Tetrahedron Letters Vol. 21, pp 1657 - 1660
0040-4039/80/0422-1657$02.00/0

SELECTIVE OXIDATION WITH t-BUTYL HYDROPEROXIDE AND ALUMINIUM REAGENTS

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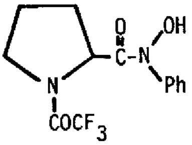
Abstract Stereoselective epoxidation of allylic alcohols is achieved with organoaluminium peroxides. Transformation of secondary alcohols to ketones with same reagents is also disclosed.

Trialkylaluminium compounds interact energetically with alkyl hydroperoxides to form organoaluminium peroxides.[1] The utility of these products as an oxidizing reagent, however, has been limited[2] because of their instability. They can react with the trialkylaluminium compounds initially used or undergo intramolecular rearrangement.[3] Here we wish to report highly stereoselective epoxidation of allylic alcohols as well as oxidation of secondary alcohols to ketones by means of ^{t}BuOOH and (^{t}BuO)$_3$Al or Me$_3$Al.

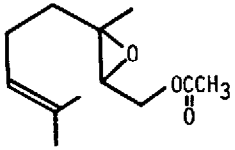
A solution of geraniol (0.31 g, 2.0 mmol) and (^{t}BuO)$_3$Al (0.74 g, 3.0 mmol)[4] in benzene (10 ml) was treated with ^{t}BuOOH[5] (0.44 g, 4.0 mmol) at 5°C and the mixture was kept there for 3.5 h. Acetylation (Ac$_2$O and C$_5$H$_5$N) and workup gave 2,3-epoxygeranyl acetate in 83% yield. The isomer, 6,7-epoxygeranyl acetate, was not detected. Other data are summarized in Table 1 together with the recorded selectivity of Sharpless' VO(acac)$_2$-^{t}BuOOH oxidation for comparison.[6]

The difference between (^{t}BuO)$_3$Al/^{t}BuOOH and VO(acac)$_2$/^{t}BuOOH system is clearly shown by runs 2, 4, and 8. Aluminium system converted (E)-allylic alcohols predominantly into *threo* products which are less favored products in vanadium case. The selective epoxidation of allylic alcohols has often been the key step in synthetic sequences of naturally occurring substances.[7]

Asymmetric epoxidation with chiral ligand I[8] gave optically active II (34% e.e.)[9] and III (38% e.e.).[10] These e.e. values are similar to those of hitherto examined transition metal-catalyzed epoxidation.[11]



I



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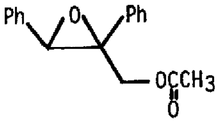
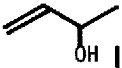
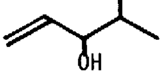
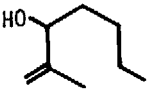
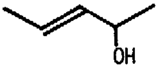
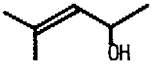
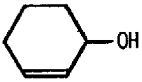
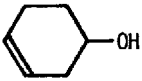


III

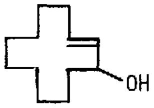
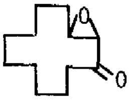
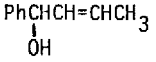
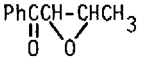
Table 1 Epoxidation of Olefinic Alcohols[a]

Run	Alcohol	Reaction Condition		Yield[b]	Product		VO(acac)$_2$-^{t}BuOOH[d]	
					threo[c] (*trans*)	*erythro*[c] (*cis*)	*threo* (*trans*)	*erythro* (*cis*)
		°C	h	%	%	%	%	%
1		25	5	70	42	58	20	80
2		25	4	78	71	29	15	85
3		25	6	<u>80</u>	13	87	2	98
4		5	6	78	64	36	29	71
5		5	4	80	>99.5	<0 5	86	14
6		5	3	72	<0.5	>99.5	2	98
7		5	3	82	<0 5	>99.5	2	98
8		5	10	<u>80</u>	83	17	29	71

[a] All reactions were performed on a 2 mmol scale [b] Isolated yields are underlined, all others are by glc relative to internal standard. Epoxy alcohols were acetylated *in situ* prior to determination of yields in run 5, 6, and 7 [c] The resulting mixtures of epoxy alcohols, epoxy acetates, or epoxy alcohol trimethylsilyl ethers were analyzed by glc on 2 m columns packed with 3% silicon OV-17 or 10% PEG 20M [d] Cited from ref 6.

The present system has found another application to the oxidation of secondary alcohols[12] into ketones in excellent yields as shown in Table 2. Certain allylic secondary alcohols produced epoxy ketones in one pot (run 5 and 6) Meanwhile, primary alcohols, such as 1-dodecanol reacted much more slowly and after prolonged period (2 days) gave a complex mixture which contained dodecanal (13% yield) and 1-dodecanol (54% recovery) Mildness of the condition and the tolerance of many functional groups[13] characterize the present method, which is illustrated as follows.

Table 2 Oxidation of Secondary Alcohols[a]

Run	Alcohol	Condition (°C)	(h)	Product[b]	Yield[c] (%)
1	$\mathrm{PhCH(OH)CH_3}$	25	6	$\mathrm{PhCOCH_3}$	90
2	cyclododecanol	25	18	cyclododecanone	85
3	2-octanol	25	12	2-octanone	(100)
4	4-t-butylcyclohexanol	25	15	4-t-butylcyclohexanone	85
5		80[d]	6		47
6	 $\mathrm{Ph\underset{OH}{C}HCH{=}CHCH_3}$	80[d]	9		48

[a] All reactions were performed on a 2 mmol scale. [b] Satisfactory spectral data have been obtained [c] Except the case of 2-octanol where yield was determined by glc, all yields were for isolated pure substances, and for $(^t\mathrm{BuO})_3\mathrm{Al}$ (3.0 mmol)-^{t}BuOOH (6.0 mmol) system $\mathrm{Me_3Al}$-^{t}BuOOH system also examined for the entire compounds in Table and found to give almost same yields of the corresponding products [d] $(^t\mathrm{BuO})_3\mathrm{Al}$ (5.0 mmol) and ^{t}BuOOH (8.0 mmol) were used.

To a stirred solution of $(^t\mathrm{BuO})_3\mathrm{Al}$ (0.74 g, 3.0 mmol)[4] and 1-phenylethanol (0.24 g, 2.0 mmol) in benzene (10 ml) was added at room temperature a solution of ^{t}BuOOH (0.44 g, 4.0 mmol) in benzene (2.0 ml) under argon The stirring was continued for 6 h and ether (10 ml) was added The organic layer was washed with 1N hydrochloric acid, $\mathrm{NaHSO_3}$, $\mathrm{NaHCO_3}$, and brine Removal of dried ($\mathrm{Na_2SO_4}$) solvents produced an oil which was purified by column chromatography on silica gel to afford acetophenone (0.22 g, 90% yield) as a colorless liquid.[14,15]

References and Notes

1. G A Razuvaev, V A Shushunov, V. A Dodonov, T G Brilkina, in "Organic Peroxides," Vol 3, D. Swern, Ed , Wiley-Interscience, New York, 1972, p 141, T Mole, E A Jeffery, "Organoaluminium Compounds," Elsevier, Amsterdam, 1972, p 205
2. A G. Davies, C. D. Hall, *J. Chem. Soc.*, 1192 (1963)
3. Y N Anisimov, S S. Ivanchev, *Zh. Obshch. Khim* , 41, 2248 (1971)
4. $\mathrm{Me_3Al}$ was effective as $(^t\mathrm{BuO})_3\mathrm{Al}$ to give similar yields.
5 ^{t}BuOOH was purchased from Nakarai (active oxygen 82%) and used without further purification
6. K. B Sharpless, R C. Michaelson, *J. Am Chem. Soc.*, 95, 6136 (1973), T Itoh, K Jitsukawa, K. Kaneda, S. Teranishi, *ibid* , 101, 159 (1979), E. D Mihelich, *Tetrahedron Lett.*, 4729 (1979), B. E. Rossiter, T R. Verhoeven, K. B. Sharpless, *ibid.*, 4733 (1979)
7. S Danishefsky, M. Hirama, K Gombatz, T Harayama, E Berman, P. Schuda, *J Am. Chem Soc.*, 100, 6536 (1978), T Nakata, G Schmid, B Vranesic, M. Okigawa, T Smith-Palmer, Y. Kishi, *ibid* , 100, 2933 (1978), S Tanaka, H. Yamamoto, H. Nozaki, K. B Sharpless, R C.

Michaelson, J D. Cutting, *ibid.*, 96, 5254 (1974)

8 Prepared by the acylation of phenylhydroxyl amine with N-trifluoroacetyl-(S)-prolyl chlorid (W E. Pereira, B Halpern, *Aust J Chem* , 25, 667 (1972)) $[\alpha]_D^{25}$ -61 3° (c 1 5, acetone) K B Sharpless, *Aldrichimica Acta*, 12, issue 4 (1979)

9 Trimethylaluminium (1 0 M solution in hexane, 3.0 ml, 3 0 mmol) was treated with I (3 6 mmol) in benzene and the solution was stirred for 1 h at room temperature Then, geraniol (2 0 mmol) and ^{t}BuOOH (4.0 mmol) were added and the resulting mixture was heated to reflux for an additional 3 h Acetylation and purification of the product gave II (0.31 g, 74% yield) $[\alpha]_D^{25}$ -8.6° (c 1 5, acetone).

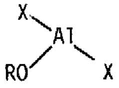
10 III $[\alpha]_D^{25}$ -16.7° (c 0.6, CCl_4). Enantiomeric excess was also checked by Eu shift reagent for II and III.

11 S. Yamada, T Mashiko, S Terashima, *J Am. Chem. Soc.*, 99, 1988 (1977) R C Michaelson R E Palermo, K. B. Sharpless, *ibid.*, 99, 1990 (1977)

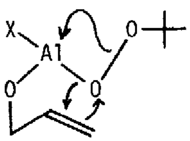
12 Oppenauer oxidation C Djerassi, *Org Reactions*, 6, 207 (1951) Al_2O_3/Cl_3CCHO G H Posner, R B Perfetti, A W Runquist, *Tetrahedron Lett.*, 3499 (1976)

13. Under the conditions described for the oxidation of secondary alcohols, 1-iodododecane, methyl dodecanoate, phenylacetylene, anisole, and dodecanal diethylene acetal were recovered in 95, 96, 98, 98, and 86% yields respectively

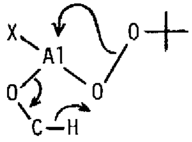
14 The observed reactions could be rationalized as follows The addition of the substrate alcohols (ROH) to aluminium reagents causes the exchange between alcohol and ^{t}BuOH or the evolution of methane gas to provide the products (A) Successive addition of ^{t}BuOOH affords intermediates B or C in which the peroxide bond is polarized by a three-centered interaction with an empty coordination site on Al. The O-O bond is cleaved by π-electrons of the suitably situated double bond (for the epoxidation of allylic alcohols) or by hydride up-take (for the oxidation of secondary alcohols) to afford the corresponding products



(A)



(B)



(C)

X ^{t}BuO-, or Me

15 Financial support by the Ministry of Education, Science, and Culture, Japanese Government (Grant-in-Aid #403022 and 475651), is acknowledged

(Received in Japan 28 January 1980)