threo-3-Hydroxycarboxylic Acids as Key Intermediates in a Highly Stereoselective Synthesis of (*Z*)- and (*E*)-Olefins and Enol Ethers

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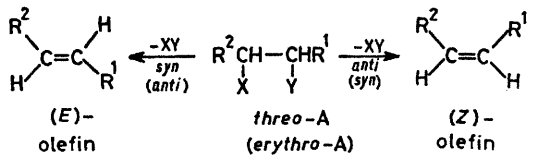
Summary *threo*-3-Hydroxycarboxylic acids, which are stereoselectively obtained from metallated carboxylic acids and aldehydes, are converted into (*Z*)-olefins and enol ethers with the triphenylphosphine–diethyl azodicarboxylate-adduct, whereas the corresponding (*E*)-isomers are prepared *via* the β-lactones.

THE (*Z*)- and the (*E*)-isomer of a particular olefin may be prepared from a common precursor molecule (*threo*- or *erythro*-A) by *syn*- and *anti*-elimination reactions (Scheme 1).



SCHEME 1

Generally, however, it is difficult to obtain the precursor (A) in diastereomerically pure form and to find sufficiently stereoselective elimination reactions. Hence, although being conceptually straightforward, this method has found application in only a few individual cases.[1] We now describe efficient and highly stereoselective procedures for the preparation of (*Z*)- and (*E*)-olefins and enol ethers from *threo*-3-hydroxycarboxylic acids; Scheme 1, X = OH, Y = CO_2H, and XY = $CO_2 + H_2O$ (decarboxylative dehydration).

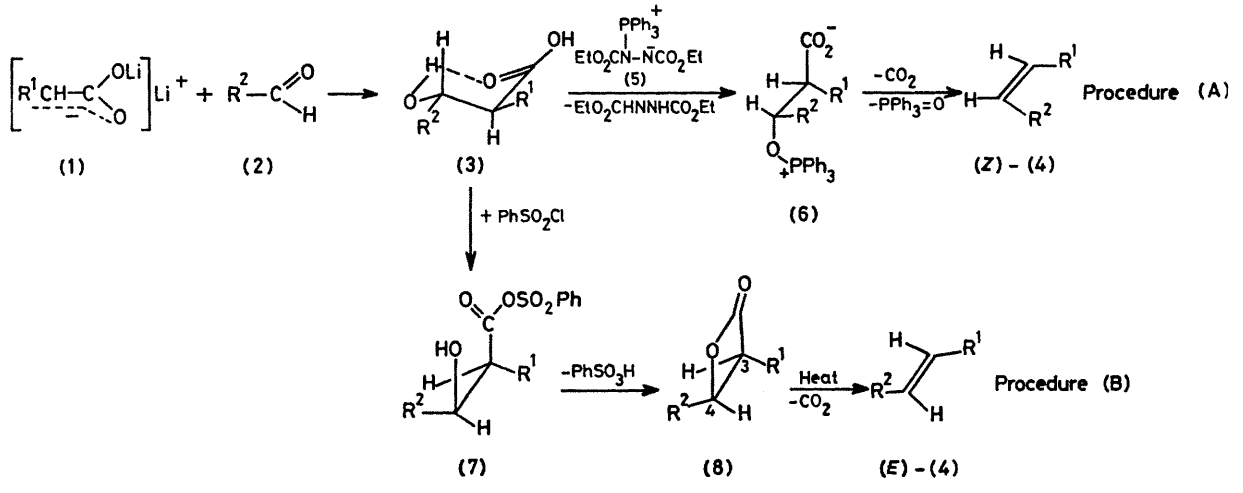
As we reported earlier,[2] the addition of the metallated carboxylic acids (**1**) to the aldehydes (**2**) stereoselectively furnishes *threo*-3-hydroxycarboxylic acids (**3**) in good yields. The diastereomeric purity of (**3**) can be easily increased to >98% (determined by ^{1}H n.m.r. analysis) by recrystallization from chloroform. Scheme 2 and the Table show how the *anti*-elimination (**3**)→(*Z*)-(**4**) is effected by treating (**3**) with the triphenylphosphine–diethyl azodicarboxylate-adduct (**5**)[3] (procedure A), whereas the corresponding *syn*-elimination (**3**)→(*E*)-(**4**) is accomplished *via* the *trans*-β-lactone (**8**) (procedure B).†

TABLE. (*Z*)- and (*E*)-Olefins and enol ethers prepared according to procedures (A) and (B).[a]

			(*E*)/(*Z*)-ratio[b] (% yield) from (**3**)	
R^1	R^2	M.p. of (**3**)/°C	(A)[c]	(B)[d]
Ph	Me	137—138	3:97 (75)	>99:1 (63)
Ph	Et	143—143·5	2:98 (68)	>99:1 (68)
Ph	Pr^n	158—159	3:97 (77)	>99:1 (71)
Ph	Bu^n	117—118	3:97 (70)	>99:1 (65)
Ph	Pr^i	139—140	2:98 (74)	>99:1 (73)
OPh	Et	141—142	<1:99 (65)	>99:1 (63)
OPh	Pr^n	122—122·5	2:98 (82)	>99:1 (78)
OPh	Bu^n	91—92	2:98 (87)	>99:1 (82)
OPh	Pr^i	137—137·5	<1:99 (67)	>99:1 (73)
OPh	Bu^t	164—164·5	<1:99 (32)	>99:1 (85)

[a] All new compounds were fully characterized by ^{1}H n.m.r. and i.r. spectroscopy, and elemental analysis. [b] Determined by capillary chromatography; experimental error *ca.* 1%. [c] Procedure (A): (**3**) + PPh_3 + EtO_2C–N=N–CO_2Et in tetrahydrofuran at 22 °C for 5 min; work up by distillation at 80—120 °C, 10 mmHg (olefins) and 60—100 °C, 0·1 mmHg (enol ethers). [d] Procedure (B): (**3**) → (**8**): (**3**) + $PhSO_2Cl$ in pyridine at 22 °C for 20 h, work up with water–pentane and distillation at 100—140 °C, 0·01 mmHg. (**8**) → (*E*)–(**4**): refluxing dimethylformamide, 2—8 h, work up with water–pentane and distillation at 80—120 °C, 10 mmHg (olefins) and 60—100 °C, 0·1 mmHg (enol ethers).

The opposite stereochemical results of Procedures (A) and (B) respectively may be rationalized by assuming that (**5**) activates (**3**) at its hydroxy-oxygen atom selectively.[4] The resulting zwitterion (**6**) undergoes a Grob-fragmentation which, as usual,[5] proceeds with *anti*-stereochemistry to give (*Z*)-(**4**). By contrast, (**8**) is formed from (**3**) presumably *via* the carboxy-oxygen-activated intermediate (**7**).[6] β-Lactones are known to eliminate CO_2 with retention of configuration.[6,7]



SCHEME 2

† The *trans*-configuration of (**8**) was established by ^{1}H n.m.r. comparison with the corresponding *cis*-β-lactones, which we prepared by an independent route. We always found that $J_{3,4}$(*cis*) = 6·5 and $J_{3,4}$(*trans*) = 4·5 Hz (*cf.* S. Sternhell, *Quart. Rev.*, 1969, **23**, 236). Similarly, δ(3-H, *cis*) > δ(3-H, *trans*) and δ(4-H, *cis*) > δ(4-H, *trans*). The geometry of the olefins and enol ethers unambiguously follows from the coupling constants [$J(Z)$ = 11·5 Hz for olefins and 6 Hz for enol ethers; $J(E)$ = 16 Hz (olefins) and 12 Hz (enol ethers)] and the chemical shifts (C. Pascual, J. Meier, and W. Simon, *Helv. Chim. Acta*, 1966, **49**, 164) of the olefinic protons in the ^{1}H n.m.r. spectra.

In summary, the method provides an olefination sequence [(**1**) + (**2**)→(**3**)→(**4**)] which, by an appropriate choice of reagents, may be directed to give either the (*Z*)- or the (*E*)-isomer in practically pure form and acceptable yield. This result is particularly valuable in the case of the enol ethers, because stereocontrolled (C, C)-connective syntheses are very rare for this class of compounds.[8]

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[1] For example, β-hydroxyselenides, A. M. Leonard-Coppens and A. Krief, *Tetrahedron Letters*, 1976, 3227; 5-trimethylsilyloctan-4-ol, P. F. Hudrlik and D. Peterson, *J. Amer. Chem. Soc.*, 1975, **97**, 1464; 2,3-dibromo-3-phenylpropanoic acid, S. J. Cristol and W. P. Norris, *J. Amer. Chem. Soc.*, 1953, **75**, 2645; E. Grovenstein and D. E. Lee, *ibid.*, p. 2639.

[2] J. Mulzer, J. Segner, and G. Brüntrup, *Tetrahedron Letters*, 1977, 4651.

[3] J. Mulzer and G. Brüntrup, *Angew. Chem. Internat. Edn.* 1977, **16**, 255; for related applications of (**5**) see F. DiNinno, *J. Amer. Chem. Soc.*, 1978, **100**, 3251 and references therein.

[4] *Cf.* O. Mitsunobu and M. Eguchi, *Bull. Chem. Soc. Japan*, 1971, **44**, 3427; O. Mitsunobu, J. Kimura, and N. Yanagida, *ibid.*, 1977, **49**, 510; T. Kurihara, Y. Nakajima, and O. Mitsunobu, *Tetrahedron Letters*, 1976, 2455; A. K. Bose, B. Lal, W. A. Hoffman, and M. S. Manhas, *ibid.*, 1973, 1619; H. Loibner and E. Zbiral, *Helv. Chim. Acta*, 1976, **59**, 2100; D. Seebach, B. Seuring, H. O. Kalinowski, W. Lubosch, and B. Renger, *Angew. Chem. Internat. Edn.*, 1977, **16**, 264.

[5] C. A. Grob, *Angew. Chem. Internat. Edn.*, 1969, **8**, 535.

[6] W. Adam, J. Baeza, and J.-C. Liu, *J. Amer. Chem. Soc.*, 1972, **94**, 2000; S. Mageswaran and M. U. S. Sultanbawa, *J.C.S. Perkin I*, 1976, 884.

[7] D. S. Noyce and E. H. Banitt, *J. Org. Chem.*, 1966, **31**, 4043.

[8] For a stereocontrolled Horner–Wittig type synthesis of enol ethers see C. Earnshaw, C. J. Wallis, and S. Warren, *J.C.S. Chem. Comm.*, 1977, 314. Stereo-uncontrolled (C, C)-connective enol ether preparations are numerous; for a recent review see G. Hesse in Houben-Weyl, 'Methoden der Organischen Chemie,' Bd. VI/1d, p. 136–179, Georg-Thieme-Verlag, Stuttgart, 1978.