Stereoselective Synthesis of Z Alkenyl Halides via Julia Olefination

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Supporting informations

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General Experimental

All reactions were carried out under a nitrogen atmosphere using dry glassware which had been flame-dried under a stream of nitrogen or oven-dried overnight. All solvents came from Aldrich Sure-Seal bottle and used as received. Commercially available reagents and bases were used as received. Reactions were monitored by thin-layer chromatography (TLC) using 0.25-mm E. Merck precoated silica gel plates. Visualization was accomplished with UV light and aqueous ceric ammonium molybdate solution followed by charring on a hot-plate. Reactions were purified using a Isco Combi-Flash system or by column chromatography performed with the indicated solvents using silica gel. NMR yields have been estimated by using an internal standard as comparison. Yields refer to chromatographically and spectroscopically pure compounds. ^1H and ^{13}C NMR spectra were recorded on a Bruker 500 MHz spectrometer at ambient temperature. ^1H and ^{13}C NMR data are reported as δ values relative to tetramethylsilane. GC-MS analysis of samples were performed using an Agilent Mass Selective Detector (EI) coupled to a gas chromatograph. One microliter of solution was injected in pulsed split mode (10:1 split ratio) and separation was achieved using an HP-1MS from Agilent (15 m long, 0.25mm internal diameter and 0.25 μm film thickness) and the temperature program was as follows: 40°C to 300°C (25°C/min) for a total run length of 11.4 min. Helium (5.0 grade) was used as carrier gas and all acquisitions were performed in scan mode (from m/z 35 to 400).

General procedure for the synthesis of *E* alkenyl halide. To a solution of sulfone (0.38 mmol, 1.0 eq) and aldehyde (0.38 mmol, 1.0 eq) in THF (1.5 mL, 0.26 M) at rt, was added magnesium bromide diethyl etherate (1.14 mmol, 3.0 eq) followed by slow addition of KHMDS (0.76 mmol, 3.0 eq, 0.5 M / toluene) via a serynge pump over 2 h. The reaction mixture was quenched with a saturated NH₄Cl solution at rt and diluted with ether. The aqueous layer was washed with ether (3x). The combined organic layers were washed with brine, dried over MgSO₄ and concentrated. The crude product was analyzed by NMR in order to evaluate the *E*:*Z* ratio and the conversion calculated with an internal standard. Purification was accomplished by flash chromatography using Et₂O / pentane.

General procedure for the synthesis of *Z* alkenyl halide. To a solution of sulfone (0.38 mmol, 1.0 eq) and aldehyde (0.38 mmol, 1.0 eq) in THF (1.5 mL, 0.26 M) at rt, was added HMPA (0.76 mmol, 2.0 eq) followed by LiHMDS (0.76 mmol, 2.0 eq, 1 M / hexanes) dropwise over 20 sec. The reaction was stirred at rt for 30 min, diluted with 3 mL of pentane, filtered through a pad of silica gel (1.5 g cartridge) and rinsed with a solution of 10% Et₂O / pentane. The crude product was analyzed by NMR in order to evaluate the *E*:*Z* ratio and the conversion calculated with an internal standard (DMF). Purification was accomplished by flash chromatography using Et₂O / pentane.

4a Z isomer (9:91)
Table 3, entry 3

id	ppm	type	mult	n	coupling
0	8.14556	compound	s	1.1	0.0
1	7.84346	compound	m	3.6	0.0
2	7.49046	compound	m	2.0	0.0
3	6.78419	compound	d	1.0	8.14
4	6.34701	compound	d	1.0	8.13

4a E isomer (71:29)
Table 2, entry 2

id	ppm	type	mult	n	coupling
0	8.13390	compound	s	0.4	
1	7.81368	compound	m	4.1	
2	7.66253	compound	s	1.0	
3	7.46647	compound	m	3.2	
4	7.24068	solvent	s	0.1	
5	6.97734	compound	d	0.9	13.66
6	6.77131	compound	m	1.1	
7	6.33830	compound	d	0.3	8.13

5a

id	ppm	type	mult	n	coupling
0	7.64403	compound	m	0.9	0.0
1	7.22440	compound	m	3.0	0.0
2	6.76820	compound	d	1.0	7.95
3	6.35901	compound	d	1.0	7.94
4	2.29904	compound	s	3.4	0.0

5a Z isomer (10:90)
Table 3, entry 5

id	ppm	type	mult	n	coupling
0	7.64403	compound	m	0.9	0.0
1	7.22440	compound	m	3.0	0.0
2	6.76820	compound	d	1.0	7.95
3	6.35901	compound	d	1.0	7.94
4	2.29904	compound	s	3.4	0.0

5a E isomer (12:88)
Table 2, entry 3

id	ppm	type	mult	n	coupling
0	7.62114	compound	m	1.0	
1	7.30062	compound	d	0.2	7.48
2	7.19646	compound	m	3.0	
3	7.02263	compound	m	0.1	
4	6.75197	compound	d	1.0	7.95
5	6.49654	compound	m	0.1	
6	6.34365	compound	d	0.9	7.94
7	3.46988	solvent	q	1.6	7.0
8	2.32402	compound	s	0.4	
9	2.27971	compound	s	3.0

5b

id	ppm	type	mult	n	coupling
0	7.60353	compound	m	0.9	0.0
1	7.26281	solvent	m	2.9	0.0
2	7.18772	compound	d	1.1	7.87
3	6.56655	compound	d	1.0	7.85
4	2.31607	compound	s	3.4	0.0

6a Z isomer (18:82)
Table 3, entry 7

id	ppm	type	mult	n	coupling
0	7.68643	compound	d	1.7	8.47
1	7.39015	compound	d	1.8	8.4
2	6.53659	compound	d	1.1	8.16
3	6.28246	compound	d	1.0	8.16

6a E isomer (27:73)
Table 2, entry 4

id	ppm	type	mult	n	coupling
0	7.67769	compound	d	6.9	8.23
1	7.62609	compound	d	2.1	8.16
2	7.38458	compound	d	6.8	8.21
3	7.24078	solvent	s	0.7	
4	7.00695	compound	d	2.2	8.14
5	6.73350	compound	m	1.1	
6	6.63853	compound	d	1.0	13.69
7	6.53276	compound	d	3.4	8.17
8	6.27536	compound	d	3.2	8.16

7a

id	ppm	type	mult	n	coupling
0	7.40526	compound	d	1.0	1.69
1	7.09639	compound	dd	1.0	8.1 1.7
2	6.84026	compound	d	1.0	8.1
3	6.55745	compound	d	1.1	8.14
4	6.17965	compound	d	1.0	8.14
5	6.01047	compound	s	2.2	0.0

id	ppm	type	mult
0	147.48565	compound	s
1	147.33769	compound	s
2	128.70018	compound	s
3	128.70758	compound	s
4	123.86937	compound	s
5	115.50266	compound	s
6	109.07267	compound	s
7	108.71295	compound	s
8	107.16217	compound	s
9	77.25055	solvent	s
10	76.93623	solvent	s
11	76.74183	solvent	s

8a

id	ppm	type	mult	n	coupling
0	7.45444	compound	d	1.8	7.56
1	7.31939	compound	m	2.1	0.0
2	7.25584	compound	m	1.3	0.0
3	7.16761	compound	dd	1.0	15.8 10.5
4	6.67577	compound	d	1.0	15.7
5	6.45581	compound	dd	0.9	10.5 7.1
6	6.06166	compound	d	0.9	7.1

8b

id	ppm	type	mult	n	coupling
0	7.46835	compound	m	2.0	0.0
1	7.33258	compound	m	2.3	0.0
2	7.26543	solvent	m	1.1	0.0
3	7.09654	compound	ddd	1.0	15.8 10.2 1.1
4	6.78034	compound	ddd	1.0	10.3 7.1 0.8
5	6.73924	compound	d	1.3	15.75
6	6.22612	compound	d	1.1	7.08

id	ppm	type	mult
0	136.63785	compound	s
1	136.06235	compound	s
2	132.70934	compound	s
3	128.67943	compound	s
4	128.29558	compound	s
5	126.77647	compound	s
6	124.33424	compound	s
7	108.47882	compound	s
8	77.22867	solvent	s
9	76.97794	solvent	s
10	76.72045	solvent	s