Pergamon

Tetrahedron Letters, Vol. 37, No. 19, pp. 3335-3338, 1996

0040-4039/96 $15.00 + 0.00

S0040-4039(96)00571-0

Catalytic Osmylation of Allenic Compounds. Synthesis of α-Hydroxyketo Amino Acid Precursors.

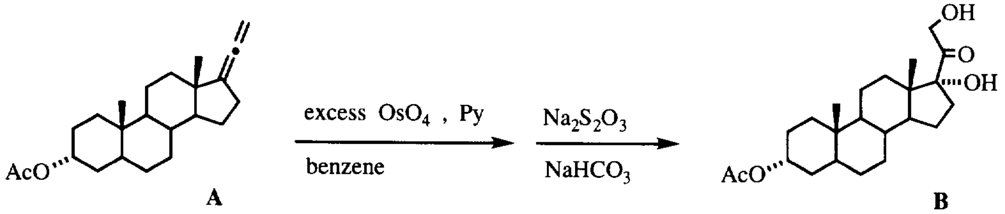
Katerine David[a], Cécile Ariente[a], Alfred Greiner[b], Jacques Goré[a] and Bernard Cazes[a]*

a) Laboratoire de Chimie Organique I, associé au CNRS, Université Claude Bernard
CPE-Lyon, 43 Bd. du 11 Novembre 1918, 69622 Villeurbanne, France.
b) Rhône-Poulenc Agrochimie, 14-20 rue Pierre Baizet, 69009 Lyon, France.

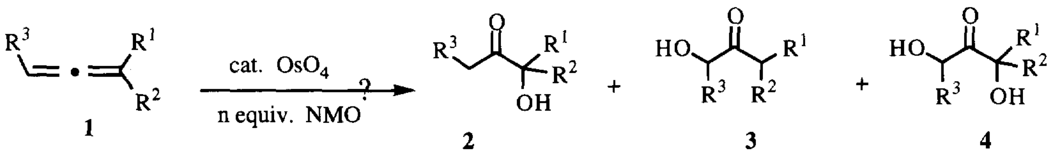
Abstract : Osmium tetroxyde-catalyzed dihydroxylation of allenic compounds in the presence of N-Methylmorpholine Oxide leads to α-ketols. Regioselectivity of this oxidation procedure with allenic α-amino acid precursors is greatly influenced by the nature and the remoteness of the protected amino acid group.

Much work has been devoted to the oxidation of allenic compounds since three decades. Earlier studies have focused on the epoxydation of allenes[1], mainly with peracids, and established that several reactive intermediates such as allene oxides[2,3], cyclopropanones[1c] and spirodioxides[4] were involved. Some of these oxides have been isolated from hindered allenes[3,4], but they usually undergo subsequent transformations (e.g addition of nucleophiles) under the reaction conditions to more stable oxidized products[1c]. Thus some selective reactions were described from functionalyzed allenes such as vinylallenes[5] or allenic alcohols[6] which respectively led to cyclopentenones and oxygen heterocycles after oxidative cyclisation. Among the other oxidants[7] tested are Payne reagent[6], H_2O_2 in the presence of catalytic amount of transition metals[6b], thallium triacetate[8] and [(diacetoxy)iodo]benzene[9] ; more recently J.K. Crandall's group reinvestigated these oxidations using dimethyldioxirane[10].

To our knowledge only one report[11] described the stoichiometric osmium tetroxyde-mediated oxidation of an allenic compound, the steroid **A** , to a α,α'-dihydroxyketo compounds **B** (53%) as shown below.



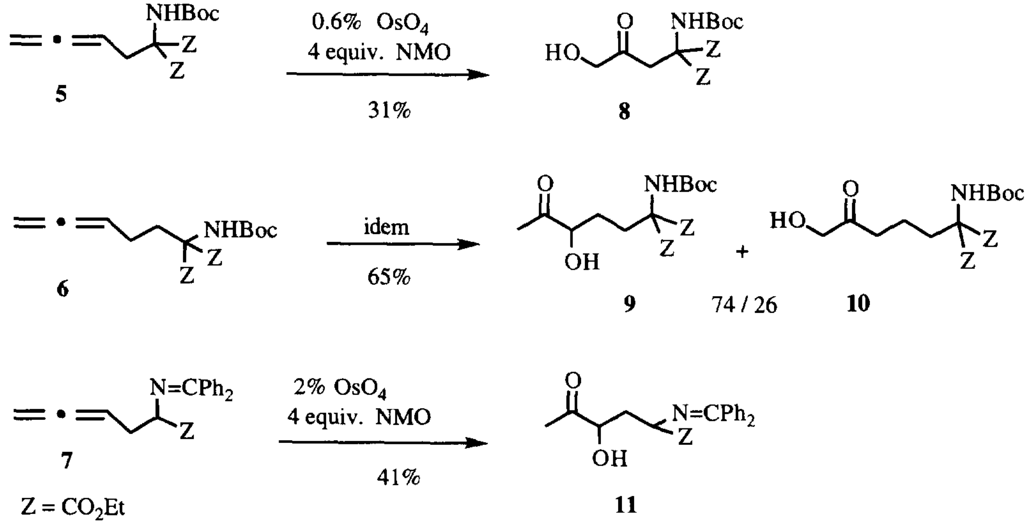
As part of a program directed towards the synthesis of α-hydroxyketo amino acids through the selective oxidation of unsaturated aminoacid precursors[12], we report herein on the osmium tetroxide-catalyzed dihydroxylation of allenic compounds which could formally lead to α-hydroxy keto **2**/**3** and/or α,α'-dihydroxyketo compounds **4**.



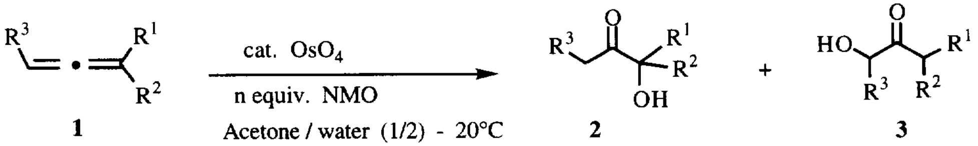
Preliminary experiments were conducted with a model monosubstituted allene, 1,2-decadiene **1a**, (see Table). Osmylation under the classical procedure for dihydroxylation of olefines[13] [0.2% OsO_4, 1.1 equivalent of N-Methylmorpholine Oxide (NMO) in acetone/water (1/2) at room temperature] led to a mixture of regiomers **2a** and **3a** (**2a**/**3a** = 72/28) with a 43% yield (run 1). Yield was improved[14] by using 4 equivalents of the oxidant NMO and a larger amount 1% of osmium tetroxyde (run 2,3 ; compare also runs 5/6 and 7/8 with allenes **1b**-**c**). However increasing the catalyst amount to 10% seemed disadvantageous (run 4) ; over oxidation to dihydroketone **4a** could not be detected. Regioselectivity was not dramatically changed by these modifications.

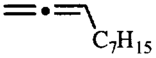
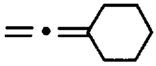
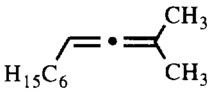
Conversely, substitution of the allenic unit by an aromatic ring as with **1b** directed the oxidation to the substituted terminus carbon (run 5,6). Dihydroxylations of allene **1c** were also totally regioselective and led to the tertiary α-ketol **2c**, demonstrating that the more electron-rich unsaturation is more easily oxidized (runs 7-9). Attempt to produce dihydroxyketone **4c** under stoichiometric conditions (run 9) did not succeed and furnished only 20% of the α-ketol **2c** ; this shows that the dihydroxylation reported by Crabbé seems specific of a steroidal substrate[11]. Trisubstituted allene **1d** gave a mixture of the two regiomers **2d**/**3d** in a nearly equal amount (run 10).

We then studied the dihydroxylation of the following allenic amino acid precursors **5**-**7**[15]. N-Boc-aminomalonate **5** led unexpectedly to the unique α-ketol **8** while its homologue **6** gave the two regiomers **9** and **10** (**9**/**10** = 74/26). This seems to prove that the bulkyness of the aminomalonate group in compound **5** inhibites the oxidation of the closest (and yet the most electronic-rich) allenic double bond. Allenic Schiff base **7** on the contrary gave only the secondary α-ketol **11**.



Table



run	Allene **1**	cat. OsO4	NMO n equiv.	Ratio **2/3***	Yield % **2** + **3**
1		0.2%	1.1 eq.	72 / 28	43%
2	**1a**	0.2%	4 eq.	77 /23	58%
3	($R^1 = C_7H_{15}$)	1%	4 eq.	76 /24	60%
4		10%	1.1 eq.	83 /17	31%
5		0.2%	4 eq.	100 / 0	30%
6	**1b** (R^1 = Ph)	1%	4 eq.	100 / 0	35%
7		0.2%	4 eq.	100 / 0	40%
8		1%	4 eq.	100 / 0	48%
9 **	**1c**	100%	0 eq.	100 / 0	20%
10	 **1d**	1%	4 eq.	56 / 44	71%

* Ratio based on isolated regiomers, separated through flash-chromatography.

** Stoichiometric reaction carried out in benzene in the presence of 2 equivalents of pyridine.

In summary, we have shown that the osmium tetroxyde-catalyzed dihydroxylation of allenic compounds leads to α-ketols, the regioselectivity of the process depending mainly on the substitution pattern and the functionality of the substituents[16]. This reaction can be used for the regioselective synthesis of α-ketol amino acids.

Acknowledgments : One of us (K.D.) gratefully thanks "Centre National de la Recherche Scientifique" (CNRS) and Rhône-Poulenc Agrochimie for a fellowship. This study has been conducted under the BIOAVENIR program financed by Rhône-Poulenc with the contribution of the "Ministère de la Recherche et de l'Espace" and the "Ministère de l'Industrie et du Commerce Extérieur".

References and notes :

1. a) Crandall, J.K. ; Machleder, W.H. *Tetrahedron Lett.* **1966**, 6037-6040.
   b) Crandall, J.K. ; Machleder, W.H. *J. Am. Chem. Soc.* **1968**, *90*, 7292-7296.
   c) Crandall, J.K. ; Machleder, W.H. ; Sojka, S.A. *J. Org. Chem.* **1973**, *38*, 1149-1152.
2. Chan, T.H. ; Ong, B.S. *J. Org. Chem.* **1978**, *43*, 2994-3002 and *Tetrahedron* **1980**, *36*, 3269-2289 and references therein.
3. a) Camp, R.L. ; Greene, F.D. *J. Am. Chem. Soc.* **1968**, *90*, 7349.
   b) Crandall, J.K. ; Machleder, W.H. *J. Heterocyclic. Chem.* **1969**, *6*, 777.
4. Crandall, J.K. ; Conover, W.W. ; Komin, J.B. ; Machleder, W.H. *J. Org. Chem.* **1974**, *39*, 1723-1725.
5. Grimaldi, J. ; Bertrand, M. *Bull. Soc. Chim. Fr.* **1971**, 957-962.
6. a) Bertrand, M. ; Dulcère, J.P. ; Gil, G. ; Grimaldi, J. ; Sylvestre-Penthet, P. *Tetrahedron Lett.* **1976**, 3305-3308.
   b) Doutheau, A. ; Goré, J. ; Diab, J. *Tetrahedron* **1985**, *41*, 329-338 and references therein.
7. For a review, see : Smadja, W. *Chem. Rev.* **1983**, *83*, 263-320.
8. Baudouy, R. ; Delbecq, F. ; Goré, J. *Tetrahedron* **1980**, *36*, 189-195.
9. Moriarty, R.M. ; Hopkins, T.E. ; Waid, R.K. ; Vaid, B.K. ; Levy, S.G. *Synthesis* **1992**, 847-849.
10. a) Crandall, J.K. ; Batal, D.J. *J. Org. Chem.* **1988**, *53*, 1340-1341.
    b) Crandall, J.K. ; Batal, D.J. ; Lin, F. ; Reix, T. ; Nadol, G.S. ; Ng, R.A. *Tetrahedron* **1992**, *48*, 1427-1448.
11. Biollaz, M. ; Haefliger, W. ; Velarde, E. ; Crabbé, P. ; Fried, J.H. *J. Chem. Soc., Chem. Comm.* **1971**, 1322-1323.
12. David, K. ; Greiner, A. ; Goré, J. ; Cazes, B. previous communication in this issue.
13. Van Rheenen, V. ; Cha, D.Y. ; Hartley, W.M. *Org. Synth.* **1988**, *Vol. 6* , 342-348.
14. **Typical experimental procedure** is as follows (run 8) : 1-acetylcyclohexanol **2c**.
    To a solution of allene **1c** (1 mmol) in an acetone/water (1/2) mixture (3 mL) was added a 2.5% solution of osmium tetroxyde in tertiobutanol (132 µL, 0.01 mmol) and N-methylmorpholine oxide (4 mmol). After two days, acetone is evaporated under vacuum and the aqueous phase was extracted with CH_2Cl_2 (5x5 mL). The combined extracts were dried over $MgSO_4$. After concentration, flash-chromatography on a silica column (Petroleum Ether/AcOEt = 75/25) afforded α-ketol **2c** (48%). ^1H NMR (200 MHz, $CDCl_3$), δ ppm : 0.88-1.79 (10H, m, $5xCH_2$) ; 2.25 (3H, s, $CO\text{-}CH_3$) ; 3.62 (1H, broad s, OH).
15. Precursors **5-7** were obtained via the alkylation of the anions of diethyl N-Boc-aminomalonate and the Schiff base of methylglycinate with α or β-allenic derivatives ; see : Cazes, B. ; Djahanbini, D. ; Goré, J. ; Genêt, J.P. ; Gaudin, J.M. *Synthesis*, **1988**, 983-985.
16. A recent work has described the regioselective oxidation of allenes with hydrogen peroxide catalyzed by cetylpyridinium peroxotungstophosphate : Sakaguchi, S. ; Watase, S. ; Katayama, Y. ; Sakata, Y. ; Nishiyama, Y. ; Ishii,Y. *J. Org. Chem.* **1994**, *59*, 5681-5686.

(*Received in France* 30 *January* 1996; *accepted* 21 *March* 1996)