppm) 7.31 (m, 10H, Ph), 5.20 (d, 2H, J = 2.1 Hz, CHO), 3.66 (m, 12H, OCH_2), 2.84 (m, 2H, CHN), 2.42 (s, 3H, NCH_3), 1.60 (m, 4H, CH_2), 0.79 (t, 6H, J = 7.2 Hz, CH_3).

^{13}C NMR: δ (ppm) 142.5, 127.7, 127.3, 126.3 (Ph), 82.6 (CHO), 71.7, 71.6, 70.5 (CH_2O), 68.1 (CHN), 37.1 (NCH_3), 18.1 (CH_2), 12.7 (CH_3).

MS (CI): m/z 442 ($M+H^+$, 100%)

Anal. Calcd. for $C_{27}H_{39}NO_4$: C, 73.44; H, 8.90; N, 3.17. Found: C, 73.08; H, 9.17; N, 3.16.

(3*R*,17*R*)-1-Aza-1-methyl-4,7,13,16-pentaoxa-3,17-diphenylcyclooctadecane (3d)

Prepared as described for **3a**, using **1a** and **2b** as the starting materials. The product was purified by flash column chromatography (Et_3N/CH_2Cl_2/petroleum ether 40-60 = 3/27/70).

Yield: 31%, $[\alpha]_D^{20}$ -84 (c=1, $CHCl_3$).

^1H NMR: δ (ppm) 7.28 (m, 10H, Ph), 4.55 (dd, 2H, J = 3.8 Hz, J = 8.2 Hz, CHO), 3.64 (m, 16H, OCH_2), 2.94 (dd, 2H, J = 8.2 Hz, J = 13.4 Hz, CH_2N), 2.62 (dd, 2H, J = 3.8 Hz J = 13.4 Hz, CH_2N), 2.46 (s, 3H, NCH_3).

^{13}C NMR: δ (ppm) 141.2, 128.1, 127.3, 126.6 (Ph), 80.6 (CHO), 70.6, 70.5, 70.3, 67.8 (CH_2O), 64.2 (CH_2N), 43.4 (NCH_3).

MS (EI): m/z 429 (M^+, 29%), 104 ($PhCH=CH_2^+$, 100%)

Anal. Calcd. for $C_{25}H_{35}NO_5$: C, 69.90; H, 8.21; N, 3.26. Found: C, 69.72; H, 8.50; N, 3.24.

(2*S*,3*R*,17*R*,18*S*)-1-Aza-1,2,18-trimethyl-4,7,10,13,16-pentaoxa-3,17-diphenylcyclooctadecane (3e)

Prepared as described for **3a**, with **1b** and **2b** as the starting materials. The product was purified by flash column chromatography (eluent: Et_3N/CH_2Cl_2/petroleum ether 40/60 = 3/15/82).

Yield: 51%, $[\alpha]_D^{20}$ -10 (c=1, $CHCl_3$), de > 95% (^1H NMR).

^1H NMR: δ (ppm) 7.20 (m, 10H, Ph), 3.91 (d, 2H, J = 4.6 Hz, CHO), 3.95-3.25 (m, 16H, CH_2O), 2.98 (dq, 2H, J = 4.6 Hz, J = 6.7 Hz, CHN), 2.34 (s, 3H, NCH_3), 1.05 (d, 6H, J = 6.7 Hz, CH_3).

^{13}C NMR: δ (ppm) 142.1, 127.4, 127.0, 126.4 (Ph), 85.4 (CHO), 70.7, 70.5, 70.2, 67.7 (CH_2O), 61.5 (CHN), 34.1 (NCH_3), 10.4 (CH_3).

MS (EI): m/z 457 (M^+, 51%), 84 ($CH_2=CHN^+(CH_3)=CHCH_3$, 100%)

Anal. Cald. for $C_{27}H_{39}NO_5$: C, 70.87; H, 8.59; N, 3.06. Found: C, 70.66; H, 8.70; N, 3.05.

(2*S*,3*R*,17*R*,18*S*)-1-Aza-2,18-diethyl-1-methyl-4,7,10,13,16-pentaoxa-3,17-diphenylcyclooctadecane (3f)

Prepared as described for **3a**, with **1c** and **2b** as the starting materials. The product was purified by flash column chromatography (eluent: Et_3N/CH_2Cl_2/petroleum ether 40-60 = 3/15/82).

Yield: 65%, $[\alpha]_D^{20}$ -29 (c=1, $CHCl_3$), de > 95% (^1H NMR).

^1H NMR: δ (ppm) 7.28 (m, 10H, Ph), 4.62 (d, 2H, J = 2.6 Hz, CHO), 3.64 (m, 16H, OCH_2), 2.66 (m, 2H, CHN), 2.56 (s, 3H, NCH_3), 1.69 (m, 4H, CH_2), 0.84 (t, 6H, J = 7.2 Hz, CH_3).

^{13}C NMR: δ (ppm) 142.5, 127.6, 126.6, 126.3 (Ph), 84.9 (CHO), 70.5, 70.4, 69.9 (CH_2O), 68.5 (CHN), 33.4 (NCH_3), 18.8 (CH_2), 12.8 (CH_3).

MS (EI): m/z 485 (M^+, 21%), 112 ($CH_3CH{=}CHN^+(CH_3){=}CHCH_2CH_3$, 100%)

Anal. Cald. for $C_{29}H_{43}NO_5$: C, 71.72; H, 8.91; N, 2.88. Found: C, 71.90; H, 9.09; N, 2.84.

General procedure for the enantioselective oxidation

At -20 °C, a solution of 41 mmol of NaOH in 1.6 mL of water was added to a solution of 2.1 mmol of ketone **4**, 2.5 mmol of triethyl phosphite, and 0.21 mmol crown ether **3a** in 15 mL of toluene. Under vigorous stirring, the reaction mixture was allowed to warm from -20 °C to +6 °C in 24 hours, as air was bubbled through the solution. The reaction mixture was poured into 50 mL of 1N HCl and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried on $MgSO_4$ and concentrated *in vacuo*. The product was purified by flash column chromatography (silicagel; eluent: **5a-e**: ether, **5f**: ether/petroleum ether 40-60 = 4/1).

(*R*)-2-Hydroxy-2-methyl-1-indanone (5a)

Yield: 93%, $[\alpha]_D^{20}$ +20 (c=1, $CHCl_3$), ee 52%, mp 52-54°C; Lit.[5] $[\alpha]_D^{25}$ +20.0 (c=2, MeOH, ee 81%).

^1H NMR: δ (ppm) 7.78 (d, 1H, J = 7.7 Hz, Ph), 7.63 (t, 1H, J = 7.7 Hz, Ph), 7.44 (d, 1H, J = 7.7 Hz, Ph), 7.40 (t, 1H, J = 7.7 Hz, Ph), 3.24 (s, 2H, CH_2), 1.45 (s, 3H, CH_3).

^{13}C NMR: δ (ppm) 208.1 (C=O), 151.1, 135.6, 133.4, 127.6, 126.6, 124.7 (Ph), 77.2 (COH), 42.2 (CH_2), 25.3 (CH_3).

IR (KBr): 3310 (OH), 1715 (C=O), 1610 (Ph), 1150 (C-OH), 727 (Hoop).

(*R*)-2-Ethyl-2-hydroxy-1-indanone (5b)

Yield: 83%, $[\alpha]_D^{20}$ +37 (c=1, $CHCl_3$), ee 43%.

^1H NMR: δ (ppm) 7.77 (d, 1H, J = 7.7 Hz, Ph), 7.63 (t, 1H, J = 7.7 Hz, Ph), 7.45 (d, 1H, J = 7.7 Hz, Ph), 7.40 (t, 1H, J = 7.7 Hz, Ph), 3.29 (d, 1H, J = 17.0 Hz, PhCH_2), 3.14 (d, 1H, J = 17.0 Hz, PhCH_2), 1.73 (m, 2H, CH_2CH_3), 0.93 (t, 3H, J = 7.2 Hz, CH_3).

^{13}C NMR: δ (ppm) 208.5 (C=O), 151.5, 135.6, 134.1, 127.5, 126.4, 124.4 (Ph), 79.9 (COH), 39.5 (PhCH_2), 31.0 (CH_2), 7.7 (CH_3).

IR (neat): 3440 (OH), 1705 (C=O), 1608 (Ph), 1152 (C-OH), 735 (Hoop).

(*R*)-2-Hydroxy-2-methyl-1-tetralone (5c)

Yield: 89%, $[\alpha]_D^{20}$ +8 (c=1, $CHCl_3$), ee 66%; Lit.[4] $[\alpha]_D^{20}$ +17.3 (c=2, $CHCl_3$, ee ≥95).

^{1}H NMR: δ (ppm) 8.03 (d, 1H, J = 7.5 Hz, Ph), 7.53 (t, 1H, J = 7.5 Hz, Ph), 7.34 (t, 1H, J = 7.5 Hz, Ph), 7.26 (d, 1H, J = 7.7 Hz, Ph), 3.86 (s, 1H, OH), 3.1 (m, 2H, CH_2), 2.2 (m, 2H, CH_2), 1.40 (s, 3H, CH_3).

^{13}C NMR: δ (ppm) 201.1 (C=O), 143.1, 133.6, 129.6, 128.6, 127.6, 126.4 (Ph), 73.2 (COH), 35.6, 26.4 (CH_2), 23.5 (CH_3).

IR (neat): 3490 (OH), 1675 (C=O), 1600 (Ph), 1155 (C-OH), 738 (Hoop)

(*R*)-2-Ethyl-2-hydroxy-1-tetralone (5d)

Yield: 95%, $[\alpha]_D^{20}$ +13 (c=1, $CHCl_3$), ee 68%; Lit[6] (*S*), $[\alpha]_D^{15}$ -11.1 (c=0.67, $CHCl_3$).

^{1}H NMR: δ (ppm) 8.01 (dd, 1H, J = 1.3 Hz, J = 7.5 Hz, Ph), 7.52 (dt, 1H, J = 1.3 Hz, J = 7.5 Hz, Ph), 7.33 (t, 1H, J = 7.5 Hz, Ph), 7.25 (d, 1H, J = 7.5 Hz, Ph), 3.81 (s, 1H, OH), 3.0 (m, 2H, CH_2), 2.35 (ddd, 1H, J = 2.6 Hz, J = 5.1 Hz, J = 13.3 Hz, CH_2), 2.17 (dt, 1H, J = 6.1 Hz, J = 13.3 Hz, CH_2), 1.6 (m, 2H, CH_2CH_3), 0.93 (t, 3H, J = 7.5 Hz, CH_3).

^{13}C NMR: δ (ppm) 201.5 (C=O), 143.1, 133.6, 130.0, 128.7, 127.5, 126.5 (Ph), 75.5 (COH), 33.3, 28.1, 26.2 (CH_2), 7.0 (CH_3).

IR (neat): 3500 (OH), 1678 (C=O), 1603 (Ph), 1154 (C-OH), 748 (Hoop).

(*S*)-2-Allyl-2-hydroxy-1-tetralone (5e)

Yield: 89%, $[\alpha]_D^{20}$ +4 (c=1, $CHCl_3$), ee 72%.

^{1}H NMR: δ (ppm) 8.02 (d, 1H, J = 7.6 Hz, Ph), 7.54 (t, 1H, J = 7.6 Hz, Ph), 7.35 (t, 1H, J = 7.6 Hz, Ph), 7.27 (d, 1H, J = 7.6 Hz, Ph), 5.88 (m, 1H, =CH), 5.17 (d, 1H, J = 10.3 Hz, $=CH_2$), 5.10 (d, 1H, J = 18.0 Hz, $=CH_2$), 3.82 (s, 1H, OH), 3.0 (m, 2H, CH_2), 2.4 (m, 3H, CH_2), 2.17 (dt, 1H, J = 6.2 Hz, J = 13.4 Hz, CH_2).

^{13}C NMR: δ (ppm) 200.4 (C=O), 143.0, 133.6, 131.9, 129.7, 128.6, 127.5, 126.4, 118.6 (Ph + C=C), 74.9 (COH), 39.9, 33.0, 25.7 (CH_2).

IR (neat): 3500 (OH), 1680 (C=O), 1640 (C=C), 1603 (Ph), 1155 (C-OH), 740 (Hoop).

(*S*)-2-hydroxy-2-(propyn-3-yl)-1-tetralone (5f)

Conversion: 82%, yield: 80%, $[\alpha]_D^{20}$ +20 (c=1, $CHCl_3$), ee 71%.

^{1}H NMR: δ (ppm) 8.05 (dd, 1H, J = 1.5 Hz, J = 7.5 Hz, Ph), 7.54 (dt, 1H, J = 1.5 Hz, J = 7.5 Hz, Ph), 7.35 (t, 1H, J = 7.5 Hz, Ph), 7.27 (d, 1H, J = 7.5 Hz, Ph),), 4.00 (s, 1H, OH), 3.08 (m, 2H, CH_2), 2.59 (m, 3H, CH_2), 2.23 (m, 1H, CH_2), 2.12 (t, 1H, J = 2.6 Hz, ≡CH).

^{13}C NMR: δ (ppm) 198.8 (C=O), 143.0, 134.0, 129.3, 128.7, 127.5, 126.6 (Ph), 78.2 (≡C), 73.9 (COH), 71.8 (≡C) 33.0, 26.8, 25.8 (CH_2).

IR (neat): 3500 (OH), 3300 (≡C-H), 2130 (C≡C), 1678 (C=O), 1602 (Ph), 1158 (C-OH), 736 (Hoop).

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