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A Short and Efficient Synthesis of Ketene O,O- and S,S-Acetals under Focused Microwave Irradiation and Solvent-Free Conditions

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Abstract: A new methodology leading to ketene O,O- and S,S-acetals is reported. The title compounds were prepared from the corresponding halogenated precursors under microwave irradiation in the absence of solvent within 5-25 minutes with excellent yields. Yields obtained under microwaves are by far the best when compared to those obtained by ultrasound or classical heating in the same conditions of time and temperature.

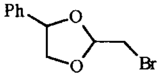
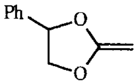
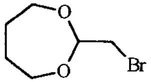
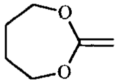
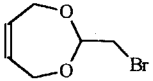
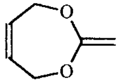
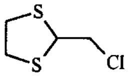
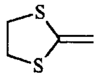
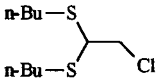
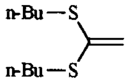
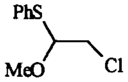
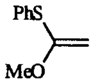
Ketene acetals and dithioacetals constitute a class of compounds of great interest in organic synthesis as well as in polymer science. Their preparations were rationalized in 1936[1] and 1919[2] respectively. However, owing to the growing importance and applications of these compounds, the synthesis of ketene O,O- and S,S-acetals has been widely studied in the last years.[3]

In 1992, we have reported a procedure to obtain cyclic ketene acetals by phase transfer catalysis without solvent coupled with ultrasound.[4] This methodology employed mild reaction conditions, allowing the title compounds in excellent yields.

Microwave irradiation under solvent-free conditions has been used to improve several synthetic processes.[5] However, to the best of our knowledge, applications of microwaves to β-elimination reactions are very uncommon.[6]

In connection with our studies to extend and delimit the scope of microwave activation in the organic reactions, we now report the preparation of ketene O,O- and S,S-acetals under microwave irradiation and solvent-free conditions. We also try here to take advantage of this study to establish a useful comparison of microwave and ultrasound activations everything equal elsewhere.

Table. β-Eliminations of halogenated acetals

				Microwaves				Ultrasound[a]	Classical Heating[a]
Entry	**Substrate**	**Product**	**Base (Equiv)**	**Power (W)**	**Temp (°C)**	**Time (min)**	**Yield (%)**	**Yield (%)**	**Yield (%)**
1			KOtBu (2) TBAB	75	75	5	87	55	36
2			KOtBu (2)	75	64	5	97	16	41
3			KOH (2.5) TBAB	75	70	25	82	58	57
4			KOtBu (1.3)	75	70	5	92	42	71
5			KOtBu (1.3) TBAB	105	89	25	79	45	15
6			KOtBu (1.3) TBAB	75	62	5	90	51	53

[a] All the reactions were carried out under the same indicated reaction conditions (nature and amount of base, temperature and reaction time)

We prepared the title compounds from the corresponding halogenated acetals[7] or thioacetals,[3f] through a β-elimination reaction with a strong base within 5-25 minutes in 79-97% yield.[8] These reactions were performed in a focused microwave reactor (monomode system) Synthewave 402 from Prolabo with measurement and control of power and temperature by infrared detection. Results are summarized in the table.

To prepare ketene O,O-acetals we started from their bromoderivatives, although ketene S,S-acetals were obtained from the corresponding chloroderivatives.[9] Reaction conditions (nature and amount of base, temperature and reaction time) were optimized for every substrate. When β-elimination yielded almost quantitatively the product (Entry 2 and 4), the phase transfer agent, tetrabutylammonium bromide (TBAB), was not necessary. This observation is in line with previous work indicating that the transfer agent is not always necessary when KOtBu is involved owing to the strength of this base.[10] In entry 3, a milder base (potassium hydroxide) was required to achieve a good yield.

Our experience in carrying out the optimization of these reactions showed that one of the most important parameters is the reaction temperature. A little change in the other factors did not produce a significant yield change. However, a change of the reaction temperature of about 10-15° C resulted in substrates not reacting (if temperature decreases) or products undergoing significant decomposition (if temperature increases).

To compare microwave irradiation with other methodologies, we carried out the reactions under ultrasound irradiation, in a cleaning bath, and under classical heating in an oil bath with the indicated reaction conditions. All these results are also summarized in the table. **They clearly show that microwave activation afforded very superior yields to those obtained under other classical or non-classical methods under similar reaction conditions (base, temperature and reaction time).**

In conclusion, microwave irradiation under solvent-free conditions induces halogenated acetals or dithioacetals to undergo dehydrohalogenation reactions leading to ketene O,O- or S,S-acetals in a fast and efficient process affording excellent yields.

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