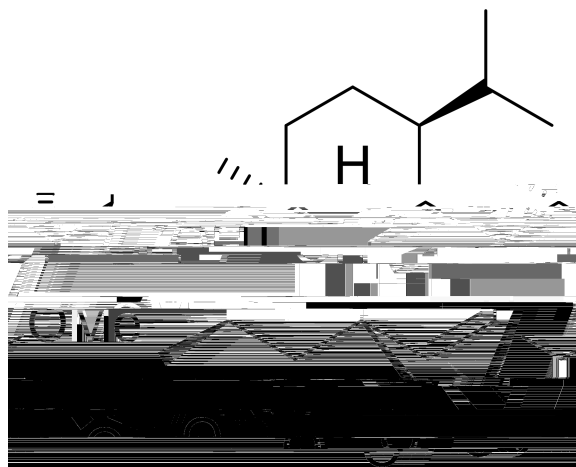
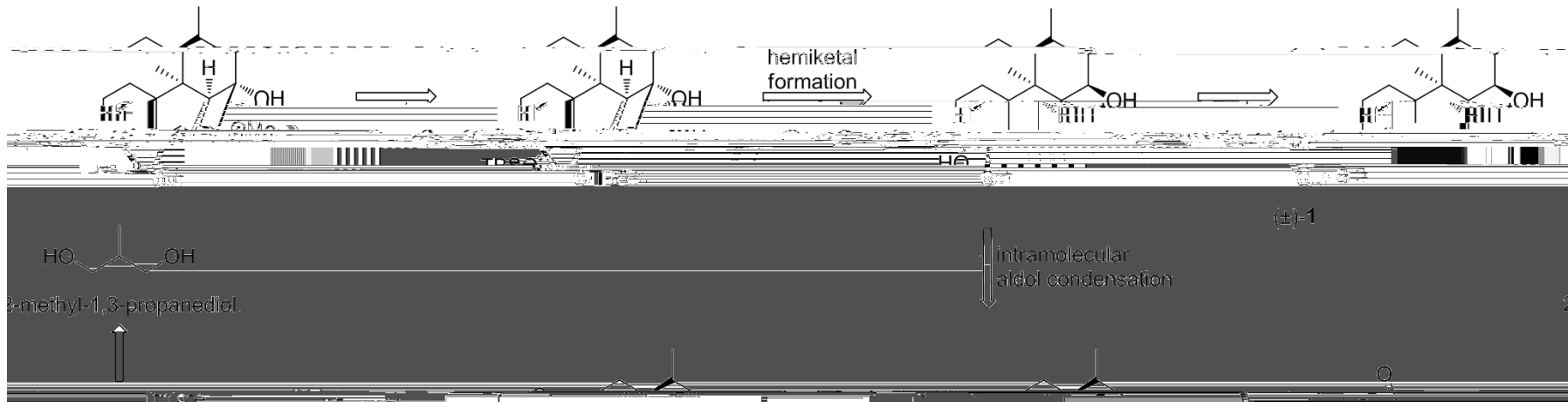


~ · °" ĭ / fĭ "fĭ ě ž ž "fĭ ĭ " " fž # / ~ ĭ ě fĭ ~ \$% ~ fĭ fĭ ž fĭ
 & ~ fĭ ě ĭ 0* (+* fĭ ĭ / ĭ ě " (~ (Angew. Chem. Int. Ed. 2015, 54, . //01. //2(



& fž ~ fĭ # ~ 3 (~ 4 fĭ ě ~ fĭ
 6 fĭ 4 ° 57
 - fĭ 5 fĭ # . ~ / 8. 2

9! f1 5L~ #/ ~ 1 1 1 1



F Racemic synthesis reported by G Hssinger in 1998.

F 33 steps longest linear sequence from thymoquinone.

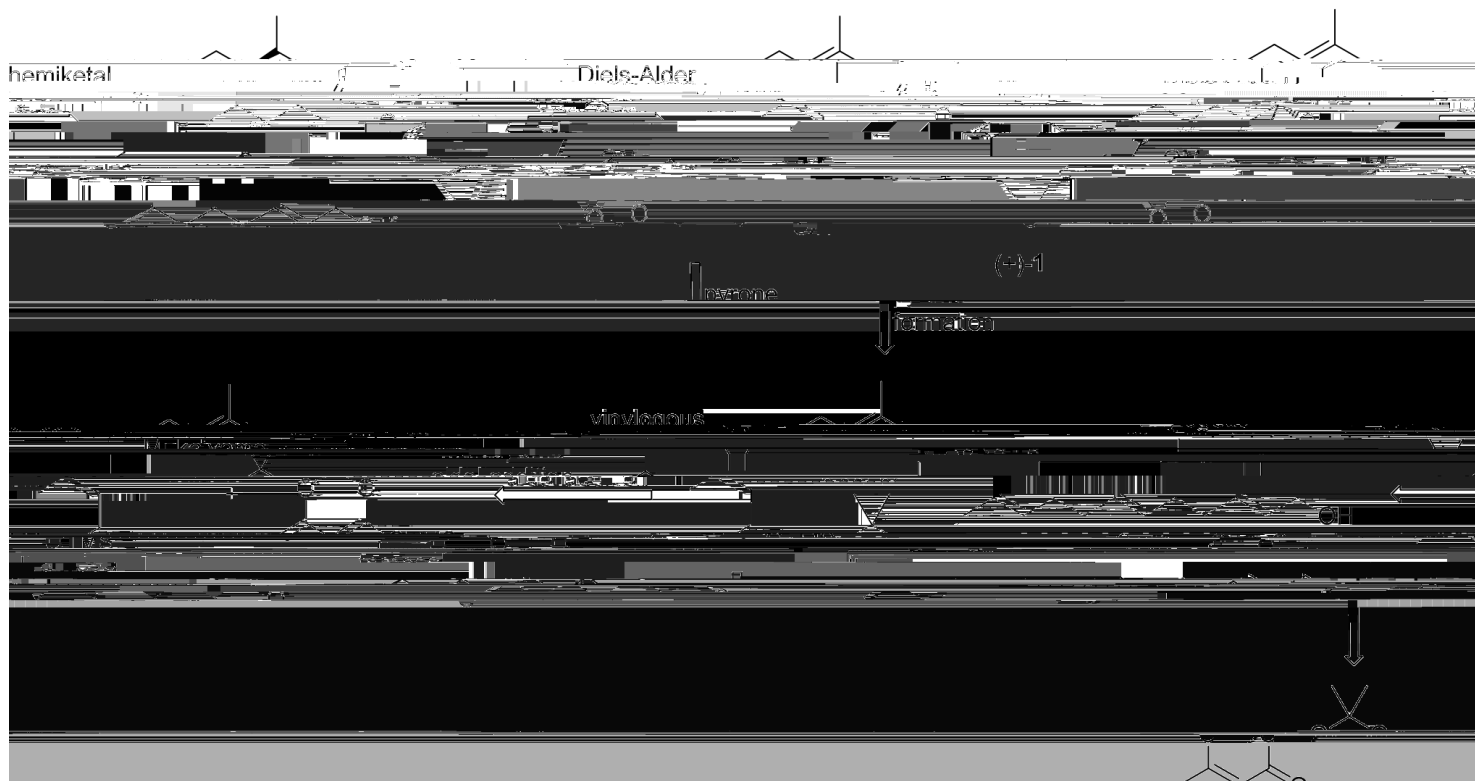
> f1 1 1 ° = ° J (K (+) f# / t ° - (+4 H 1 1 1 1 ° = ° i (+4 ° 5 l t ° A (+* t / L ° 4 (Monatsh. Chem. 1994, 125, MM1. 8. 8 (M 1 °, f i ~ 0
 ~~~~~ Z Y = 5 f i H O  
 > f# / t ° - (+4 H 1 1 1 1 ° = ° i (+A P Z f e C (+\* t / L ° 4 (+9 5 = 1 ; t ° A (Angew. Chem. Int Ed. 1998, 37, ///21///E(

9°! fl 5L~ #/ ~ | 1 1 1

F Enantioselective synthesis achieved by Deslongchamps in 2003.

F

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F Exceedingly acid-sensitive hemiketal moiety formed in the penultimate step.

F Intramolecular Diels-Alder cyclization with pyrone diene to set four of the final product's seven stereocenters.

F Vinylogous Mukaiyama aldol addition to combine two fragments containing all necessary carbon atoms.

D

X' °B fi; ~ #/ ~ 1 7fL

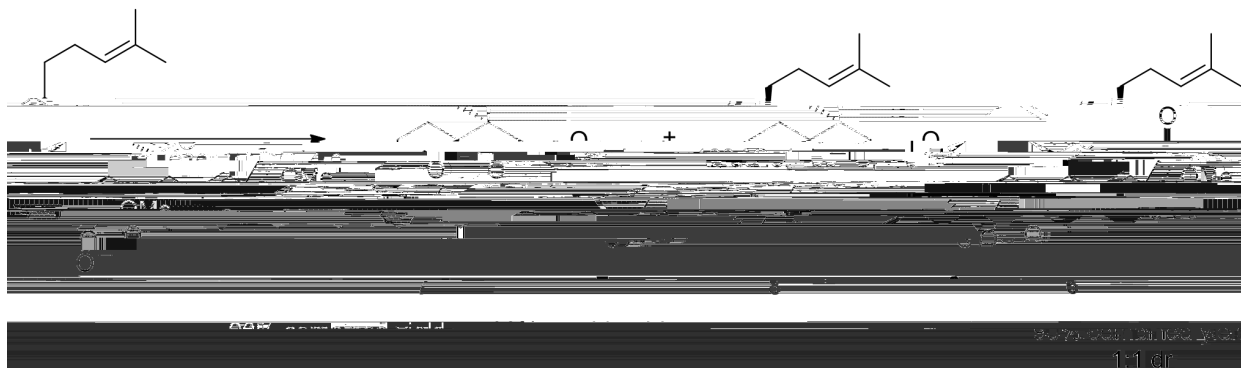
K\* 9YK11)\* fi'f'7i °fi; f'f'f'  
&~ fi' ~ ()\* (+\* f'f'f' /f' ~ (- (Angew. Chem. Int Ed. 2015, 54, . //01. //2(  
1 7Z! 1L, W(i (-5L'f'f'f' ~(-<fL; f'<(+X5f/ 1L, [ (+9f'f'f' fL,\* (+%~ ' \5f'f'f' )6fL9.

# X' °B fi; ~ #/ ~ ~ t 7fl



6K > Y ZT f5, ; flL 7° 7#Zi, flt +K\* 9YKtE)\* fi "fl ~ 7i °fl; fl flt +K: 9i > Y N,N-; flL 7° 7#Zi) t ~ #Zi flt  
 & fi ~ 0)\* (+\* fl) /t ~ (- (Angew. Chem. Int. Ed. 2015, 54, . //01. //2(  
 Xt ~ t E ~ > +%fi t flfi i (~\* (J. Org. Chem. 2003, 68, MUQ1MEO(

# X' °B fi; ~ #/ ~ t Lfl



F Diastereomers 7 and 8 separable by column chromatography.

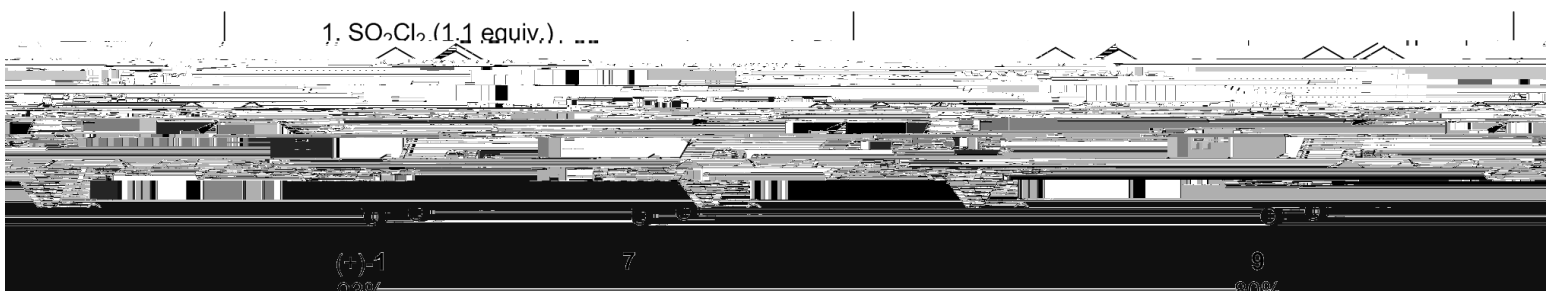
F Only decarboxylated products obtained when attempted with triflate 5.

F Significant decarboxylation also observed in more polar solvents (DMF, acetonitrile), and at higher temperatures (120 °C).

F Cyclization reaction was markedly sluggish at 80 °C.



X' °B fi; ~ #/ ~ 1 7fl



M

& fi ~ ()\* (+\* fl) ' / t ~ (- (Angew. Chem. Int. Ed. 2015, 54, . //01. //2(



\* 1 ž f/f, t\_

K 1 t) \* fi "f/ 9l ° fl ; f/f f/ t ~ @Sf/ fi'f/ /



1 t'Z! t L, W(i (+-5t "fzffl~-(+<fL; fl<(+X5l / 1 t\_ [ (+9fi'fi fL\_\* (+%~ ' \5t t fZ) 6fLf i' 1 ,K (+4 fi'z]fi~-(~\* (+W l ž t\_ W(+  
 ~~~~4 f/f tP5t ° ,> (+%5t ! fi~-(~\* (+@ž"fi~-(i (Chem. Eur. J. 2009, 15, //UQ1/UM(

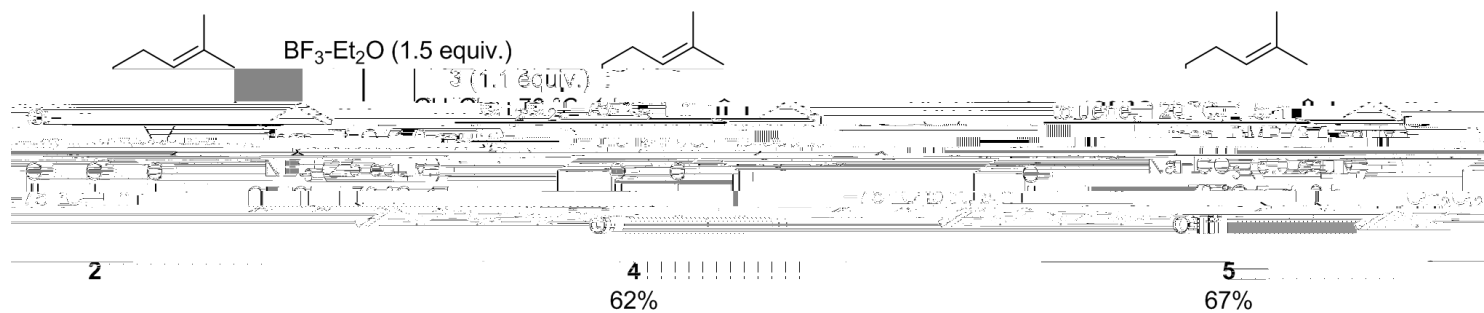
* 1 ž f/f, t



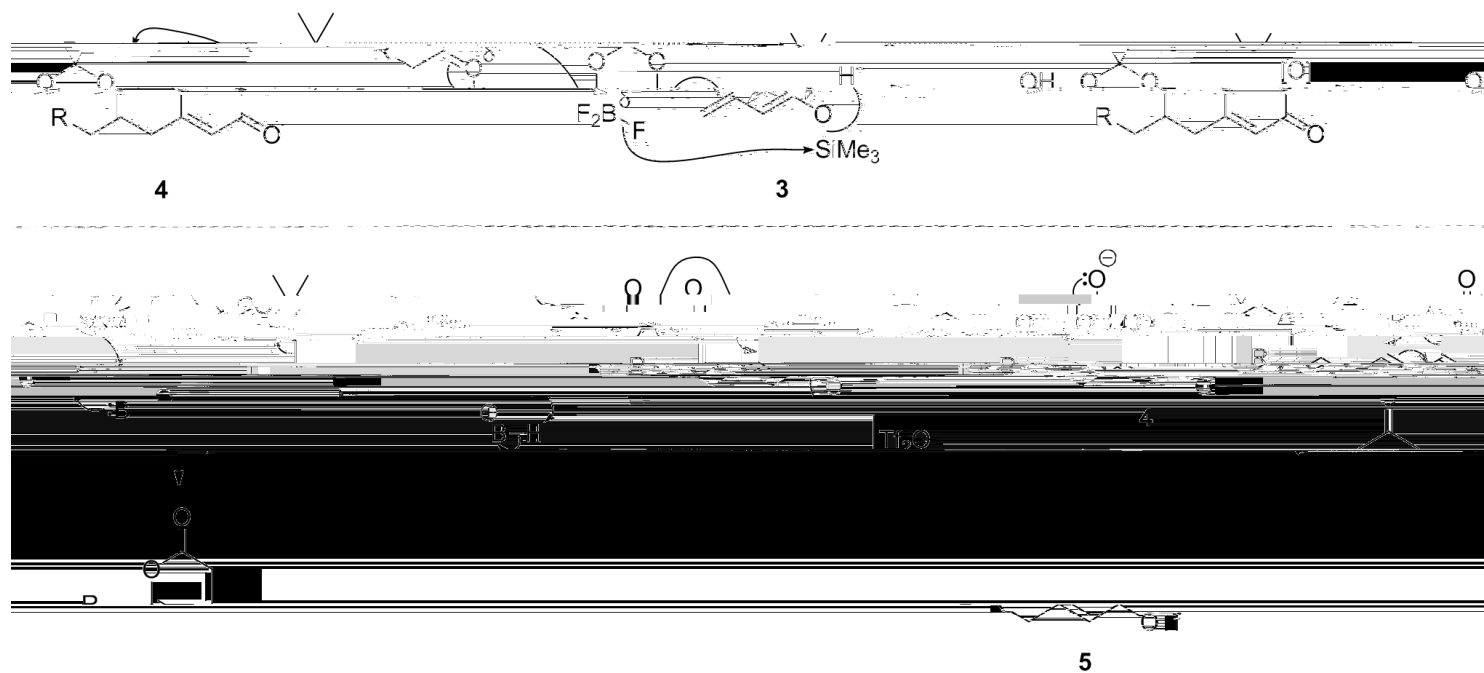
./

* f/f (f/f) (Angew. Chem. Int. Ed. 2006, 45, Q M01Q M0)

* 1 ž f/ fl, t



vinylogous Mukaiyama aldol addition



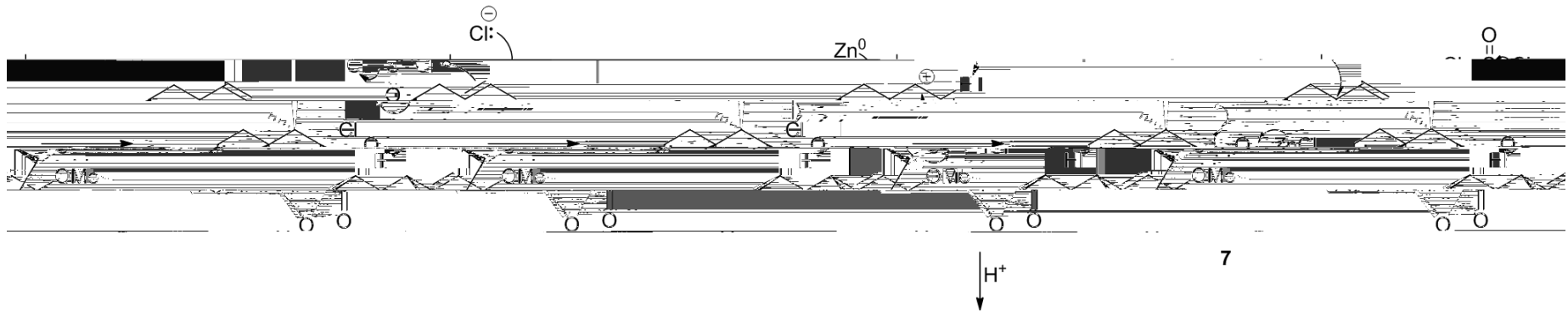
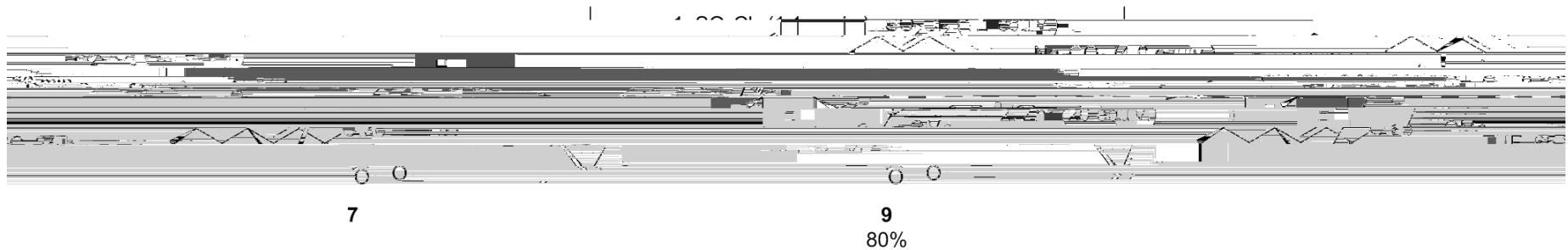
* 1 ž ~ f/x fl, 7

* 1 ž ~ f i / f l , 7

.D

& ~ f i , ~ 0 * (+ * f f l) ' / f , ~ (- (

* 1 ž ~ fi/fl, t



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

