SYNTHESIS OF AN ARYL PHOSPHONATE VIA THE ANIONIC PHOSPHO-FRIES REARRANGEMENT

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ABSTRACT

Zearalenone (**1**) is a mycotoxin, which reduces fertility in sheep and leads to substantial production losses in New Zealand. Catalytic antibodies are proposed as a potential approach to reducing the problem. This thesis describes progress toward the synthesis of the aromatic fragment of a transition-state analogue for the hydrolysis of the zearalenone lactone. The key step in the synthesis is an anionic phospho-Fries rearrangement; this relatively novel transformation is reviewed. α-Resorcylic acid (**36**) was converted to three different substrates, each with potential to undergo the O→C transfer of the dimethylphosphoryl moiety. Methyl 3-dimethylphosphato-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]benzoate (**117**) was prepared in three steps and 40% overall yield, but the *tert*-butyldimethylsilyl (TBDMS) protecting group was found to be unstable to phenolate anions. (2-Bromo-3,5-dibenzyloxyphenyl)-1,3-dioxolane (**154**) was prepared but further elaboration required hydrogenolytic cleavage of the benzyl ethers which was incompatible with the Ar-Br linkage. Finally, Ethyl 3-dimethylphosphate-5-(*p*-methoxybenzoxy)benzoate (**167**) was prepared in three steps and 25% overall yield. Treatment with LDA at –78 °C led to the formation of **166**, rather than the desired regioisomer **165**, as a result of lithium preferentially coordinating to the phosphoryl and OPMB groups.

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ABBREVIATIONS.

Ar-M	aromatic metal species
BDH	British drug house
BuLi	*n*-butyl lithium
COSY	correlation spectroscopy
°C	degrees Celsius
d	doublet
DDQ	2,3-dichloro-5,6-dicyanoquinone
DEPT	distortionless enhancement by polarization transfer
DIA	N,N-diisopropylamine
DIEA	N,N-diisopropylethylamine
DMAP	N,N-dimethylaminopyridine
DMF	N,N-dimethylformamide
DMSO	dimethylsulfoxide
δ	chemical shift
EI	electron impact
equiv.	molar equivalent(s)
FAB	Fast atom bombardment
HMBC	heteronuclear multiple bond coherence
HMQC	heteronuclear multiple quantum coherence
HPLC	high performance liquid chromatography
hr(s)	hour(s)

HRMS	high resolution mass spectroscopy
Hz	Hertz
J	coupling constant
LDA	lithium diisopropylamide
$LiAlH_4$	lithium aluminum hydride
LRMS	low resolution mass spectroscopy
m	multiplet
MeCN	acetonitrile
min(s)	minute(s)
mmol	millimole
m.p.	melting point
MS	mass spectrometry
m/z	mass to charge ratio
NBA	Nitrobenzyl alcohol
NBS	*N*-Bromosuccinimide
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect spectroscopy
Pd/C	palladium on carbon
PMB	*p*-methoxybenzyl
ppm	parts per million
p-TSA	para-toluene sulfonic acid
q	quartet
R*f*	Retardance factor
rt	room temperature

§	section
t	triplet
TBAF	tetrabutylammoniumfluoride
TBDMS	*tert*-butyldimethylsilyl
TBDMSCl	*tert*-butyldimethylsilyl chloride
THF	tetrahydrofuran
tlc	thin layer chromatography
UV	ultra violet