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Microwave-assisted synthesis of symmetric and asymmetric viologens

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ABSTRACT

Viologens are generally synthesized by N-alkylating 4,4′-bipyridine with alkyl halides. Under conventional heating conditions, however, their synthesis suffers from long reaction times and, often, low yields. In this work, symmetric and asymmetric viologens were synthesized under the assistance of microwave irradiation in good to excellent yields and in short reaction times.

Viologens are diquaternary derivatives of 4,4′-bipyridine[1] with attractive redox properties. As a result, they have become convenient building blocks of multifunctional materials for the fabrication of liquid crystal displays,[2,3] light emitting diodes,[4] solar cells,[5–8] and biosensors.[9–11] However, they are generally synthesized in good yields only when prolonged reaction times, from a few hours to days, are used.[1,12–19] Thus, the identification of efficient and fast synthetic routes to access these compounds can have significant implications on diverse areas of research.

In this work, the use of microwave technology in the synthesis of symmetric, asymmetric viologens and a bis-viologen was investigated with the objective of improving yields and shortening reaction times, relative to conventional heating conditions. To the best of our knowledge, only one report on microwave assistance to viologen synthesis has appeared in the literature so far, but only a few examples were investigated in this study.[20] We have extended this approach to the preparation of 17 derivatives and investigated systematically the influence of the experimental conditions on these reactions.

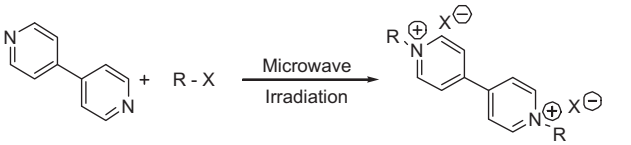
Symmetric viologens were synthesized by reacting 4,4′-bipyridine with various alkyl halides under microwave irradiation conditions[21] to give compounds **1**–**5** in good to excellent yields according to Scheme 1.

Methyl viologen (**1**) was synthesized in yields ranging from 34% to 83% by varying the equivalents of methyl iodide relative to 4,4′-bipyridine, the temperature, reaction time and solvent (Table 1). **1** was obtained in a yield of 83%, when 20 equiv of methyl iodide were used in acetonitrile at 80 °C. The reaction was completed in 10 min only. Shorter reaction times and higher temperatures resulted in lower yields. The reaction was also performed in methanol, but the expected product was obtained in a much lower yield (34%).

The reaction of excess ethyl bromide with 4,4′-bipyridine in DMF afforded ethyl viologen (**2**) in a yield of 84% (Table 2). Significantly lower yields were obtained in MeCN and MeOH.

Propyl viologen (**3**) was synthesized in yields ranging from 11% to 60% by irradiating the reaction mixture for 10 min at 130 °C and by using different reaction solvents, like toluene, acetonitrile, and DMF (Table 3).

DMF and a large excess of the alkyl halide had to be employed to get good yields. Use of 5 or 10 equiv, resulted in much lower yields, below 25%. Other solvents, such as toluene and acetonitrile, also resulted in low yields.



1 R = -CH_3
2 R = -CH_2CH_3
3 R = -$CH_2CH_2CH_3$
4 R = -CH_2Ph
5 R = -$CH_2(CH_2)_6CH_3$

Scheme 1. Synthesis of symmetric viologens.

Table 1
Reaction conditions for the synthesis of methyl viologen (**1**)

MeI (equiv)	*T* (°C)	Time (min)	MeCN (mL)	MeOH (mL)	Yield (%)
5	130	2.5	—	5	34
10	80	3	5	—	50
10	80	5	5	—	59
10	80	10	5	—	74
20	80	10	5	—	83
20	100	10	5	—	76
20	100	15	5	—	79
20	80	120	5	—	50

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Table 2
Reaction conditions for the synthesis of ethyl viologen (**2**)

EtBr (equiv)	*T* (°C)	Time (min)	MeCN (mL)	MeOH (mL)	DMF (mL)	Yield (%)
10	130	3	5	—	—	56
10	130	5	—	5	—	Traces
10	130	10	—	—	5	84

Table 3
Reaction conditions for the synthesis of propyl viologen (**3**)

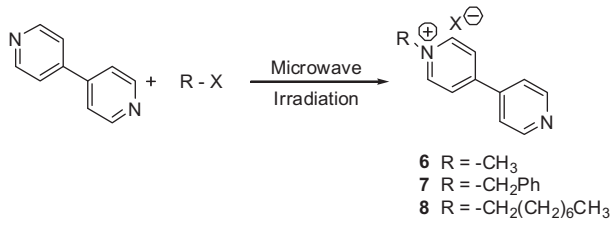
PrBr (equiv)	*T* (°C)	Time (min)	MeCN (mL)	PhMe (mL)	DMF (mL)	Yield (%)
20	130	10	5	—	—	16
20	130	10	—	—	5	60
5	130	10	—	5	—	Traces
10	130	10	5	—	—	11
30	130	10	5	—	—	21

Table 4
Reaction conditions for the synthesis of benzyl viologen (**4**)

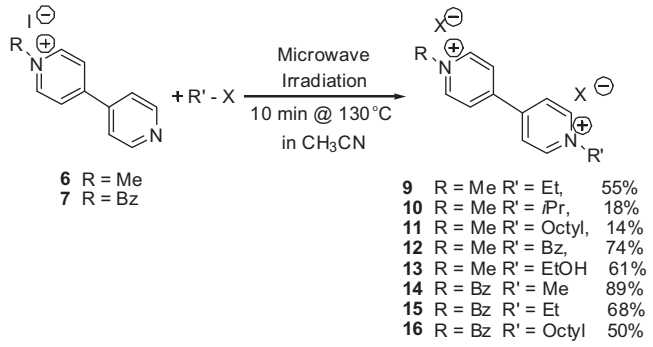
BzBr (equiv)	*T* (°C)	Time (min)	MeCN (mL)	PhMe (mL)	Yield (%)
5	130	10	—	5	71
10	130	10	5	—	82
10	80	10	5	—	77
10	100	10	5	—	84

Table 5
Reaction conditions for the synthesis of octyl viologen (**5**)

OctBr (equiv)	*T* (°C)	Time (min)	MeCN (mL)	Yield (%)
10	130	10	5	31
10	100	10	5	20
20	130	30	5	27



Scheme 2. Synthesis of monoalkylated bipyridine derivatives.



Scheme 3. Synthesis of asymmetric viologens **9**–**16**.

Benzyl viologen (**4**) was synthesized in yields ranging from 71% to 84% by varying the equivalents used of benzyl bromide, temperature, and solvent according to Table 4.

Table 6
Reaction conditions for the synthesis of 1-methyl-[4,4′]bipyridinyl-1-ium (**6**)

MeI (equiv)	*T* (°C)	Time (min)	MeCN (mL)	DCM (mL)	Yield (%)
1	130	10	—	5	6
1	130	20	—	5	4
1	130	20	5	—	Traces
1	50	20	—	5	52
0.5	60	20	—	2	72

Compound **4** was obtained in excellent 84% and 82% yields when 10 equiv of benzyl bromide were used in acetonitrile at 100 or 130 °C, the reaction was completed in 10 min. Employing other solvents, such as toluene, and increasing or decreasing the reaction temperature resulted in slightly lower yields.

Octyl viologen **5** was synthesized in yields ranging from 27% to 31% (Table 5).

The highest yields were obtained by using 10 equiv of octyl bromide in acetonitrile at 130 °C. The reaction was completed in 10 min. Longer reaction times or larger number of equivalents of the alkyl halide did not improve the overall yield.

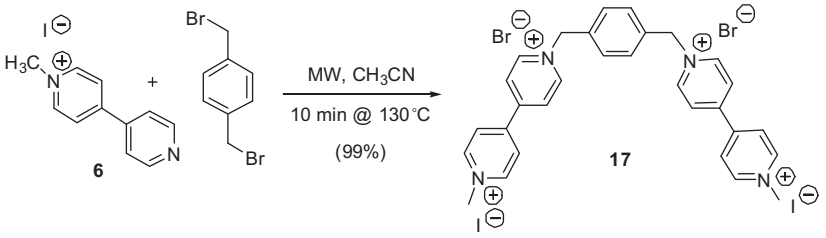
The excellent results obtained for the synthesis of symmetric viologens prompted us to investigate whether it was possible to synthesize viologens bearing different alkyl groups (asymmetric). In order to achieve this goal, it was first necessary to synthesize a monoalkylated bipyridine derivative (Scheme 2) and then perform a second alkylation with a different alkyl halide (Scheme 3).

Table 7
Reaction conditions for the synthesis of 1-benzyl-[4,4′]bipyridinyl-1-ium (**7**)

BzBr (equiv)	*T* (°C)	Time (min)	PhMe (mL)	MeCN (mL)	DCM (mL)	Yield (%)
0.5	130	10	4	—	—	4
1	130	10	3	—	—	22
0.9	70	5	—	—	2	Traces
0.9	70	5	—	2	—	14
0.9	100	10	2	—	—	14
1	50	60	—	—	4	47
1	60	60	—	—	4	51
0.5	60	60	—	—	2	91

Table 8
Reaction conditions for the synthesis of 1-octyl-[4,4′]bipyridinyl-1-ium (**8**)

OctylBr (equiv)	*T* (°C)	Time (min)	MeCN (mL)	Yield (%)
1	130	10	4	14
1	60	60	4	28
0.5	60	60	2	41



Scheme 4. Synthesis of bis-viologen **17**.

Monoalkylated bipyridine derivatives **6**–**8** were synthesized under microwave irradiation according to the conditions in Tables 6–8 in 72%, 91%, and 41% yields, respectively.

Good yields of compounds **6**–**8** were obtained, although temperatures in the range of 50–60 °C and longer reaction times than for the synthesis of viologens **1**–**5** had to be used.

Asymmetric viologens were then synthesized by reacting **6** and **7** with 10 equiv of various alkyl halides under microwave conditions to give compounds **9**–**16** in good yields and in 10 min only (Scheme 3).

A bis-viologen (**17**) was also synthesized in good yield by reacting 1-methyl-[4,4′]bipyridinyl-1-ium (**6**) with excess α,α′-dibromo-*p*-xylene under microwave irradiation (Scheme 4).

In conclusion, our experiments showed that the best general conditions to access symmetric viologens entailed using either MeCN (for very reactive alkyl halides) or DMF, and the reaction times of 10 min with 10 equiv of the alkyl halide. The reaction temperatures of 130 °C worked well in most cases but methyl viologen required a lower temperature (80 °C). Monoalkylation of 4,4′-bipyridine was best accomplished by irradiating the reaction mixture for 20–60 min in DCM at 60 °C using 0.5 equiv of the alkyl halide. The general synthesis of asymmetric viologens entails using conditions identical to those of symmetric molecules, but MeCN was the best solvent.

In summary, viologens **1**–**5**, and **9**–**17** were successfully synthesized by using microwave irradiation in short reaction times (when compared to traditional heating methods) and in good to excellent yields.

Acknowledgments

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