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Diastereoselective Hydroformylation of Certain Protected Allylic Alcohols

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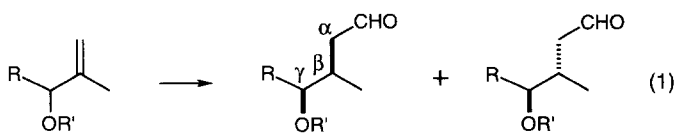
***Abstracts**: The diastereoselective hydroformylation of 2-methyl-1-alken-3-ol and 5-t-butyl-2-methylene-cyclohexanol derivatives gave threo- and erythro-γ-hydroxyalkanal derivatives in ratios up to 82 : 18, contrary to the results observed for hydroxy-directed hydrogenation of the corresponding allylic alcohols.*

The hydroformylation of alkenes is one of the most important industrial reactions using homogeneous catalysts.[1] Although much effort has been focused on the efficiency of the rhodium(I) complex-catalyzed hydroformylation of a variety of alkenes and on the high linear selectivity for 1-alkenes, it is generally difficult to control the regio- and stereoselectivity in the hydroformylation of internal alkenes with the exception of a few elegantly designed synthetic approaches.[2,3] Herein we wish to report diastereocontrol in the rhodium(I)-catalyzed hydroformylation of 1,1-disubstituted alkenes that contain an allylic hydroxy group. These substrates can undergo hydroformylation exclusively at the terminus[4] leading to a γ-hydroxyalkanal, the equivalent to an aldol adduct with a homoenolate,[5] thereby creating a new stereogenic center at the β-position (eq 1). Although the hydroxy-directed hydrogenation[6] and hydroboration[7] of allylic alcohols using a rhodium(I) complex catalyst are well documented, the analogous hydroformylation aimed at possible diastereocontrol has not been reported.[8] Thus, the influence of the C*-OR (R = H or a protecting group) stereogenic center adjacent to the alkene moiety on the stereochemical outcome of the hydroformylation was examined.



2 R = octyl
5 R = *c*-hexyl

threo-**3** R = octyl
threo-**6** R = *c*-hexyl

erythro-**4** R = octyl
erythro-**7** R = *c*-hexyl

A typical example is given below. A toluene solution of the catalyst $Rh(acac)(CO)_2$ (**1**) (1 mol %) and a given allylic alcohol (0.2 M) was heated in a glass-lined autoclave under an appropriate pressure of hydrogen and carbon monoxide. The hydroformylation of 2-methyl-1-undecen-3-ol (**2a**) and its derivatives (**2b-d**) was found to complete in 48 h at 80 °C under 60 atm of the syn gas (H_2 / CO = 1), as shown in Table 1. The reaction of **2a** (R'=H) gave a 53 : 47 mixture of *threo*-**3a** and *erythro*-**4a** (R'=H) diastereomers. The stereochemistry was unambiguously determined after PCC oxidation of the products.[9] The observed lack of diastereoselectivity is rather amazing from a mechanistic standpoint. We have attempted the diastereo-controlled hydroformylation of several hydroxy-protected derivatives of **2a**. Although no obvious effect was observed in the case of the benzoate derivative **2b**, slightly enhanced selectivities were detected in both the pivalate **2c** and the TBDPS (*t*-butyldiphenylsilyl) ether **2d**, with ratios of 61 : 39 (Table 1).[10] However, it is worth mentioning that the present hydroformylation is more or less syn (threo) selective, a result opposite to that observed for the hydroxy-directed hydrogenation in which high anti (erythro) selectivity is preferred.[6]

We have also examined the hydroformylation of substrates **5a-e** (see eq. 1) which bear a bulkier cyclohexyl group at the allylic position. The reactions of **5** proceeded in 48 h at 80 °C under 80 atm of the syn gas (H_2 / CO = 1) (Table 2). As is seen from Table 2, the diastereoselectivity was again found to be low in the case of alcohol **5a**. However, a marked enhancement of selectivity was observed in acyl derivatives **5b** and **5c**, respectively, with *threo*-**6** : *erythro*-**7** being formed in ratios up to 82 : 18. On the contrary, the TBS (*t*-butyldimethylsilyl) ether **5d** (75 : 25) and the TBDPS ether **5e** (69 : 31) exhibited no effective trend in selectivity. Based on these results, it seems reasonable to assume that the stereoelectronic effect of the acyl groups rather than the simple steric effect of the silyl groups may control the diastereoselectivity in the present hydroformylation.

Table 1. Hydroformylation of 2-methyl-1-undecen-3-ol derivatives (**2**).[a]

Entry	Substrate	Yield / %[b]	*threo*-**3** : *erythro*-**4**
1	**2a**, R' = H	99	53 : 47
2	**2b**, R' = Bz	99	54 : 46
3	**2c**, R' = Piv	90	61 : 39
4	**2d**, R' = TBDPS	99	61 : 39

a $Rh(acac)(CO)_2$ (1 mol %), 60 atm (H_2 : CO = 1 : 1), 80 °C, 48 h. *b* Conversion

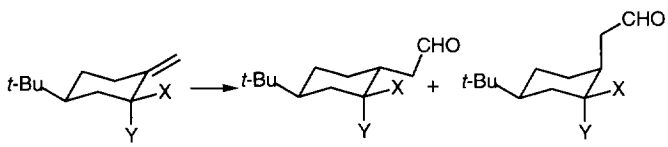
Table 2. Hydroformylation of 1-cyclohexyl-2-methyl-2-propenol derivatives (**5**).[a]

Entry	Substrate	Yield / %[b]	*threo*-**6** : *erythro*-**7**
1	**5a**, R' = H	96	52 : 48
2	**5b**, R' = Ac	84	78 : 22
3	**5c**, R' = Piv	89	82 : 18
4	**5d**, R' = TBS	91	75 : 25
5	**5e**, R' = TBDPS	96	69 : 31

a $Rh(acac)(CO)_2$ (1 mol %), 80 atm (H_2 : CO = 1 : 1), 80 °C, 48 h. *b* Isolated yield.

This stereoelectronic effect is more obvious in the hydroformylation of a cyclic system **8** or **11**, methylenecyclohexanes that again contain a hydroxy group in the allylic positions. The results of these studies are given in Table 3. Thus, the rhodium(I)-catalyzed hydroformylation of *cis*-5-*t*-butyl-2-methylenecyclohexanol **8a** (R = H) and the protected derivative **8b** (R = Piv) proceeds *via* axial attack to avoid torsional strain with the C-O bond at an equatorial position of the substrate. Product **9** (rather than **10**) is thus isolated in ratios of 64-67 : 36-33 (Entries 1, 2). On the other hand, remarkable stereoselectivity was observed in the reaction of *trans*-5-*t*-butyl-2-methylenecyclohexyl pivalate **11b** (R = Piv), giving, as the major product, **13b** that results from the preferential addition of the catalyst species from the same side as the axial C-O bond (equatorial attack) (Entries 3, 4). Substrate **11a** (R = H) exhibits the same selectivity, though to a lesser extent. Thus, it is evident that the stereoelectronic effect of the carbon-acyloxy bond can enhance selectivity when addition of an enormously bulky rhodiumcarbonyl hydride species[11] takes place preferentially at the alkene moiety bearing either an equatorial[12] or, particularly, axial acyloxy group in the allylic position.

Table 3. Hydroformylation of 5-*t*-butyl-2-methylenecyclohexanol derivatives (**8**) and (**11**).[a]



8 X = OR, Y = H
11 X = H, Y = OR

9 X = OR, Y = H
12 X = H, Y = OR

10 X = OR, Y = H
13 X = H, Y = OR

Entry[a]	Substrate	Yield / %[b]	Stereoselectivity
1	**8a**, R = H	85	**9a** : **10a** = 67 : 33
2	**8b**, R = Piv	95	**9b** : **10b** = 64 : 36
3	**11a**, R = H	84	**12a** : **13a** = 36 : 64
4	**11b**, R = Piv	99	**12b** : **13b** = 20 : 80

[a] $Rh(acac)(CO)_2$ (1 mol %), 80 atm (H_2 / CO = 1), 40 °C, 45 h. *b* Isolated yield.

In summary, we have demonstrated that unusual stereocontrol in the hydroformylation of 1,1-disubstituted allylic alcohol derivatives can be achieved, based mainly on the stereoelectronic rather than steric effects of the allylic carbon-acyloxy bond.

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REFERENCES AND NOTES

1. Cornils, B. In *New Syntheses with Carbon Monoxide*; Fable, J. Ed.; Springer-Verlag: New York, 1980. Tolman, C. A.; Faller, J. In *Homogeneous Catalysis with Metal Phosphine Complexes*; Pignolet, L. H. Ed.; Plenum Press: New York, 1983; Chapt. 2. Dickson, R. S. In *Homogeneous Catalysis with Compounds of Rhodium and Iridium*; Ugo, R.; James B. R. Eds.; D. Reidel Publish Company: Dordrecht, 1985. Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W. *J. Mol. Cat. A* **1995**, *104*, 17-85. For a recent review of asymmetric hydroformylation, see: Agbossou, F.; Carpentier, J.-F.; Mortreux, A. *Chem. Rev.* **1995**, *95*, 2485-2506.
2. For the regiocontrolled hydroformylation of bulky silyl group-substituted (*Z*)-alkenes, see: (a) Doyle, M. M.; Jackson, W. R.; Perlmutter, P. *Tetrahedron Lett.* **1989**, *30*, 233-234. (b) Crudden, C. M.; Alper, H. *J. Org. Chem.* **1994**, *59*, 3091-3097.
3. For examples of stereoselectivity in the rhodium-catalyzed hydroformylation, see: Lazzaroni, R.; Pucci, S.; Bertozzi, S.; Pini, D. *J. Organomet. Chem.* **1983**, *247*, C56-58. Azzaroni, F.; Biscarini, P.; Bordoni, S.; Longoni, G.; Venturini, E. *J. Organomet. Chem.* **1996**, *508*, 59-67. For the phosphine-directed hydroformylation, see: Burke, S. D.; Cobb, J. E. *Tetrahedron Lett.* **1986**, *27*, 4237-4240. Burke, S. D.; Cobb, J. E.; Takeuchi, K. *J. Org. Chem.* **1990**, *55*, 2138-2151. Jackson, W. R.; Perlmutter, P.; Suh, G.-H. *J. Chem. Soc., Chem. Commun.* **1987**, 724-725. Jackson, W. R.; Perlmutter, P.; Tasdelen, E. E. *Tetrahedron Lett.* **1990**, *31*, 2461-2462. For the phosphite-directed hydroformylation, see: Jackson, W. R.; Moffat, M. R.; Perlmutter, P.; Tasdelen, E. E. *Aust. J. Chem.* **1992**, *45*, 823-834.
4. For simple examples of 1,1-disubstituted alkenes, see: Botteghi, C.; Consiglio, G.; Ceccarelli, G.; Stefani, A. *J. Org. Chem.* **1972**, *37*, 1835-1837. Hoffmann, W.; Siegel, H. *Tetrahedron Lett.* **1975**, 533-526. Opposite regioselectivity, see: Kollár, L.; Consiglio, G.; Pino, P. *Chimia* **1986**, *40*, 428-429. Gladiali, S.; Pinna, L. *Tetrahedron: Asymmetry* **1991**, *2*, 623-632.
5. For a review of homoenolates, see: Kuwajima, I.; Nakamura, E. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I.; Heathcock, C. H. Eds.; Pergamon Press: Oxford, 1991; Vol. 2, p.441.
6. Brown, J. M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 190-203.
7. Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917-6918. For a recent review of substrate-directed chemical reactions, see: Hoveyda, A. H; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307-1370.
8. No diastereoselection in the hydroformylation was observed where a chiral hydroxy substituent was present in the allylic position, see ref. 2a.
9. The products **3a** and **4a** were observed as a diastereomer mixture of hemiacetals.
10. No significant change in the diastereoselectivity was observed when the hydroformylation was carried out using $Rh(acac)(CO)_2$ with 3 equiv. of a phosphine or a phosphite ligand [triphenylphosphine, tri-(*o*-tolyl)phosphine, 1,2-bis(diphenylphosphino)ethane, 1,4-bis(diphenylphosphino)butane (dppb), and triphenylphosphite]. The hydroformylation did not proceed by the cationic rhodium complex, [Rh(nbd)(dppb)]ClO_4, which is effective in the hydroxy-directed hydrogenation (nbd = norbornadiene).
11. Hydrogenation of 4-*t*-butylcyclohexanone catalyzed by a bulky iridium hydride or rhodium hydride species proceeds *via* equatorial attack (ca. 96%), see *Org. Syn.*; John Wiley & Sons Inc.: New York, 1988; Coll. Vol. 6, p 215
12. The hydroformylation of 4-*t*-butylmethylenecyclohexane using the present catalyst precursor **1** gave rise to a 1 : 1 mixture of *cis*- and *trans*-4-*t*-butylcyclohexylacetaldehyde in quantitative yield.

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