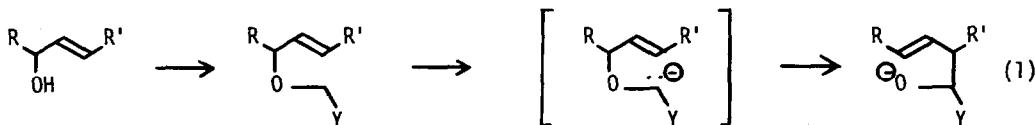


THE [2,3]WITTIG REARRANGEMENT OF 2-ALKENYLOXYACETIC ACIDS AND ITS APPLICATIONS TO THE STEREOCONTROLLED SYNTHESIS OF β,γ -UNSATURATED ALDEHYDES AND CONJUGATED DIENOIC ACIDS¹⁾

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ABSTRACT: Dianions generated from 2-alkenyloxyacetic acids readily undergo the [2,3]sigmatropic rearrangement which can constitute the versatile synthetic sequences for the stereocontrolled synthesis of β,γ -unsaturated aldehydes and conjugated dienoic acids.

Conceptually, the [2,3]sigmatropic rearrangement involving an α -oxycarbanion as the migrating terminus (*i.e.*, the [2,3]Wittig rearrangement) allows the regio- and stereoselective substitution of the hydroxy group of an allylic alcohol with a functionalized carbon moiety (eq 1) which has currently received increasing attention.²⁾

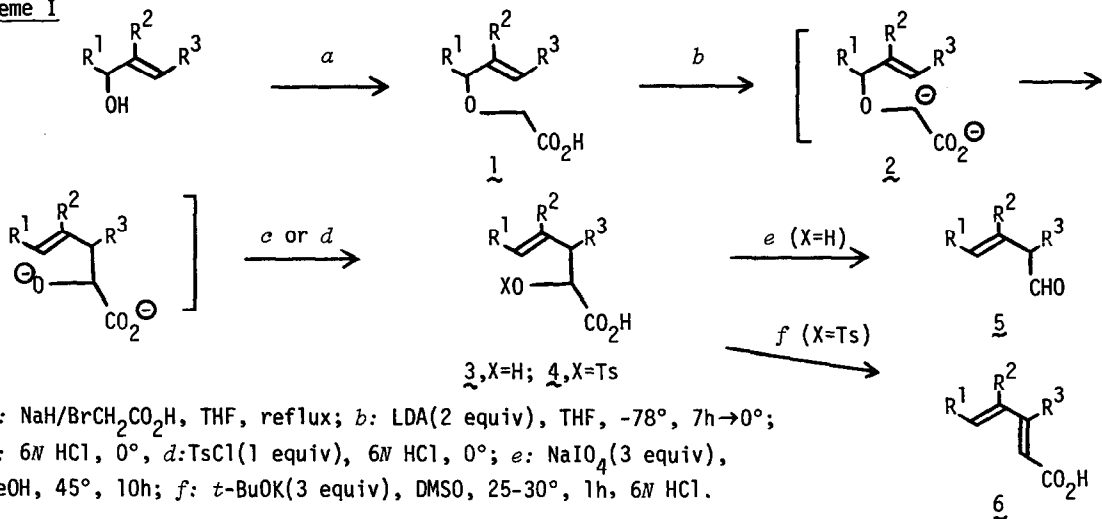


From the standpoint of synthetic utility, however, the anionic [2,3]sigmatropic approach has generally suffered from positional complications in terms of the possibilities for [2,3] *vs.* [1,2]sigmatropic process except for several cases.^{3,4)} As part of our general interest in the development of the synthetic potential of [2,3]sigmatropic rearrangements, we have now examined rearrangements of dianions generated from the 2-alkenyloxyacetic acids (1) readily accessible from allylic alcohols and bromoacetic acids.⁵⁾ In this communication, we wish to report that these dianions (2) undergo exclusively the [2,3]sigmatropic rearrangement which can constitute the versatile synthetic sequences for the stereocontrolled synthesis of β,γ -unsaturated aldehydes (5) and conjugated dienoic acids (6). The overall process is depicted in Scheme I.

First of all, we found that dianions generated *in situ* from 1 with 2 equiv of lithium diisopropylamide (LDA) in THF at -78°C readily underwent rearrangement at that temperature for *ca.* 7h to give exclusively the [2,3]-rearranged products. Subsequent treatment of the resultant mixture with hydrochloric acid and with tosyl chloride afforded the α -hydroxy- (3) and α -tosyl-oxy- γ,δ -unsaturated acids (4), respectively, in high isolated yields (Table 1).

Of particular interest are the following stereochemical outcomes;⁶⁾ (i) the [2,3]Wittig rearrangement of 1 derived from a secondary allylic alcohol resulted exclusive formation of the *E* double bond in the product (entries 1, 2, 6, and 7);⁷⁾ (ii) the rearrangement where the stereochemistry about the newly formed carbon-carbon single bond is present afforded a diastereomeric mixture of the product (entries 3, 4, 8, and 9);⁸⁾ (iii) a high preference for equatorial entry was observed across the convex face of cyclohexylidene ring system (entry 5).⁹⁾

Scheme 1



To illustrate the synthetic potential of this genuine [2,3]Wittig rearrangement, we have first studied the oxidative decarboxylation of the α -hydroxy acids (3) to the β,γ -unsaturated aldehydes (5). In practice, it is very difficult to prepare β,γ -unsaturated aldehydes because they readily isomerize to the more stable α,β -unsaturated isomers under either acidic or basic conditions. In fact, despite numerous reports that *protected* β,γ -unsaturated aldehydes could be prepared cleanly *via* various [2,3]sigmatropic rearrangements,¹⁰⁾ regenerations of the aldehyde function often lead to complete or partial double bond transposition. We found that use of sodium periodate *in methanol*¹¹⁾ as the oxidizing reagent afforded the desired β,γ -unsaturated aldehydes free from its α,β -unsaturated isomer (entries 1 and 2) except for entry 4. Neither conventional procedures using sodium periodate in acetic acid nor lead tetraacetate in benzene gave satisfactory results. It should be noted that the stereochemistry of 3 described above is completely preserved in this subsequent elaboration, thus making the overall reaction process a useful procedure for the stereoselective synthesis of β,γ -unsaturated aldehydes.¹²⁾

To access further the utility of the [2,3]Wittig process described above, we have explored the transformation of the α -tosyloxy acids (4) to the conjugated dienoic acids (6) of which the stereocontrolled synthesis has been the subject of current synthetic studies.¹³⁾ We found that treatment of 4 with potassium *t*-butoxide (3 equiv) in DMSO¹⁴⁾ gave the desired dienoic acids (6) in acceptable yields (entries 6-9). Of great significance is the stereochemical outcome, indicating clearly that this elimination reaction proceeds exclusively in a *trans* fashion. Thus the two olefinic stereochemistries in the dienoic acid can be controlled through the [2,3]Wittig process followed by the stereoselective elimination process, making the overall reaction process a general method of choice for the stereoselective synthesis of (*E,E*)-2,4-alkadienoic acids in which the α,β double bond is disubstituted (entries 6 and 7). Notably, (*E,E*)-2,4-decadienoic acid thus obtained has been utilized as a synthetic precursor of pellitorine, a natural insecticide isolated from *Anacyekus pyrethrum* roots.¹⁵⁾

Table 1

Entry	Acid 1 [Stereochemistry] ^a	Acid 3 or 4 (%Yield) ^b [Stereochemistry] ^e	Aldehyde 5 or Acid 6 (%Yield) ^b [Stereochemistry] ^e
1	R ¹ = <i>n</i> -C ₇ H ₁₅ , R ² =H	(80) [<i>E</i> >95%]	(78) [<i>E</i> >95%]
2	R ¹ = <i>n</i> -C ₅ H ₁₁ , R ² =CH ₃	(74) [<i>E</i> >95%]	(94) [<i>E</i> >95%]
3			
4			
5			
6	R ¹ =CH ₃	(87) [<i>E</i> >95%]	(81) [<i>E,E</i> >95%]
7	R ¹ = <i>n</i> -C ₅ H ₁₁	(64) [<i>E</i> >95%]	(53) [<i>E,E</i> >95%]
8			
9			

^a Refers to the stereochemistry of the allylic alcohol employed. ^b Isolated yield, not optimized. ^c Determined by careful analyses of NMR and IR spectra. The spectral data will be published in a full paper. ^d The diastereomeric ratio was not determined. ^e Refers to the ratio of *threo* vs. *erythro*. The stereochemical assignments were made as reported in the literature: B. B. Snider and J. W. van Straten, *J. Org. Chem.*, **44**, 3567 (1979). ^f The NMR spectrum indicated that the product consisted of a 19 : 81 mixture of the α,β - and β,γ -unsaturated aldehyde. ^g The stereochemical assignment was unequivocally made through spectral comparisons of its carboxylic acid with an authentic sample: cf. T. Nakai and K. Mikami, *Chem. Lett.*, 1979, 1081.

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- 8) For the diastereoselection in related [2,3]sigmatropic rearrangements, see: ref 4a, 4b, and 4c. The diastereoselection in various [2,3]Wittig rearrangements including the present variant will be the subject of a forthcoming paper from our laboratory.
- 9) For other [2,3]sigmatropic variants exhibiting high preferences for equatorial entry in the same ring systems, consult: D. A. Evans, C. L. Sims, and G. C. Andrews, *J. Am. Chem. Soc.*, 99, 5453 (1977). For one exception, see: T. Nakai and K. Mikami, *Chem. Lett.*, 1979, 1081.
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