Influence of the Trimethylsilyl Group on the Diastereoselectivity of an Adjacent Claisen Amide-acetal Rearrangement

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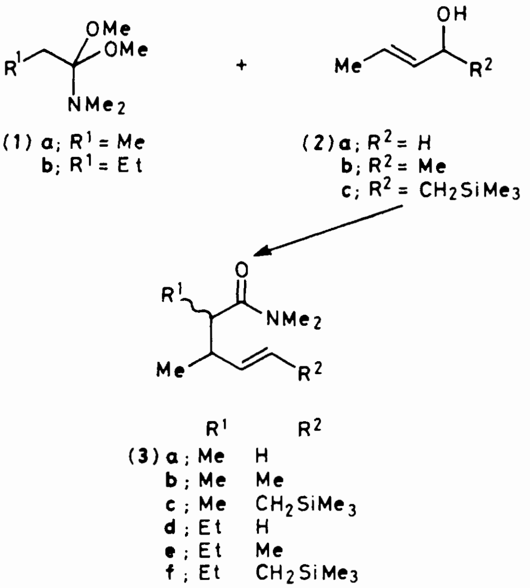
In contrast to their reactions with other (*E*)-allylic alcohols, the amide-acetals (**1a**, **b**) react with (*E*)-1-trimethylsilylpent-3-en-2-ol to give mixtures of product amides in which the *threo*-diastereoisomers marginally predominate.

In 1971 Sucrow reported on the good *erythro*-diastereoselectivity of the Claisen amide-acetal rearrangement of (*E*)-allylic alcohols using 1,1-dimethoxy-1-(dimethylamino)-propane (**1a**) as the amide-acetal component.[1] We now report on the reactions of (**1a**) and the homologous butane (**1b**) with but-2-en-1-ols (**2a**—**c**) which show the particular effects on diastereoselectivity of a trimethylsilyl group vicinal to the pericyclic system.



(1) a; R^1 = Me
b; R^1 = Et

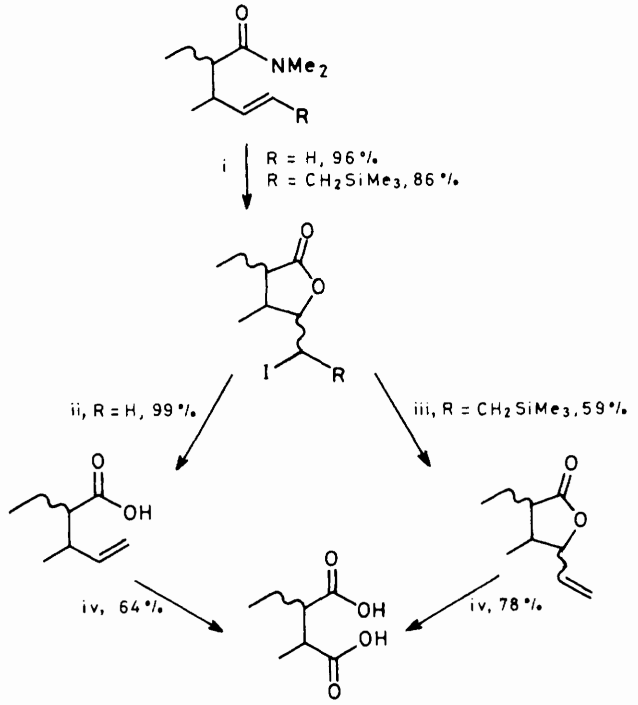
(2) a; R^2 = H
b; R^2 = Me
c; R^2 = CH_2SiMe_3

	R^1	R^2
(3) a	Me	H
b	Me	Me
c	Me	CH_2SiMe_3
d	Et	H
e	Et	Me
f	Et	CH_2SiMe_3

Table 1. Reaction of the amide-acetals (**1a, b**) with the alcohols (**2a—c**) to give the amides (**3a—f**).

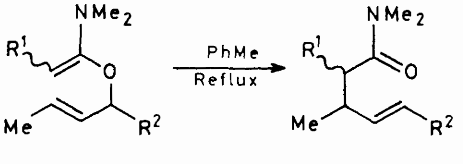
	erythro : *threo*			
Amide	This work	Ref. 1	Reaction time/h	Yield,[a] %
(**3a**)	16 : 1[b]	19 : 1	12	36
(**3b**)	17 : 1	(11.5 : 1)[c]	12	23
(**3c**)	1 : 1.15		3	46[d]
(**3d**)	8 : 1[b]		12	70
(**3e**)	3 : 2		2.5	52
(**3f**)	1 : 1.2		3	55

[a] Isolated yields. [b] Corrected for the content of *Z*-isomer in starting alcohol. [c] Alcohol was (*E*)-EtCH=CH·CH(OH)Et. [d] By ^{1}H n.m.r.



(4)

Scheme 1. *Reagents:* i, I_2, aqueous tetrahydrofuran, 0 °C; ii, Zn, Et_2O, trace AcOH; iii, SiO_2; iv, KIO_4, $KMnO_4$, K_2CO_3.



(5) (3)

Reaction of (**1a, b**) with the alcohols (**2a—c**) (Na-dried toluene, reflux) gave the amides (**3a—f**)† (Table 1). ^{1}H N.m.r. data given in Sucrow's report[1] had indicated that the chemical shift of the *N*-methyl groups in the product 2,3-dialkyl-amides were at uniformly lower field (0.29—0.37 p.p.m.) in the *erythro*- compared to the *threo*-series. A downfield shift (0.05 p.p.m.) in the spectrum of the amide mixture (**3d**) led us to assign tentatively the *erythro*-stereochemistry to the major diastereoisomer. This assignment was confirmed by degradation of amide (**3d**) to a mixture of diastereoisomeric 2-ethyl-3-methylsuccinic acids (**4**)[2] (Scheme 1), comprising predominantly the *erythro*-isomer as shown by ^{13}C n.m.r. spectroscopy[3] (ratio between 7.5 : 1 and 4.5 : 1 *erythro* : *threo* by comparison of corresponding sp^3-carbons). The major diastereoisomers of the amides (**3b, e**) were assigned the *erythro*-configuration on the basis of the above ^{1}H n.m.r. diagnostic test. Vicinal, olefinic coupling constants from the 250 MHz n.m.r. spectra of amide mixtures (**3b, e**) established that all diastereoisomers contained a double bond of *E*-configuration [vicinal, olefinic coupling constants, (**3b**): 15.0, 15.0 Hz; (**3e**): 15.0, 15.0 Hz].

In contrast the silyl-amides (**3c, f**) appeared to contain approximately equal amounts of isomers again established as *erythro–threo* pairs rather than *Z–E* pairs by ^{1}H n.m.r. spectroscopy [vicinal, olefinic coupling constants, (**3c**): 15.3, 15.3 Hz; (**3f**): 15.0, 15.5 Hz]. Degradation of (**3f**) to the succinic acid (**4**) (Scheme 1) showed that the marginally *minor* isomer had the *erythro*-configuration.‡

The diastereoisomeric composition of the amide (**3f**) proved to be independent of the temperature of its formation in the Claisen rearrangement (benzene, room temperature, 17 h; xylene, reflux, 15 min). Neither isomer, *erythro*- nor *threo*-(**3f**), epimerised on subjecting it to the conditions of the Claisen rearrangement in the presence of the amide-acetal (**1b**) (1 equiv.). Thus the loss of diastereoselectivity in forming (**3f**) reflects a kinetic requirement of the overall reaction and we assume that this holds for (**3c**) too.

Loss of diastereoselectivity may occur by (a) loss of stereochemical integrity at the allyl double bond during, or after, formation of the presumed intermediate (**5**), (b) similar loss at the enamine double bond, or (c) an equal probability of chair- and boat-like transition states.

Recovery of (**2c**) as the pure *E*-isomer after partial rearrangements with (**1a, b**) precludes possibility (a). An early, boat-like transition state[4,5] is stereoelectronically unfavourable requiring overlap of non-colinear orbitals and, in the absence

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† Compounds (**3b, d, e, f**) were fully characterised spectroscopically and by accurate mass and/or microanalytical methods; (**3c**) was contaminated with the alcohol (**2c**) from which it could be clearly distinguished in the 250 MHz ^{1}H n.m.r. spectrum.

‡ Degradation of *erythro*-(**3f**) led to some epimerisation in the resultant (**4**) under conditions in which *threo*-(**3f**) gave cleanly *threo*-(**4**).

of the conformational constraints present in cyclic allylic alcohols,[5] we believe that it does not play a significant role in the present case.[6] However, a non-synchronous, concerted reaction in which bond cleavage precedes bond formation would result in a lower bond order in the enamine double bond, thus allowing greater rotational flexibility. Assistance to such cleavage could be provided by silicon by hyperconjugation,[7] bridging,[8] or by inductive affects.[9] The last may be of greatest importance in view of the low diastereoselectivity exhibited in the formation of (**3e**) for which the first two effects are unlikely. These points are being examined further.

The Claisen ester-enolate rearrangement of the propionate ester of alcohol (**2c**) proceeds with good diastereoselectivity, presumed to be *erythro*.[10]

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References

1 W. Sucrow and W. Richter, *Chem. Ber.*, 1971, **104**, 3679; W. Sucrow, B. Schubert, W. Richter, and M. Slopianka, *ibid.*, p. 3689.

2 J. H. Golden and R. P. Linstead, *J. Chem. Soc.*, 1958, 1732; E. Berner and R. Leonardsen, *Liebigs Ann. Chem.*, 1939, **538**, 1, 23, 30; H. Brockman and D. Müller-Enoch, *Chem. Ber.*, 1971, **104**, 3704; J. Bode and H. Brockman, *ibid.*, 1972, **105**, 34.

3 L. Ernst and W. Trowitsch, *Chem. Ber.*, 1974, **107**, 3771.

4 H.-J. Hansen and H. Schmid, *Tetrahedron*, 1974, **30**, 1959.

5 R. J. Cave, B. Lythgoe, D. A. Metcalfe, and I. Waterhouse, *J. Chem. Soc., Perkin Trans.* 1, 1977, 1218.

6 Ireland has invoked a boat-like transition state in an ester-enolate rearrangement on an *acyclic* alcohol; R. E. Ireland and C. S. Wilcox, *Tetrahedron Lett.*, 1977, 2839.

7 R. W. Bott, C. Eaborn, and P. M. Greasley, *J. Chem. Soc.*, 1964, 4804; H. J. Berwin, *J. Chem. Soc., Chem. Commun.*, 1972, 237; C. Eaborn, *ibid.*, 1972, 1255; C. Eaborn, *J. Organomet. Chem.*, 1975, **100**, 43.

8 A. W. P. Jarvie, A. Holt, and J. Thompson, *J. Chem. Soc. B*, 1969, 852; A. J. Bourne and A. W. P. Jarvie, *J. Organomet. Chem.*, 1970, **24**, 335; M. A. Cooke, C. Eaborn, and D. R. M. Walton, *J. Organomet. Chem.*, 1970, **24**, 301.

9 J. B. Lambert and R. B. Finzel, *J. Am. Chem. Soc.*, 1982, **104**, 2020.

10 S. R. Wilson and M. F. Price, *J. Am. Chem. Soc.*, 1982, **104**, 1124; E. H. Smith and N. D. Tyrrell, unpublished results.