MS, m/e 148, 91, 78, 71. 2,4-DNP derivative: mp 121–2 °C (methanol). Anal. Calcd for $C_{16}H_{16}N_4O_4$: C, 58.53; H, 4.91; N, 17.07. Found: C, 58.71; H, 4.96; N, 16.75.

17β-Acetoxy-5β-(4-methylphenyl)estran-3-one: mp 186–187 °C (methanol); $[\alpha]^{21}_D$ −21.8° (c 1.0, $CHCl_3$); IR (KBr) 1730, 1700, 810 cm^{-1}; NMR 7.4–7.0 (m, 4 H), 4.65 (t, 1 H), 2.8 (q AB system, 2 H), 2.3 (s, 3 H), 2.3–1.1 (m, 20 H), 2.05 (s, 3 H), 0.85 (s, 3 H) ppm; MS, m/e 409 $(M + 1)^+$, 408 (M^+), 351, 350, 290. Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.31; H, 8.73.

1-[2-(2-Methylphenyl)cyclohexyl]ethan-1-one: oil; IR (neat) 3020, 1700, 1600, 1440, 1340, 1160, 780, 700 cm^{-1}; NMR 7.4–6.9 (m, 4 H), 3.2–2.4 (m, 3 H), 2.3 (s, 3 H), 2.2–1.1 (m, 7 H), 1.7 (s, 3 H) ppm; MS, m/e 216 (M^+), 173, 131, 111, 105, 91. 2,4-DNP derivative: mp 122–3 (ethanol). Anal. Calcd for $C_{21}H_{24}N_4O_4$: C, 63.62; H, 6.10; N, 14.13. Found: C, 63.74; H, 5.94; N, 14.13.

Preparation and Reaction of the Mixed Reagent, (4-Tolyl)cyclohexylzinc. In 20 mL of dry toluene and 2 mL of dry THF 652 mg (4 mmol) of cyclohexyl bromide, 910 mg (4 mmol) of zinc bromide, and 150 mg (21 mmol) of lithium wire were sonicated as described above. After consumption of the organic halide (TLC check), 684 mg (4 mmol) of 4-bromotoluene in 1 mL of THF was added and sonication was effected for another 30-min period.

Following the standard procedure, 288 mg (3 mmol) of cyclohexenone and 15 mg of $Ni(acac)_2$ in 1 mL of THF were added to the reagent at room temprature and the reaction was allowed to proceed for 10 min. After quenching and workup as usual and purification on a silica gel column, 3-(4-methylphenyl)cyclohexanone **14** was obtained in 64% yield.

3-(4-Methylphenyl)cyclohexanone: oil; IR (neat) 1705, 1500, 1220, 810, 800 cm^{-1}; NMR 7.1 (s, 4 H), 3.2–1.5 (m, 9 H), 2.3 (s, 3 H) MS, m/e 189 $(M + 1)^+$, 188 (M^+), 145, 131, 118, 91. Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.65; H, 8.67.

Conjugate Addition–Alkylation of 2-Hexenal. Bis(2-methylphenyl)zinc (5 mmol) in 23 mL of dry THF were prepared as described above and transferred under argon into a round-bottom flask with magnetic stirrer. $Ni(acac)_2$ (20 mg) in 1 mL of THF was added and the mixture was cooled to −40 °C. 2-Hexenal (0.442 g, 4.5 mmol) was added in 2 mL of THF and stirring was continued for 30 min; 2 mL of dry HMPA were then introduced followed 3 min later by 2.8 mL of methyl iodide (ca. 10 equiv). After 55 min of stirring, the mixture was quenched with saturated aqueous NH_4Cl at 0 °C, then extracted with diethyl ether. The organic phase was washed with aqueous sodium thiosulfate, then worked up as usual to give an oil which was purified by column chromatography. Compound **17** (oil, 0.449 g, 49% yield) was obtained as a 3:1 mixture of diastereomers which could not be resolved by silica-gel or vapor-phase chromatography: IR (neat) 3050, 3010, 2850, 2700, 1720, 1485, 1460, 1380, 920, 895, 760, 730 cm^{-1}; NMR 9.7 (d, 1 H, major isomer), 9.5 (d, 1 H, minor isomer), 7.3 (s, 4 H), 3.2 (m, 1 H), 2.6 (m, 1 H), 2.3 (s, 3 H), 1.8–1.4 (m, 3 H), 1.3–0.7 (m, 4 H), 1.16 (d, 3 H of minor isomer), 0.87 (d, 3 H of major isomer) ppm; MS, m/e 204 (M^+), 147, 105, 91. 2,4-DNP derivative: mp 169–170 (methanol). Anal. Calcd for $C_{20}H_{24}N_4O_4$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.63; H, 6.28; N, 14.49.

Enolate Trapping Experiments. Diphenylzinc (4 mmol) was prepared in THF as described in the general procedure. Cyclohexenone **7** (3 mmol) and $Ni(acac)_2$ catalyst were added in 1 mL of THF to the reagent, and the mixture was stirred for 2 h at room temperature. After the mixture was cooled to 0 °C (ice bath), 30 mmol (10 equiv) of methyl iodide were added over a 5-min period. The mixture was allowed to warm up and stirred at room temperature for 12 h. After the usual quenching and workup the crude mixture was purified by column chromatography to give 2-methyl-3-phenylcyclohexanone (**15**) in 71% yield: oil; IR (neat) 3050, 3020, 1700, 1600, 1450, 1220, 1020, 920, 780, 750, 700 cm^{-1}; NMR 7.2 (m, 5 H), 2.8–2.3 (m, 4 H), 2.2–1.5 (m, 4 H), 0.8 (d, 3 H) ppm; MS, m/e 188 (M^+), 117, 97, 91. Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.81; H, 8.66. 2,4-DNP derivative: mp 220–221 °C (ethanol) lit.[32] 220–221 °C. Following the same procedure, compound **16** was obtained in 51% yield.

3-Methyl-3-(phenylmethyl)bicyclo[2.2.1]heptan-2-one (16): mp 54 °C (hexane–trace of ethyl acetate); IR (film) 3050, 3010, 1735, 1600, 1480, 1460, 1440, 1360, 1050, 740, 700 cm^{-1}; NMR 7.2 (s, 5 H), 2.7 (s, 2 H), 2.6 (m, 1 H), 2.3–1.3 (m, 7 H), 0.8 (s, 3 H) ppm; MS, m/e (215 $(M + 1)^+$, 214 (M^+), 186, 146, 145, 117, 95, 91. Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.11; H, 8.61.

Acknowledgment. Financial support from the CNRS (LA 332, ATP Chimie Fine) is acknowledged. We wish to thank Prof. A. E. Greene and A. Rassat for their constant interest in this work and Prof. E. Negishi and B. Waegell for stimulating discussions.

3,3′-Disubstituted 2,2′-Biphenols: Synthesis of Nonplanar, Tetradentate Chelating Ligands

Thomas N. Sorrell* and Debora J. Ellis

Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514

Received March 14, 1985

The Claisen rearrangement of 2,2′-bis(allyloxy)biphenyl provides an appropriate starting material for the preparation of free and benzyl-protected 3,3′-bis(2-hydroxyethyl)- and 3,3′-bis(3-hydroxy-1-propyl)-2,2′-biphenol. The alcohols are converted via their mesylates to several new metal chelating agents, 3,3′-bis(2-X-ethyl)- and 3,3′-bis(3-Y-propyl)-2,2′-biphenol (X = methylthio or 1-pyrazolyl and Y = methylthio or dimethylamino).

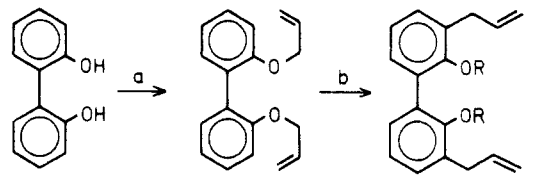
Our interest in preparing models for the active site of the molybdenum oxidases[1] led us to consider the synthesis of new ligands that would bind to a metal ion, leaving two vacant cis-coordination sites. For Mo(VI) complexes, a flexible ligand would have been sufficient since most Mo(VI) systems have two cis Mo=O groups in their coordination spheres that dictate the overall geometry.[2] However, we desired a rigid ligand framework because catalytically active Mo complexes cycle through the +4, +5, and +6 valences and we wanted to be able to minimize reorganization of the coordination environment during catalysis. At the same time, we recognized that the creation of vacant cis sites by ligand design should have wide

(1) Spence, J. T. *Coord. Chem. Rev.* **1983**, *48*, 59.

(2) (a) Tatsumi, K.; Hoffmann, R. *Inorg. Chem.* **1980**, *19*, 2656. (b) Stiefel, E. I. *Prog. Inorg. Chem.* **1973**, *22*, 1.

0022-3263/85/1950-5765$01.50/0

Scheme I[a]

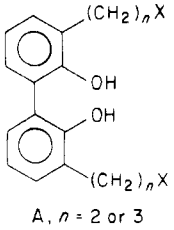


1 2 R = Ac 3 R = H 4 R = CH_2Ph

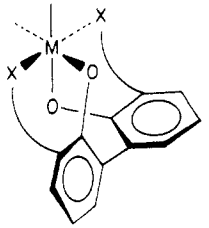
[a] a, NaH, CH_2=$CHCH_2Cl$; b, $PhNEt_2$, Ac_2O, Δ; OH^-; NaH, DMF, $PhCH_2Cl$.

applicability in catalysis using other metal complexes.[3]

We report here our work on one such system, A, that molecular models showed might coordinate to a metal ion as illustrated by B.



A, n = 2 or 3



B

Results and Discussion

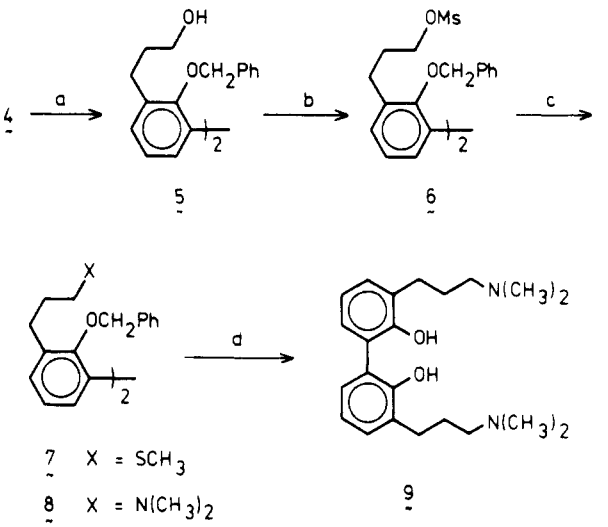
While models demonstrated that the biphenol system could bind to metal ions in the desired manner, they did not enable us a priori to choose between those compouds having two-carbon instead of three-carbon side chains. Therefore we adopted a strategy employing a common precursor to allow us to prepare representative derivatives of each group.

The synthetic plan for preparing the compounds appeared straightforward. A Claisen rearrangement of the known diallyl ether 1[4] provides a ready entry into the necessary biphenyl derivatives (Scheme I)[5] which we could easily functionalize. We initially attempted to conduct the transformation from 1 to 3 directly but found purification to be more facile if the acetate 2 was isolated first. Hydrolysis of 2 to 3 followed by benzylation gave the protected precursor 4.

Ligands with Three-Carbon Side Chains. Hydroboration of diene 4 occurred to give the hydroxypropyl compound 5, which was smoothly converted to its mesylate derivative (Scheme II). Nucleophilic displacement of the leaving group with methylmercaptide ion or dimethylamine gave the protected form of two of the ligands. The dimethylamino compound 8 could be deprotected by hydrogenolysis although the product 9 is apparently unstable, discoloring rapidly in air. The sulfide 7, on the other hand, could not be readily debenzylated; so we examined another route to its unprotected analog (Scheme III).

The benzyl group in 5 was removed by hydrogenolysis, and the resulting diol 10 was treated under standard

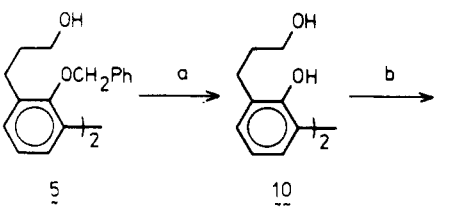
Scheme II[a]

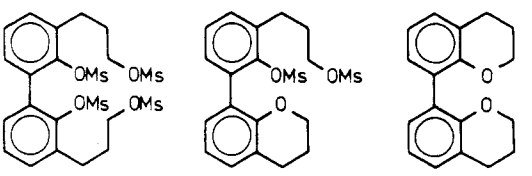


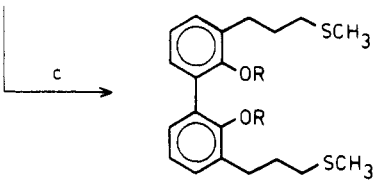
7 X = SCH_3 8 X = $N(CH_3)_2$ 9

[a] a, BH_3·SMe_2, NaOH, H_2O_2; b, MsCl, NEt_3, CH_2Cl_2; c, CH_3S^- or $(CH_3)_2NH$; d, H_2, Pd/C.

Scheme III[a]







14 R = Ms 15 R = H

[a] a, H_2, Pd/C; b, MsCl, NEt_3, CH_2Cl_2; c, $CH_3S^-Na^+$; 20% NaOH.

conditions with methanesulfonyl chloride and triethylamine.[6] The desired tetrakis(mesylate) 11 was obtained in 32% yield after chromatography to separate it from the benzotetrahydropyran derivatives 12 and 13. Although we did not optimize the yield of this reaction, an inverse addition of 10 to MsCl and Et_3N would probably give a higher yield of 11 as we demonstrated later for compound 18 (see Experimental Section). The tetrakis(mesylate) 11 was subsequently converted to the methyl sulfide derivative 14 by nucleophilic displacement, and the two re-

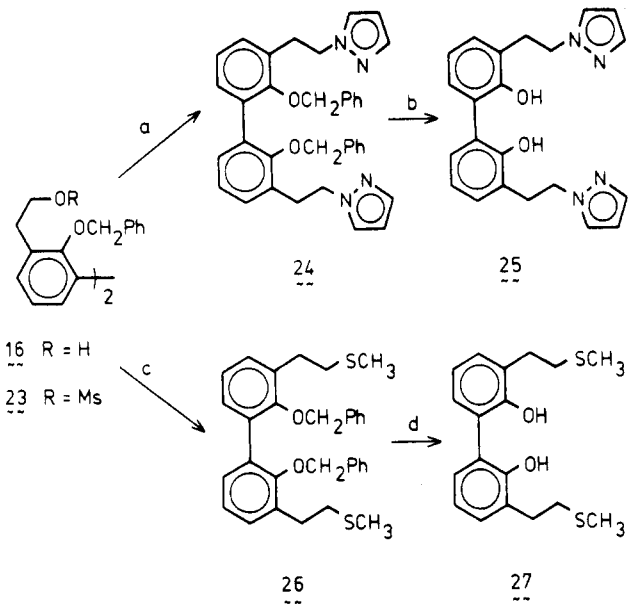
(3) Collman, J. P.; Hegedus, L. S. "Principles and Applications of Organotransition Metal Chemistry"; University Science Books, Mill Valley, CA, 1980.

(4) Pearson, D. P. J.; Leigh, S. J.; Sutherland, I. O. *J. Chem. Soc.; Perkin* Trans. *1* **1979**, *12*, 3113.

(5) Abbreviations used in this paper: DMF, *N,N*-dimethylformamide; Ms, methanesulfonyl; THF, tetrahydrofuran.

(6) Fieser, M.; Fieser, L. F. "Reagents for Organic Synthesis"; Wiley: New York, 1974; Vol. 4, p 326.

Scheme IV[a]



[a] a, $Na^+C_3H_3N_2^-$, DMF; b, H_2, Pd/C; c, $CH_3S^-Na^+$; d, $BF_3 \cdot OEt_2$, C_2H_5SH.

maining mesylate groups were saponified with 20% NaOH to give the ligand **15**.

Ligands with Two-Carbon Side Chains. Based on our results with the ligands having three-carbon side chains, we first attempted a strategy similar to that shown in Scheme III but using bis(hydroxyethyl)biphenol **17** (cf. **10**) instead. Formation of the tetrakis(mesylate) **18** (cf. **11**) and attempted displacement with methylmercaptide ion gave little of the desired product (cf. **27**) because of competing ring closure to benzodihydrofurans. As a result, we explored an alternate route to these ligands (Scheme IV).

Using the benzyl-protected diol **16**, we prepared the bis(mesylate) **23**, which underwent smooth reaction with methylmercaptide or pyrazolate ion to give protected ligands **24** and **26**. The pyrazolyl derivative could be deprotected by hydrogenolysis to give **25**, but the sulfide ligand **27** was obtained after treatment with ethanethiol and boron trifluoride etherate.[7] Note that while **25** has only two carbons in the side chain, there are *three atoms* between the aromatic ring and the donor nitrogen. Attempts to prepare a ligand having a nitrogen donor γ to the ring by displacing the mesylate groups with dimethylamine appeared to proceed without problem, but the desired product could not be obtained in pure form perhaps as a result of facile elimination to form a styrene derivative.

Summary. Ligands **9**, **15**, **25**, and **27** are members of a new class of chelating agents that may prove useful for binding metals in such a way so as to leave vacant cis-coordination sites.[8] Other derivatives, for example phosphine-substituted analogues, have not been examined yet but ultimately may be more desirable especially for applications in homogeneous catalysis. Another, possibly more important, use for these compounds would be for the synthesis of crown ethers having functionalized sidearms, the so-called "podandocoronands".[4,9] The intermediates described here should provide ready entry into these other systems.

Experimental Section

All reagents and solvents were purchased from commercial sources and used as received unless noted otherwise. Tetrahydrofuran (THF) was distilled from sodium–benzophenone ketyl under nitrogen. Triethylamine was purified by heating under reflux with acetic anhydride for 12 h followed by fractional distillation. Methanesulfonyl chloride (MsCl) was distilled at reduced pressure before use. Melting points were obtained with use of a Fisher-Johns apparatus and are uncorrected. Flash chromatography[10] was performed using Merck Kieselgel 60 (230–400 mesh). Microanalyses were performed by MicAnal Laboratories Inc., Tucson, AZ.

^1H NMR spectra were recorded on a Perkin-Elmer R-24B or Varian EM-360 at 60 MHz, or a Bruker WM 250 instrument at 250.13 MHz. All chemical shifts are reported in ppm relative to an internal standard of tetramethylsilane.

3,3′-Bis(2-propen-1-yl)-2,2′-bis(benzyloxy)biphenyl (4). A solution of 5.9 g (0.017 mol) of 3,3′-bis(2-propen-1-yl)-2,2′-diacetoxybiphenyl (**2**)[4] in 100 mL of 3% methanolic KOH was heated under reflux for 2 h. The methanol was evaporated and 5% HCl was added until the solution was neutral. The resulting mixture was extracted with three 50-mL portions of ether. The ether layers were combined, washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography with toluene gave 4.2 g (90%) of **3** as a pale tan oil. ^1H NMR ($CDCl_3$): δ 3.44 (d, 4 H, $-CH_2-$), 5.10 (m, 4 H, $-C{=}CH_2$), 5.42 (s, 2 H, –OH), 6.0 (m, 2 H, $-HC{=}C$), 6.86–7.24 (m, 6 H, Ar H).

Under a dinitrogen atmosphere,10.9 g (0.041 mol) of crude phenol **3** in 25 mL of DMF was added dropwise to a mechanically stirred slurry of 4 g (0.167 mol) of NaH in 150 mL of DMF. After stirring for 2 h, the solution was treated dropwise with 15.6 g (0.123 mol) of benzyl chloride in 25 mL of DMF. After 5 h, a small amount of water was carefully added to destroy excess NaH. Six hundred milliliters of water was added, and this mixture was extracted with three 100-mL portions of toluene which were subsequently washed with water, dried over $MgSO_4$, filtered, and concentrated. Distillation gave 12 g (66%) of a yellow oil; bp 210 °C (0.1 torr). An analytical sample was purified further by distillation at 150 °C (3×10^{-4} torr). ^1H NMR ($CDCl_3$): δ 3.48 (d, 4 H, CH_2), 4.53 (s, 4 H, OCH_2Ar), 5.0 (s, 2 H, C=CH), 5.09 (d, 2 H, C=CH), 5.85–6.16 (m, 2 H, C=CH), 7.45–7.36 (m, 16 H, Ar H). Anal. Calcd for $C_{32}H_{30}O_2$: C, 86.06; H, 6.77. Found: C, 86.24; H, 6.75.

3,3′-Bis(3-hydroxy-1-propyl)-2,2′-bis(benzyloxy)biphenyl (5). Three milliliters (31.8 mmol) of borane–methyl sulfide was added slowly by syringe to a mechanically stirred solution of 6 g (13.4 mmol) of alkene **4** in 100 mL of anhydrous ether at 0 °C under a dinitrogen atmosphere. After stirring at room temperature for 2 h, the reaction mixture was cooled to 0 °C and treated carefully with 18 mL of 3 N NaOH followed by 18 mL of 30% H_2O_2. The solution was stirred at room temperature for 15 min and heated under reflux for 2 h. Ice water was added and the mixture extrcted with three 100-mL portions of ether. The combined ether layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography with 2:3 ethyl acetate ethyl acetate–hexanes yielded 5.2 g (80%) of **5**. An analytical sample was further purified by distillation at 170 °C (4×10^{-3} torr). ^1H NMR ($CDCl_3$): δ 1.79 (q, 4 H, CH_2), 2.23 (s, 2 H, OH), 2.75 (t, 4 H, $ArCH_2$), 3.40 (t, 4 H, CH_2O), 4.50 (s, 4 H, $-OCH_2Ar$), 6.94–7.38 (m, 16 H, Ar H). Anal. Calcd for $C_{32}H_{34}O_4$: C, 79.64; H, 7.10. Found: C, 79.57; H, 7.13.

3,3′-Bis[3-((methylsulfonyl)oxy)-1-propyl]-2,2′-bis(benzyloxy)biphenyl (6). A solution of 100 mL of methylene chloride, 5.84 g (12.1 mmol) of diol **5**, and a 50% molar excess of triethylamine was cooled to 0 °C. Three grams (26 mmol) of

(7) Fieser, M.; Danheiser, R. L.; Roush, W. "Reagents for Organic Synthesis"; Wiley: New York, 1981; Vol. 9, p 63.

(8) We have been unable so far to prepare any Mo(VI) complexes of the ligands reported here. Other metal ions such as Cu(II) appear to form complexes but preliminary studies suggest that they are polymeric. While CPK models indicate that these ligands should bind as desired, the formation of eight-membered rings within the chelate structure may be entropically unfavorable.

(9) Weber, E.; Vögtle, F. In "Topics in Current Chemistry"; Vögtle, F., Ed.; Springer-Verlag: Berlin; 1981; Vol. 98, p 14.

(10) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

methanesulfonyl chloride was added dropwise over 30 min, and after an additional 10 min, a white precipitate appeared. Water was added to the reaction mixture which was then allowed to stir for 24 h to remove unreacted methanesulfonyl chloride. The methylene chloride layer was separated from the aqueous layer which was subsequently extracted with two 50-mL portions of methylene chloride. The combined methylene chloride layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated to give 6.57 g (85%) of an oil which was purified by flash chromatography with 2:3 ethyl acetate–hexanes. ^1H NMR ($CDCl_3$): δ 1.95 (q, 4 H, CH_2), 2.75 (t under s, 10 H, CH_2 –SO_2CH_3), 4.0 (t, 4 H, CH_2), 4.40 (s, 4 H, OCH_2Ar), 6.90–7.35 (m, 16 H, Ar H).

3,3′-Bis[3-(methylthio)-1-propyl]-2,2′-bis(benzyloxy)biphenyl (7). To a slurry of 0.93 g (13 mmol) of sodium methylmercaptide in 30 mL of anhydrous ethanol under N_2 was added 3.13 g (4.9 mmol) of the bis(mesylate) **6** in 15 mL of anhydrous THF. The mixture was stirred for 12 h, and the solvent was evaporated under vacuum. The reaction mixture was extracted with three 30-mL portions of methylene chloride. The combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated. This procedure yielded 1.78 g of a white solid (67%), which was recrystallized from ethanol–pentane. ^1H NMR ($CDCl_3$): δ 1.95 (m under s, 10 H, CH_2, $-SCH_3$), 2.3–2.9 (overlapping t, 8 H, CH_2, CH_2), 4.4 (s, 4 H, OCH_2Ar), 7.1 (m, 16 H, Ar H). Anal. Calcd for $C_{34}H_{38}O_2S_2$: C, 75.23; H, 7.06; S, 11.81. Found: C 75.31; H, 7.04; S, 11.91.

3,3′-Bis[3-(dimethylamino)-1-propyl]-2,2′-biphenol (9). A Parr bottle was charged with 1.66 g (2.6 mmol) of the bis(mesylate) **6** and 30 mL of anhydrous ethanol and cooled to 0 °C in an ice bath. The bottle was flushed with nitrogen, and 15 mL of anhydrous dimethylamine was added. The Parr bottle was tightly capped and the solution allowed to stir for 12 h at room temperature. A white precipitate gradually formed. After cooling in an ice bath, the Parr bottle was carefully opened. Ethanol and excess dimethylamine were removed under vacuum, and 10% NaOH was added to make the mixture basic. The solution was then extracted with three 50-mL portions of methylene chloride. The combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated to give 1.1 g of **8** as a tan oil (79%).

Hydrogenolysis of 3.22 g (6 mmol) of the benzyl-protected biphenol **8** in ethanol with 2.3 g of 5% palladium on charcoal was completed in 2 days. The solution was filtered through a celite pad and concentrated to give a white solid. The white solid rapidly discolored in solution and could not be crystallized. High-vacuum sublimation at 110 °C (5×10^{-5} torr) yielded a white powdery solid. ^1H NMR ($CDCl_3$): δ 1.95 (q, 4 H, CH_2), 2.35 (s, 6 H, NCH_3), 2.42 (t, 4 H, $ArCH_2$), 2.80 (t, 4 H, NCH_2), 6.90 (t, 2 H, Ar H), 7.10 (d of d, 2 H, Ar H), 7.21 (d of d, 2 H, Ar H). Anal. Calcd for $C_{22}H_{32}N_2O_2$: C, 74.12; H, 9.05; N, 7.85. Found: C, 72.76; H, 9.05; N, 6.94. The apparent oxygen sensitivity of the product precluded obtaining a better analysis.

3,3′-Bis(3-hydroxypropyl)-2,2′-biphenol (10). The same procedure was followed as reported for the preparation of **9** to give an oil which was purified by flash chromatography (80%). ^1H NMR ($CDCl_3$): δ 1.75 (q, 4 H, CH_2), 2.7 (t, 4 H, $ArCH_2$), 3.45 (t, 4 H, CH_2O), 5.45 (s, 2 H, ArOH), 7.0 (m, 6 H, Ar H).

Methanesulfonylation of 10. The experimental procedure for mesylation was followed as outlined for **6**. The three products obtained were separated by flash chromatography (elution order: **13**, **12**, **11**) with 1:1 ethyl acetate–hexanes followed by recrystallization from hot benzene and ethanol with a small amount of ethyl acetate. The desired tetrakis(mesylate) **11** was obtained in 32% yield, mp 128–129 °C. ^1H NMR of **11** ($CDCl_3$): δ 2.15 (q, 4 H, CH_2), 2.44 (s, 6 H, $ArOSO_2CH_3$), 2.96 (m, 4 H, $ArCH_2$), 3.02 (s, 6 H, $-SO_2CH_3$), 4.30 (t, 4 H, OCH_2), 7.38 (m, 6 H, Ar H). Anal. Calcd for $C_{22}H_{30}O_{12}S_4$: C, 42.99; H, 4.88; S, 20.86. Found: C, 43.16; H, 4.78; S, 19.86.

^1H NMR of **12** ($CDCl_3$): δ 2.0 (m, 2 H, CH_2), 2.16 (m, 2 H, CH_2), 2.30 (s, 3 H, $ArOSO_2CH_3$), 2.90–3.02 (m under s, 5 H, $-SO_2$–CH_3, $ArCH_2$), 4.18 (t, 2 H, OCH_2), 4.32 (t, 2 H, OCH_2–), 6.9–7.3 (m, 6 H, Ar H). Anal. Calcd for $C_{20}H_{24}O_7S_2$: C, 54.53; H, 5.45; S, 14.56. Found: C, 54.18; H, 5.22; S, 14.02.

^1H NMR of **13** ($CDCl_3$): δ 2.0 (q, 4 H, CH_2), 2.84 (t, 4 H, CH_2), 4.12 (t, 4 H, OCH_2), 6.76–7.12 (m, 6 H, Ar H).

3,3′-Bis[3-(methylthio)-1-propyl]-2,2′-biphenol (15). The bis(thioether) **14** was prepared as reported for **7** and was obtained as an oil which was purified by flash chromatography with 1:2 ethyl acetate–hexanes (75%). ^1H NMR ($CDCl_3$): δ 2.0 (q, 4 H, CH_2), 2.14 (s, 6 H, $-SO_2CH_3$), 2.41 (s, 6 H, $-SO_2CH_3$), 2.58 (t, 4 H, $ArCH_2$–), 2.94 (m, 4 H, CH_2), 7.33 (m, 6 H, Ar H).

Under dinitrogen, a mixture of 25 mL of 20% NaOH and 0.57 g (1.1 mmol) of the thioether **14** was heated under reflux for 24 h. The solution remained heterogeneous during that time. The mixture was cooled and extracted with methylene chloride. The dried methylene chloride layer was filtered and concentrated to give an oil which was purified by chromatography in 1:2 ethyl acetate–hexane yielding 0.24 g (60%) of the free ligand **15**. An analytical sample was further purified by high-vacuum distillation at 170 °C (2×10^{-3} torr). ^1H NMR ($CDCl_3$): δ 1.94 (q, 4 H, CH_2), 2.07 (s, 6 H, SCH_3), 2.52 (t, 4 H, $ArCH_2$), 2.79 (t, 4 H, SCH_2), 5.84 (br. s, OH), 6.92 (t, 2 H, Ar H), 7.08 (d of d, 2 H, Ar H), 7.16 (d of d, 2 H, Ar H). Anal. Calcd for $C_{20}H_{26}O_2S_2$: C, 66.26; H, 7.23; S, 17.69. Found: C, 66.98; H, 7.60; S, 16.50.

3,3′-Bis(2-hydroxyethyl)-2,2′-bis(benzyloxy)biphenyl (16). Ozone was bubbled through a solution of 3 g (6.7 mmol) of alkene **4** in 50 mL of anhydrous ethanol at −78 °C for 10 min. A white precipitate appeared as the reaction progressed. A solution of 1.14 g (30 mmol) of $NaBH_4$ and 0.83 g (21 mmol) of NaOH in 25 mL of 50% aqueous ethanol was added to the ozonide while the reaction temperature was maintained at −78 °C. As the solution warmed to room temperature the color changed from colorless to pale yellow. After stirring overnight the solution was no longer yellow but appeared turbid. Ethanol was removed under vacuum, and the mixture was extracted with three 25-mL portions of ether. The ether layers were combined, washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated. Diol **16** was purified by flash chromatography with 3:2 ethyl acetate–hexanes to give 2.6 g (85%) of product. An analytical sample was purified further by high-vacuum sublimation at 160 °C (3×10^{-4} torr); mp 65–70 °C. ^1H NMR ($CDCl_3$): δ 1.66 (t, 2 H, OH), 2.94 (t, 4 H, $ArCH_2$), 3.80 (m, 4 H, CH_2O), 4.52 (s, 4 H, OCH_2Ar), 6.88–7.40 (m, 16 H, Ar H). Anal. Calcd for $C_{30}H_{30}O_4$: C, 79.27; H, 6.67. Found: C, 79.46; H, 6.70.

3,3′-Bis(2-hydroxyethyl)-2,2′-biphenol (17). The same procedure as outlined for the preparation of **9** was used for 7 g (15 mmol) of **16** and yielded a white solid. Recrystallization from ethanol–benzene gave 2.9 g (70.5%) of **17**, mp 125–126 °C. ^1H NMR ($CDCl_3$): δ 2.94 (t, 4 H, $ArCH_2$), 3.87 (t, 4 H, OCH_2), 6.89 (s, 4 H, OH), 7.13 (m, 6 H, Ar H). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.01; H, 6.62. Found: C, 70.09; H, 6.49.

Methanesulfonylation of 17. A solution of 30 mL of methylene chloride containing a 50% excess of triethylamine and 2.6 g (9.5 mmol) of diol **17** was cooled to 0 °C. During the dropwise addition of 2.4 g (20.7 mmol) of methanesulfonyl chloride, a white solid precipitated. After stirring an additional 10 min at 0 °C, the solution was treated with water to quench the reaction. The methylene chloride–water mixture was left stirring vigorously for 24 h to remove excess methanesulfonyl chloride. The methylene chloride layer was separated from the aqueous layer which was extracted with two 50-mL portions of methylene chloride. The combined methylene chloride extracts were dried over $MgSO_4$ filtered, and concentrated to give a mixture of two products, **19** and **20**. The two products were separated by flash chromatography with 1:1 ethyl acetate–hexanes, the bis(benzodihydro*furan*) **20** (cf. **13**) being eluted first. Compound **19** (cf. **12**) was recrystallized from benzene–ethanol to give 1.6 g (42%), mp 116–118 °C. ^1H NMR of **19** ($CDCl_3$): δ 2.49 (s, 3 H, $ArOSO_2CH_3$), 2.86 (s, 3 H, $-SO_2CH_3$), 3.20–3.31 (m, 4 H, ring CH_2, $ArCH_2$), 4.46–4.61 (m, 4 H, ring OCH_2, OCH_2), 6.89–7.40 (m, 6 H, Ar H). Anal. Calcd for $C_{18}H_{10}O_7S_2$: C, 52.41; H, 4.85; S, 15.55. Found: C, 52.50; H, 4.92; S, 15.32.

Recrystallization from a benzene–ethanol mixture yielded 0.4 g (19%) of diether **20**, mp 129–130 °C. ^1H NMR of **20** ($CDCl_3$): δ 3.24 (t, 4 H, $ArCH_2$), 4.56 (t, 4 H, OCH_2), 6.88 (t, 2 H, Ar H), 7.13 (d of d, 2 H, Ar H), 7.45 (d of d, 2 H, Ar H). Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.93. Found: C, 80.30; H, 6.00.

3,3′-Bis(2-hydroxyethyl)-2,2′-biphenol Tetrakis(methanesulfonate) (18). A solution of 2.8 g (10 mmol) of the diol **17** in 15 mL of methylene chloride and 11.5 mL of triethylamine was added dropwise to 6.2 g (54 mmol) of methanesulfonyl chloride

cooled to −15 °C. The reaction was stirred at −15 °C for 5 min and then at 0 °C for 15 min before water was added. After stirring for 24 h, the methylene chloride layer was separated and the aqueous layer extracted with two 50-mL portions of methylene chloride. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to give 3.0 g (50%) of tetrakis(mesylate) **18** with the two-carbon side chain (cf. **11**) after recrystallization from hot benzene and several drops of methylene chloride, mp 149–150 °C. ^1H NMR ($CDCl_3$): δ 2.45 (s, 6 H, $ArOSO_2CH_3$), 3.0 (s, 6 H, SO_2CH_3), 3.16–3.32 (m, 2 H, diastereotopic –CH of $ArCH_2$), 3.32–3.48 (m, 2 H, diastereotopic –CH of $ArCH_2$), 4.56 (m, 4 H, OCH_2), 7.40 (m, 6 H, Ar H). Anal. Calcd for $C_{20}H_{26}O_{12}S_4$: C, 40.95; H, 4.47; S, 21.86. Found: C, 40.73; H, 4.35; S, 21.48.

3,3′-Bis(2-((methylsulfonyl)oxy)ethyl)-2,2′-bis(benzyloxy)biphenyl (23). The same procedure was used as for the preparation of **6** and yielded 6.35 g (86%) of bis(mesylate) **23** which was purified by flash chromatography using 2:3 ethyl acetate–hexanes: ^1H NMR ($CDCl_3$) δ 3.78 (s, 6 H, SO_2CH_3), 3.10 (t, 4 H, $ArCH_2$), 4.34 (t, 4 H, CH_2), 4.50 (s, 4 H, OCH_2Ar), 7.0–7.43 (m 16 H, Ar H). Anal. Calcd for $C_{32}H_{34}O_8S_2$: C, 62.93; H, 5.61; S, 10.50. Found: C, 62.56; H, 5.61; S, 10.61.

3,3′-Bis[2-(1-pyrazolyl)ethyl]-2,2′-biphenol (25). Sodium pyrazolate was generated by the addition of 0.58 g (8.5 mmol) of pyrazole in 10 mL of DMF to a slurry of 0.323 g (13.5 mmol) of NaH in 30 mL of DMF under dinitrogen. After 2 h, 2.6 g (4.3 mmol) of the bis(mesylate) **23** in 10 mL of DMF was added dropwise to the sodium pyrazolate solution. The reaction was stirred for 24 h, treated with 150 mL of water, and extracted with three 50-mL portions of toluene. The combined toluene layers were washed with water, dried over $MgSO_4$, filtered, and concentrated. After flash chromatography with 1:1 ethyl acetate–hexanes, 1.0 g (42%) of the protected product **24** was obtained as an oil. ^1H NMR ($CDCl_3$): δ 3.15 (t, 4 H, $ArCH_2$), 4.20 (t, 4 H, NCH_2), 4.40 (s, 4 H, OCH_2Ar), 6.75 (t, 2 H, Pz H), 6.95–7.30 (m, 18 H, Ar H, Pz H), 7.35 (d, 2 H, Pz H).

Hydrogenolysis was carried out by the same experimental procedure described for **9**. A tan solid was obtained which was soluble in hot ethanol. Attempts at recrystallization lead to decomposition and the solid **25** was purified by high-vacuum sublimation at 175 °C (3×10^{-2} torr); mp 168–169 °C. ^1H NMR ($CDCl_3$): δ 3.45 (t, 4 H, $ArCH_2$–), 4.47 (t, 4 H, NCH_2–), 6.23 (t, 2 H, Pz H), 6.93–7.19 (m, 6 H, Ar H), 7.32 (, 2 H, Pz H), 7.54 (d, 2 H, Pz H), 8.88 (s, 2 H, ArOH). Anal. Calcd for $C_{22}H_{22}N_4O_2$: C, 70.57; H, 5.92; N, 14.96. Found: C, 69.64; H, 5.32; N, 14.50. The compound is somewhat unstable and decomposes to unidentified products upon standing. This may account for the poor analytical results.

3,3′-Bis[2-(methylthio)ethyl]-2,2′-bis(benzyloxy)biphenyl (26). The same experimental procedure was followed as reported for the synthesis of **7**. Recrystallization from ethanol–pentane yielded 2.0 g (75%) of the thioether **26**, mp ~27 °C. ^1H NMR ($CDCl_3$): δ 2.0 (s, 6 H, SCH_3), 2.5–3.1 (m, 8 H, CH_2CH_2), 4.5 (s, 4 H, OCH_2Ar), 7.2 (m, 16 H, Ar H). Anal. Calcd for $C_{32}H_{34}O_2S_2$: C, 74.66; H, 6.66; S, 12.46. Found: C, 74.66; H, 7.30; S, 11.03. Compound **26** was difficult to purify because of its low melting point.

3,3′-Bis[2-(methylthio)ethyl]-2,2′-biphenol (27). Two milliliters of ethanethiol was added to 0.26 g (0.5 mmol) of thioether **26** followed by the dropwise addition of 2.0 mL of $BF_3{\cdot}OEt_2$. The reaction mixture was stirred for 24 h in a stoppered flask. Water was added and the mixture extracted with methylene chloride. The combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated. The resulting oil was purified by flash chromatography with 3:1 methylene chloride–hexanes. The oil from chromatography solidified and was crystallized from methanol–benzene, mp ~28 °C. ^1H NMR ($CDCl_3$): δ 2.16 (s, 6 H, SCH_3), 2.80 (t, 4 H, $ArCH_2$), 3.0 (t, 4 H, SCH_2), 5.56 (br s, 2 H, –OH), 6.88–7.30 (m, 6 H, Ar H). Anal. Calcd for $C_{18}H_{22}O_2S_2$: C, 64.64; H, 6.63; S, 19.17. Found: C, 64.80; H, 6.93; S, 18.7.

Acknowledgment is made to the National Institutes of Health and to the University of North Carolina for a Junior Faculty Development Award for support of this work.

Enantioselective Preparation of 3-Substituted-4-pentenoic Acids via the Claisen Rearrangement

Mark J. Kurth* and Owen H. W. Decker

Department of Chemistry, University of California, Davis, Davis, California 95619

Received July 23, 1985

Asymmetric C–C bond formation via the diastereoselective aza-Claisen rearrangement of *N*-allylketene *N,O*-acetal **4** is described. The starting materials, allylic alkylating agent **1** and optically pure oxazoline **2**, are easily prepared and, in a one-pot procedure, generate rearranged oxazolines **5** in 52–94% diastereomeric excess. The overall chemical yields for **2** → **5** range from 51 to 78%. The aza-Claisen rearrangement (**4** → **5**) proceeds with excellent *N,O*-acetal face selectivity and with good to excellent chair selectivity. Hydrolysis of rearranged oxazoline **5** completes an enantioselective synthesis of 3-substituted pent-4-enoic acids.

Achieving absolute stereocontrol in the construction of acyclic systems is a particularly challenging goal in organic synthesis. While the Claisen rearrangement and its variants have been gainfully employed in addressing this challenge, all but a few of these Claisen protocols are self-immolative[1] at the original chiral center.[2] As one approach to nonimmolative asymmetric induction, we recently reported the diastereoselective chiron-mediated[3] aza-Claisen rearrangement of *N*-allylketene *N,O*-acetals.[4] The methodology developed in that work, which was based on the pioneering aza-Claisen work of Ireland and Willard,[5] provides a general, highly enantioselective preparation of 2-substituted-4-pentenoic acids by C(α) asymmetric in-

(1) Mislow, K. "Introduction to Stereochemistry"; Benjamin: New York, **1965**; p. 131.
(2) For example, see: (a) Ziegler, F. E.; Thottathil, J. K. *Tetrahedron Lett.* **1982**, *23*, 3531. (b) Kurth, M. J.; Yu, C.-M. *Tetrahedron Lett.* **1984**, *25*, 5003. (c) Kurth, M. J.; Yu, C.-M. *J. Org. Chem.*, in press.
(3) Hanessian, S. In "Total Synthesis of Natural Products: The 'Chiron' Approach"; Baldwin, J. E., Ed.; Pergamon Press Ltd.: New York, 1983; p. 21.
(4) Kurth, M. J.; Decker, O. H. W.; Hope, H.; Yanuck, M. D. *J. Am. Chem. Soc.* **1985**, *107*, 443.
(5) Ireland, R. E.; Willard, A. K. *J. Org. Chem.* **1974**, *39*, 421.

0022-3263/85/1950-5769$01.50/0