

Contents

1	Introduction	1
1.1	Hederagonic Acid	1
1.1.1	Natural Occurrence	2
1.1.2	Biological Activity	3
1.1.3	Previous Syntheses	4
1.2	C–H Activation	6
1.2.1	Stoichiometric C–H Oxidation	6
1.2.1.1	Baldwin’s Cyclopalladation Reaction	6
1.2.2	Catalytic C–H Oxidation	9
1.2.2.1	Palladium Catalysed C–H Acetoxylation	9
2	Results and Discussion	13
2.1	Objectives	13
2.2	Preliminary Results	14
2.2.1	Halolactone Oxime	14
2.2.1.1	Chlorolactone Oxime	14
2.2.2	C–H Activation at position C-23	16
2.2.2.1	Palladium Catalysed C–H Acetoxylation	16
2.2.3	Deacetylation and Deoximation	16
2.2.4	Retro-halolactonisation	17
2.3	Optimisation of the Synthetic Sequence	18
2.3.1	Halolactone Oxime	18
2.3.1.1	Chlorolactone Oxime	18
2.3.1.2	Bromolactone Oxime	24
2.3.2	C–H Activation at position C-23	26
2.3.2.1	Palladium Catalysed C–H Acetoxylation	26
2.3.2.2	Copper Catalysed C–H Hydroxylation	31
2.3.3	Deacetylation and Deoximation	33

2.3.4	Retro-halolactonisation	35
2.4	Final Synthetic Route to Hederagonic Acid	36
2.4.1	Economic Considerations	38
2.5	Summary and Outlook	39
3	Experimental Section	41
3.1	General Information	41
3.2	Experimental Procedures	42
3.2.1	12 α -Chloro-3 β -hydroxyolean-28,13 β -olide (26a)	42
3.2.2	12 α -Bromo-3 β -hydroxyolean-28,13 β -olide (26b)	43
3.2.3	12 α -Chloro-3-oxo-olean-28,13 β -olide (27a)	45
3.2.4	12 α -Bromo-3-oxo-olean-28,13 β -olide (27b)	46
3.2.5	12 α -Chloro-3-(hydroxyimino)-olean-28,13 β -olide (6a)	47
3.2.6	12 α -Bromo-3-(hydroxyimino)-olean-28,13 β -olide (6b)	48
3.2.7	12 α -Chloro-3-(methoxyimino)-olean-28,13 β -olide (29a)	50
3.2.8	23-Acetoxy-3-(acetoxyimino)-12 α -chloro-olean-28,13 β - olide (7a)	51
3.2.9	23-Acetoxy-3-(acetoxyimino)-12 α -bromo-olean-28,13 β - olide (7b)	52
3.2.10	12 α -Bromo-23-hydroxy-3-oxo-olean-28,13 β -olide (8b)	53
3.2.11	Hederagonic acid (23-Hydroxy-3-oxo-olean-12-en-28- oic acid) (1)	54
	References and Notes	57