Pergamon

Tetrahedron Letters 39 (1998) 8071–8072

TETRAHEDRON
LETTERS

Boron Trifluoride Induced Fragmentation of β-Aryl-β-Hydroxyketones

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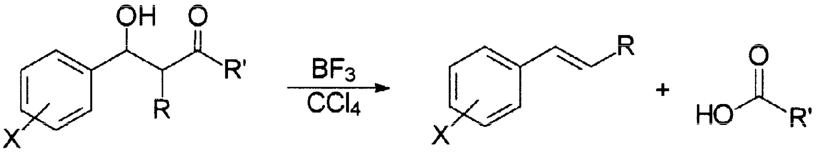
Received 2 June 1998; revised 27 July 1998; accepted 12 August 1998

Abstract: β-Aryl-β-hydroxy ketones are readily cleaved by boron trifluoride in non-protic solvents. The reaction appears to proceed via a non-synchronous Grobe fragmentation pathway.

Fragmentation reactions play an important role in organic synthesis.[1, 2,3] We wish to report that β-aryl-β-hydroxy carbonyl compounds are readily cleaved by boron trifluoride in non-protic solvents[4] to form the corresponding styrene derivative along with a carboxylic acid.



X	R	R'	% Yield (Alkene)	% Yield (Acid)
H	*n*-Pr	*n*-Bu	54	68
o-Cl	*n*-Pr	*n*-Bu	73	72
m-NO_2	*n*-Pr	*n*-Bu	62	70
p-CF_3	*n*-Pr	*n*-Bu	62	70
o-Cl	Me	Ph	33	58
p-CH_3	*n*-Pr	*n*-Bu	50	68

At present, it would appear that the reaction is limited to β-aryl derivatives in that all β-alkyl-β-hydroxy carbonyl compounds examined to date have simply produced the corresponding α,β-unsaturated carbonyl compound via a straightforward dehydration reaction. Retro-aldol and dimerization reactions also occur and can lead to loss of product. Dimerization occurs most readily when electron donating substituents are present on the β-aryl group.

Although a detailed study of the mechanism of the reaction has not been completed, the consistent formation of the (E)-alkene products derivatives from isomeric mixtures of *syn* and *anti* β-aryl-β-hydroxy ketones[5] as well as the fact that β-arylsubstituents appear to be required[6] would point toward the intermediacy of a carbocation derivative. Hydrogen NMR analyses of the reaction mixtures reveal a resonance corresponding to one hydrogen at 11.5 δ suggesting the formation of a carboxylic

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PII: S0040-4039(98)01777-8

acid prior to hydrolysis. A reasonable mechanism would involve the formation and subsequent non-synchronous ring opening of a lactol. This is reminiscent of two-step Grob[7] fragmentations that have been reported for *N*-halo-α-amino acids[8] and cyclobutane hemiacetals[9] as well as the acid catalyzed fragmentation of β-hydroxyacetals.[10,11]

The preparation of (E)-1-(*o*-chlorophenyl)-1-pentene is representative: BF_3 is bubbled[12] into a stirred solution of 1-hydroxy-1-(*o*-chlorophenyl)-2-propyl-3-heptanone (283 mg, 1.00 mmol) in CCl_4 (10 mL). The reaction is monitored by TLC and upon completion (< 5 minutes) is quenched with distilled water (10 mL), the product extracted into ether (3 x 10 mL), and the ether layer dried over anhydrous $MgSO_4$. The solvent is removed under reduced pressure and the mixture purified by flash chromatography to yield 132 mg (73%) of (E)-1-(*o*-chlorophenyl)-1-pentene and 74 mg (72%) of pentanoic acid. It is important to note that the reaction can be carried out sequentially. Thus, *o*-chlorobenzaldehyde reacts with the 5-nonanone in hexane in the presence of BF_3 to yield (E)-1-(*o*-chlorophenyl)-1-pentene but the reaction requires more stringent conditions.

The reaction yields are dependent on the stability of the product in the presence of boron trifluoride. Thus simple styrenes readily dimerize in a relatively short time under the reaction conditions. Whereas enhanced product yields can sometimes be obtained in instances where retro-aldol reactions occur by simply increasing the reaction time or elevating the temperature. We are currently examining reaction temperatures, solvent systems, and the quantity of BF_3 required to generate maximum yields.

Acknowledgements: We wish to thank the U.S. Department of Energy and the Robert H. Cole Foundation for support of this research. We also wish to thank Professor Scott Denmark for his insightful comments.

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4. Reactions have been successfully run in hexane, carbon tetrachloride and toluene.
5. Control experiments reveal that (Z)-1-phenyl-1-alkenes do not isomerize to the corresponding (E)-isomers under the reaction conditions.
6. For example, 7-hydroxy-6-*n*-propyl-5-tridecanone forms the corresponding α,β-unsaturated ketone upon addition of BF_3. Dehydration also occurs with 1,3-diaryl-β-hydroxyketones.
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12. Preliminary experiments indicate that boron trifluoride etherate may also be used in the fragmentation.