

Highly Selective Catalytic Hydrogenation of Cyclic Enones

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Abstract: *Cyclic enones are hydrogenated to the allylic alcohols with high chemoselectivity in the presence of a homogeneous Ir/diop catalytic system.*

Cyclic enols are important precursors to a variety of natural products, and much effort has been made towards their asymmetric synthesis.

We already reported¹ that Ir/diphosphine systems are active and selective as hydrogenation catalysts with benzylideneacetone as substrate. Now we find that simple cyclic enones are reduced to the allylic alcohols with high chemoselectivity and optical purities up to 28% in the presence of an "in situ" catalytic system formed by [Ir(cod)(OMe)]₂ and diop [diop=(+)-O-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane].

Only a few stoichiometric reduction systems are able to perform this reaction cleanly and with good enantioselectivity²⁻⁵, while most of them also give some 1,4-hydrogen addition and/or overreduction products. To the best of our knowledge, homogeneous catalytic hydrogenation systems capable of reducing the carbonyl group in these substrates selectively and asymmetrically are not known, and we found only one example in the literature of chemoselective reduction to the allylic alcohol by hydrogen transfer⁶.

A selection of our results is reported in the table. The typical procedure is that previously reported¹ with minor variations. Best results are achieved by operating at high substrate to iridium ratios. Furthermore, chemoselectivity seems to be a function of reaction time, and the formation of the selective catalytic species is accelerated by temperature and excess of substrate. Even unsubstituted enones, which are known to be highly susceptible to 1,4-attack, are reduced to the allylic alcohols with selectivities over 90%. Substitution on the olefinic bond leads to higher steric interactions and hence to even higher selectivities. Reduction of carvone is extremely slow, nevertheless the reaction is highly selective even in the presence of a terminal olefinic bond.

¹H and ³¹P NMR experiments show that the iridium monohydride HIr(diop)₂ forms initially, which in turn evolves, at high hydrogen pressure and in the presence of excess substrate, into different species which give complex spectra. The same pattern is shown starting from the cationic precursor [Ir(diop)₂]⁺, together with the signals due to the *cis*-dihydride¹. The formation of polynuclear hydridic species with bridging diop is possible in these conditions and is well documented in the literature in the case of larger diphosphines which give seven-membered rings on chelation to the metal.^{7,8}

The potential applicability of this system to various natural products of interest including six- and five-membered unsaturated cycles is being evaluated. A full characterization of the selective species present in solution under these experimental conditions is also being currently attempted.

Table. Hydrogenation of Cyclic Enones ^a

substrate	t(h)	% conv.	% enol	sel ^b	e.e. ^c
2-cyclopenten-1-one	118	54	50	92	12
2-cyclohexen-1-one	68	65	62	95	25
4,4-(Me) ₂ -2-cyclohexen-1-one	72	47	46	98	--
3-Me-2-cyclohexen-1-one ^d	144	67	66	99	12
R-(-)-carvone [5R-isopropenyl-2-Me-2-cyclohexen-1-one]	144	10	9	91 ^e	28 ^f

Notes

- a. Cat=[Ir(cod)(OMe)]₂+diop; diop/Ir=5; sub/Ir=500; solvent toluene; [Ir]=7x10⁻⁴ M; T=100°C; p_{H2}=20 atm.
- b. Sel= % unsaturated alcohol/% conversion.
- c. Absolute configuration R.
Calculated by optical rotation measurement on the basis of the following values for the optically pure alcohols:²
2-cyclohexen-1-ol: [α]_D=112.0 (c 0.60, CHCl₃).
2-cyclopenten-1-ol: [α]_D=129.0 (c 1.14, CHCl₃).
3-Me-2-cyclohexen-1-ol: [α]_D=96.3 (c 0.458, CHCl₃).
- d. Sub/Ir=250.
- e. %carveol/% conversion. (carveol=5-isopropenyl-2-Me-2-cyclohexen-1-ol).
1% 5-isopropyl-2-Me-2-cyclohexen-1-one also produced.
- f. Determined by GLC. Major product: *cis*-(5R,1R)-carveol.

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