Aspects of Organoselenium Chemistry

A thesis presented for the degree of

Doctor of Philosophy

by

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ABSTRACT

A range of β-amidoalkyl phenylselenides were prepared in order to explore their cyclisation *via* oxidation of the selenium moiety to the selenone followed by intramolecular displacement. At first, the β-amidoalkyl phenylselenides were prepared in one-step from the alkenes. However, the one-step preparation was complicated by side-reactions and a two-step method was found to give clean reactions and higher yields of a wide range of the desired amido selenides.

Along with the expected oxazolines, isomeric *N*-acylaziridines were obtained from the cyclisation reaction. Formation of *N*-acylaziridines by cyclisation of amides is unusual, and variation of the conditions was explored in order to optimise this novel aziridine-forming reaction. It was found that conducting the oxidation reaction at low temperature favoured the aziridine products. In this way, the aziridines derived from all prepared β-amido selenides were obtained in good to excellent yield. From some substrates, the aziridine was obtained as the exclusive product.

The low temperature generation of a selenone from the corresponding selenide had not been reported previously. Experiments were carried out which provided evidence for the supposition that the intermediate in the cyclisation reaction was the selenone.

The preparation of β-amido selenides was also investigated using silver ion to sequester the halide of the selenium reagent, rendering the selenium species more electrophilic and its addition to the alkene to give a seleniranium ion, irreversible. The seleniranium ion was generated in the presence of nitrile to allow attack by the

weak nitrile nucleophile upon the seleniranium ion, giving a nitrilium ion. With addition of water to the nitrilium ion, β-amido selenides were formed in moderate yield. Thus, it was shown that the β-amido selenides could be prepared without the use of strong acid. Addition of azide to the nitrilium ion gave a tetrazole, which demonstrated that this methodology could provide access to selenides substituted at the β-position with groups other than the amido group.

β-Benzamidocyclohexyl phenyl selenoxide and β-benzamidocyclohexyl phenyl selenone were prepared, and hydrogen bonding in the two compounds was examined spectroscopically. An X-ray crystal structure of the selenoxide showed intermolecular hydrogen bonding between the amide hydrogen and the seleninyl oxygen, in contrast to proposals in the literature that analogous selenoxides were stabilised by intramolecular hydrogen bonding in the solid state.

Three γ-hydroxy selenides were prepared and their low-temperature oxidation and cyclisation was explored with a view to obtaining the corresponding oxetanes. The low-temperature procedure did not translate successfully to the cyclisation of γ-hydroxy selenides to oxetanes, instead giving complex mixtures. However, with reference to literature conditions for the preparation of methoxy-substituted oxetanes, the γ-hydroxy selenides were cyclised to the corresponding oxetanes by oxidation in methanol at room temperature, demonstrating that the scope of this method could be widened to a more generalised preparation of oxetanes.

STATEMENT OF ORIGINALITY

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ABBREVIATIONS

General	Ac	acetate
	AIBN	azobisisobutyronitrile
	Bn	benzyl, $C_6H_5CH_2$
	Bu_3SnH	tri-butyltin hydride
	CH_2Cl_2	dichloromethane
	$CHCl_3$	chloroform
	de	diastereomeric excess
	DMF	dimethyl formamide
	DMSO	dimethyl sulfoxide
	ee	enantiomeric excess
	Et_2O	diethyl ether
	EtOAc	ethyl acetate
	EtOH	ethanol
	HMPA	hexamethylphosphoramide
	i-PrOH	isopropanol
	KOH	potassium hydroxide
	LDA	lithium diisopropylamide
	m-CPBA	*meta*-chloroperbenzoic acid
	Me	methyl, CH_3
	MeOH	methanol
	$MgSO_4$	magnesium sulfate
	N_2	nitrogen
	$NaBH_4$	sodium borohydride
	NaCl	sodium chloride

	NaH	sodium hydride
	$NaHCO_3$	sodium hydrogen carbonate
	Nu	nucleophile
	OTf	trifluoromethanesulfonate, triflate
	Ph	phenyl, C_6H_5
	Pr	propyl, C_3H_7
	r.t.	room temperature
	t-BuOK	potassium *tertiary*-butoxide
	TfOH	trifluoromethanesulfonic acid, triflic acid
	THF	tetrahydrofuran
	TLC	thin layer chromatography
NMR	d	doublet
	Hz	hertz
	m	multiplet
	MHz	megahertz
	ppm	parts per million
	q	quartet
	qn	quintet
	s	singlet
	sept	septet
	t	triplet
	δ	chemical shift

IR	br	broad
	cm^{-1}	wavenumbers (reciprocal centimeters)
	KBr	potassium bromide pressed disc
	s	strong
	w	weak
MS	EI	electron impact
	ESI	electrospray
	FAB	fast atom bombardment
	HRMS	high resolution mass spectrum
	M	molecular ion
	m/z	mass per unit charge