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Regio- and Stereo-selective Oxidation of gem-Dimethyl Olefins via [2,3]-Sigmatropic Rearrangement of Allyl Amine Oxides

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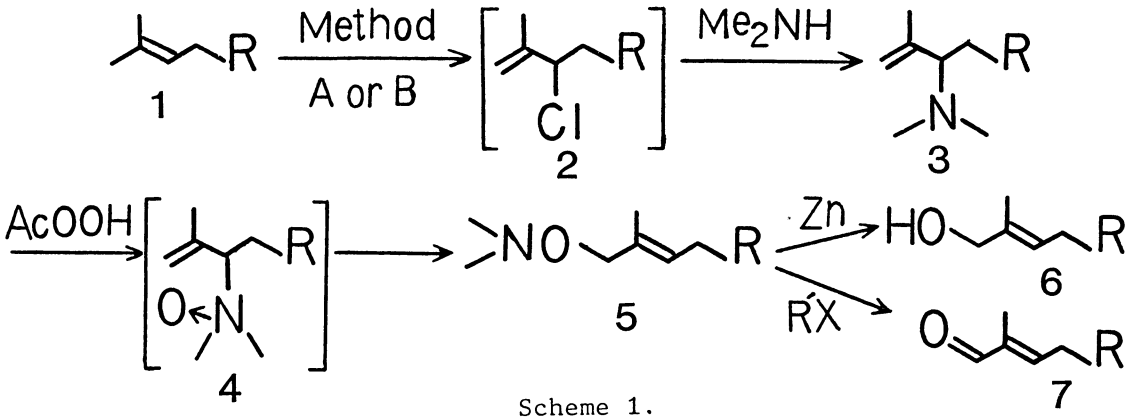
Highly regio- and stereo-selective oxidation sequences are described for the efficient conversion of the gem-dimethyl olefin terminus of acyclic terpenes to terminal trans-allylic alcohols and trans-α,β-unsaturated aldehydes.

Allylic oxidations of gem-dimethyl olefins **1** are extremely important for the synthesis of naturally occurring oxygenated isoprenoids. Hence a number of methods have been reported for the synthesis of terminal trans-allylic alcohols and α,β-unsaturated aldehydes.[1] Here, we report facile, regio- and stereo-selective oxidations of gem-dimethyl olefins **1** as shown in Scheme 1.



Scheme 1.

Allyl chlorides **2** were prepared by ene-type chlorination[2] of olefins **1** using calcium hypochlorite.[3] To a stirred mixture of **1** (10 mmol) and calcium hypochlorite (active chlorine 60%; 1.3 g; 11 mmol) in CH_2Cl_2 (100 ml) and water (10 ml) were added slowly pieces of dry ice at 10 °C. The mixture was filtered and extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude chloride **2** was stirred in 50% aq. dimethylamine (50 ml) and ethanol (17 ml) at room temperature for 3-5 d. The reaction mixture was evaporated in vacuo and the residue was extracted with AcOEt. The solvent was evaporated off to give crude product, which was purified by column chromatography on silica gel (elution with 10-50% AcOEt/n-C_6H_{14}) to provide the corresponding allylamine **3** in good yield. In case of the chlorination of geraniol (**1d**) the use of CH_2Cl_2—sat. aq Na_2SO_4 (Method B) as the solvent in stead of CH_2Cl_2-H_2O (Method A) des-

cribed in the original paper[3] led to fewer amount of by-products, hence resulted in higher yield of **3d**.

Subsequent [2,3]-sigmatropic rearrangement[4] was carried out by oxidation of allylamines **3** with peracetic acid followed by heating the crude allylamine oxides **4**. Peracetic acid (40%; 1.0 g; 5.5 mmol) was added dropwise to a mixture of **3** (5.0 mmol) and solid Na_2CO_3 (0.6 g; 5.5 mmol) in CH_2Cl_2 (50 ml) at -50 °C with vigorous stirring. After 30 min the mixture was warmed to room temperature, poured into half-saturated brine and extracted with AcOEt. The combined organic layer was warmed at 40-50 °C for 30 min. The solvent was removed in vacuo, and the residue was chromatographed on silica gel (elution with 5-20% AcOEt/n-C_6H_{14}) to provide trans-allyloxy amines **5**, which was not contaminated by the cis-isomer as evidenced by NMR analysis.

The attempted cleavage of nitrogen-oxygen bond of allyloxy amines **5** by $LiAlH_4$ in refluxing THF (24 h)[5] afforded only a trace of product (as judged by TLC), however, treatment of **5** with excess of zinc dust[6] cleanly afforded terminal trans-allylic alcohols **6**. A mixture of **5** (1.0 mmol) and Zn dust (0.3 g) in AcOH-H_2O (1:1; 6 ml) was stirred vigorously at room temperature for 1-2 d. The mixture was filtered and extracted with Et_2O. The combined organic layer was washed with saturated aqueous Na_2CO_3 several times, dried over $MgSO_4$, and concentrated to give the pure alcohol **6** in quantitative yield.

Recently A. Liguori and co-workers reported a ring-opening elimination of isoxazolidines to α,β-enones using trimethyl phosphate.[7] Therefore, we investigated the N-alkylation of allyloxy amines **5** and the subsequent Hofmann-like elimination of the resulting quaternary ammonium salts **8** to prepare terminal trans-α,β-unsaturated aldehydes **7**. The results are shown in Table 1.

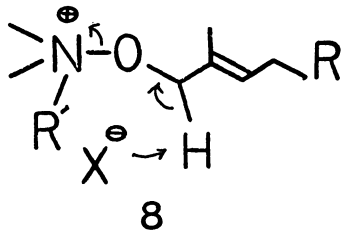


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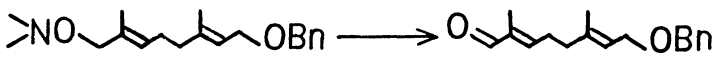
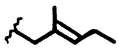
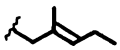
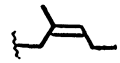
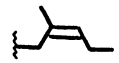
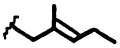
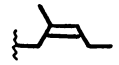
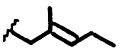
Table 1. Transformation of allyloxy amines **5** to terminal trans-α,β-unsaturated aldehydes **7**

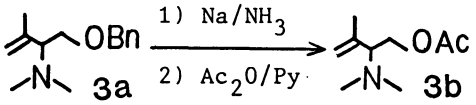


Reagent	Conditions	Yield/%
$(MeO)_3PO$	diglyme, refl.	trace
MeI	$CHCl_3$, refl., 3 h	quant.
CH_2=$CHCH_2Br$	$CHCl_3$, refl., 3 h	trace
	TBAI(5 mol%), $CHCl_3$, refl., 4 h	quant.
$PhCH_2Cl$	TBAI(5 mol%), $CHCl_3$, refl., 4 h	0
	TBAI(5 mol%), DMF, 100 °C , 4 h	70

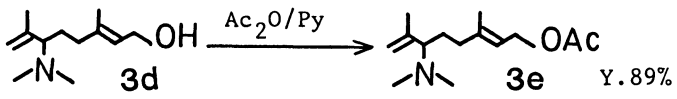
Table 2. Transformation of isoprenoids 1 to allylamines 3, allyloxy amines 5, terminal trans-allylic alcohols 6, and trans-α,β-unsaturated aldehydes 7

Isoprenoid 1 R	Method of Chlorination[a)]	Yield/%[b)] 3	5	6	7
OBn (1a)	A	77	93	quant.	quant.
OAc (1b)	-	--	86[c)]	quant.	quant.
OPh (1c)	A	80	92	quant.	quant.
 OH (1d)	A	57	--	--	--
	B	73			
 OAc (1e)	-	--[d)]	86[e)]	quant.	quant.
 OH (1f)	B	75	--	--	--
 OAc (1g)	-	--[d)]	83[f)]	quant.	quant.
 OBn (1h)	A	70	80	quant.	quant.
 OBn (1i)	A	74	71	quant.	quant.
 SO_2Tol (1j)	A	64[g)]	89	quant.	quant.

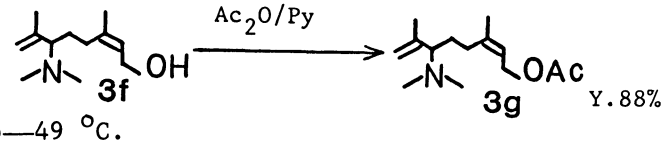
a) Method A: $Ca(OCl)_2$—dry ice, CH_2Cl_2—H_2O, 10 °C. Method B: $Ca(OCl)_2$—dry ice, CH_2Cl_2—H_2O saturated with Na_2SO_4, 10 °C. b) All compounds gave satisfactory spectral data. c) Yield from **3b** which was prepared as follows;



d) When acetates **2e** and **2g** were used in amination, deacetylated products **3d** and **3f**, respectively, were obtained. e) Yield from **3e** which was prepared as follows;



f) Yield from **3g** which was prepared as follows;



g) mp 48.5—49 °C.

Treatment of allyloxy amines 5 with N-alkylating reagents such as iodomethane alone or allyl bromide in the presence of tetrabutylammonium iodide (TBAI) cleanly gave the desired aldehydes 7. A solution of 5 (1.0 mmol) and

iodomethane (3 ml) in $CHCl_3$ (6 ml) was refluxed for 3 h. The mixture was poured into water and extracted with Et_2O. The combined organic layer was washed with water, dried over $MgSO_4$, and concentrated to give the pure aldehyde **7** quantitatively.

The versatility of the method for the terminal allylic oxidations mentioned above was demonstrated on the various isoprenoids **1** and results are summarized in Table 2.

We are currently investigating the application to the synthesis of natural products.

References

1) D. A. Evans, G. C. Andrews, T. T. Fujimoto, and D. Wells, Tetrahedron Lett., 1973, 1385; T. Nakai, H. Shino, and M. Okawara, Chem. Lett., 1975, 249; M. A. Umbreit and K. B. Sharpless, J. Am. Chem. Soc., 99, 5526 (1977); Y. Masaki, K. Hashimoto, and K. Kaji, Tetrahedron 40, 3481 (1975); J. E. McMurry and P. Kocovsky, Tetrahedron Lett., 25, 4187 (1984).
2) A. J. Mura, Jr., D. A. Bennett, and T. Cohen, Tetrahedron Lett., 1975, 4433; B. Chabaud and K. B. Sharpless, J. Org. Chem., 44, 4202 (1979); S. Torii, K. Ueneyama, T. Nakai, and T. Yasuda, Tetrahedron Lett., 22, 2291 (1981); L. W. Hertel and L. A. Paquette, J. Am. Chem. Soc., 101, 7620 (1979); W. Sato, N. Ikeda, and H. Yamamoto, Chem. Lett., 1982, 141; S. Torii, H. Tanaka, N. Tada, S. Nagao, and M. Sasaoka, ibid., 1984, 877.
3) S. G. Hegde, M. K. Vogel, J. Saddler, T. Hrinyo, N. Rockwell, R. Haynes, M. Oliver, and J. Wolinsky, Tetrahedron Lett., 21, 441 (1980).
4) A. C. Cope and P. H. Towle, J. Am. Chem. Soc., 71, 3423 (1949).
5) A. E. Walts and W. R. Roush, Tetrahedron, 41, 3463 (1985).
6) R. Huisgen, R. Grashey, H. Hauck, and H. Seidl, Chem. Ber., 101, 2548 (1968).
7) A. Liguori, G. Sindona, and N. Uccella, Tetrahedron, 40, 1901 (1984).

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