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Synthesis of an octahydro-1,1′-binaphthyl thioether ligand and comparison with unhydrogenated binaphthyl analogues

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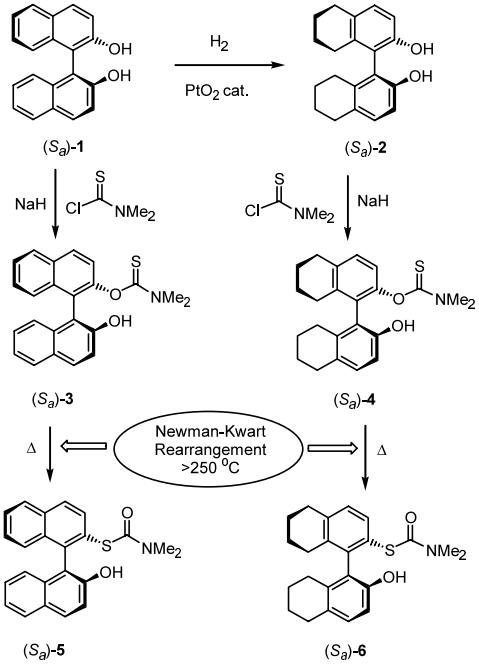
Abstract—Acylation of octahydro-BINOL with $Me_2NC(=S)Cl$, in the presence of NaH, allows the formation of 2-(OH)-2′-($Me_2NC(S)O$)-1,1′-$C_{10}H_{20}$. Subsequent Newman–Kwart rearrangement (275°C, 12 min) proceeds cleanly with a small amount of racemisation (96–97% ee). The equivalent BINOL-derived species undergoes an identical rearrangement (but with higher racemisation, 79–80%) and appreciable amounts of a thiophene by-product are formed. Semi-empirical calculations (PM3) predict a higher racemisation barrier for the octahydro compound and suggest that the Newman–Kwart rearrangement could proceed via a concerted pathway. The H_8-BINOL derived compound can be modified to 2-(OH)-2′-(SBu^n)-1,1′-$C_{10}H_{20}$ and the BINOL species to 2-(OH)-2′-(SBu^t)-1,1′-$C_{10}H_{12}$. The former promotes the 1,4-addition of $AlMe_3$ to non-3-en-2-one in 57% ee the latter in 63% ee.

1. Introduction

Despite the fact that 2,2′-dihydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl (H_8-BINOL, **2** shown in Scheme 1 as it S_a enantiomer) is easily prepared by direct hydrogenation of BINOL **1**[1] it, and its derivatives, have not yet attained the popularity of BINOL as ligands and additives in asymmetric catalysis. However, recent examples of catalysts bearing ligands derived from **2** show that its use often results in the formation of more soluble and selective catalysts. For example, higher enantioselectivities are attained with **2** ligand cores in catalytic aldehyde allylation,[2] hetero Diels–Alder reactions[3] and metathesis[4] reactions than with their 1,1′-binaphthylene parent ligands. Similarly, the octahydro version of Feringa's MonoPhos ligand shows superior performance in Rh-catalysed acetamidocinnamic ester hydrogenation.[5] Recently, Chan has shown that octahydrobinaphthyl-based ligands lead to the formation of rather selective catalysts for the 1,4-additions of $AlMe_3$[6] and $ZnEt_2$[7] to cyclohexenone. As we have demonstrated[8] that the thioether ligand (S_a)-$\mathbf{L_A}$ is of some utility in catalytic asymmetric conjugate addition



Scheme 1. Preparation of thiocarbamates from BINOL and H_8-BINOL and their rearrangement.

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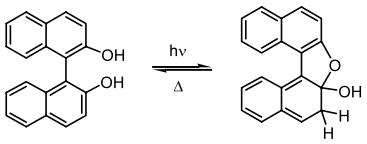
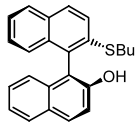


Scheme 2. Known isomerisation of BINOL.

of $AlMe_3$ (80–93% ee) to linear aliphatic enones, (*E*)-RCH=CHCOMe (R = alkyl) we became interested in this field. We sought to modify the 1,1′-binaphthyl backbone in $\mathbf{L_A}$ to its octahydro analogue to see if it had a positive or negative outcome on the stereoselectivity of the $AlMe_3$ conjugate addition and our initial results are described herein.

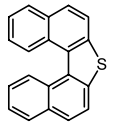


(S_a)-$\mathbf{L_A}$

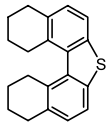
2. Newman–Kwart studies

One succinct route to the desired ligand would be thiocarbamylation of the known diol (S_a)-**2** with $Me_2NC(=S)Cl$ to yield (S_a)-**4** followed by its Newman–Kwart rearrangement[9] at high temperature. It is known that the presence of free OH groups often leads to low yields of rearranged products in Newman–Kwart chemistry. However, as protecting the hydroxy function significantly lengthens the overall synthetic procedure the reaction trials were conducted on the transformation of (S_a)-**4** to (S_a)-**6** anyway. For comparison the equivalent 1,1′-binaphthyl chemistry was investigated in parallel (Scheme 1).

Reaction of BINOL (S_a)-**1** with $Me_2NC(=S)Cl$ and 1 equiv. of NaH in DMF is known to form (S_a)-**3**[10] and an identical procedure cleanly afforded (S_a)-**4** from H_8-BINOL (S_a)-**2**. The ^1H NMR spectrum of (S_a)-**4** clearly indicates breaking of the C_2 symmetry in the original octahydrobinol. When (S_a)-**3** and (S_a)-**4** are subjected to thermolysis between 275 and 280°C both undergo rearrangement generating the key C–S bonds, however, the detailed behaviour of the two compounds is distinctly different. As we anticipated (S_a)-**3** underwent a rather unclean, sometimes partial, conversion in which the major product is the racemic **7**, which is a common by-product in related chemistry.[11] Surprisingly, when (S_a)-**4** is heated under identical conditions the rearranged product (S_a)-**6** is the only product and no trace of the expected thiophene by-product **8** is present.



7
major by-product



8
not formed

The mechanism for formation of the thiophene **7** is probably closely related to the observation of Zandomeneghi who noted that BINOL undergoes photochemical cyclisation via a keto-tautomer, to **A** (Scheme 2) which can thermally or photochemically relax back to BINOL with some racemisation.[12] A similar pathway seems to operate for the formation of **7** under the vigorous Newman–Kwart conditions, however, in this case the intermediate aromatises. The reason for the absence of **8** under the Newman–Kwart conditions is most likely the greater loss of resonance energy involved in tautomerisation of the phenol in **6** versus naphthol in **5**.

Because of the high temperatures involved in the Newman–Kwart rearrangement racemisation of both the starting materials and products through 1,1′-rotation is possible. The enantiomers of **3**–**6** are all separable by HPLC using a Diacel-AD column allowing the enantiopurity of these compounds to be determined as a function of heating time (Table 1). The optical rotational data of the derived **6** showed a similar trend but these data are less reliable due to the tendency of these compounds to strongly occlude variable amounts of solvent when isolated. While the quality of the HPLC data do not allow the extraction of accurate kinetic rate data they do indicate that octahydro-based **6** undergoes racemisation slower that its BINOL-derived analogue **5**.

3. Computational studies

In an effort to rationalise the above observations, we have investigated the use of semi-empirical calculations to estimate racemisation barriers for compounds **3**–**6** and activation energies for the corresponding Newman–Kwart rearrangements.

Table 1. Enantiopurities (% ee) as a function of Newman–Kwart reaction time[a]

Compound	0 min	10 min	12 min	15 min	20 min
(S_a)-**3**	100		>98		
(S_a)-**4**	100	98	–	98	
(S_a)-**5**	–		79–80[b]		
(S_a)-**6**	–	–	96–97[b]	93–96[b]	90

[a] Carried out under vacuum at 275–280°C, enantiopurities measured on a Diacel-AD column.
[b] Range for three runs.

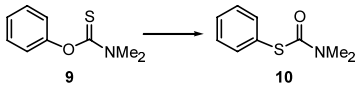
Previously it has been demonstrated that semi-empirical calculations (PM3, AM1) can give reasonable estimations of the barriers to racemisation for C_2-symmetric 1,1′-binaphthyls.[13] Unsymmetrical substitution, coupled with the degrees of freedom associated with the 2,2′-substituents, and (in the case of the octahydronaphthalene) the cyclohexenyl ring system, make it difficult to apply a study of this type to compounds **3**–**6**. Bearing this in mind, we initially investigated the simpler binaphthyl systems **3** and **5**. PM3 calculations performed on these compounds suggest that they should racemise preferentially via *syn*-transition states in which the two connected aryl rings experience similar out-of-plane deformation (Fig. 1a). The nature of the ring deformation and the apparent preference for a *syn*-transition state are in close agreement with previous findings involving 2,2′-dibromo-1,1′-binaphthyl.[13a] Extending this study to the corresponding octahydrobinaphthyl derivatives **4** and **6** suggested that similar *syn*-transition states for racemisation should also be preferred (Fig. 1b).

Activation energies (E_a) obtained (Table 2) are in broad agreement with experimental results (Table 1) and suggest that, in general, barriers to racemisation are higher for the octahydronaphthalene derivatives. These findings are consistent with the expectation that aryl ring distortion is predominantly responsible for the barrier to rotation and that the energy requirement for this would be higher for octahydronaphthalene.

We next considered possible transition states for the Newman–Kwart rearrangement. As far as we are aware no calculations have previously been reported for this reaction process, however experimental data would appear to support a concerted rearrangement.[14] In order to investigate this computationally we initially considered the rearrangement of dimethylthiocarbamate **9** (Scheme 3).

Optimised transition state structures for this rearrangement were calculated using PM3, B3LYP/6-31G(d) and MP2/6-31G(d). All three methods generated similar transition state geometries and activation energies (Fig. 2, Table 3). In addition, the activation energies predicted by B3LYP/6-31G(d) and MP2/6-31G(d) are in good agreement with experimental data,[14b] suggesting that this is indeed the likely reaction pathway.

In order to probe the likelihood of racemisation versus rearrangement for compounds **3** and **4** we next examined these rearrangements using PM3. For each substrate there are two possible diastereoisomeric transition states and calculated activation energies leading to these are shown in Figure 3.



Scheme 3.

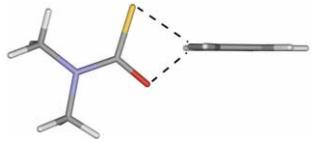
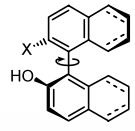


Figure 2. B3LYP/6-31G* transition state for rearrangement **9** to **10**.



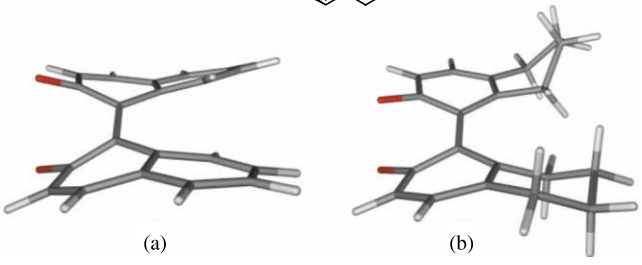


Figure 1. Lowest energy (*syn*-) transition state structures found for (a) binaphthyl and (b) octahydrobinaphthyl systems (2,2′-substituents omitted for clarity).

Table 2. Calculated (PM3) barriers to rotation (kcal mol^{-1})[a]

Compound	E_a	Compound	E_a
3	38.0	**4**	39.8
5	39.5	**6**	46.1

[a] Based on the lowest energy *syn*-transition state located.

Table 3. Calculated activation energies (kcal mol^{-1}) and transition state Ar–X bond lengths (Å) for the concerted rearrangement of **9** to **10**

	PM3	B3LYP/6-31G*	MP2/6-31G*
E_a	35.3	38.7	38.3
C–O	1.71	1.86	1.80
C–S	2.13	2.26	2.21

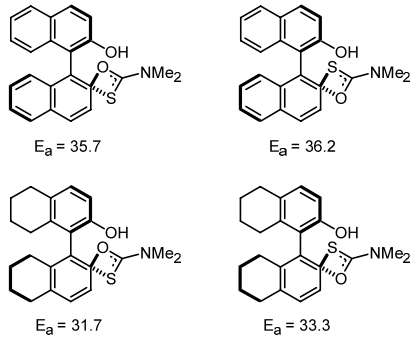
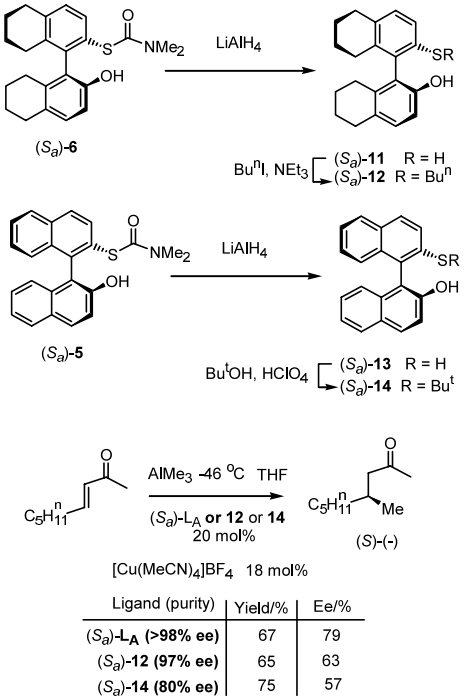


Figure 3. PM3 calculated activation energies (kcal mol^{-1}) for rearrangements **3** to **5** and **4** to **6**.

As can be seen, PM3 calculations predict that the activation energy for Newman–Kwart rearrangement should be lower in the case of the octahydronaphthalene substrate **5**. The same level of theory predicts that the barrier to racemisation should be higher for the octahydronaphthalene derivatives (Table 2). Taken together these results would appear to be consistent with the experimental results (Table 1) which show that the substrates rearrange faster than they racemise, and that the rearranged octahydronahthalene product **6** is significantly less prone to racemisation.

4. Ligand preparation and testing

The desired ligand could be accessed by $LiAlH_4$ cleavage of the thiocarbamate (S_a)-**6** (95% ee) to yield the air sensitive H_8-monothiobinaphthol (S_a)-**11** (Scheme 4). Because of the reactive nature of the thiol it was immediately alkylated to the (S_a)-**12** octahydro analogue of $\mathbf{L_A}$. Because of the availability of compound (S_a)-**5** we decided to deprotect this with $LiAlH_4$ fashioning the known MTB ligand (S_a)-**13**[8,10] that could be transformed into the *t*-butyl analogue of $\mathbf{L_A}$ using $Bu^tOH/HClO_4$ in AcOH. In this way the effect of increasing the steric demand in both the thioether and binaphthyl backbone of ligand $\mathbf{L_A}$ could be tested. The ligand promoted the 1,4-addition of $AlMe_3$ to (*E*)-non-3-en-2-one under appropriate conditions (Scheme 4). We have noted that the performance of this reaction is intimately dependent on the quality of the $AlMe_3$.[10] In the control reaction, with $\mathbf{L_A}$ and this particular $AlMe_3$, the stereoselectivity was slightly below our normal range. However, even allowing for this and the variation in ligand enantiopurity between (S_a)-$\mathbf{L_A}$ (>98% ee), (S_a)-**12** (97% ee), and (S_a)-**14** (80% ee) it appears that the parent ligand is still the best.



Ligand (purity)	Yield/%	Ee/%
(S_a)-$\mathbf{L_A}$ (>98% ee)	67	79
(S_a)-**12** (97% ee)	65	63
(S_a)-**14** (80% ee)	75	57

Scheme 4. Ligand preparation and testing in asymmetric catalytic conjugate addition of $AlMe_3$ to nonenone.

5. Conclusion

The desired octahydrobinaphthyl thioether ligand (S_a)-**12** could be prepared in four steps from (S_a)-H_8-BINOL. Unusually, the Newman–Kwart rearrangement of the key intermediate (S_a)-**4** proceeds cleanly, even though a protic OH group is present. The performance of this ligand in copper-catalysed catalytic conjugate additions of $AlMe_3$ when compared to the parent ligand $\mathbf{L_A}$ was inferior. This coupled to the lack of a crystalline intermediate to allow the enantiopurity of (S_a)-**12** to be assured mitigates against its use. The closely related *t*-butyl compound (S_a)-**14** also performed poorly (even allowing for its reduced optical purity). However, syntheses of these compounds provides some interesting insights into the nature of the transition states responsible for racemisation and Newman–Kwart rearrangement in 1,1′-binaphthyl ligands and their octahydro analogues.

6. Experimental

Nuclear magnetic resonance spectra were recorded in $CDCl_3$ on Varian VXR-300 (300 MHz) and Bruker AV-400 (400 MHz) spectrometers ^1H, chemical shifts are reported in ppm downfield from internal Me_4Si, J values are given in Hz. Carbon-13 NMR spectra were recorded on the AV-400 machine (100 MHz). Melting points were obtained with a Leitz Laborlux S melting point apparatus and are not corrected. Procedures involving moisture sensitive intermediates were carried out under nitrogen using standard Schlenk techniques. Tetrahydrofuran (THF) was distilled from sodium benzophenone immediately prior to use. Solvents were dried and distilled under nitrogen before use. Optical rotations were measured on a Perkin–Elmer model 241 polarimeter, *c* is in g per 100 cm^3 of solvent. Column chromatography and TLC analysis were performed on silica gel. TLC analyses were carried out in 4:1 light petroleum:ethyl acetate mixtures for H_8-BINOL derived compounds and dichloromethane (for BINOL derived species, with the exception of **12** for which the former solvent mix was used). Commercial reagents (Aldrich) were used as received. HPLC analyses were carried out on a Chiralcel AD using a flow rate of 0.3 ml min^{-1} and a 97.5:2.5 hexane:isopropanol mixture. Both hands of all ligands were prepared to facilitate the extraction of accurate HPLC data. Only the (S_a) enantiomer data are reported here. The spectroscopic properties for compounds **3**[10] and **11**[8,10] have already been reported.

6.1. (−)-(S_a)-2-(*N*,*N*-Dimethylthiocarbamoyloxy)-2′-hydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl (S_a)-4

Solid NaH (0.147 g, 6.15 mmol, 60% oil dispersion) was combined with the (S_a)-octahydroBINOL (S_a)-**1** (1.80

g, 6.15 mmol) in dry DMF (30 ml) under nitrogen and stirred for (1 h). Solid *N*,*N*-dimethylthiocarbamoyl chloride (0.760 g, 6.15 mmol) was added to the yellow solution which was stirred (85°C, 1 h). The reaction was allowed to cool whilst being stirred for a further 5 h, during which time the solution turned green. Aqueous potassium hydroxide solution (100 ml, 1% w/w), was added to the green solution. The resulting creamy precipitate was extracted with dichloromethane, washed with water (3×200 ml), and then dried (Na_2SO_4). The solution was evaporated to yield the crude product (2.34 g). Column chromatography using a petroleum ether and ethyl acetate solvent gave the pure product as a colourless solid, mp 94–96°C (4:1, R_f 0.29, 1.04 g, 45%). $[\alpha]_D^{20} = -208$ (*c* 0.53, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): 1.56–1.85 (8H, m, ring-CH_2), 2.00–2.15 (2H, m, ring-CH_2), 2.33–2.47 (2H, m, ring-CH_2), 2.68–2.77 (2H, m, ring-CH_2), 2.77–2.88 (2H, m, ring-CH_2), 2.94 (3H, s, NMe), 3.25 (3H, s, NMe), 5.40 (1H, s, OH), 6.79 (1H, d, $J=8.0$ Hz, Ar), 6.93 (1H, d, $J=8.0$ Hz, Ar), 6.98 (d, $J=8.0$ Hz, 1H), 7.19 (d, $J=8.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 22.7 (NMe), 22.9 (NMe), 23.2, 23.3, 26.9, 27.6, 29.4, 29.8, 38.1, 43.1, 114.9 (Ar*C*H), 120.7 (Ar*C*H), 123.3 (q), 128.8 (Ar*C*H), 129.4 (Ar*C*H), 129.8 (2C, q), 135.7 (q), 136.0 (q), 138.3 (q), 150.4 (q), 151.0 (q), 188.2 (*C*=S); IR: ν_{max} ($CHCl_3$ solution)/cm^{-1} 3381br (OH), 2928s, 1591m, 1540s, 1470w, 1396s, 1291s, 1224s, 1170w, 810m, 758w; *m*/*z* (EI): 381 (M^+, 76%), 292 (33), 251 (3), 207 (3), 151 (7), 89 (9), 88 (100). [Found (HRMS, EI): M^+, 381.1749 $C_{23}H_{27}NO_2S$ requires M 381.1762].

6.2. (−)-(S_a)-2-(*N*,*N*-Dimethylcarbamoylthio)-2′-hydroxy-1,1′-binaphthyl (S_a)-5

Samples of the thiocarbamoyloxy compound (S_a)-**3** (0.50 g, 1.35 mmol) were pre-heated to a liquid (mp <100°C, gentle use of a commercial heatgun, ca. 3 min) before being thermalised in a furnace at 275°C with rotation for 12 min under reduced pressure (0.8 mm Hg) during which time the reaction mixture became very dark. The samples were removed from the oven and the conversion checked by TLC which indicated partial conversion [4:1 light petroleum:ethyl acetate; (S_a)-**3** R_f 0.57, (S_a)-**5** R_f 0.19] together with other uncharacterised by-products. Some runs were conducted at 280°C, or for longer times or heated for a second time to check racemisation (see Table 1). The product was isolated by column chromatography on silica gel; yields for three separate runs: 24, 34, 55%. mp 82–84°C. $[\alpha]_D^{20} = -277$ (*c* 0.52, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): 2.91 (3H, s, NMe), 2.96 (3H, s, NMe), 5.28 (1H, s, OH), 6.87 (1H, d, $J=8.4$ Hz, plus unresolved long range couplings, Ar), 7.11–7.36 (5H, m, Ar), 7.48–7.55 (1H, m, Ar), 7.75 (1H, d, $J=8.4$ Hz, Ar), 7.86 (1H, d, $J=8.7$ Hz, Ar), 7.89 (1H, d, $J=9.0$ Hz, Ar), 7.94 (1H, d, $J=8.4$ Hz, Ar), 8.01 (1H, d, $J=8.7$, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): 37.2 (NMe), 37.4 (NMe), 119.2 (q), 119.6 (Ar*C*H), 123.4 (Ar*C*H), 124.6 (Ar*C*H), 126.6 (q), 127.0 (q), 127.2 (Ar*C*H), 127.5 (Ar*C*H), 128.1 (Ar*C*H), 128.2 (Ar*C*H), 128.8 (Ar*C*H), 128.9 (Ar*C*H), 129.7 (Ar*C*H), 129.8 (Ar*C*H), 133.4 (q), 133.8 (q), 134.1 (Ar*C*H), 134.4 (q), 140.4 (q), 152.6 (q), 169.2 (*C*=O); IR: ν_{max} ($CHCl_3$ solution)/cm^{-1} 3683s, 3020bs (OH), 2399s, 2244w, 1973w, 1884w, 1521s, 1476s, 1423s, 1334m, 1228s, 1016s, 929s, 849m, 627s; *m*/*z* (EI): 373 (M^+, 52%), 284 (20), 239 (7), 141 (4), 113 (5), 72 (100). [Found (HRMS, EI): M^+, 373.1141 $C_{23}H_{19}NO_2S$ requires M 373.1136.].

6.3. (−)-(S_a)-2-(*N*,*N*-Dimethylcarbamoylthio)-2′-hydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl (S_a)-6

Samples of the thiocarbamoyloxy compound (S_a)-**4** (0.50 g, 1.30 mmol) were gently pre-heated to a liquid using a commercial heatgun (ca. 3 min) and then heated in an oven (275°C) and recovered as above. Column chromatography using dichloromethane (R_f 0.18, yielded (S_a)-**6** as a colourless solid (typically 0.26 g, 51%). Mp 82–84°C. $[\alpha]_D^{29} = -155$ (*c* 0.93, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): 1.57–1.79 (8H, m, ring-CH_2), 1.86–1.96 (1H, m, ring-CH_2), 1.98–2.16 (2H, m, ring-CH_2), 2.28–2.38 (1H, m, ring-CH_2), 2.75 (2H, m, ring-CH_2), 2.84 (2H, m, ring-CH_2), 2.93 (6H, s, br, NMe_2), 6.22 (1H, s, br, OH), 6.80 (2H, d, $J=8.4$ Hz, Ar), 6.99 (2H, d, $J=8.4$ Hz, Ar), 7.15 (2H, d, $J=8.0$ Hz, Ar), 7.38 (2H, d, $J=8.0$ Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): 22.8 (2×N*Me*), 23.4, 23.5, 23.7, 27.8, 28.2, 29.8, 30.1, 30.6, 115.6 (Ar*C*H), 126.3 (q), 128.1 (q), 129.6 (q), 129.7 (Ar*C*H), 130.3 (Ar*C*H), 134.7 (Ar*C*H), 135.4 (q), 138.5 (q), 141.0 (q), 143.2 (q), 151.7 (q), 170.4 (*C*=O); IR: ν_{max} ($CHCl_3$ solution)/cm^{-1} 3542br (OH), 2928s, 2856m, 2344w, 1592s, 1475s, 1455m, 1328w, 1293w, 1278m, 1241s, 1213w, 1189s, 1155s, 938s, 860m, 808s, 770w; *m*/*z* (EI): 381 (M^+, 60%), 309 (14), 292 (15), 149 (9), 72 (100). [Found (HRMS, EI): M^+, 381.1755 $C_{23}H_{27}NO_2S$ requires M 381.1762].

6.4. (−)-(S_a)-2-Hydroxy-2′-mercapto-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl (S_a)-11

The rearranged product (S_a)-**6** (0.83 g, 2.17 mmol) was dissolved in dry THF (25 ml) under nitrogen and to this solution $LiAlH_4$ (0.17 g, 4.5 mmol) was added slowly at room temperature forming an effervescent mixture. The mixture was stirred at ambient temperature (16 h) such that there was complete hydrolysis of the thiocarbamate (S_a)-**6** (TLC). The reaction solution was quenched by dropwise addition of hydrochloric acid solution (10% w/w, aq.) and the crude product extracted, under nitrogen, with diethyl ether in combination with a small amount of dichloromethane, before being dried (Na_2SO_4) and evaporated to produce a white crystalline solid (R_f 0.65, 0.62 g, 92%). TLC analysis indicated that only a single product but due to it's air sensitivity it was used as obtained. Mp (dec. above 50°C); $[\alpha]_D^{20} = -73$ (*c* 0.56, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): 1.62–1.80 (8H, m, ring-CH_2), 2.04–2.38 (4H, m, ring-CH_2), 2.68–2.84 (4H, m, ring-CH_2), 3.16 (1H, s, SH), 4.35 (1H, s, br, OH), 6.82 (1H, d, $J=8.0$, Ar), 7.02 (1H, d, $J=8.0$, Ar), 7.05 (1H, d, $J=8.0$, Ar), 7.19 (1H, d, $J=8.0$, Ar); *m*/*z* (EI): 310 (M^+, 100). [Found (HRMS, EI): M^+, 310.1385 $C_{20}H_{22}OS$ requires M 310.1391].

6.5. (−)-(S_a)-2-*S*-*n*-Butyl-2′-hydroxymercapto-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl (S_a)-12

Freshly prepared (S_a)-**11** (0.58 g, 1.9 mmol) was combined with Bu^nI (0.35 ml, 0.035 mmol) and Et_3N (0.60 ml, 7 mmol) in dry methanol (40 ml) and stirred at room temperature under nitrogen. After 70 h, TLC analysis indicated good conversion to the target compound. The reaction solution was acidified by dropwise addition of hydrochloric acid solution (10% w/w) and extracted with dichloromethane, before being dried (Na_2SO_4) and evaporated to produce the crude product (0.99 g). Product purification was by column chromatography utilizing petroleum ether (bp 40–60°C) and ethyl acetate solvent (4:1, R_f 0.70, 0.49 g, 70%) to yield a pale oil. $[\alpha]_D^{20}=-30$ (*c* 0.57, $CHCl_3$); ^{1}H NMR ($CDCl_3$, δ): 0.88 (3H, t, $J=7.2$, Me), 1.34–1.43 (2H, m, CH_2Me), 1.53–1.59 (2H, m, CH_2CH_2Me), 1.63–1.79 (8H, m, ring-CH_2), 2.03–2.34 (4H, m, ring-CH_2), 2.69–2.82 (6H, m, ring-CH_2 and SCH_2), 4.34 (1H, s, br, OH), 6.79 (1H, d, $J=8.4$ Hz, Ar), 7.04 (1H, d, $J=8.4$ Hz, Ar), 7.11 (2H, apparent s, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.6 (CH_2Me), 22.0 (CH_2Me), 23.1 (CH_2CH_2Me), 23.1, 26.9, 27.1, 29.2, 29.6, 30.3, 30.8, 31.5, 65.8 (SCH_2), 112.5 (Ar*C*H), 123.2 (Ar*C*H), 124.3 (q), 125.4 (q), 129.1 (q), 129.8 (2×Ar*C*H), 132.8 (q), 134.7 (q), 135.7 (q), 137.3 (q), 149.8 (q); IR: ν_{max} ($CHCl_3$ solution)/cm^{-1} 3043br (OH), 2938s, 2868m, 1777w, 1442m, 1384m, 1350m, 1321w, 1261s, 1200s, 1182s, 1157m, 1118s, 1077s, 1052m, 1022s, 978m, 906s, 869s, 816s, 756w; *m*/*z* (EI): 366 (M^+, 100%). [Found (HRMS, EI): M^+, 366.2003 $C_{24}H_{30}OS$ requires M 366.2017].

6.6. (−)-(S_a)-2-*S*-*t*-Butyl-2′-hydroxymercapto-1,1′-binaphthyl (S_a)-14

A. Monothiobinaphthol (S_a)-**13**. The Newman–Kwart rearranged product (S_a)-**5** (1.14 g, 3.07 mmol) was dissolved in dry THF (25 ml) under nitrogen and to this solution $LiAlH_4$ (0.30 g, 8.0 mmol) was added slowly at room temperature forming an effervescent mixture. The mixture was stirred at room temperature (16 h) for complete hydrolysis (assured by TLC: R_f 0.65). The reaction was acidified by HCl solution (10% w/w aq.) and extracted with dichloromethane, before being dried (Na_2SO_4) and rotoevaporated to produce a white crystalline solid (0.80 g, 87%); ^{1}H NMR ($CDCl_3$, 300 MHz): 3.39 (1H, s, SH), 4.86 (1H, s, br, OH), 7.01 (1H, d, $J=8.4$ Hz plus unresolved long range couplings, Ar), 7.13 (1H, d, $J=8.4$ Hz plus unresolved long range couplings, Ar), 7.24–7.47 (5H, m, Ar), 7.59 (1H, d, $J=8.4$ Hz, Ar), 7.89 (1H, d, $J=8.1$ Hz, Ar), 7.90 (1H, d, $J=8.7$ Hz, Ar). The air sensitive monothiobinaphthol (S_a)-**11** had literature properties[8,10] and was used immediately as attained.

B. Monothiobinaphthol alkylation. Concentrated $HClO_4$ (0.4 ml) was added to an ice cold solution of acetic acid (3 ml), acetic anhydride (1.5 ml), containing MTB (S_a)-**11** (0.27 g, 0.89 mmol) and the mixture allowed to stir (20 min) under an inert atmosphere. A solution of *t*-butanol (0.33 g, 4.5 mmol) in acetic acid (5 ml) was added. Conversion of (S_a)-**11** was complete after 24 h (TLC). The reaction solution was neutralised by dropwise addition of sodium hydroxide solution (10% w/w aq.) and extracted with dichloromethane, dried (Na_2SO_4) and rotoevaporated to yield the crude product, 0.20 g. Proton NMR analysis of this indicated the desired *t*-butylated product and the *t*-butyl thioether of MTB where the 2′-OH group had been acylated. The crude product was dissolved in dry THF (20 ml) under nitrogen and $LiAlH_4$ (0.13 g, 3.1 m mol) was added slowly forming an effervescent mixture. The mixture was stirred at room temperature (3 h) and the reaction solution was acidified by dropwise addition of HCl (10% w/w, aq.). Extraction with dichloromethane, and subsequent column chromatography using a petroleum ether and ethyl acetate solvent (4:1, R_f 0.58), yielded (S_a)-**14** (0.09 g, 18%). Mp 57–60°C; $[\alpha]_D^{20}=-32$ (*c* 0.47, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): 1.22 (9H, s, *t*-Bu), 4.69 (1H, s, br, OH), 6.94 (1H, d, $J=8.4$ Hz, Ar), 7.17–7.36 (5H, m, Ar), 7.50 (1H, d, $J=8.7$, Ar), 7.83–7.99 (5H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): 32.0 (3×Me), 47.7 (*C*Me), 117.5 (Ar*C*H), 118.5 (q), 123.3 (Ar*C*H), 125.2 (Ar*C*H), 126.4 (Ar*C*H), 126.7 (Ar*C*H), 126.8 (Ar*C*H), 127.3 (Ar*C*H), 128.1 (q), 128.2 (Ar*C*H), 128.7 (Ar*C*H), 128.9 (Ar*C*H), 130.0 (Ar*C*H), 133.3 (q), 133.5 (q), 134.0 (q), 134.0 (q), 135.1 (Ar*C*H), 135.9 (q), 150.6 (q); IR: ν_{max} ($CHCl_3$ solution)/cm^{-1} 3381br (OH), 3001m, 2925s, 2852m, 1674s, 1593m, 1492s, 1452m, 1372s, 1352m, 1304m, 1261w, 1181m, 1064m, 984s, 890m, 815m, 786w, 756s, 733m, 718m, 692s, 648m; *m*/*z* (EI): 358 (M^+, 64%), 302 (100). [Found (HRMS, EI): M^+, 358.1397 $C_{24}H_{22}OS$ requires M 358.1391].

6.7. Catalytic studies

To a stirred 0.028 M solution of (S_a)-$\mathbf{L_A}$ (35 mg, 0.098 mmol) or and $[Cu(MeCN)_4]BF_4$ (28 mg, 0.089 mmol) in absolute THF at −45°C was simultaneously added 250 mg (1.783 mmol) (*E*)-3-nonen-2-one in THF (0.72 M) and a 1.40 M solution of $AlMe_3$ in THF (0.72 M) with a syringe pump over a period of 20 min. After stirring for 16 h at −45°C, the reaction solution was diluted with Et_2O and quenched with aqueous 1 M HCl. Yields and ee values were determined by GC (ee 85%, oktakis-(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin[15]) against an internal undecane standard as described before.[8]

6.8. Computational methodology

Spartan'02 version 1.0.2 (Wavefunction, Inc., Irvine, CA, USA) was employed for all calculations reported here. Second derivative (frequency) calculations were performed for all PM3 and B3LYP/6-31G* calculations to confirm the nature of stationary points and to quantify zero point energies. Frequency calculations at MP2/6-31G* level were not performed due to prohibitive computational overheads and so B3LYP/6-31G* zero point energies were used for structures generated by this method. Activation energies (E_a) quoted are based on the energy difference between fully-optimised equilibrium geometries and fully-optimised transition state geometries at the appropriate

level of theory. Unscaled ZPE corrections have been used in all cases.

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