Pergamon

Tetrahedron Letters 41 (2000) 3713–3716

TETRAHEDRON
LETTERS

Stereoselective intermolecular oxymercurations of trisubstituted allylic ethers

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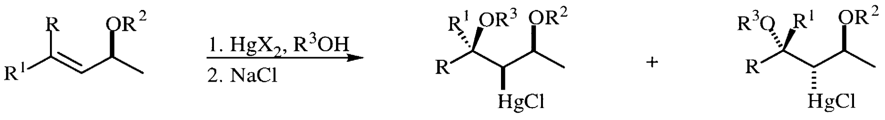
Received 21 December 1999; accepted 21 March 2000

Abstract

Trisubstituted allylic ethers undergo intermolecular oxymercurations with good to excellent diastereoselectivity compared to the corresponding allylic alcohols. © 2000 Published by Elsevier Science Ltd. All rights reserved.

We have recently reported studies on the structural features of allylic ethers which are important in order to achieve useful levels of diastereoselectivity in intra- and inter-molecular oxymercurations of disubstituted allylic ethers.[1–4] In this letter we report on the results of a related study involving intermolecular oxymercurations of tri-substituted allylic ethers (Eq. (1)).



1a-g **2a-g** **3a-g** (1)

1	R	R^1	R^2
a	Me	Me	OH
b	Me	Me	OBPS*
c	*n*-Pr	*n*-Bu	OH
d	*n*-Pr	*n*-Bu	OBPS
e	Me	Ph	OH
f	Me	Ph	OBPS

* BPS = *tert*-butyldiphenylsilyl

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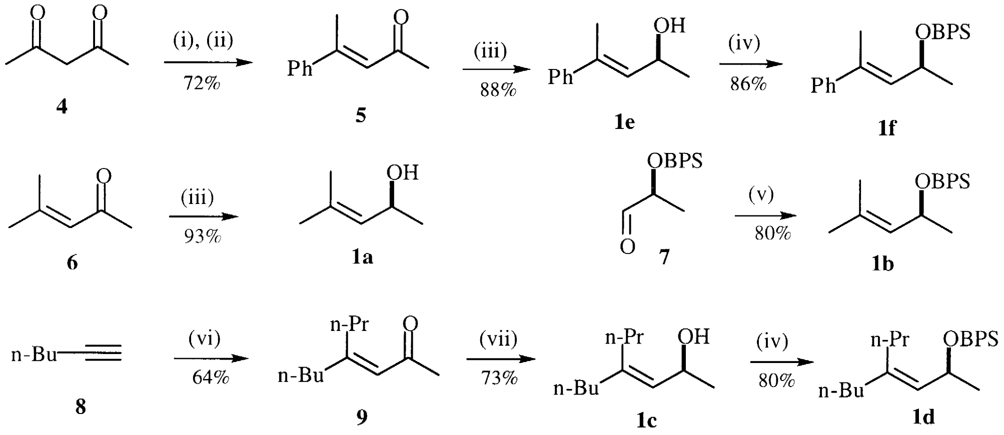
PII: S0040-4039(00)00472-X

Scheme 1 outlines the preparation of the allylic systems **1a**–**f**. All the alkenes except **1b** were prepared by sequential 1,2-reduction and silylation of known precursor alkenones. Thus, **1a** was prepared from mesityl oxide[5] in 93% overall yield and diastereoselectivity and **1b** was prepared by olefination of protected lactaldehyde (**7**) in 80% overall yield.[6] Alkenone **9**, required for **1c** and **1d** was prepared by carbocupration of 1-hexyne followed by in situ acylation with acetyl chloride.[7] Finally, alkenone **5** was prepared by Grignard addition to 2,4-pentanedione followed by dehydration.[8]

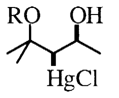
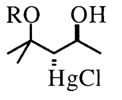
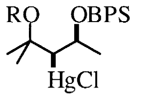
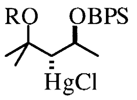
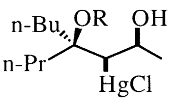
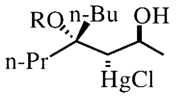
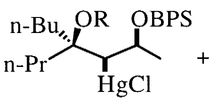
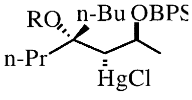
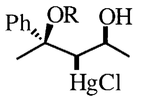
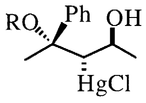
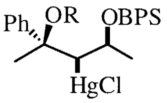
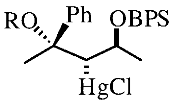


Scheme 1. Synthesis of oxymercuration precursors **1a**–**f**. (i) PhMgBr, Et_2O; (ii) 6N HCl, MeOH; (iii) $NaBH_4$; (iv) BPSCl, DMAP (cat.), DMF, Et_3N; (v) $Ph_3PCH(CH_3)_2I$, $NaN(TMS)_2$, −78°C; (vi) (a) *n*-PrCu·$MgBr_2$ (b) AcCl; (vii) $LiAlH_4$, Et_2O, −78°C

Oxymercurations were initially carried out using $Hg(OAc)_2$ in methanol at room temperature.[2] Hence in these reactions the solvent was also the nucleophile. In all cases regioselectivity was, not unexpectedly, very high. As is evident from Table 1 all the alkenes in this study underwent methoxymercuration with reasonable to excellent efficiency. An X-ray crystal structure determination was carried out on adduct **2f** and is shown in Fig. 1. This clearly shows that this adduct possesses the same relative stereochemistry as that expected from our previous studies of both intramolecular[1,3,4] and intermolecular[2] oxymercurations. The results in Table 1 also confirm our previous observations[2] that only the *tert*-butyldiphenylsilyl (BPS) ethers (as opposed to their corresponding unprotected allylic alcohols) display high levels of diastereoselectivity (compare entries 1–3, 7 and 9 with, respectively, entries 4–6, 8, 10 and 11). Oxymercurations of **1a**, **1b** and **1f** with benzyl alcohol and trimethylsilylethanol were also briefly examined. We were very pleased to find that, in most cases examined, these also proceeded with very similar levels of diastereocontrol (see entries 2, 3, 5, 6 and 11) to those obtained from methoxymercurations. Trimethylsilylethoxymercuration of **1f** (entry 12) failed, returning unchanged starting material. The success of the benzyloxymercurations has the obvious advantage of including an easily removable protecting group from the newly-introduced ether substituent.

The origin of the high diastereoselection obtained in the reactions involving silyl ethers appears to be a combination of conformational and coordination effects. The former has been described earlier by us in the context of intramolecular oxymercurations.[1] The latter is supported by examination of several crystal structures of organochloromercurials we have prepared, each of which bears an adjacent silylether oxygen (as in **2f**). In all of these cases there is clear evidence for coordination between the mercury atom and the ether oxygen.[9] For the silyl ethers, such as **2f** (R=Me) below, reductive removal of the chloromercurial substituent is readily achieved using tributylstannane/AIBN.[10] However, attempts

Table 1
Results from intermolecular oxymercurations[a,b] of trisubstituted alkenes **1a–h**

Entry	Alkene	Products	R	Yield ^{c}(%)	Time (h)	Ratio (2:3)
1	**1a**	 (**2a**) +  (**3a**)	Me	48	1	2:1
2			Bn	36	1	4:1
3			TSE	41	2	5:1
4	**1b**	 (**2b**) +  (**3b**)	Me	80	1	16:1
5			Bn	89	2	>20:1
6			TSE	68	24	>20:1
7	**1c**	 (**2c**) +  (**3c**)	Me	50	1	6:1
8	**1d**	 (**2d**) +  (**3d**)	Me	80	1	>10:1
9	**1e**	 (**2e**) +  (**3e**)	Me	70	2	3.5:1
10	**1f**	 (**2f**) +  (**3f**)	Me	83	48	>20:1
11			Bn	87^{d}	72	18:1
12			TSE	0	120	-

(a) All reactions were carried out at r.t., using 1.2 eq. of $Hg(OAc)_2$ in the appropriate alcoholic solvent. The reaction mixtures were treated with aq. NaCl to effect ligand exchange on mercury. (b) All new compounds gave satisfactory spectroscopic and elemental analysis. (c) Total isolated yield. (d) Based on unrecovered starting material.

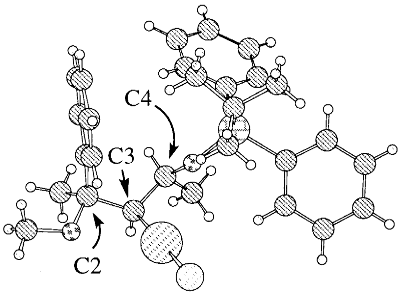
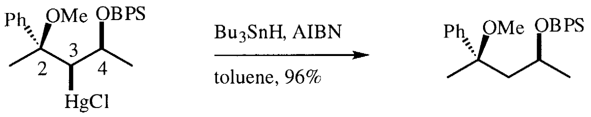


Fig. 1. X-Ray crystal structure of methoxymercuration adduct **2f** (R=Me)

to reductively demercurate the corresponding alcohol **2e** led to regeneration of allylic alcohol **1e**. This further emphasises the usefulness of the silyl ethers in this overall process.



2f (R= Me) **10**

In conclusion we have demonstrated that the intermolecular oxymercuration of the BPS ethers of trisubstituted allylic alcohols proceeds with complete regioselectivity and very high levels of diastereoselectivity. These results should be of value in the preparation of skipped polyols, especially those containing tertiary alcohols.

Acknowledgements

Financial support from the Australian Research Council is gratefully acknowledged. We thank Dr. Gary D. Fallon for determining the X-ray crystal structure of compound **2f** (R=Me).

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