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STRUCTURAL REQUIREMENTS IN CHIRAL DIPHOSPHINE-RHODIUM COMPLEXES. VII[1]. USE OF Z-METHYL-α-ACYLAMINOCINNAMATES AS STRUCTURAL PROBES FOR DIOP-RHODIUM(I) COMPLEXES.

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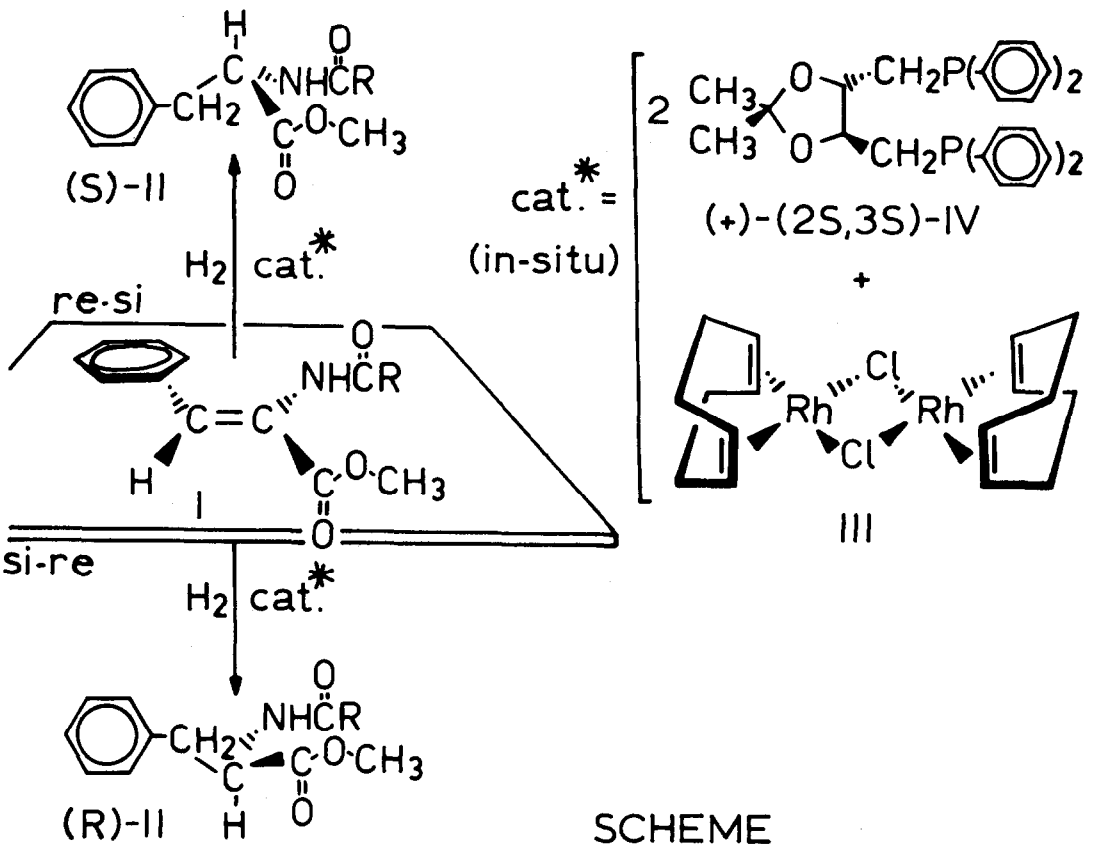
Summary: (+)-(2S,3S)-DIOP was used in neutral rhodium(I)-diphosphine complexes to catalyze the asymmetric hydrogenation of Z-methyl-α-acylaminocinnamates. Increasing steric bulk in the acyl function (NHCOR, where R is a hydrocarbon moiety) resulted in a decrease in optical purity of the N-acylphenylalanine methyl ester products. The optical purity decreased from 69 % ee (S) [Me], 15 % ee (S) [i-Pr], to 0 % ee [t-Bu and 1-adamantyl]. The α-formamido substrate decreased in optical purity [58 % ee (S)] relative to the Me analogue. The α-trifluoroacetamido analogue gave a reversal in chirality [22 % ee (R)].

As part of our continuing interest in the structural requisites of diphosphine-rhodium(I) hydrogenation complexes,[1] we have prepared Z-methyl-α-acylaminocinnamates [I] as topographical probes. We decided to make a systematic study of these complexes by utilizing the above-mentioned unsaturated substrates having increasing steric bulk in the α-acylamino moiety. These dehydroamino esters underwent hydrogenation to the corresponding N-acylphenylalanine methyl esters [II] using a neutral rhodium(I) catlyst prepared *in-situ* from chloro(1,5-cyclooctadiene)rhodium(I) dimer [III] and (+)-(2S,3S)-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane[2,3] (DIOP) [IV]. (see scheme)

The results of these studies are listed in the table. In the case of α-acylamino (NHCOR) unsaturated substrates having a hydrocarbon moiety R, it is seen that the enantiomeric excess of the reaction product decreases as the amide steric bulk is systematically increased from Me [69 % ee (S)], i-Pr [15 % ee (S)], to t-Bu (0 % ee) or 1-adamantyl (0 % ee). The α-formamido analogue shows a decrease in optical purity [58 % ee (S)] relative to the corresponding α-acetamide, yet the formamido group is smaller in steric bulk than the acetamido group. Moreover, the trifluoro-acetamido moiety shows a reversal in chirality of the major product isomer [22 % ee (R)].



SCHEME

The trifluoromethyl group has been described by Pirkle *et.al.*[4] as having a van der Waals diameter (5.1 Å) that is intermediate between that of methyl (4.0 Å) and t-butyl (6.2 Å). In terms of steric bulk alone, it would have been expected that the percent (S)-enantiomeric excess for CF_3 would be smaller than that for Me. Yet, the chirality of the CF_3 major product isomer is (R) rather than (S). The deviations of the formamido and trifluoroacetamido analogues from the NHCOR substrates in which R is a hydrocarbon moiety may be interpreted in terms of polar factors as well as steric ones. Thus, one preliminary interpretation of this data might be that the α-acylamino group undergoes a polar-type of interaction with another moiety within the catalytic complex in such a manner that the carbonyl C-atom in the NHCOR group prefers an electron donating group (such as methyl) bonded adjacent to it. A change from Me to H (in the formamide) or to CF_3 would thus be expected to result in a lower stereospecificity for the reaction. The strong electron withdrawing nature of the trifluoromethyl group might be the factor to change the preferential attack from the *re-si* to the *si-re* prochiral face of the unsaturated substrate within the (2S,3S)-DIOP·Rh hydrogenation complex.[5]

The sharp decrease in enantioface differentiation exhibited as a function of increasing steric bulk (of the hydrocarbon residue R within the NHCOR moiety) is in marked contrast to analogous

Table ASYMMETRIC HYDROGENATION OF Z-METHYL-α-ACYLAMINOCINNAMATES, $C_6H_5CH=C(NHCOR)COOCH_3$, WITH CHLORORHODIUM·(+)-(2S,3S)-DIOP[a]

R	% conversion[b]	$[\alpha]_D^{25}$	% opt. yield[c]	abs. config.
H	∿100 %	+57.8[d]	58 %[e]	S
Me[f]	∿100 %	+70.4[d]	69 %[g]	S
CF_3	89 %	-21.6[d]	22 %[h]	R[i]
i-Pr	∿100 %	+13.8[d]	15 %[j]	S
t-Bu	∿100 %	0	0 %	-
1-Ada	∿100 %	0	0 %	-
Ph	∿100 %	-16.0[k]	35 %[l,m]	S

[a] [Rh] = 3.0 mmol l^{-1}; [DIOP]/[Rh] = 1.1; [substrate]/[Rh] = 25; [abs. ethanol]/[benzene] = 2.3; total volume 10 ml; 1 atm. H_2; and 25°C. (+)-(2S,3S)-DIOP $[\alpha]_D^{22}$ +12.1° (C 1.0, C_6H_6) lit.[2] $[\alpha]_D^{22}$ -12.3° (C 4.57, C_6H_6) for (-)-(2R,3R)-DIOP. Experimental procedure as described in ref. 1a. Structures of all new compounds were in agreement with their respective elemental analysis, N.M.R., and infrared spectra. [b] determined by theoretical uptake of H_2 and N.M.R. or V.P.C. [c] percent enantiomeric excess; ± 1 %. [d] (C 1, $CHCl_3$); $[\alpha] \times 10^{-1}$ = degree g^{-1} cm^2. [e] based upon N-formyl-(S)-phenylalanine methyl ester, $[\alpha]_D^{25}$ +99.0° (C 1.0, $CHCl_3$). [f] data from ref. 1a. [g] based upon N-acetyl-(S)-phenylalanine methyl ester, $[\alpha]_D^{25}$ +101.3° (C 1, $CHCl_3$). [h] based upon N-trifluoroacetyl-(S)-phenylalanine methyl ester, $[\alpha]_D^{25}$ +100.0° (C 1.0, $CHCl_3$).[7] [i] sample from same source as used in footnote "h" gave $[\alpha]_D^{25}$ -8.9° (C 2.0, abs. EtOH) lit. $[\alpha]_D^{25}$ -7.2° (abs. EtOH). [j] based upon N-isobutyryl-(S)-phenylalanine methyl ester, $[\alpha]_D^{25}$ +90.8° (C 1.0, $CHCl_3$). [k] (C 1, 95 % EtOH). [l] based upon N-benzoyl-(S)-phenylalanine methyl ester, $[\alpha]_D^{25}$ -45.3° (C 1.3, 95 % EtOH) ref. 8. [m] lit.[8] 37.5 % ee.

changes in the COOR group.[1a] In earlier studies with Z-α-acetamidocinnamate esters,[6] it was found that when the alcohol moiety was systematically increased in steric bulk from Me, Et, i-Pr, to t-Bu, the optical purity of the reaction product increased slightly from 69 % ee to 76 % ee.[1a] However, when the alcohol moiety was increased still more in steric bulk from t-Bu to 1-adamantyl, the enantiomeric excess of the reaction product decreased to 71 % ee.[1a] The relatively more bulky 1-adamantyl ester was subsequently shown to undergo Z,E-isomerization prior to hydrogenation (this isomerization was not found to be appreciable in the case of the t-Bu ester analogue).[1c] The differences in behavior between the present α-acylamino series and the earlier ester series may provide clues as to the steric requirements in the vicinity of each of the two above-mentioned functional groups within the catalytic complex.

Additional studies dealing with the corresponding free acids as well as other substrates are now in progress.

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