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STEREOSPECIFIC SYNTHESIS OF Z- AND E-1-ALKOXY-1,3-BUTADIENES

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Summary: A stereospecific, highly efficient, generally applicable synthesis of Z- and E-1-alkoxy-1,3-butadienes involving dehydrative decarboxylations of 4,5-unsaturated-2-alkoxy-3-hydroxy-carboxylic acids is described.

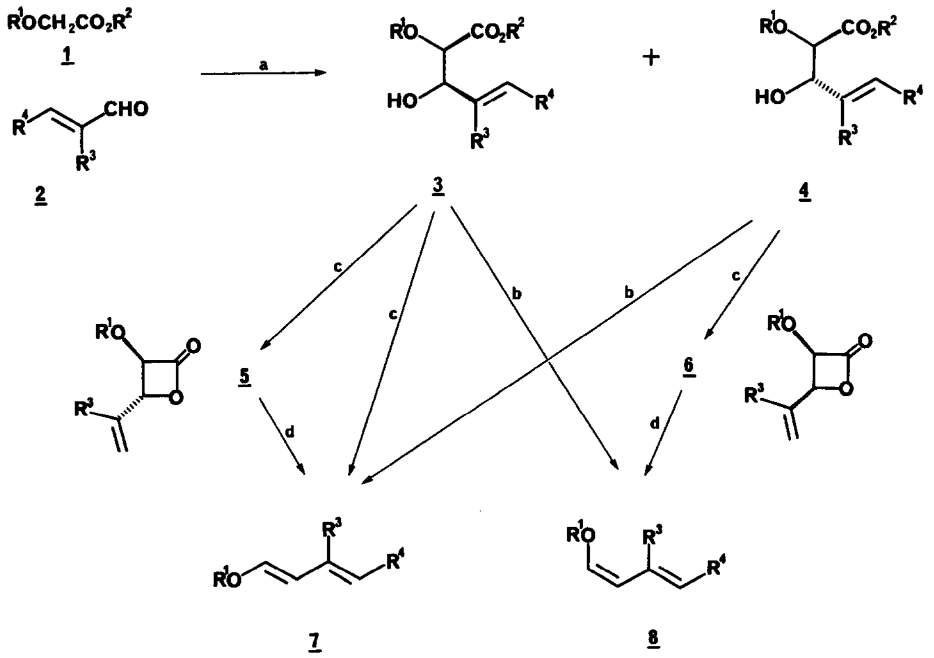
The Diels-Alder reaction of substituted 1-alkoxy-1,3-dienes[1] has been extensively employed in the synthesis of a wide range of natural products, most notably in the synthesis of polycyclic quinones[2], such as daunomycinones, and carbohydrates[3]. These dienes are usually obtained either by pyrolysis of the corresponding β-alkoxy-acetal[4] or by Wittig reaction of unsaturated carbonyls with alkoxy-phosphoranes[5]. In addition, in recent years several more elaborate syntheses of 1-alkoxy-1,3-butadienes have been developed[6]. However, it should be noted that all of these methods suffer from a lack of stereochemical control at the oxygenated double bond, providing usually inseparable mixtures of Z- and E-dienes in varying ratios. This limits considerably the scope of the Diels-Alder and related cycloaddition reactions in the cases where the stereochemistry of the resulting adducts is of crucial importance[7]. We wish to report that the highly efficient, stereospecific synthesis of Z- or E-1-alkoxy-1,3-butadienes can be achieved by application of two dehydrative decarboxylation methods[8] to the readily separable erythro-and threo-4,5-unsaturated-2-alkoxy-3-hydroxycarboxylic acids, 3 and 4, respectively[9].

The intermediate hydroxy acids 3 and 4 were obtained by alkylation of alkoxy-acetic acids 1 (R_2= H) or their esters 1 (R_2= Et) with unsaturated aldehydes 2 (Table I)[10]. In all cases, the erythro-isomer 3 was the major diastereomer, with the ratio varying from 1.25 to 2.5 and both diastereomers, 3 and 4, were found to be easily separable. The erythro-hydroxy acids 3 (R_2= H) were conveniently obtained pure after a couple of recrystallizations of the mixtures of 3 and 4 (R_2= H) from hexanes-ether. Alternatively, the hydroxy esters 3 and 4 (R_2= Me,Et) (obtained by either esterification of the hydroxy acids with diazomethane or alkylation of ethyl alkoxy-acetates) could be separated by flash chromatography or by preparative HPLC (Waters, Prep 500) and quantitatively hydrolyzed to the hydroxy acids with lithium hydroxide in methanol-water without epimerization. The assignment of the stereochemistry of 3 and 4 was made through stereospecific conversion of the hydroxy acids to the 1-alkoxy-1,3-butadienes 7 and 8 by using two different methods as illustrated in Scheme I.

Anti dehydrative decarboxylation of the hydroxy acids was effected in high yields (>80%) with dimethylformamide dineopentylacetal in methylene chloride after 20 min at 0°C (Table II)[11]; the work-up of the reaction was done by simple evaporation of the solvent followed by chromatographic purification of the product on silica gel. The use of diethylazodicarboxylate-triphenylphosphine[12], a more common reagent for this transformation, resulted in decomposition of the sensitive dienol ether products. The configurations of 7 and 8 were assigned using ^{1}H NMR spectroscopy; the *E*- isomers showed a $^{3}J_{1,2}$ of 11.1-12.8 Hz, in contrast with 6.0-7.1 Hz for the *Z*- isomers.

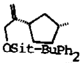
Alternatively, syn dehydrative decarboxylation was realized via lactonization; thus, treatment of the hydroxy acids with benzenesulfonyl chloride at 0°C in dry pyridine[13] afforded smoothly the corresponding β-lactones 5 and 6 (Table II)[13]. Interestingly, the lactone 5b, produced from 3b, was found to be thermally labile even at 0°C, undergoing spontaneous decarboxylation under the reaction conditions to give the crystalline *E*-diene 7b[14]. The decarboxylation of the β-lactones was found to be very sensitive to the solvent used[15]. When the reaction was done neat or in a decalin solution, the thermolysis took place at 155-160°C. However, the temperature of the reaction was lower when using more polar solvents, such as DMF (100°C, 2h) or DMSO (85°C, 2h)[16]; under these conditions, the decarboxylation is stereospecific and the yields of the dienes are almost quantitative.

In this way, by using complementary syn and anti dehydrative decarboxylation methods of the pure 4,5-unsaturated-2-alkoxy-3-hydroxycarboxylic acids 3 and 4, both *E*- and *Z*-1-alkoxy-1,3-butadienes 7 and 8 were obtained in good yields with a stereoisomeric purity over 98%.



Scheme I Conditions : (a) 1, LDA (2.5 equiv), THF, -78°C, 30 min; 2 (2.5 equiv), -78°C, 1h. (b) DMF dineopentyl acetal (5.5 equiv), dichloromethane, 0°C, 20 min. (c) PhSO$_2$Cl (5 equiv), pyridine, 0°C, 1.5 h. (d) DMF, 100°C, 2h.

Table I : Alkylation of α-alkoxy enolates with unsaturated aldehydes 2

Compounds	R^1	R^2	R^3	R^4	Ratio of 3:4 (% yield)	mp (°C) 3	mp (°C) 4
a		H	CH_3	H	2.5:1 (85)	72-73°	*
b	Ph	H	H	Ph	2.1:1 (41)	129-130°	*
c	Ph	H	CH_3	H	1.6:1 (62)	105-106°	93-94°
d	$PhCH_2$	H	H	H	1.3:1 (69)	76-78°	*
e[9]		Et	CH_3	H	2.4:1 (87)	*	*

* : these compounds could not be crystallized

Table II : Synthesis of β-lactones 5, 6 and 1-alkoxy-1,3-butadienes 7, 8[ψ]

trans-lactone	% yield from 3	E-diene	% yield from 4 reaction b	% yield from 5 reaction d
5a	86	7a	84[θ]	88
		7b	87[θ]	41
5c	71	7c	93	93
5d	68	7d	82	98
5e	72	7e	86	100

cis-lactone	% yield from 4	Z-diene	% yield from 3 reaction b	% yield from 6 reaction d
6a	64[θ]	8a	86	100
		8b	88	
6c	74	8c	81	93
6d	62	8d	80	89
6e	77	8e	91	95

ψ : yields are given for isolated compounds purified by flash chromatography

θ : estimated based on the diastereomeric purity of the starting materials

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References and notes

1. For a review, see: a) Petrzilca, M.; Grayson, J. I. Synthesis **1981**, 753. See also: b) Gouesnard, J. P. Tetrahedron **1978**, 34, 2083. c) Broekhuis, A. A.; Scheeren, J. W.; Nivard, R. J. F. Recl. Trav. Chim. Pays-Bas **1980**, 99, 6.

2. a) Kelly, T. R.; Gillard, J. W.; Goerner, R. N.; Lyding, J. M. J. Am. Chem. Soc. **1977**, 99, 5513. b) Kelly, T. R.; Montury, M. Tetrahedron Lett. **1978**, 4309, 4311. c) Fariña, F.; Prados, P. Tetrahedron Lett. **1979**, 477. d) Carretero, J. C.; Cuevas, J. C.; Echevarren, A.; Fariña, F.; Prados, P. J. Chem. Research **1984**, (S) 6; (M) 0147.

3. a) Schmidt, R. R.; Abele, W. Angew. Chem., Int. Ed. Engl. **1982**, 21, 302. b) Forrest, A. K.; Schmidt, R. R. Tetrahedron Lett. **1984**, 25, 1769.

4. Martin, G. J.; Gouesnard, J. P. Bull. Soc. Chim. Fr. **1969**, 2501.

5. a) Kelly, T. R. Tetrahedron Lett. **1978**, 1387. b) Mandai, T.; Osaka, K.; Wada, T.; Kawada, M.; Otera, J. Tetrahedron Lett. **1983**, 24, 1171.

6. These include: a) Peterson reaction, Kende, A. S.; Blacklock, T. J. Tetrahedron Lett. **1980**, 3119. b) base-induced ring opening of β,γ-unsaturated cyclic acetals, Steinbeck, K.; Osterwinter, B. Tetrahedron Lett. **1980**, 21, 1515. c) base treatment of α,β-unsaturated-γ-alkoxy bromomethyl sulfones, Block, E.; Aslam, M. J. Am. Chem. Soc. **1983** 105, 6164. d) base treatment of bis-ethers of 2-butene-1,4-diols, Everhardus, R. H.; Peterse, A.; Vermeer, P.; Brandsma, L.; Arens, J. F. Recl. Trav. Chim. Pays-Bas **1974**, 93, 90.

7. For a comparison in reactivities of the Z- and E-1-methoxy-1,3-butadienes, see: a) Rucker, C.; Lang, D.; Sauer, J.; Friege, H.; Sustmann, R. Chem. Ber. **1980**, 113, 1663. For a study of the stereochemistry in the Diels-Alder reactions of isomeric 1,4-dialkoxy-1,3-butadienes, see: b) Hiranuma, H.; Miller, S. I. J. Org. Chem. **1983**, 48, 3096.

8. a) Mulzer, J.; Pointner, A.; Chucholowski, A.; Brüntrup, G. J. Chem. Soc., Chem. Commun. **1979**, 52. b) Caron, G.; Lessard, J. Can. J. Chem. **1973**, 51, 981.

9. One specific application of this approach has been recently reported by us in conjunction with the synthesis of trichothecene-like skeleton: Koreeda, M; Luengo, J. I. J. Org. Chem. **1984**, 49, 2079.

10. a) Mulzer, J.; Segner, J.; Brüntrup, G. Tetrahedron Lett. **1977**, 4651. b) Adam, W.; Fick, H. H. J. Org. Chem. **1978**, 43, 772.

11. a) Ruttimann, A.; Wick, A.; Eschenmoser, A. Helv. Chim. Acta **1975**, 58, 1450. b) Hara, S.; Taguchi, H.; Yamamoto, H.; Nozaki, H. Tetrahedron Lett. **1975**, 1545. c) Mulzer, J.; Kühl, U.; Brüntrup, G. Tetrahedron Lett. **1978**, 2953.

12. Mulzer, J.; Brüntrup, G.; Chucholowski, A. Angew. Chem. Int. Ed. Engl. **1979**, 18, 622.

13. a) Adam, W.; Baeza, J.; Liu, J. C. J. Am. Chem. Soc. **1972**, 94, 2000. b) Adam, W.; Fick, H. H. J. Org. Chem. **1978**, 43, 4574.

14. The assignment of the β-lactones (2-oxetanones) was made based on the difference in ${}^3J_{3,4}$ values exhibited by the cis (6.0 Hz) and trans (3.8 Hz) isomers in their 360 MHz ^{1}H NMR spectra.

15. Mulzer, J.; Zippel, M. Tetrahedron Lett. **1980**, 751.

16. The use of other solvent systems, such as formamide, acetone-water, trifluoroethanol and hexafluoroisopropanol resulted in decomposition of either the starting materials or the products.

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