Asian Journal of Chemistry Vol. 22, No. 9 (2010), 7213-7218

Microwave-Assisted Synthesis of Di-*sec*-butyl Disulphide by Phase Transfer Catalysis under Solvent-Free Conditions

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Di-*sec*-butyl disulphide was synthesized by phase transfer catalysis under microwave irradiation and solvent-free conditions. The optimal experiment conditions were obtained by single-factor and orthogonal designs. The samples synthesized under the optimal conditions were characterized by infrared spectrometer, ^{1}H-nuclear magnetic resonance and gas chromatograph.

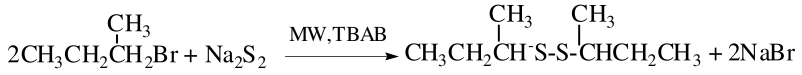
Key Words: Microwave-assisted synthesis, Solvent-free, Phase transfer catalysis, *Sec*-butyl bromide, Di-*sec*-butyl disulphide.

INTRODUCTION

Organic disulphide is an important organic sulphide possessing unique and crucial chemistry status in the synthetic and biochemical areas[1]. Large disulphide-linked aggregates are prevalent in proteins and many other bioactive molecules. Large disulphide-linked aggregates are prevalent in proteins and many other bioactive molecules. Industrially, disulphides have wide applications as vulcanizing agents for rubbers, giving them excellent tensile strength[2]. They are used as intermediates for the synthesis of medicine, dyes, agrochemical containing sulphur[3] and so on.

The developments in disulphide synthesis are rather rapid. Synthetic technique is being improved, from normal reaction to reaction using many new techniques such as microwave and new phase transfer catalysis[4,5].

Di-*sec*-butyl disulphide is a symmetrical disulphide. Several methods of preparation of disulphide have been reported in the literatures[6-15]. Most of them used 2-butanethiol as a reagent, various oxidants or catalysts involved such as N_2O_4/charcoal or PVP-N_2O_4, N-chlorosuccinimide, oxygen catalyzed by a rhodium complex, molecular bromine, *bis*[trinitratocerium(IV)] chromate ($[Ce(NO_3)_3]_2CrO_4$), copper(II) chloride or sulphur. These oxidants and catalysts are either expensive or difficult to remove. 2-Butanethiol is volatile, has an offensive odor and does damage to the equipment and environment. So the synthetic route using 2-butanethiol as a reagent is seldom employed industrially. Sodium sulphide is an important nucleophile and reducing agent derived from H_2S. It can be used for the synthesis of thiols, thioethers and disulphides[2] as a reducing agent. In this work, we used sodium sulphide and sulphur to form disulphide anion in water and organic solvent-free under microwave irradiation condition and then reacted with *sec*-butyl bromide to afford di-*sec*-butyl disulphide in good to excellent yield in short time. The synthetic route is as follows:



$$2CH_3CH_2\overset{CH_3}{C}H_2Br + Na_2S_2 \xrightarrow{MW,TBAB} CH_3CH_2\overset{CH_3}{C}H\text{-}S\text{-}S\text{-}\overset{CH_3}{C}HCH_2CH_3 + 2NaBr$$

EXPERIMENTAL

In all experiments, distilled water was used. Sulphur, sodium sulfate and tetrabutyl ammonium bromide and sodium sulphide were supplied by Tianjin Kermel Chemical Reagent Co. and were of AR grade with purity higher than 99.5 %. *Sec*-butyl bromide was supplied by Sanmenxia Aoke Chemical Industry Co., Ltd. Di-*sec*-butyl disulphide (the authentic sample) was supplied by Germany Chemical Co., Ltd.

Apparatus and procedure: Microwave irradiations were carried out with a KD23C-BA commercial microwave oven at 750W. IR spectra were measured for KBr discs using a Nicolet IR300 FT-IR spectrometer. ^{1}H NMR spectra (400 MHz) were recorded in $CDCl_3$ using a Bruker DPX-400 spectrometer. GC spectra were measured by GC-9800TFP. All the matters used were weighed by an electronic balance (Mettler Toledo AB204-N) with an accuracy of ± 0.0001 g. Vacuum filtration was operated using SHB-III multi-use of recycled water pump.

General procedure: Sulphur powder 3.2 g (0.1 mol) was added to a mixture of sodium sulphide 9.755 g and water (35 mL) after which the reaction mixture was irradiated for at 270 W an appropriate period. The solution changed from colourless to brownish red. After dissolution, the reaction mixture was cooled to room temperature and TBAB (2 % of the mass of *sec*-butyl bromide) was added. Then *sec*-butyl bromide (0.16 mol) was added and the reaction mixture was irradiated for 50 min under the same irradiation power. The progress of the reaction was monitored by GC. The organic layer was washed well with water and dried over sodium sulfate. The solid inorganic salt was separated by filtration. The organic layer was concentrated under reduced pressure to afford di-*sec*-butyl disulphide.

RESULTS AND DISCUSSION

Effect of microwave irradiation power on yield of reaction: Methods as employed, only microwave irradiation power was changed. Results are shown in Table-1. It showed that when microwave irradiation power was 90 W, the reaction was inadequate and the yield was low. Yield increased with the increment of microwave irradiation power. But when microwave irradiation powers were beyond 270 W, yield decreased. That was because part of *sec*-butyl bromide volatilized and part of

TABLE-1
EFFECT OF MICROWAVE IRRADIATION POWER

Irradiation power (W)	90	180	270	360	450
Yield (%)	45.01	62.36	86.23	80.92	65.74

catalyst was broken down due to high temperature aroused by high microwave irradiation power.

Effect of mole ratio of sodium disulphide to *sec*-butyl bromide on yield of reaction: Methods as employed, only mole ratio was changed. Results are shown in Table-2. It showed that when mole ratio was 1.0:1.6, yield of the reaction was 87.98 %, equal to that of 1.0:1.4 more or less. But when mole ratio increased, yield decreased. That was because part of *sec*-butyl bromide was in inadequate reaction. Considering various factors, mole ratio 1.0:1.6 was preferred.

TABLE-2
EFFECT OF MOLE RATIO ON YIELD OF REACTION

$n(Na_2S_2)$:$n(C_4H_9Br)$	1.0:0.8	1:1	1.0:1.2	1.0:1.4	1.0:1.6	1.0:1.8
Yield (%)	86.2	86.23	87.12	88.05	87.98	86.08

Effect of amount of catalyst on yield of reaction: Methods as employed, only amount of catalyst was changed. Results are shown in Table-3. It showed that the reaction was able to operate without catalyst, but yield is rather low. That was because most of the raw material didn't react. Increased amount of catalyst, the reaction rate of main reaction increased and so did the side reaction. 2 and 3 % were more or less.

TABLE-3
EFFECT OF AMOUNT OF CATALYST ON YIELD OF REACTION

Amount of catalyst (%)	0	1	2	3	4
Yield (%)	32.16	74.63	87.98	88.02	87.24

Effect of microwave irradiation time on yield of reaction: Methods as employed, only microwave irradiation time was changed. Results are shown in Table-4. It showed that when irradiation time was short, the reaction was inadequate and the yield was low. Yield increased with the increment of microwave irradiation time. But when microwave irradiation time was beyond 40 min, yield decreased. That was because part of *sec*-butyl bromide volatilized and part of catalyst was broken down due to long irradiation time.

TABLE-4
EFFECT OF MICROWAVE IRRADIATION TIME ON YIELD OF REACTION

Irradiation time (min)	20	40	60	80	100
Yield (%)	84.43	88.12	87.98	86.87	82.65

Results of orthogonal design: Factors of the experiment were microwave irradiation power, mole ratio of sodium disulphide to *sec*-butyl bromide, amount of catalyst and microwave irradiation time. Orthogonal design was adopted to further afford better conditions. The results are listed in Table-5.

TABLE-5
RESULTS OF ORTHOGONAL DESIGN

Entry	Irradiation power (A)	Mole ratio (B)	Amount of catalyst (%) (C)	Irradiation time (D)	Yield (%)
1	225	1:1.5	1.5	30	84.35
2	225	1:1.6	2	40	88.21
3	225	1:1.7	2.5	50	86.97
4	270	1:1.5	2	50	88.00
5	270	1:1.6	2.5	30	87.86
6	270	1:1.7	1.5	40	87.42
7	315	1:1.5	2.5	40	84.20
8	315	1:1.6	1.5	50	85.63
9	315	1:1.7	2	30	85.74
Mean value k_1	86.510	85.517	85.800	85.983	–
Mean value k_2	87.760	87.233	87.317	86.610	–
Mean value k_3	85.190	86.710	86.343	86.867	–
Range R	2.570	1.717	1.517	0.883	–

The factors followed the order microwave irradiation power > mole ratio of sodium disulphide to *sec*-butyl bromide > amount of catalyst > microwave irradiation time by the mean values. The optimum combination was A2, B2, C2, D3.

Results of orthogonal design under the optimal experiment conditions: The optimum combination was not presented in the orthogonal design. So another two experiments were carried out according to the optimum combination. The results were listed in Table-6.

TABLE-6
RESULTS OF ORTHOGONAL DESIGN UNDER
THE OPTIMAL EXPERIMENT CONDITIONS

Entry	Yield (%)
1	88.36
2	88.42

Product analysis and characterization

GC Analysis: A gas chromatograph (Shanghai Kechuang, model: GC-9800 TFP) was used to determine the course of reaction. The chromatograph was equipped with a flame ionization detector and a capillary column (SE-54, 0.32 mm × 30 m). The samples were examined under the following conditions: temperature: injector = 533.2 K; column = 453.2 K; detector = 533.2 K. The uncertainty in temperatures was 0.5 K. The procedure was that column temperature sustained 7 min at 453.2 K, temperature rose to 513.2 K at the heating rate of 20 K/min and then sustained 5 min. The carrier gas was nitrogen. The component mean retention time was *sec*-butyl bromide = 2.828 min, di-*sec*-butyl sulphide = 3.796 min, di-*sec*-butyl disulphide = 6.407 min, di-*sec*-butyl trisulphide = 9.959 min and the other two peaks were the peak of decomposition products of TBAB. The mean uncertainty in the measurements of mass fractions was 0.05.

IR Characterization: IR spectrogram was measured for KBr discs using a Nicolet IR300 FT-IR spectrometer. The spectrogram was shown in Fig. 2. The wave numbers were 1454, 1374, 1284, 1215, 1145, 1054, 999.9, 953 and 787 cm^{-1} in the order, in accord with that in the literature[16].

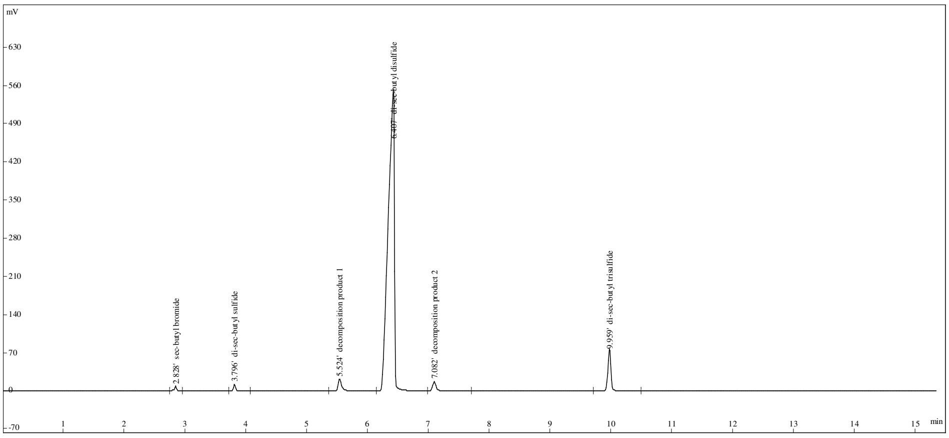


Fig. 1. GC spectrum of the course of reaction

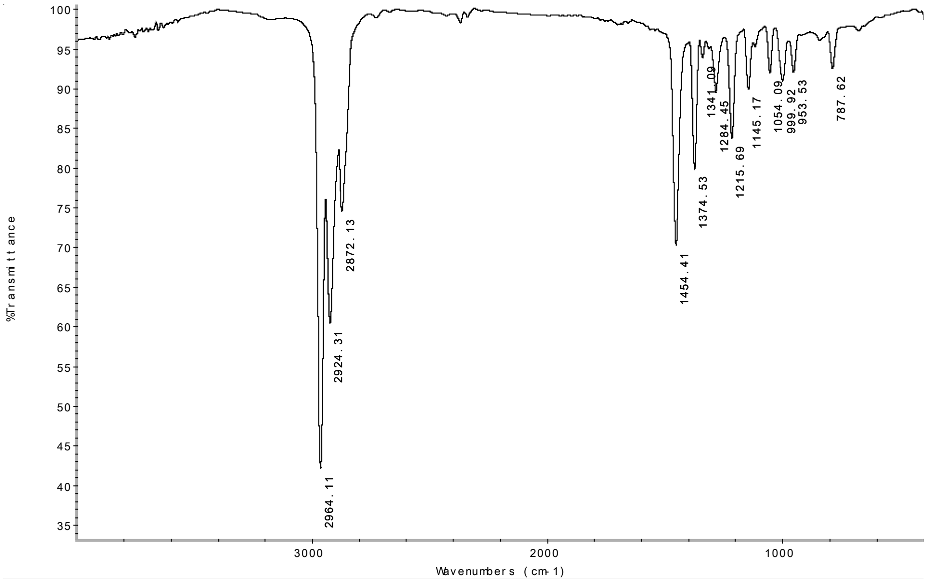


Fig. 2. FT-IR spectrum of di-*sec*-butyl disulfide synthesized

^{1}H NMR spectrum: ^{1}H NMR of the authentic sample and the product synthesized were recorded in $CDCl_3$ using a Bruker DPX-400 spectrometer. The NMR spectrums showed that di-*sec*-butyl disulphide synthesized and the authentic sample were in perfect accord. δ 2.70-2.75 (m, 2 × -S-S-CH), 1.45-1.74 (m, 2 × $-CH_2$), 1.27-1.29 (d, 2 × CH_3-CH-), 0.96-1.00 (t, 2 × CH_3-).

Conclusion

The optimal experiment conditions were obtained by single-factor and orthogonal designs. Results were microwave irradiation power 270 W, mole ratio of sodium disulphide to *sec*-butyl bromide 1.0:1.6, amount of catalyst 2 % and microwave irradiation time 50 min. The samples synthesized were characterized by infrared spectrometer (IR), ^{1}H NMR and gas chromatograph. They had satisfactory IR and ^{1}H NMR and were compared with the authentic sample.

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(*Received*: 30 January 2010; *Accepted*: 22 June 2010) AJC-8821