

Construction of pyrazole fused spiroketals by a (3 + 2) annulation reaction

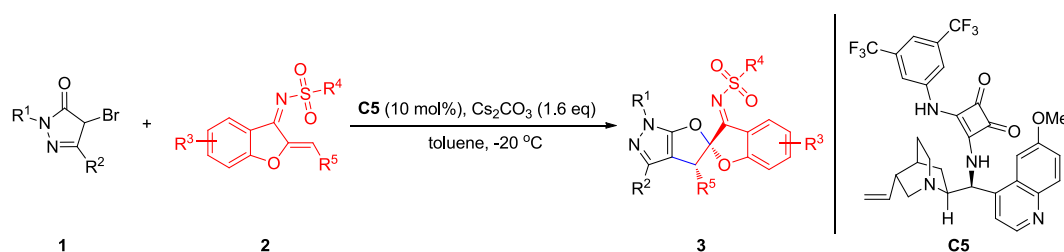
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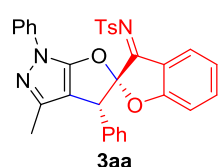
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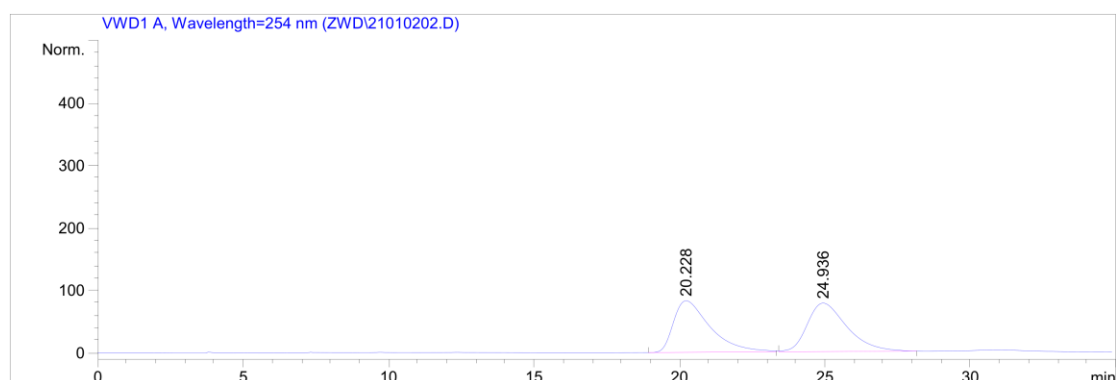
1. Characterization of enantiomeric excess for the asymmetric (3 + 2) annulation product



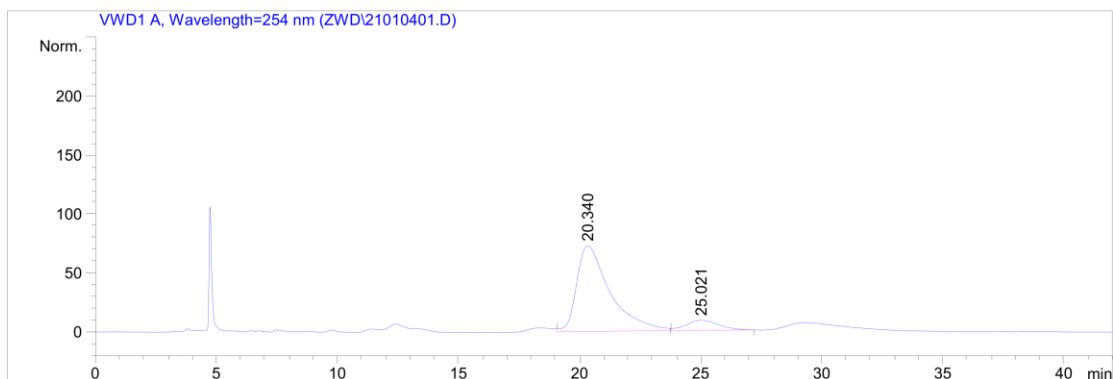
A Schlenk tube equipped with a magnetic stir bar was charged with 4-bromo pyrazolone **1** (0.15 mmol, 1.5 equiv.), benzofuran-derived azadiene **2** (0.10 mmol, 1.0 equiv.), **C5** (10 mol%), toluene (1 mL) under nitrogen atmosphere at -20 °C. After stirring for 3-5 min, Cs₂CO₃ (0.16 mmol, 1.6 equiv.) was added. The resulting mixture was stirred at -20 °C. Progress of the reaction was monitored by TLC. After completion of the reaction, the crude product was purified by column chromatography (petroleum ether/ethyl acetate = 10/1-5/1) on silica gel to give the product **3**.



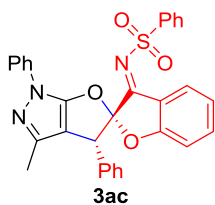
Prepared according to the procedure within 10 min as a light yellow solid (89% yield, dr > 20:1); **Enantiomeric excess** was determined to be 79% (determined by HPLC using chiral OD-H column, hexane/2-propanol = 95/5, $\lambda = 254 \text{ nm}$, 30 °C, 0.8 mL/min, $t_{\text{major}} = 20.3 \text{ min}$, $t_{\text{minor}} = 25.0 \text{ min}$).



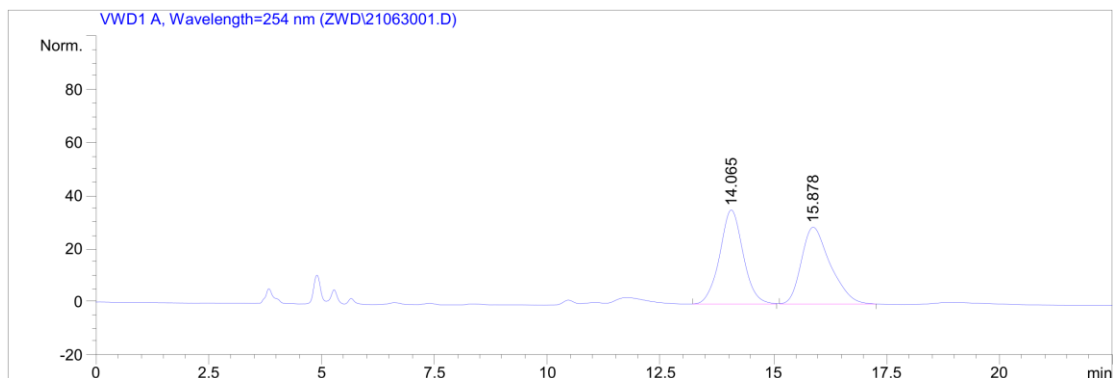
Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	20.228	BB	1.3089	7286.44531	82.70372	49.6302
2	24.936	BB	1.3968	7395.02686	77.72697	50.3698



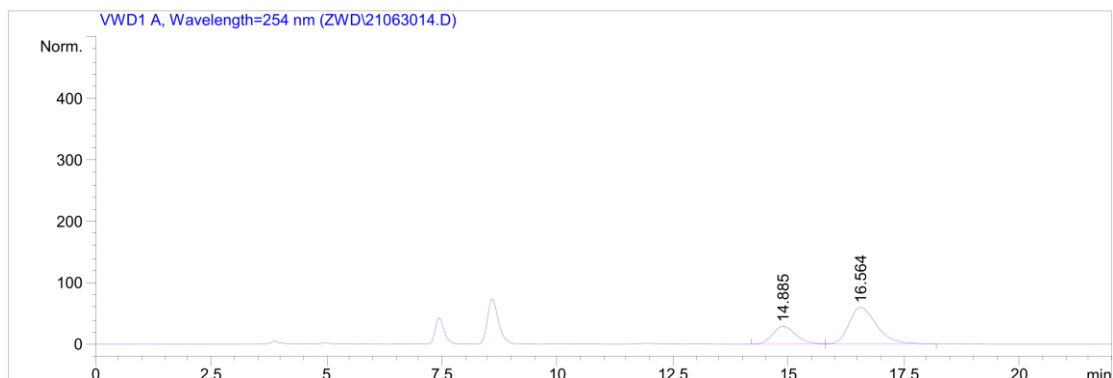
Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	20.340	VB	1.3985	7000.15967	72.79925	89.4386
2	25.021	BB	1.1640	826.61804	8.69824	10.5614



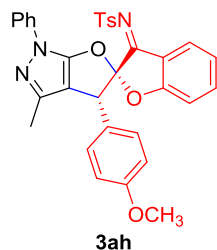
Prepared according to the procedure within 2 h as a light yellow solid (43% yield, dr > 20:1); **Enantiomeric excess** was determined to be 42% (determined by HPLC using chiral OD-H column, hexane/2-propanol = 90/10, $\lambda = 254$ nm, 30 °C, 0.8 mL/min, $t_{\text{minor}} = 14.9$ min, $t_{\text{major}} = 16.6$ min).



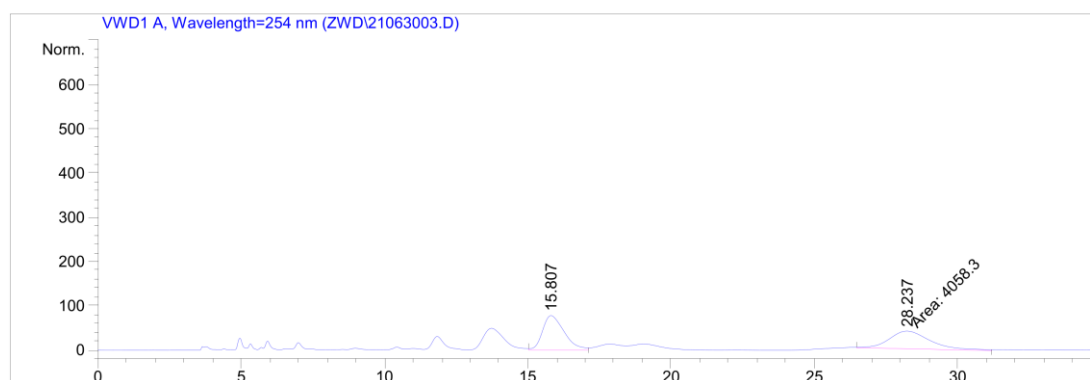
Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	14.065	BB	0.5465	1285.19141	35.47011	49.8705
2	15.878	BB	0.6595	1291.86426	28.99769	50.1295



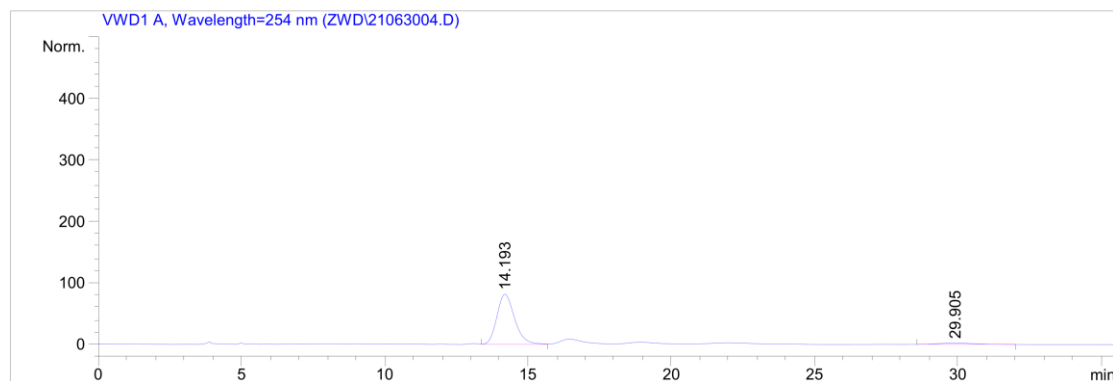
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.885	BV	0.5373	1021.19128	29.01307	29.1134
2	16.564	VB	0.6415	2486.44214	59.71934	70.8866



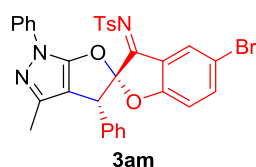
Prepared according to the procedure within 4 h as a light yellow solid (72% yield, dr > 20:1); **Enantiomeric excess** was determined to be 89% (determined by HPLC using chiral OD-H column, hexane/2-propanol = 90/10, $\lambda = 254$ nm, 30 °C, 0.8 mL/min, $t_{\text{major}} = 14.2$ min, $t_{\text{minor}} = 29.9$ min)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.807	VV	0.7886	4105.42871	78.01667	50.2887
2	28.237	MM	1.6787	4058.29590	40.29240	49.7113

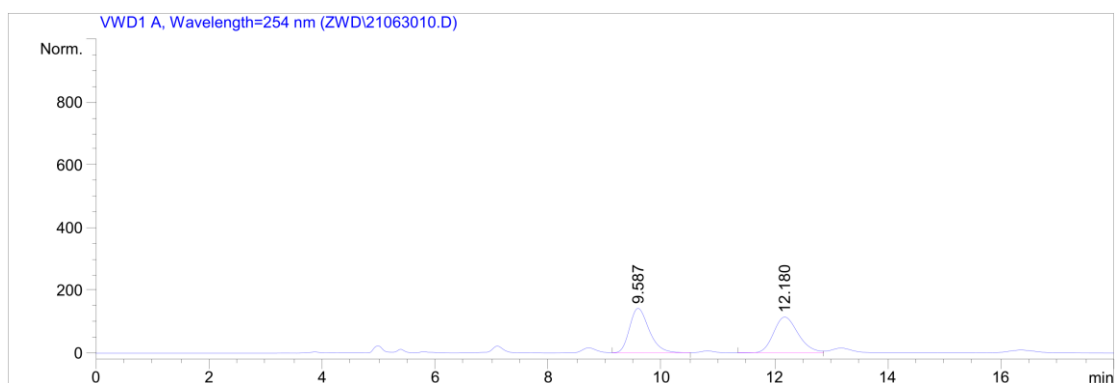


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.193	VB	0.6575	3530.92139	81.86845	94.5040
2	29.905	BB	1.0376	205.34433	2.35166	5.4960

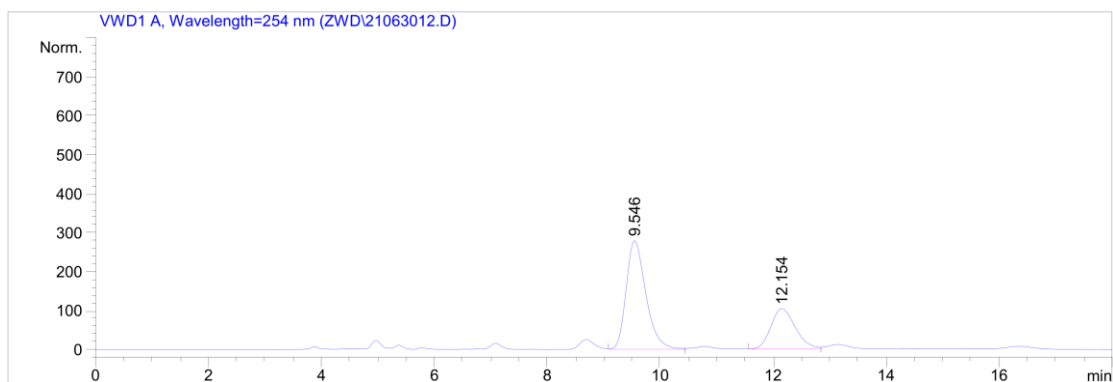


Prepared according to the procedure within 11 h as a light yellow solid (22% yield, dr > 20:1); **Enantiomeric excess** was determined to be 37% (determined by HPLC using chiral OD-H column, hexane/2-propanol = 90/10, $\lambda = 254$ nm, 30 °C, 0.8 mL/min, $t_{\text{major}} =$

9.5 min, $t_{\text{minor}} = 12.2$ min)



Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	9.587	VV	0.3719	3456.73706	142.46994	49.9520
2	12.180	VV	0.4689	3463.38159	114.18127	50.0480



Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	9.546	VV	0.3719	6774.60840	279.19775	68.2734
2	12.154	BV	0.4675	3148.16162	103.77524	31.7266

2. NMR spectra for compounds 3aa-3am

