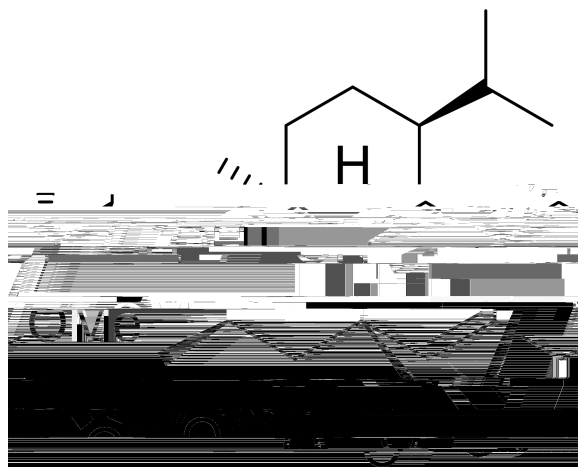
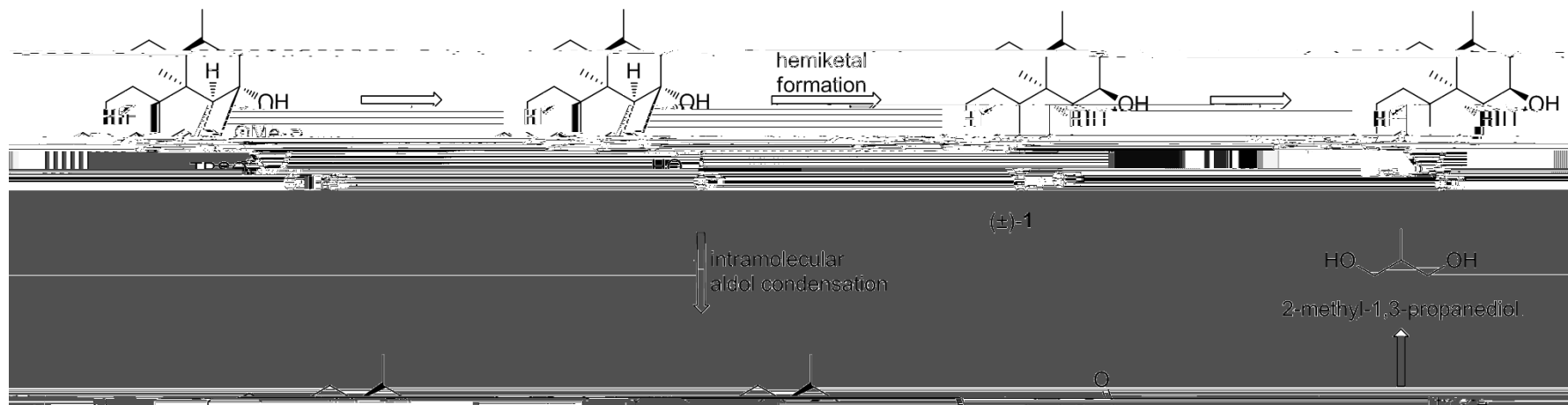


! "#\$%& ' () (\$*" +, -, . \$*/ , & 0 "\$) - & 1 (\$! , +* +& " 2& 3 !) \$) (. * (4 !) " % & 5 6 7 8 6 9 & 8) * : " (, % & 0 6 & ; 6 & *Angew. Chem. Int. Ed.* **2015**, 54, <==> ? <==@ 6



4) . !) # 1 & A 6 & B * C + \$ #)
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G#, /*"C+& 1(\$!, +, +



T Racemic synthesis reported by Gvssinger in 1998.

T 33 steps longest linear sequence from thymoquinone.

L*. !W, #K, #%& X&Y69&L*K(, #%&; 69&BV++*(K, #%& ' 69&B#CW, #%&O69& 8, (Z%&B&Monatsh. Chem. **1994**, 125, [[<?<F<F6&\B, # :) (& > &&&&-) (KC) K,]

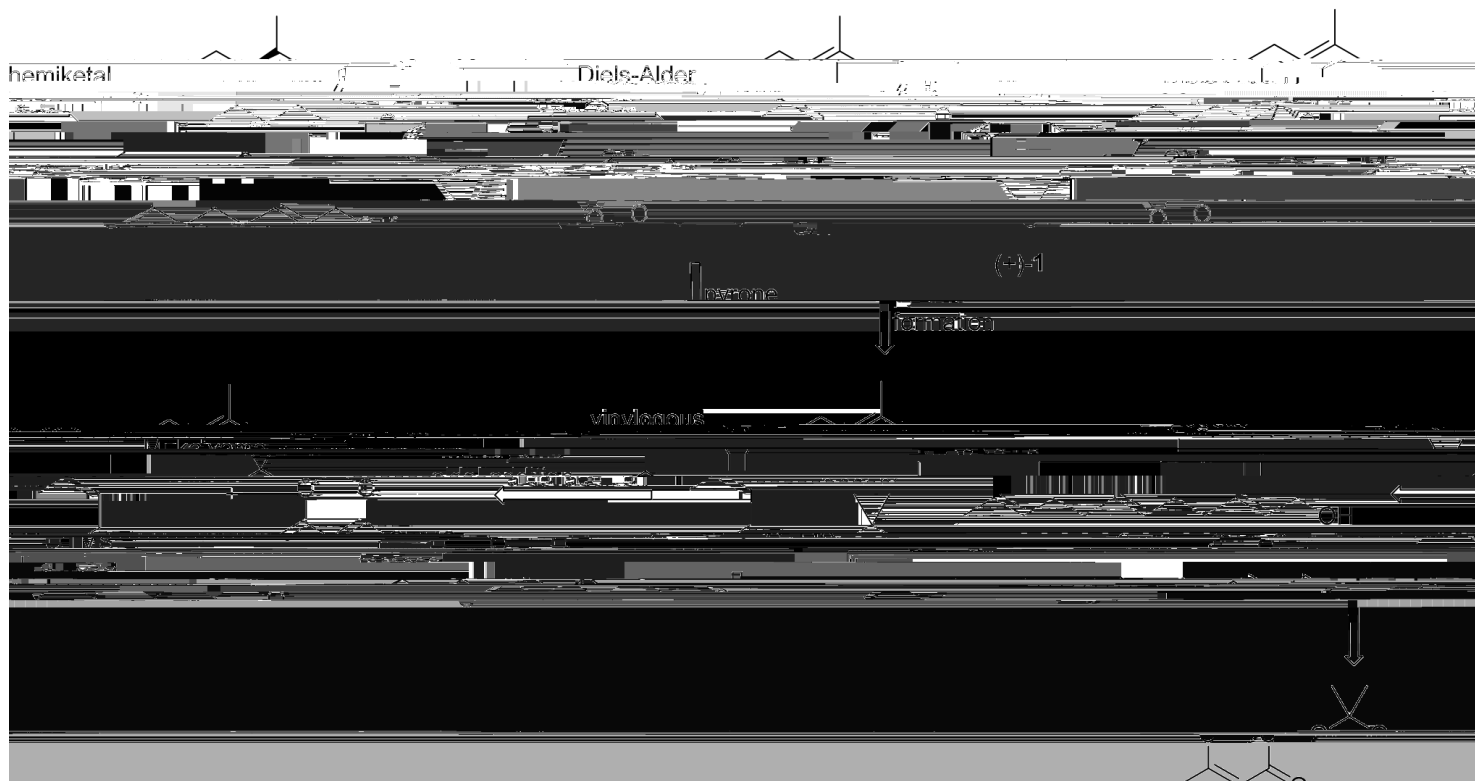
L*K(, #%&; 69&BV++*(K, #%& ' 69&O^! - *K%&Q69& 8, (Z%&B69&G2-CK+, I, #%&O6&Angew. Chem. Int. Ed. **1998**, 37, ===@?===S6

G#, /*"C+& 1(\$!, +, +

T Enantioselective synthesis achieved by Deslongchamps in 2003.

T

\d]71&e , \$#" +1 (\$! , +*+



- T Exceedingly acid-sensitive hemiketal moiety formed in the penultimate step.
- T Intramolecular Diels-Alder cyclization with pyrone diene to set four of the final product's seven stereocenters.
- T Vinylogous Mukaiyama aldol addition to combine two fragments containing all necessary carbon atoms.

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f"#P)#I& 1(\$!,+*+

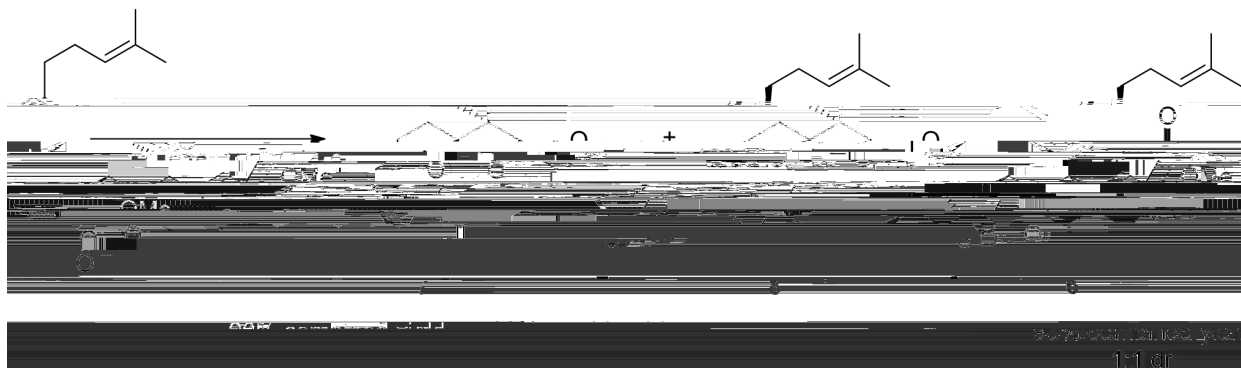
Y 8 G&g&Y,++7 8)#\$*(&E, #*"I*(,)
4!) "%&5 67 8 69& 8)* : "(, %&0 6&6&Angew. Chem. Int. Ed. **2015**, *54*, <==>?<==@6
' +\$h/, Z%& e 6& ' 69&; C+\$*.*)%&; 69& J) ZI*%& J 69& fC, (\$, +%& i 69&G)#I)+%& 8 69&3 !" jC, +*--"7D)ZG%

f"#P)#I& 1(\$!,+*+



DYL&g&-*\$!*C : &I**+"E#"E1-) : *I,9&Y 8 G&g&Y, ++7 8)#\$(&E, #*"I*() (, 9&YHG ' L&g&M%N-I**+"E#"E1-7N7, \$!1-) : *(,
 4!)"%&5 6 7 8 6 9 & 8)* : "(, %&0 6 & 6 & Angew. Chem. Int. Ed. **2015**, 54, <==>?<==@6
 f, \$\$, +%&L 9 & 3)##, *)%&' 6 & 8 6 & J. Org. Chem. **2003**, 68, [=c_?[=S>6

f"#P)#I& 1(\$!,+*+



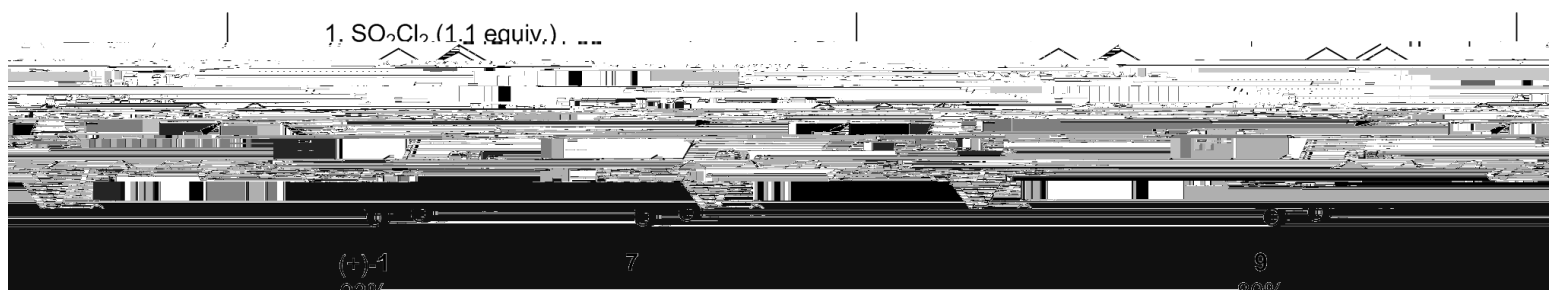
T Diastereomers **7** and **8** separable by column chromatography.

T Only decarboxylated products obtained when attempted with triflate **5**.

T Significant decarboxylation also observed in more polar solvents (DMF, acetonitrile), and at higher temperatures (120 IC).

T Cyclization reaction was markedly sluggish at 80 IC.

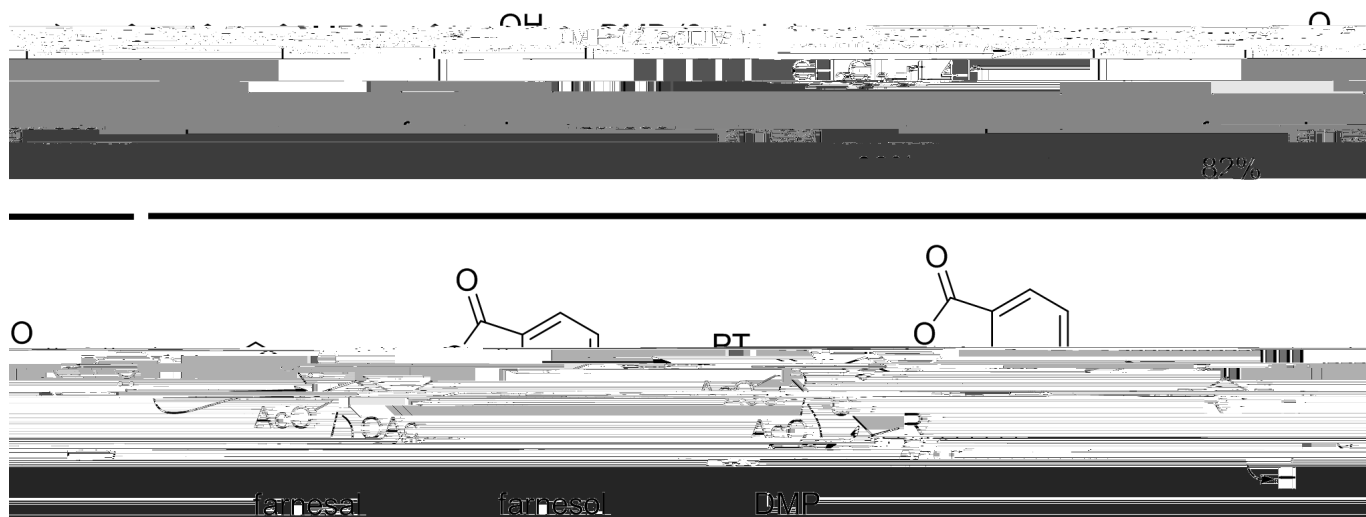
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4!) "%&567869&8)* : "(, %&06&6&Angew. Chem. Int. Ed. **2015**, *54*, <===>?<===@6

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 Y , + + 7 8) # \$ * (& G , # * " I * () (, & Na * I) \$ * " (



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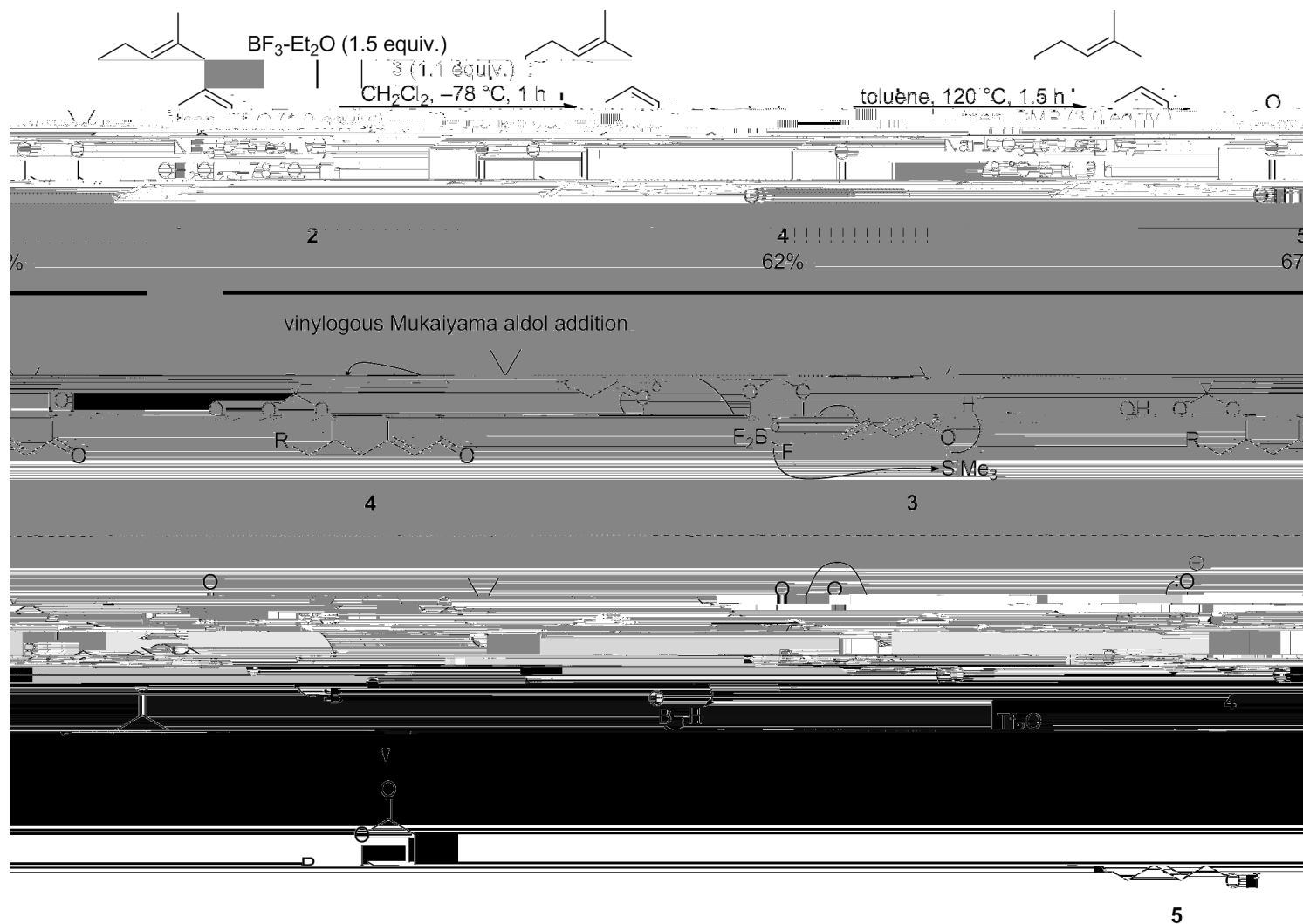
' + \$ h / , Z % e 6 k ' 6 9 k ; C + \$ * . *) % k ; 6 9 k J) Z I * % k J 6 9 k f C , (\$, + % k i 6 9 k G) # I) + % k 8 6 9 k 3 ! " j C , + * -- " 7 D) Z) # \$, % k Y 6 9 k B) # . k) % k ; 6 k 8 6 9 k e " W - , + % k e 6 9 k & k & k & k B) (+ ^ C , # % k L 6 9 k 3 C , # /) % k ; 6 k 8 6 9 k N - \$ #) % k ; 6 k ' 6 k Chem. Eur. J. **2009**, *15*, ==c_?=c [<6

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8, .!) (*+ : +



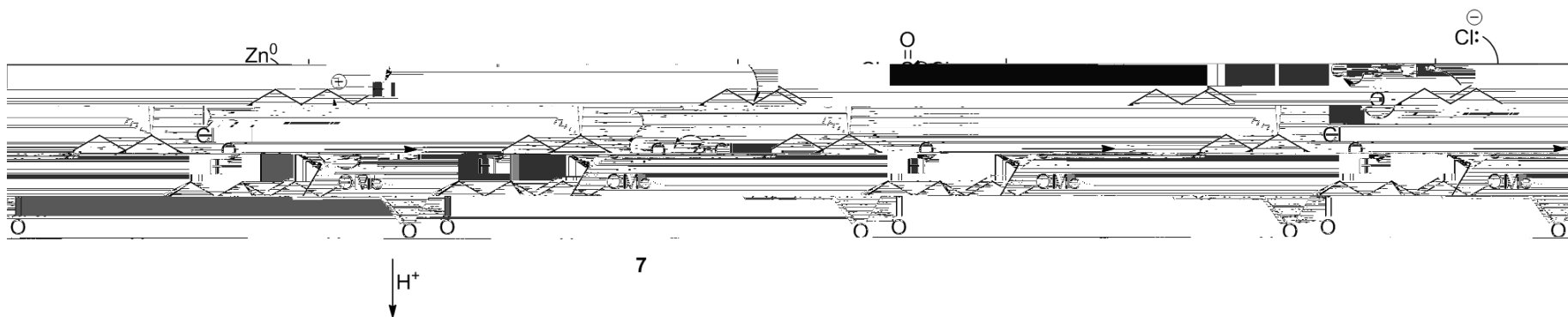
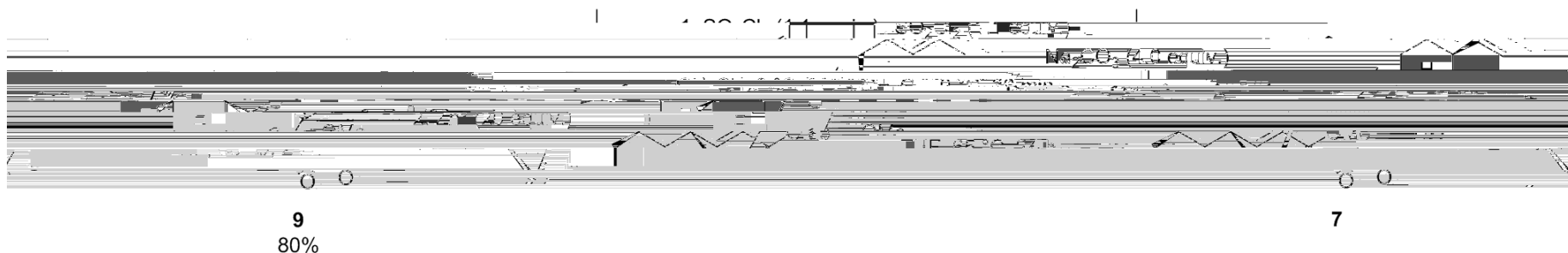
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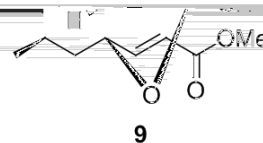
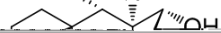
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4!) " % & 5 6 7 8 6 9 & 8) * : " (, % & 0 6 & ; 6 &

8, .!) (*+ : +



T A hemiketal formation mechanism involving intramolecular attack of a zincate on the lactone carbonyl is also plausible.



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