Synthesis of Optically Pure 2,2′-Dimercurio-1,1′-binaphthyl Compounds: Catalysis of Diels−Alder Reactions of *O*-Ethyl Crotonthioate

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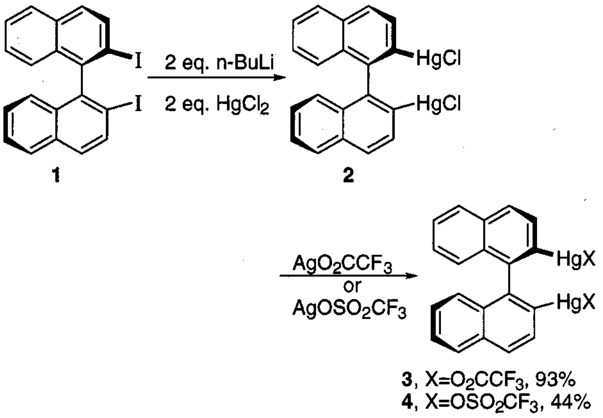
Optically pure 2,2′-bis(chloromercurio)-1,1′-binaphthyl, 2,2′-bis(trifluoroacetatomercurio)-1,1′-binaphthyl, and 2,2′-bis(trifluoromethanesulfonatomercurio)-1,1′-binaphthyl compounds have been synthesized. The dimercurio compounds show catalytic activity in the asymmetric Diels–Alder reactions with *O*-ethyl crotonthioate.

Introduction

The complexation of anions by multidentate Lewis acids has received attention only recently.[1] The interaction between bidentate Lewis acids with neutral carbonyl groups is an even less-well studied phenomenon. The carbonyl group is one of the most important functional groups in organic chemistry, making its interaction with, and activation by, Lewis acids an area of central importance. This issue has led to the development of chiral Lewis acids in asymmetric reactions.[2] Even more recent is the development of multidentate Lewis acids and chiral multidentate Lewis acids for this activation.[3d−3f] We have shown that simultaneous coordinations are possible with an *N*,*N*-dimethylcrotonthioamide substrate with mercuric bidentate Lewis acids.[4] As part of our work in this area, we report the synthesis of optically pure 2,2′-dimercurio-1,1′-binaphthyl compounds and demonstrate their catalytic activity in a Diels−Alder reaction with ethyl crotonthioate.

Results and Discussion

The asymmetric synthesis of the 2,2′-dimercurio-1,1′-binaphthyl compounds was accomplished from the optically pure 2,2′-diiodo-1,1′-binaphthyl compound **1** (Scheme 1).[5] The dianion of the binaphthyl compound is generated from compound **1**[6] with two equivalents of butyllithium at −42 °C, quenched with two equivalents of $HgCl_2$, and then allowed to warm to room temperature to give compound **2**. The optical integrity of the reaction was examined by ^1H NMR spectroscopy of racemic and chiral α-methylbenzylamine complexes of compound **2**. The ^1H NMR spectrum of the complex formed from compound **2** and one equivalent of (±)-α-methylbenzylamine shows a clean separation of the racemic amine. There is a separation of 0.37 ppm of the methine hydrogen of the amine and a 0.23 ppm separation of the methyl group between the enantiomers [methine-H, 4.30 ppm, methyl-H, 0.90 ppm; (+)-(*R*)-isomer; methine-H, 3.93 ppm, methyl-H 1.13 ppm, (−)-(*S*)-isomer]. The ^1H NMR spectrum of compound **2** complexed with (−)-(*S*)-α-methylbenzylamine shows only one enantiomer of compound **2** within the detection limit of a 360 MHz NMR spectrometer. These results show the potential of these compounds for use as chiral shift-reagents for chiral amines.[7] The chloride of compound **2** can be readily exchanged with $Ag(O_2CCF_3)$ or $Ag(OSO_2CF_3)$ to give the trifluoroacetate or trifluoromethanesulfonate compounds **3** and **4**.[8]



Scheme 1. Synthesis of chiral bidentate Lewis acids

Our initial examination of compound **2** as a catalyst in the Diels−Alder reaction with methacrolein and cyclopentadiene showed poor catalytic activity. The reaction of ethyl crotonthioate with cyclopentadiene is catalyzed by compound **2** (Scheme 2).[9] The reaction took two days at

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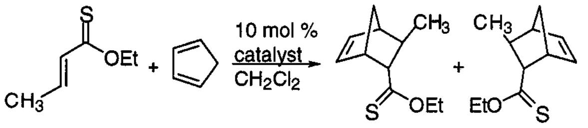
−23 °C with 10 mol-% of the catalyst, and only the *endo* Diels−Alder adduct was obtained in 30% yield favoring the (−)-isomer. The thioester moiety of the product was hydrolyzed to the acid (1. KOH, EtOH/H_2O; 2. 1 M HCl) and the acid converted into the amide [oxalyl chloride, (−)-(*S*)-α-methylbenzylamine]. Analysis of the ^1H NMR spectrum showed 38% *ee*. When the reaction was catalyzed by the more Lewis acidic compounds **3** and **4**, the reaction went to completion in less than 1 h at −78 °C. The enantioselectivities were 58% *ee* and 29% *ee*, respectively (Table 1). Again, only the *endo* isomers were obtained. Intriguing was the fact that the reaction catalyzed by compounds **3** and **4** favors the (+)-enantiomers. The more Lewis acidic compounds **3** and **4** must therefore catalyze the reaction through a different mechanism than the weaker Lewis acidic catalyst **2**. The exact nature of the mechanism is not yet understood. Clearly, these mercuric Lewis acids are much better at activating ethyl crotonthioate than methacrolein dienophiles.



Scheme 2. Diels−Alder reaction of ethyl crotonthioate

Table 1. Diels Alder reactions of ethyl crotonthioate and cyclopentadiene

Lewis acid	Temp., time	Ee(%)	$[\alpha]_D$[a]	Yield(%)
2	−23 °C, 2 d	38	−69	30
3	−23 °C, 1 h	58	+129	44
4	−78 °C, 1 h	29	+65.5	57

In order to gain an insight into the mechanism we examined the complexes of compounds **2** and **3** with *N*,*N*-dimethylcrotonthioamide (**5**).[10] Our attempts to examine the reaction with ethyl crotonthioate failed due to decomposition in the presence of the bidentate mercuric Lewis acids. Infrared absorption of the carbonyl functional group of the trifluoroacetate of the bidentate Lewis acid is indicative of whether simultaneous coordination is taking place. In the presence of two equivalents of **5**, the trifluoroacetate carbonyl stretch shifts from 1692.4 to 1660.2 cm^{-1} indicating a greater single-bond character and coordination of the mercury atoms to the thiocarbonyl group. With two equivalents of *N*,*N*-dimethylcrotonthioamide **5**, there should be one *N*,*N*-dimethylcrotonthioamide coordinated to each mercuric site. With one equivalent of *N*,*N*-dimethylcrotonthioamide two carbonyl stretches were observed at 1693.4 and 1659.6 cm^{-1} thus indicating that there is a coordinated and a free mercuric site. Additional investigations of the catalytic activity were carried out. A comparison of phenylmercury trifluoroacetate and the 2,2′-bis(trifluoroacetatomercurio)-1,1′-binaphthyl compound showed similar activities, suggesting that compounds **3** and **4** catalyze the reaction by monocoordination to the ethyl crotonthioate.

Experimental Section

All reactions were conducted under a protective atmosphere of either dry nitrogen or argon. Glassware was dried in an oven or flame-dried under vacuum prior to use. All solvents were dried and distilled prior to use. Standard ^1H and ^{13}C NMR analyses were conducted on a Bruker AM 360 Model 360 MHz spectrometer with $CDCl_3$ or $[D_6]$DMSO as the solvent in 5 mm NMR tubes. Infrared spectra were on a Perkin−Elmer Model 1600 FTIR infrared spectrometer. Optical rotations were obtained at ambient temperature on a Perkin−Elmer Model 243B polarimeter using a polarimetry cell with a 0.1000 dm path length. All reported melting points were obtained in capillary tubes and are uncorrected. All compounds reported are estimated to be at least 98% pure by the NMR spectral data.

(−)-2,2′-Bis(chloromercurio)-1,1′-binaphthyl (2): To a stirred solution of the (*R*)-(+)-2,2′-diiodo-1,1′-binaphthyl compound (0.50 g, 0.99 mmol) in dry diethyl ether (50 mL) at −42 °C (dry ice/acetonitrile bath) was added dropwise *n*-butyllithium (1.4 mL, 2.2 mmol, 1.6 M solution in hexanes). The solution immediately turned yellow. After 5 min, solid mercury(II) chloride (2.7 g, 9.9 mmol) was added in one portion at −42 °C. The yellow color faded immediately. The mixture was slowly brought to room temperature and was stirred for 12 h. The solvent was removed in vacuo to afford a crude yellow/white solid. This solid was dissolved in hot methanol (200 mL) and the insoluble material was removed by filtration. The colorless filtrate was allowed to cool to room temperature and was then diluted with an equal volume (200 mL) of distilled water. After 10 min a white precipitate formed which was recovered by suction filtration. The white solid was then dried in a heated vacuum desiccator to give 0.67 g (94%) of a white solid. Analytical samples were prepared by dissolving the compound in dichloromethane/hexanes until turbidity appeared. Removal of solvent provided an off-white solid of analytical purity after trituration. ^1H NMR (360 MHz, $[D_6]$DMSO): δ = 7.00 (d, J = 8.5 Hz, 2 H), 7.28 (t, J = 7.7 Hz, 2 H), 7.46 (t, J = 7.2 Hz, 2 H), 7.88 (d, J = 8.3 Hz, 2 H), 7.98 (d, J = 7.6 Hz, 4 H). − ^{13}C NMR (90 MHz, $[D_6]$DMSO): δ = 126.0, 126.1, 126.3, 127.2, 128.0, 132.6, 132.7, 133.1, 147.4, 154.7. − FTIR (KBr pellet): $\tilde{\nu}$ = 3049, 1577, 1499, 812, 743 cm^{-1}. − $[\alpha]_D$ = −8.0 (c = 1.5, DMSO).

(−)-2,2′-Bis(trifluoroacetatomercurio)-1,1′-binaphthyl (3): To a stirred suspension of the chiral 2,2′-bis(chloromercurio)-1,1′-binaphthyl (0.20 g, 0.27 mmol) in a 1:1 mixture of dry benzene (1.0 mL) and dry dichloromethane (1.0 mL) at room temperature was added solid silver trifluoroacetate (0.12 g, 0.54 mmol). The resulting mixture was then refluxed for 15 min and cooled to ambient temperature. The white silver chloride precipitate was then removed by suction filtration. Concentration of the filtrate and trituration of the resulting oil with 98:2 hexanes/EtOAc led to the isolation of 0.22 g (93%) of the desired product as a white solid. ^1H NMR (360 MHz, $CDCl_3$): δ = 7.16 (d, J = 8.6 Hz, 2 H), 7.33 (dt, J = 8.4, 0.9 Hz, 2 H), 7.53 (dt, J = 7.0, 0.9 Hz, 2 H), 7.60 (d, J = 8.5 Hz, 2 H), 7.98 (d, J = 8.3 Hz, 2 H), 8.02 (d, J = 8.5 Hz, 2 H). − ^{13}C NMR (90 MHz, $CDCl_3$): δ = 113.6, 116.7, 120.0, 123.1, 126.9, 127.5, 127.7, 128.7, 129.9, 132.0, 133.5, 133.8, 147.6. −

FTIR (KBr pellet): $\tilde{\nu}$ = 3054, 2956, 1682, 1410, 1188 cm^{-1}. − $[\alpha]_D$= −115.8 (c = 1.2, DMSO).

(−)-2,2′-Bis(trifluoromethanesulfonatomercurio)-1,1′-binaphthyl (4): This compound was synthesized using the same procedure as for compound **3**. Concentration of the filtrate and trituration of the resulting oil with hexanes led to the isolation of 0.059 g (44%) of the desired product as an off-white solid. ^{1}H NMR (360 MHz, [D$_6$]DMSO): δ = 7.01 (d, J = 8.6 Hz, 2 H), 7.32 (t, J = 7.6 Hz, 2 H), 7.49 (t, J = 7.5 Hz, 2 H), 7.77 (d, J = 8.4 Hz, 2 H), 8.02 (t, J = 7.2 Hz, 4 H). − ^{13}C NMR (90 MHz, [D$_6$]DMSO): δ = 118.8, 122.4, 126.3, 126.5, 126.5, 127.6, 128.0, 132.7, 132.8, 147.8. − FTIR (KBr pellet): $\tilde{\nu}$ = 3053, 2958, 1500, 1260, 1028, 642 cm^{-1}. − $[\alpha]_D$ = −48.2 (c = 1.1, DMSO).

Representative Cycloaddition Reaction Procedure: To a stirred solution of the ethyl thioester (0.039 g, 0.30 mmol) in dry dichloromethane (1.5 mL) at −78 °C was added the solid mercuric catalyst **4** (0.030 mmol) in one portion. After approximately 5 min, cyclopentadiene was added dropwise and the mixture was stirred for 1 h at −78 °C. The mixture was then diluted with 1 mL of a saturated aqueous $NaHCO_3$ solution and the organic layer was removed. The remaining aqueous layer was then extracted with dichloromethane (3 × 10 mL). The organic phases were combined, dried ($MgSO_4$) and concentrated in vacuo to yield a yellow residue. Purification by flash chromatography on silica gel (98:2, hexanes/EtOAc) provided 33 mg (57%) of a pale yellow oil. ^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.36 (t, J = 7.2 Hz, 3 H), 1.42 (qd, J = 8.6, 1.8 Hz, 1 H), 1.56−1.59 (m, 1 H), 1.98−2.06 (m, 1 H), 2.44 (m, 1 H), 2.71 (dd, J = 4.6, 3.6 Hz, 1 H), 3.21 (m, 1 H), 4.45 (q, J = 14.2, 7.2 Hz, 2 H), 5.95 (dd, J = 5.7, 2.8 Hz, 1 H), 6.24 (dd, J = 5.6, 3.1 Hz, 1 H). − ^{13}C NMR (90 MHz, $CDCl_3$): δ = 13.6, 20.9, 40.5, 46.2, 48.4, 49.1, 63.9, 67.8, 133.0, 138.2, 223.4. − FTIR (film): $\tilde{\nu}$ = 3061, 2960, 2869, 1262, 1182 cm^{-1}. − $[\alpha]_D$ = +65.5 (c = 1.65, $CHCl_3$). − TLC (SiO_2, 32:1 hexanes/EtOAc): R_f = 0.48.

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