Bayesian Optimization-assisted Screening to Identify Improved Reaction Conditions for Spiro-dithiolane Synthesis

Masaru Kondo,[1,2] H. D. P. Wathsala, [1] Kazonori Ishikawa,[1] Daisuke Yamashita,[3] , Takeshi Miyazaki,[3] Yoji Ohno, [3] Hiroaki Sasai,[1] Takashi Washio,[1] and Shinobu Takizawa*[1]

[1]*SANKEN, Osaka University, Mihogaoka, Ibaraki-shi, Osaka 567-0047, Japan*

[2]*Department of Materials Science and Engineering, Graduate School of Science and Engineering, Ibaraki University, Nakanarusawa-cho, Hitachi-shi, Ibaraki 316-8511, Japan*

[3]*Asahi Chemical Co. Ltd., Yodogawa-ward, Osaka 532-0035, Japan*

[4]*Graduate School of Pharmaceutical Sciences, Osaka University, Suita-shi, Osaka 565-0871, Japan*

E-mail: taki@sanken.osaka-u.ac.jp

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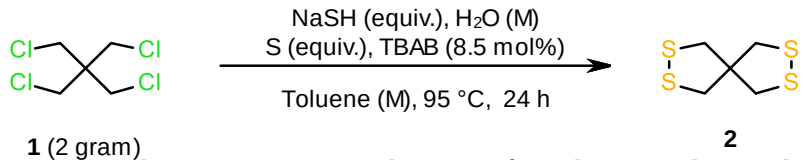
1. BO-assisted multiparameter screening of sulfurization

As a result, we can get many advantages from them in order to enhance Asahi`s products demand.



1 (2 gram) **2**

Optimization Table S1: As a result, we can get many advantages from them in order to enhance Asahi`s products demand.

entry	NaSH (eq.)	H_2O (M)	S (eq.)	Toluene (M)	GC conv.%
1	6.0	1.38	3.0	2.36	68
2	6.5	1.67	2.4	1.42	65
3	4.5	1.21	2.4	3.32	51
4	5.5	1.98	3.0	0.9	39

5	5.5	0.99	1.2	1.42	76
6	6.5	1.11	2.0	3.32	66
7	4.5	1.61	1.2	0.9	52
8	5.8	1.02	1.4	1.46	78
9	5.5	5.3	2.1	4.54	67
10	2.7	7.0	3.3	2.16	31
11	6.9	18.4	2.7	1.42	68
12	8.3	4.3	0.9	0.84	48
13	4.1	10.0	1.5	1.06	66
14	6.7	16.2	2.7	1.5	70
15	6.5	9.2	2.0	2.26	78
16	7.0	29.8	1.3	4.54	89
17	7.0	29.8	1.3	4.54	87[a]
19	7.0	29.8	1.3	4.54	81[b]

Reaction condition: **1**(2gram), NaSH (eq), Sulphur (eq), H_2O (M), Toluene (M), TBAB (8.5 mol %) at 95 °C for 24 h; a) 20g scale; b) 100g scale

Calculation of Molarity (M):

H_2O (M): mmol of **1**/H_2O volume

Toluene (M): mmol of **1**/Toluene volume

H_2O Volume: H_2O weight/density

Toluene volume: Toluene weight/density

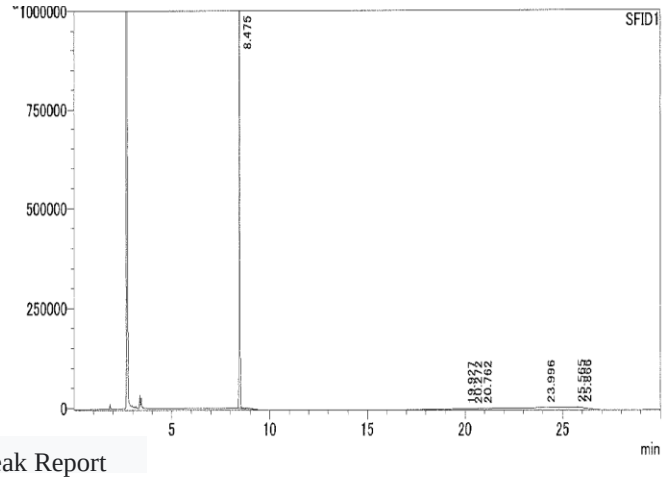
H_2O weight: WR1*NaSH weight

Toluene weight: WR2* weight of **1**

2. Calculation of GC yield from GC conversion chart: Table 2, entry 03 (100g scale)

a) Pure GC chart of tetrachloropentaerythritol (4Cl): **8:4 min** (1.46 mol/L)

Chromatogram

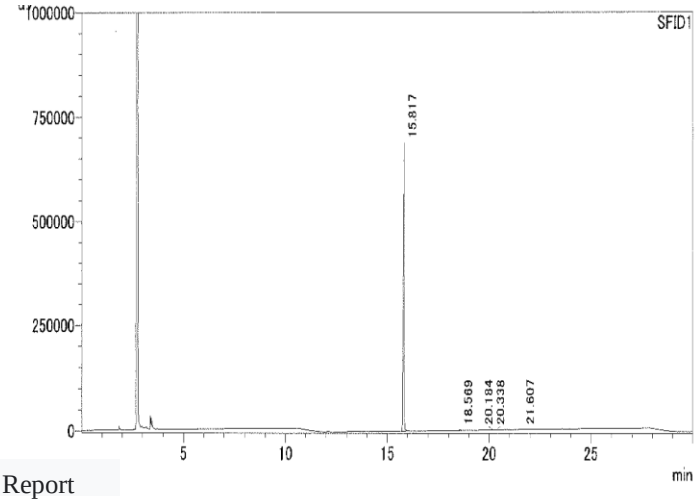


Peak Report

Peak#	tR (min)	Area	Hight	Area%	Mark	Compound name
1	8.475	4693741	1609896	99.691		
2	19.927	1321	110	0.028		
3	20.272	1660	112	0.035	V	
4	20.762	2303	175	0.049	V	
5	23.996	1689	311	0.036		
6	25.565	1678	280	0.036	V	
7	25.866	5912	394	0.126		
合計		4708304	1611278	100.000		

b) Pure GC chart of Spiro-dithiolane (4S): **15.8 min** (1.46 mol/L)

Chromatogram

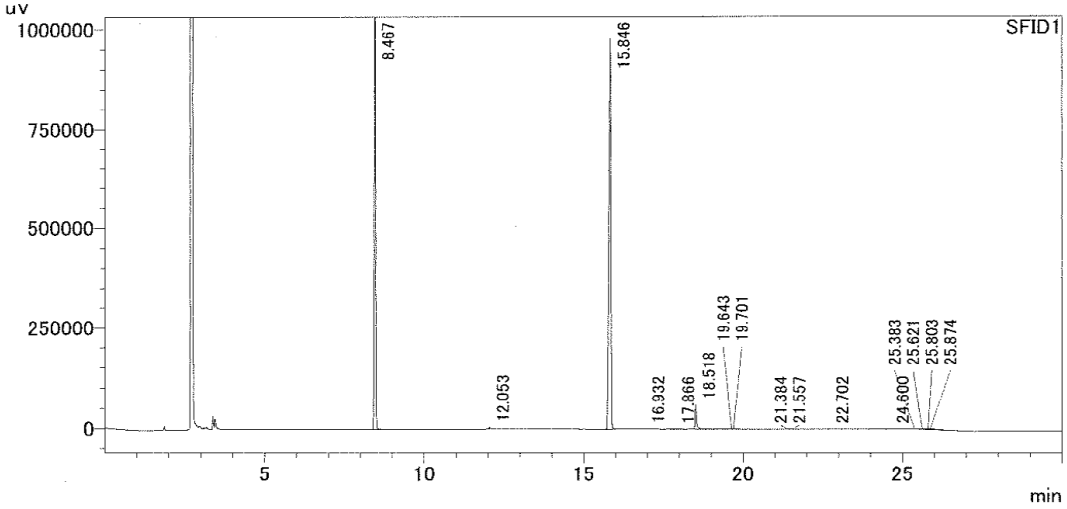


Peak Report

Peak#	tR (min)	Area	Hight	Area%	Mark	Compound name
1	15.817	2328234	682949	99.391		
2	18.569	9123	1594	0.389		
3	20.184	2535	147	0.108	V	
4	20.338	1571	187	0.067	V	
5	21.607	1042	109	0.044		
合計		2342505	684987	100.000		

b) 1:1 ratio of tetrachloropentaerythritol (50%) and Spiro-dithiolane (50%): (1.46 mol/L)

Chromatogram

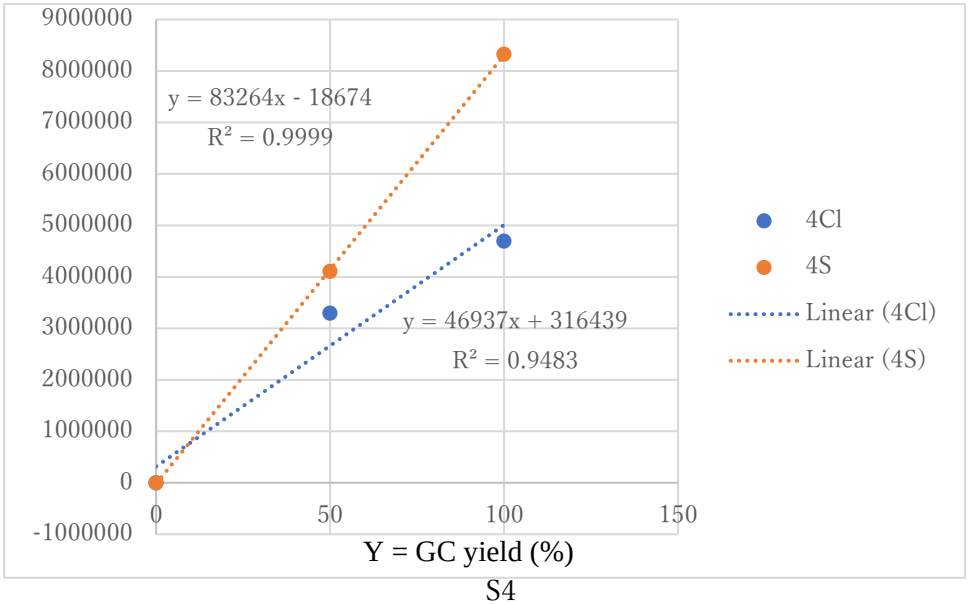


Peak Report

Peak#	tR (min)	Area	Hight	Area%	Mark	Compound name
1	8.467	3296188	1237215	42.466		
2	12.053	21424	4619	0.276		
3	15.846	4107187	974362	52.915	S	
4	16.932	14960	938	0.193	V	
5	17.866	4785	286	0.062	V	
6	18.518	214134	60164	2.759	SV	
7	19.643	1352	336	0.017	TV	
8	19.701	4285	389	0.055	TV	
9	21.384	4557	808	0.059		
10	21.557	1240	221	0.016	V	
11	22.702	1269	244	0.016	V	
12	24.600	1173	107	0.015		
13	25.383	3226	435	0.042	V	
14	25.621	21606	1452	0.278	V	
15	25.803	10260	1884	0.132	V	
16	25.874	54273	2139	0.699	V	
合計		7761918	2285598	100.000		

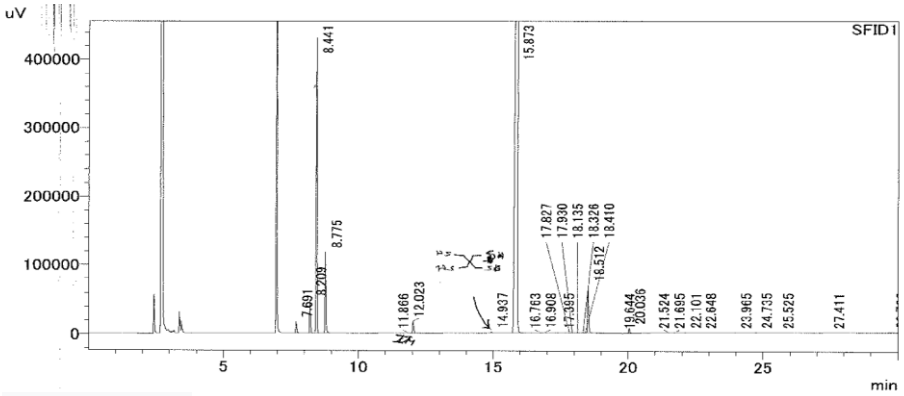
d) Draw a graph GC area vs GC yield) Graph of GC area vs GC yield

X = GC area (-)



e) 100g scale GC chart (Table 2, entry 3): (1.46 mol/L)

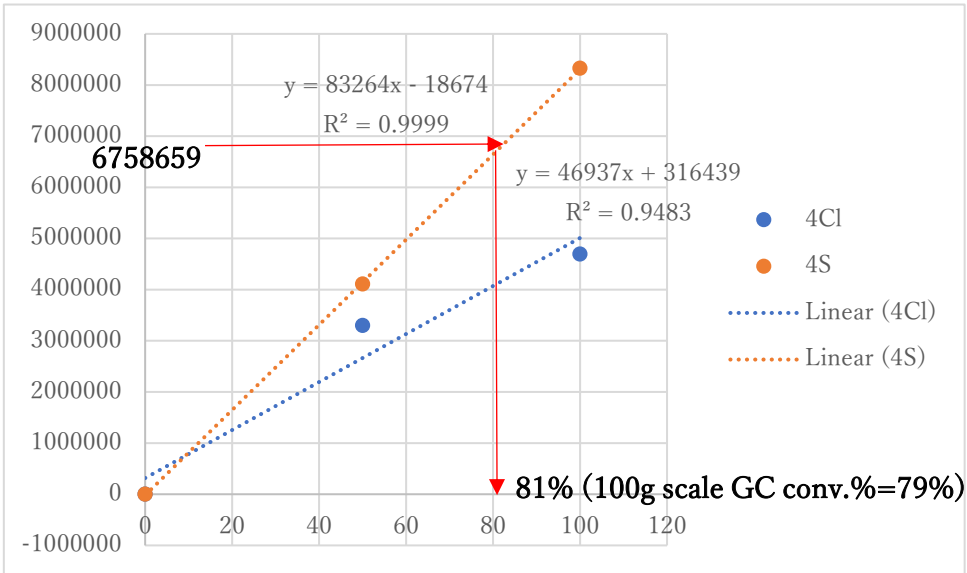
Chromatogram



Peak Report

Peak#	tR (min)	Area	Hight	Area%	Mark	Compound name
1	7.691	48635	16815	0.567	M	
2	8.209	118017	47676	1.376		
3	8.441	992121	426902	11.570	V	
4	8.775	279507	116476	3.260		
5	11.866	3422	674	0.040		
6	12.023	57992	17445	0.676	V	
7	14.937	11490	1822	0.134		
8	15.873	6758659	1310948	78.817	S	
9	16.763	1734	276	0.020	TV	
10	16.908	6155	619	0.072	TV	
11	17.395	1080	278	0.013		
12	17.827	1623	233	0.019	V	
13	17.930	3189	325	0.037	V	
14	18.135	5747	470	0.067	V	
15	18.326	4410	649	0.051	V	
16	18.410	2894	747	0.034	V	
17	18.512	208957	68043	2.437	V	
18	19.644	2883	818	0.034		
19	20.036	25712	7748	0.300		
20	21.524	1416	396	0.017	V	
21	21.695	1199	289	0.014		
22	22.101	4088	951	0.048		

Area of **6758659** = GC yield??



Calculation [1]:

$$Y = 83264X - 18674$$

$$6758659 + 18674/83264 = X$$

$$X = 81\%$$

GC conversion yield ≈ GC calculated yield±2

Reference

1. https://www.shimadzu.com/an/service-support/technical-support/analysis-basics/fundamentals/results.html

3. Calculation of the correlation coefficient between the conversion yield of 1 and each loading of chemicals afforded the corresponding values.