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THE STEREOCHEMISTRY OF METAL CATALYSED HYDROGEN CYANIDE ADDITION TO ALKENES

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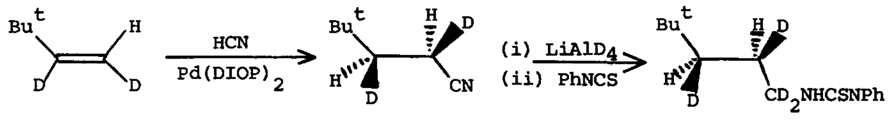
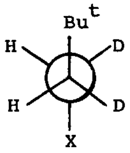
Abstract: Reactions of both terminal and cyclic alkenes have been shown to occur in a stereospecifically *cis* - manner with deuterium cyanide when a catalyst system based on $Pd(DIOP)_2$ was used. Reactions of cyclohexene give only the products of equatorial cyanide incorporation.

Hydrocyanation of alkenes is an important, established industrial process but very little information has been reported as to the stereochemistry or mechanism of this reaction.[1] One example of *cis* - addition of hydrogen cyanide to a terminal acyclic alkene has recently been reported.[2] We wish to report that addition of hydrogen cyanide to both acyclic and cyclic alkenes is stereospecifically *cis* when reactions were catalysed by a zerovalent compound of palladium with the chelating diphosphine DIOP, 2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane.[3]

The methodology developed by Whitesides and his co-workers to study the stereochemistry of additions to terminal acyclic alkenes was first employed.[4] Addition of hydrogen cyanide to *cis*-1,2-dideuterio-3,3-dimethylbut-1-ene (1) gave the nitrile (2) which was reduced with lithium aluminium deuteride and the resulting amine converted into the thiourea derivative (3). The conditions chosen for hydrocyanation were deliberately mild so as to minimise the chance of isotope exchange reactions, the yield of (2) was thus restricted to *ca.* 10%. The vicinal coupling constants $J_{2,3}$ were determined to be 5.8 Hz in the nitrile (2) and 4.3 Hz in the thiourea (3) from spectra recorded at 270 MHz with broadband deuterium decoupling. These values were consistent with (2) and (3) having the *threo*-stereochemistry with the preferred conformation (4), even in the case of the nitrile which has low conformational requirements.[5] None of the *erythro*-diastereoisomers (8) could be detected within the limits of nmr experiments (<5%). The *erthyro* diastereoisomers (8) were the major products from reactions of *trans*-1-deuterio-3,3-dimethylbut-1-ene (5) with deuterium cyanide. The coupling

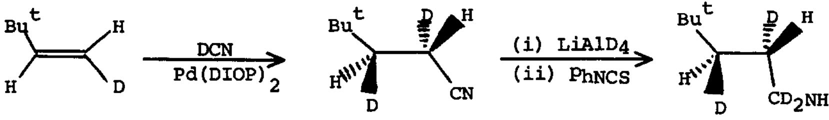


(1) (2) (3)

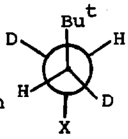


(4)

constants $J_{2,3}$ were now 10.6 Hz for (6) and 12.6 Hz for (7), thus confirming the cis-stereochemistry of addition of hydrogen cyanide. No threo-products were observed from the DCN reaction but the DCN contained a significant amount of HCN as impurity. Signals arising from the products of HCN addition had to be subtracted from the spectra and the limits of detection of the minor isomer was estimated to be ca. 10%, greater than in the experiment with HCN.

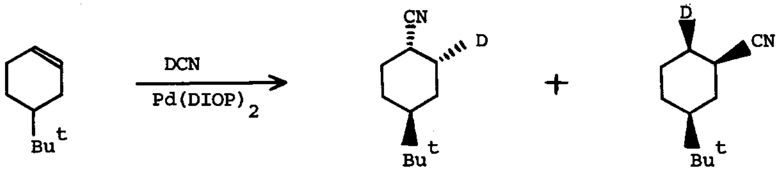


(5) (6) (7)



(8)

Reaction of 4-t-butylcyclohex-1-ene (9) with deuterium or hydrogen cyanide gave the equatorial cyanides (10) and (11) in equal amounts. No axial cyanides could be detected by glc (<1%). The stereochemistry of deuterium incorporation was established by examination of the 270 MHz spectra of the products. In the fully protonated samples resulting from HCN addition, the α-protons absorbed as two triplets of triplets at δ 2.32 (10) and 2.40 (11) p.p.m. with J_{aa} 12.3 Hz and J_{ae} 3.7 Hz in the ^1H n.m.r. spectrum. The spectrum of a product of a DCN reaction was observed with deuterium decoupling and the α-protons now absorbed at δ 2.31 and 2.39 p.p.m. as doublets of triplets. Only one large axial-axial coupling constant was observed (J 12.2 Hz) whereas two equatorial-axial couplings were present (J 4.1 Hz). Clearly the deuterium had been incorporated into the axial position in (10) and (11). This observation was confirmed from a study of the high resolution ^2H spectrum of the mixture which showed the deuterium atoms in (10) and (11) as quartets with $^2J_{^1H^2H} = {}^3J_{^1H_{ax}{}^2H} = 2Hz$, and $^3J_{^1H_{eq}{}^2H} < 0.6$ Hz. No signals attributable to equatorial substituted deuterium were observed.



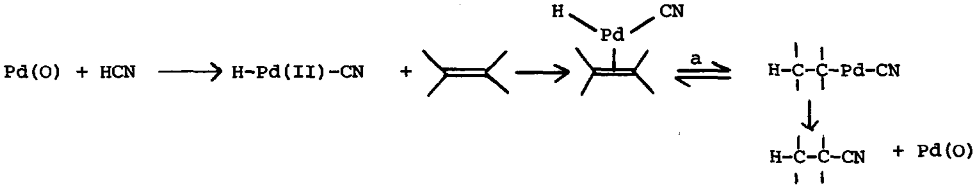
(9) (10) (11)

Similar cis-di-exo- addition of DCN to both norbornene and norbornadiene was observed for reactions using the $Pd(DIOP)_2$ catalyst system.[6] No endo-deuterium or nitrile was observed even though the nitriles were obtained in high yields (>80%) from these reactions.

When the catalyst system based on $Ni[P(OPh)_3]_4$ and zinc chloride was used[7] both intra- and intermolecular scrambling of the deuterium label occurred.[8] 4-t-Butylcyclohex-1-ene rapidly equilibrated to give a mixture containing an equimolar amount of 3-t-butylcyclohex-1-ene together with a trace of 2-t-butylcyclohex-1-ene. However, the two cyanides (10) and (11), (as fully protonated compounds) were the only products arising from a reaction of (9) with HCN using the nickel phosphite based catalyst system. The cyanides were isolated in ratio 1(10) : 2(11) suggesting that this catalyst system may show similar stereochemistry to the Pd(DIOP)$_2$ based one. The regiospecificity of reaction of the 3-t-butylcyclohex-1-ene at the 1-position is in keeping with a large steric requirement for the reaction, again similar to the Pd(DIOP)$_2$ system.[3]

The alkenes were also hydroformylated using HRh(CO)(PPh$_3$)$_3$ as catalyst.[9] Similar reactions are known to display high cis-stereochemistry.[10] The aldehydes from reaction of (1) with H_2 + CO and (5) with D_2 + CO were oxidised with silver oxide and converted into the corresponding amides. The amide from (1) predominantly had the threo-stereochemistry (4; X - CONH$_2$) similar to that obtained by hydrolysis of the nitrile (2) with $J_{2,3}$ 4.7 Hz. In each case however, about 10% of the amide of the alternative stereochemistry was observed suggesting that at least with this catalyst system hydroformylation is not as stereospecific as hydrocyanation. A lack of complete stereoselectivity was shown in the hydroformylation of the cyclohexene (9) which gave ca. 10% of axial aldehydes in addition to the equatorial aldehydes corresponding to (10) and (11).

The adverse susceptibility of the hydrocyanation reaction to bulky substituents,[3] the exclusive formation of equatorial nitriles, and the cis-stereochemistry of addition point to a mechanism similar to that discussed previously.[1] Oxidative addition of HCN is followed by olefin insertion. The σ-bonded palladium species is sterically demanding and exclusively adopts the terminal position (with alk-1-enes) or an equatorial position (with cyclohexenes). Cyano-carbon bond formation then occurs with retention of configuration. The regioselectivity of insertion of a group RX in palladium catalysed reactions involves formation of a bond between the palladium atom and the most substituted carbon atom.[11] However, R in all cases was alkyl or aryl and it appears to us that it is highly probable that the substituted palladium atom will be more sterically demanding than hydrogen.



The olefin insertion step "a" appears to be reversible only in the presence of zinc chloride leading to alkene isomerisation when possible and deuterium-hydrogen exchange.

Acknowledgements

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