Chiral Recognition in Silver(I) Olefin Complexes with Chiral Diamines. Resolution of Racemic Alkenes and NMR Discrimination of Enantiomers

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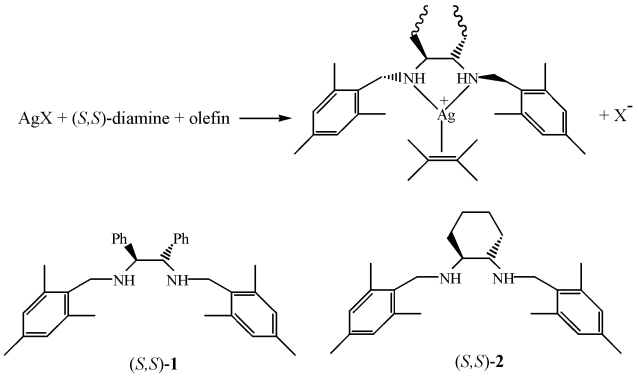
Summary: The fragment [(chiral diamine)Ag]$^+$ is a very useful reagent, both for the resolution of racemic alkenes and for the ^1H or ^{13}C NMR determination of the enantiomeric abundances of chiral olefinic compounds.

Chiral recognition in the coordination of olefins to chiral transition-metal fragments is a topic of great interest,[1] not only because of its involvement in metal-promoted enantioselective syntheses[2] but also because it can offer simple procedures for the thermodynamic[3] or kinetic[4] resolution of racemic mixtures or for the analytical determination of relative enantiomeric abundances.[5]

We recently reported a detailed investigation of trigonal Cu(I) olefin complexes with the chiral diamine *N*,*N*′-bis(mesitylmethyl)-1,2-diphenyl-1,2-ethanediamine (**1**), which led to a fairly good understanding of the factors affecting stereoselectivity in these species.[6] One remarkable property of the [(*S*,*S*)-**1**-Cu]$^+$ fragment proved to be the ability to selectively coordinate the *R* enantiomer of secondary allylic alcohols, providing a simple and effective method for the resolution of these compounds.[3a,6] Following our studies on Cu(I) complexes, we were prompted to prepare analogous Ag(I) species, both to determine whether the larger size of the metal ion could affect the stereochemical properties of the complexes and to investigate whether its higher lability and air stability could be exploited in practically useful methods. Although silver−olefin adducts are about the oldest metal π-complexes known,[7] very few studies on chiral species appear to have been reported in the literature, and these are essentially limited to the use of silver salts, in combination with chiral lanthanide shift reagents, for the NMR discrimination of enantiomeric olefins.[5a,b] In this communication we report the use of the [(*S*,*S*)-**1**-Ag]$^+$ and [(*S*,*S*)-**2**-Ag]$^+$ adducts as effective reagents for the resolution of racemic olefins (especially allylic alcohols) and for the NMR determination of the enantiomeric excess of chiral olefinic compounds.

Scheme 1



Tricoordinate cationic complexes of general formula [(N−N)Ag(olefin)]$^+$ were rapidly formed by suspending a silver salt (triflate, fluoroborate, or nitrate) in dichloromethane (0.1 mmol/mL) at room temperature and adding 1 equiv of the diamine and an excess (from 3 to 5 equiv) of the appropriate olefin (Scheme 1).

The nitrate salts are generally less soluble and best suited to achieve an optimal resolution of chiral olefins. They separated from the reaction mixture as a gelatinous solid by addition of diethyl ether (in the case of allylic alcohols) or pentane (in the case of hydrocarbon olefins).[8] The gel generally showed a poor to moderate diastereomeric enrichment, but when the mixture was stirred overnight, it was converted in better than 95% yield (based on Ag) to a crystalline material which contained the enantiomerically enriched olefin in up to 99% ee, the best resolutions being achieved in the case of secondary allylic alcohols and diamine **1** (Table 1).[9]

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(8) If diethyl ether is used to precipitate the complexes of hydrocarbon olefins, partial or even total loss of the olefin may take place by a displacement reaction.

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Table 1. Resolution of Olefins via [(diamine)Ag(olefin)]X Complexes. Enantiomeric Excesses in the Precipitated Product[a]

diamine	X^-	olefin	amt, equiv[b]	ee, %
(*S*,*S*)-**1**	NO_3^-	CH_2=CHCH(OH)Me	3	93
		CH_2=CHCH(OH)$(CH_2)_4$Me	3	85
			4	94
			5	>98
		(*E*)-MeCH=CHCH(OH)Me	5	>98
		CH_2=CHCH(Me)CMe_3	5	81[c]
		CH_2=CHCH(Me)$CHMe_2$	5	41
		CH_2=CHCH(Me)CH_2Me	5	39
(*S*,*S*)-**1**	BF_4^-	CH_2=CHCH(OH)Me	5	67
		CH_2=CHCH(Me)CMe_3	5	25
(*S*,*S*)-**2**	NO_3^-	CH_2=CHCH(OH)Me	5	85
		CH_2=CHCH(Me)CMe_3	5	60

[a] In all the cases, chemical yields (based on silver) were close to 95%. In the case of allylic alcohols, the *R* enantiomer was obtained. [b] Equivalents of racemic olefin used to prepare the complex. [c] *R* enantiomer.

Although a detailed stereochemical investigation of the complexes is out of the scope of the present communication, we point out that they are very likely to be isostructural with the previously investigated Cu(I) adducts,[6] since the same olefinic enantiomer (*R* in the case of secondary allylic alcohols) is enriched upon coordination. In our previous study concerning Cu(I) complexes,[6] the resolution of secondary allylic alcohols could be ascribed to the preferential coordination of one enantiomer with 95−98% selectivity. In the case of silver complexes the selectivity appears to be substantially lower, as indicated by the counterion dependence of the ee's and by the fact that the initially precipitated amorphous solids did not display large enantiomeric excesses of the olefin. Nevertheless, the final crystalline solids (nitrate salts) showed in all the cases a better diastereomeric purity than for the corresponding copper(I) derivatives.[10] This indicates the concurrence of a moderate preferential coordination of one enantiomer with a lower solubility of the corresponding diastereomer in achieving the final good resolution.

With respect to the metal−olefin bond, the complexes of hydrocarbon olefins appear to be very weak and labile, while those with allylic alcohols are more stable and robust, very likely because of a stabilizing intramolecular interaction between the oxygen atom and the metal ion.[6,12] Accordingly, two different procedures were adopted to recover the resolved alkene. In the case of hydrocarbon olefins (procedure i), the complex was dissolved in the minimum amount of dichloromethane and ethylene was gently bubbled through the solution while simultaneously adding pentane. This caused the immediate and nearly quantitative precipitation of the ethylene complex, while the resolved olefin could be isolated by fractional distillation of the mother liquor. This procedure has the advantage of leaving the $[(N-N)Ag]^+$ fragment intact and directly available to coordinate a further batch of olefinic compound. In the case of allylic alcohols (procedure ii), ethylene is not able to displace the coordinated olefin, and therefore the solid complex was treated with NaI (1.5 equiv) and aqueous HCl (3 M) with vigorous stirring, and the resolved allylic alcohol was recovered from the slurry in better than 95% yield by extraction with pentane and successive fractional distillation of the extract. The diamine was recovered from the residual aqueous suspension by addition of NaOH, extraction with dichloromethane, and evaporation of the solvent (ca. 95% yield).[11] Both procedures i and ii are remarkably simple, involving few steps and little workup, and are suitable to recycle the same crop of chiral diamine to resolve successive batches of olefinic compound.

The enantiomeric excess could be directly estimated from the ^{1}H NMR spectrum of the isolated crystalline complex in $CDCl_3$, CD_2Cl_2, or acetone-d_6, since many signals of the minor diastereomer are well separated from those of the major one. The large differences in the coordination shifts of the two enantiomers is most likely due to the different shielding effects by the mesityl rings of the diamine ligand. As shown in our previous study on analogous Cu(I) species,[6] in the most stable conformation the mesityl rings protrude forward to "envelop" the sides of the third coordinative position (as schematically shown in Scheme 1), thus generating shielding effects on the coordinated olefin which are very sensitive to the spatial location of each proton. This prompted us to explore the use of $[(N-N)Ag]NO_3$ and $[(N-N)Ag]OTf$ salts as chiral shift reagents for the NMR discrimination of enantiomeric olefins.[13] Such reagents would indeed be complementary or even advantageous over those containing lanthanide ions,[5a,b] due to the lack of line broadening caused by the paramagnetic ions. Of

(9) Selected data for representative complexes are as follows. **[(*S*,*S*)-1-Ag-(*R*)-1-buten-3-ol]NO_3** (major diastereomer). Anal. Calcd for $C_{38}H_{48}AgN_3O_4$: C, 63.51; H, 6.73; N, 5.85. Found: C, 63.15; H, 6.95; N, 5.64. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 0.93 (d, 3H, Me), 2.19 (s, 12H, *o*-Me_{N-N}), 2.21 (s, 6H, *p*-Me (N−N)), 3.32 (br, 1H, C*H*OH), 3.42−3.60 (m, 6H, CH_2 (N−N) and NH), 3.72 (d, 1H, OH), 4.07 (d, 1H, =CH^{1Z}), 4.26 (m, 2H, CH (N−N)), 4.54 (d, 1H, =CH^{1E}), 5.31 (ddd, 1H, =CH^2). ^{13}C NMR (100.6 MHz, CD_2Cl_2): δ 19.9 (*o*-Me(N−N)), 21.0 (*p*-Me (N−N)), 23.5 (Me), 46.8 (CH_2 (N−N)), 66.9 (CHOH), 69.3 (CH (N−N)), 94.1 (br, $=CH_2$), 135.5 (br, =CH). **[(*S*,*S*)-1-Ag-(*S*)-1-buten-3-ol]NO_3** (minor diastereomer). ^{1}H NMR (400 MHz, CD_2Cl_2): δ 1.06 (d, 3H, Me), 4.01 (br, 1H, C*H*OH), 4.60 (d, 1H, =CH^{1Z}), 4.68 (d, 1H, =CH^{1E}), 5.50 (ddd, 1H, =CH^2). **[(*S*,*S*)-1-Ag-(*R*)-1-octen-3-ol]NO_3**. Anal. Calcd for $C_{42}H_{56}AgN_3O_4$: C, 65.11; H, 7.28; N, 5.42. Found: C, 65.37; H, 7.45; N, 5.32. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 0.90 (t, 3H, Me), 2.22 (br, 18H, Me (N−N)), 3.13 (br, 1H, C*H*OH), 3.45−3.60 (m, 6H, CH_2 (N−N) and NH), 3.92 (d, 1H, OH), 4.03 (d, 1H, =CH^{1Z}), 4.35 (m, 2H, CH (N−N)), 4.47 (d, 1H, =CH^{1E}), 5.20 (ddd, 1H, =CH^2). ^{13}C NMR (100.6 MHz, CD_2Cl_2): δ 14.3 (Me), 20.0 (*o*-Me (N−N)), 21.0 (*p*-Me (N−N)), 23.2, 25.8, 32.5, 37.9 ($4CH_2$), 46.9 (CH_2 (N−N)), 69.4 (CH (N−N)), 70.7 (CHOH), 93.7 (br, $=CH_2$), 134.1 (br, =CH). **[(*S*,*S*)-1-Ag-(*R*)-3,4,4-Me_3-1-pentene]NO_3** (major diastereomer). Anal. Calcd for $C_{42}H_{56}AgN_3O_3$: C, 66.48; H, 7.44; N, 5.54. Found: C, 66.17; H, 7.35; N, 5.62. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 0.81 (s, 9H, 3Me), 0.82 (d, 3H, CH*Me*), 1.77 (dq, 1H, C*H*Me), 2.12 (s, 12H, *o*-Me (N−N)), 2.21 (s, 6H, *p*-Me (N−N)), 2.96 (br, 2H, NH), 3.56 (m, 4H, CH_2 (N−N)), 4.03 (m, 2H, CH (N−N)), 4.57 (dd, 1H, =CH^{1E}), 4.81 (dd, 1H, =CH^{1Z}), 5.60 (ddd, 1H, =CH^2). ^{13}C NMR (100.6 MHz, CD_2Cl_2): δ 16.4 (CH*Me*), 19.8 (*o*-Me (N−N)), 21.0 (*p*-Me (N−N)), 27.5 (3Me), 32.9 (*C*Me_3), 46.7 (CH_2 (N−N)), 48.6 (*C*HMe), 69.2 (CH (N−N)), 107.5 (br, $=CH_2$), 140.1 (br, =CH). **[(*S*,*S*)-1-Ag-(*S*)-3,4,4-Me_3-1-pentene]NO_3** (minor diastereomer). ^{1}H NMR (400 MHz, CD_2Cl_2): δ 0.80 (s, 9H, 3Me), 0.90 (d, 3H, CH*Me*), 4.82 (dd, 1H, =CH^{1E}), 4.85 (dd, 1H, =CH^{1Z}), 5.74 (ddd, 1H, =CH^2).

(10) It should be noted that in the case of the Cu(I) complexes, to prevent oxidation, nitrate could not be used as a counterion.

(11) Silver can be easily and quantitatively recovered as pure metal by reduction of the precipitated AgI with Zn powder in 0.1 M aqueous HCl and successive removal of the excess Zn with 5 M aqueous HCl.

(12) It is known that olefinic alcohols can form chelate adducts with silver ions; see: Novak, M.; Aikens, D. A.; Closson, W. D. *Inorg. Nucl. Chem. Lett.* **1974**, *10*, 1117−1121. Moreover, on the sole basis of inductive effects on the Ag−olefin bond, allylic alcohols would be expected to give *less* stable adducts than, for example, ethylene, which implicitly supports the existence of an O···Ag stabilizing interaction in their complexes. See: Herberhold, M. In *Metal π-Complexes*; Elsevier: Amsterdam, London, New York, 1974; Vol. 2, part II, pp 150−151. An additional stabilization could in principle arise from an intramolecular N−H···O bond, which, however, seems unlikely since X-ray diffraction data show that such an H-bond is *not* present in the analogous Cu(I) complexes.[6]

the two diamines, (*S*,*S*)-**1** appears to be better suited to the purpose, both because the silver salts of (*S*,*S*)-**2** have a pronounced tendency to darken and because the ^{1}H NMR signals of (*S*,*S*)-**2** obscure a wider spectral range. An NMR sample suitable for the accurate determination of enantiomeric abundances contained a 10−30 mM solution of the [(N−N)Ag]X salt (X = NO_3, OTf) and 1−3 equiv of the olefin in $CDCl_3$, CD_2Cl_2, or acetone-d_6. In either solvent the olefin is in fast exchange (on the NMR time scale) on the silver ions and therefore gives signals whose shifts are averaged between the free and coordinated molecules. Since the chemical shifts of the olefin in the diastereomeric complexes are generally different, the $[(N-N)Ag]^+$ fragment does indeed act as a chiral shift reagent, and many of the NMR signals of the olefin's enantiomers present in the sample are well separated (Figure 1).

In the presence of an excess of olefin, or other potentially coordinating species, the magnitude of the signal separation results from a balance of the different coordination shifts of the two enantiomers and of their binding affinities to the chiral metal fragment. Accordingly, the solvent and the counterion may have a substantial effect on the magnitude of the signal separation, depending on their coordinating ability. In the case of the more weakly bound hydrocarbon olefins, the signal separations generally increase in the counterion order $OTFA^- < NO_3^- < OTf^-$ and in the solvent order acetone < $CDCl_3$ (Table S1 in the Supporting Information).[14] Due to the dissociation and exchange equilibria, the amount of signal inequivalence is of course affected by the concentrations of the olefin and of the chiral metal fragment. While the particular choice of the concentrations is usually not crucial (thus adding flexibility to the method), this dependence can be turned into an advantage, because in the case of fortuitous overlapping of important resonances, the addition of a small amount of silver salt or olefin usually removes the incidental degeneracy and results in a satisfactory separation of the signals.

In conclusion, (chiral diamine)−Ag^+ salts, in addition to being useful resolving agents, appear to provide a simple method for the NMR determination of the enantiomeric abundances of a variety of chiral olefins. Although the method was only tested on olefins bearing a chiral center adjacent to the double bond, its possibly wider scope and ramifications are currently under investigation.

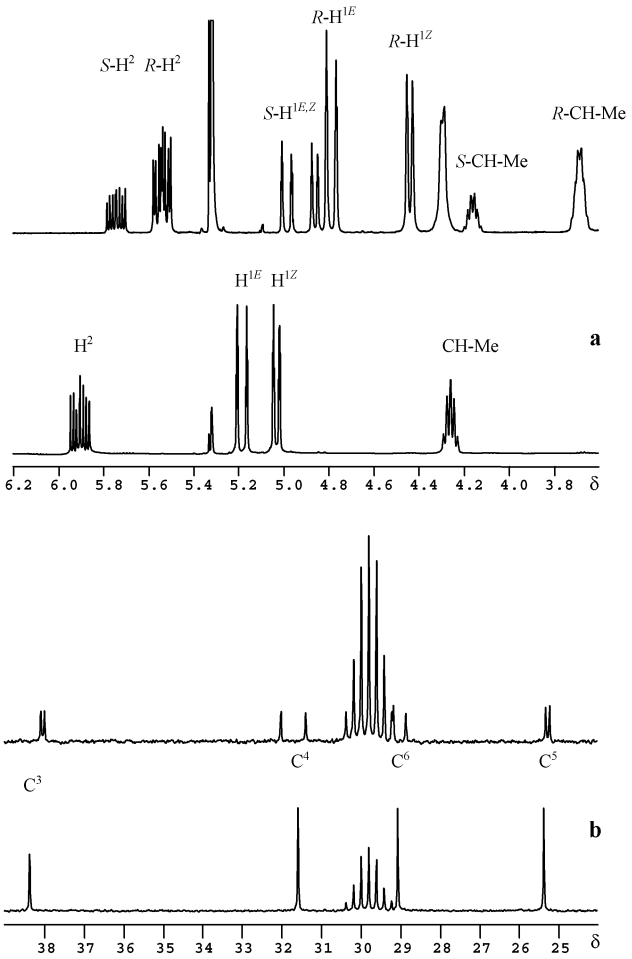

Figure 1. (a) Middle part of the 400 MHz ^{1}H NMR spectrum (CD_2Cl_2) of 1-buten-3-ol (enriched in *R* isomer). (b) Middle part of the 100.6 MHz ^{13}C NMR spectrum (acetone-d_6) of racemic 3-vinylcyclohexene. Lower traces show the olefin alone and upper traces the olefin in the presence of [(*S*,*S*)-**1**-Ag]OTf. Concentrations: (a) 13 mM complex, 40 mM olefin; (b) 35 mM complex, 40 mM olefin.

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Supporting Information Available: A table giving ^{1}H NMR shift differences between olefin enantiomers as affected by solvent and counterion. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) These salts could be either formed directly in the NMR tube, by mixing stoichiometric amounts of chiral diamine and silver nitrate or triflate, or prepared and stored separately in larger amounts. The crude adducts can be obtained by mixing stoichiometric amounts of silver salt ($AgNO_3$ or AgOTf) and chiral diamine in dichloromethane solution and successive evaporation of the solvent. In the case of the nitrate salt a cleaner product could be obtained by bubbling ethylene in the solution and precipitating the ethylene complex with pentane. Upon drying under vacuum (0.1 mmHg) at 40 °C, ethylene was lost and the pure $[((N-N))Ag]NO_3$ salt was obtained. The corresponding triflate salt does not lose ethylene under vacuum.

(14) Solvent and counterion effects can be rationalized more likely as a consequence of olefin displacement equilibria rather than ion-pair formation, since the switch to a supposedly more coordinating anion moves *all* the chemical shifts of *both* enantiomers toward those of the free olefin. Indeed, in the case of hydrocarbon olefins, such equilibria are independently evidenced by the partial olefin loss when diethyl ether rather than pentane is used in the precipitation of the complex[8] and by the loss of ethylene from the complex $[(N-N)Ag(C_2H_4)]NO_3$ when drying it under vacuum.[13]