# Diallyl disulfides: comparison between classical and microwave-assisted synthesis

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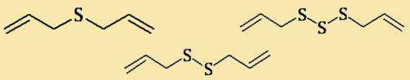
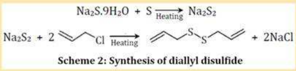
## Context and objectives

Garlic (*Allium sativum* L.) is recognized for its therapeutic effects in various ancestral medicines. Its properties are mainly related to the organosulfur compounds that are freed when the plant is crushed. Among those interesting compounds, diallyl sulfides (DAS) possess antioxidant and antitumor properties[1], and could lower the cholesterol level[2]. The most common one is the diallyl disulfide (DADS), but the diallyl monosulfide (DAMS) is also formed in garlic (scheme 1).



**Scheme 1: diallyl monosulfide (DAMS), diallyl disulfide (DADS) and diallyl trisulfide (DATS)**

Regarding those potential benefits for health, it is important to find a simple way to obtain these molecules, in order to experiment deeper their effects. Various synthetic routes exist, leading to different yields and purity in DADS, DAMS but also diallyl trisulfide (DATS). Our objective was thus to optimize the synthesis of DADS (scheme 2).




**Scheme 2: Synthesis of diallyl disulfide**

Two processes are suggested in the literature: a classical synthesis according to Maloney et al.[3], and a microwave-assisted one according to Yuan et al[4].

## Material and methods

In order to optimize the yield and the purity of DADS in the synthesis, two parameters have been studied (scheme 3): the thermal treatment and the phase transfer catalysis (PTC).

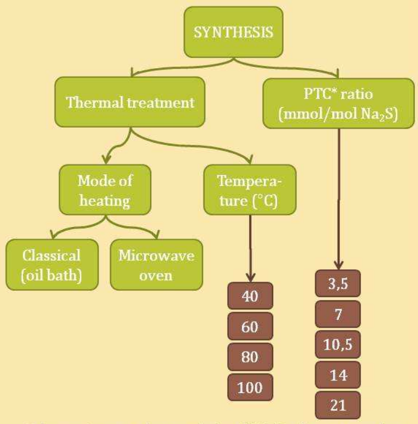
For the first step of the synthesis, an equimolar solution containing 1,3 mol/L of sodium sulfur and sulfur is heated for 2 hours. Then, an equimolar amount of allyl bromide is added. The mixture is stirred for 2 hours at the choosen temperature.
The conditions tested are summarized in table 1.

The microwave heating is performed in a Milestone STARTS MW oven in closed vessels conditions. The samples in the oil bath are also closed.
We choose tetrabutylammonium bromide as PTC, as suggested by Yuan et al[4]. The PTC tests were done in an oil bath at 60°C.

| | | Conditions | | | | |
|---|---|---|---|---|---|---|
| Thermal treatment | Oil bath | 40°C | 60°C | 80°C | 100°C | |
| | Microwave | | | | | |
| PTC ratio (mmol/mol of Na2S) | | 3,5 | 7 | 10,5 | 14 | 21 |

**Table 1: experimental plan**

The products have been identified by GC-MS (Agilent 6890N-5973N), on an HP-5ms column and by $^1H$ and $^{13}C$ NMR (Varian Unity 600). Then, the amount of DAS is measured by GC-FID.




**Scheme 3: experimental plan (*PTC: phase transfer catalyst)**

## Influence of the phase transfer catalyst amount

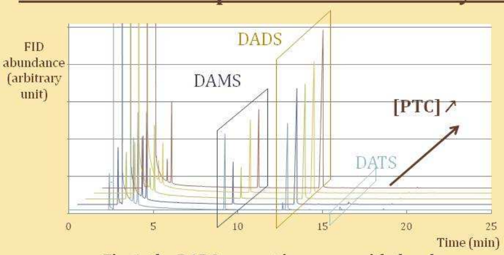



**Fig. 1: the DADS amount increases with the phase transfer catalyst (PTC) concentration**

**On the yield** (figure 1)
The PTC seems to enhance the production of DADS : in the presence of 21 mmol of PTC/$Na_2S$ mol the yield increase by a factor 3,5 while the amount of DAMS doesn't increase.

**On the formation of side-products** (figure 2)
The absence of PTC leads to lots of impurities (>40 %). The PTC addition allows to decrease the impurity level to less than 20 %, but doesn't enhance the proportion of DADS compared to the other DAS (only 8 % more DADS with a 6-fold amount of PTC addition)

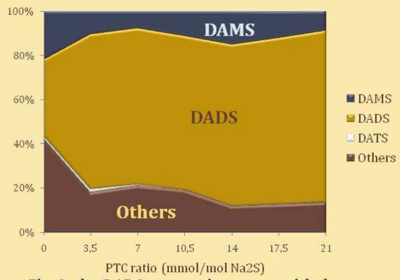



**Fig. 2: the DADS amount increases with the phase transfer catalyst (PTC) concentration**

## Influence of the temperature and heating process

**On the yield** (figure 3)
The highest amount of DADS is found at 40°C under microwave treatment, and this amount slightly increases between 40 and 80°C under classical heating conditions with a maximum at 80°C. Furthermore, the amount of DAMS increases constantly with the temperature.

**On the formation of side-products** (figure 4)
High temperatures lead to a diminution of the DADS proportion, in particular in the microwave-assisted synthesis in which the DAMS takes the largest part of the proportion from 80°C.

**Heating process**
The classical oil bath heating seems to provide a better reproducibility as well as a higher amount of DADS under 100°C. This technique is therefore preferred.

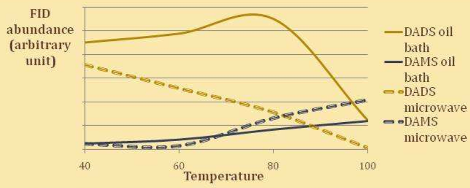



**Fig. 3: the DADS amount goes down with the temperature**

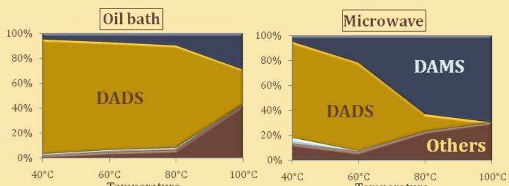



**Fig. 4: the DADS rate decreases with the temperature, especially in the microwave oven**

## Conclusion

- The presence of a phase transfer catalyst is recommended to increase both the quantity of DADS in this synthesis and the purity of the final product. The use of other PTC could eventually improve further those results.
- At the opposite, the rise of temperature leads to a loss of purity and a huge decrease in yield.

**We recommend a temperature of 40°C and the presence of a phase transfer catalyst to improve the amount of DADS in the synthesis**

### Literature cited

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### Acknowledgments

The authors thank Virginie Van den Broeck, Danny Trisman and Vincent Hote for their technical assistance.

### For further information

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