

Acceleration of Ortho Ester Claisen Rearrangement by a Commercial Microwave Oven

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Microwave irradiation, using a commercial microwave oven accelerates (in 10–15 min) the three-step ortho ester Claisen rearrangement of allyl and propynyl alcohols in dry DMF in open Erlenmeyer flasks.

The ability to form γ,δ -unsaturated esters, e.g. **4**, as well as the ease with which quaternary centres are formed in one-pot reactions from allylic alcohols (e.g. **1** via the mixed ortho ester **2** and the ketene acetal **3**) makes the ortho ester Claisen rearrangement a very useful and dependable reaction in organic synthesis.¹ Although several chemical applications involving microwave ovens have been reported, it is only recently that

microwave rapid heating techniques have been used in organic synthesis to accelerate organic reactions and reduce the reaction times substantially.² Applications concern both dry organic reactions and those occurring in solution. The latter are generally carried out in sealed Teflon or glass (with extra precautions) vessels. We report herein a simple and convenient procedure for the acceleration of the three-step ortho ester

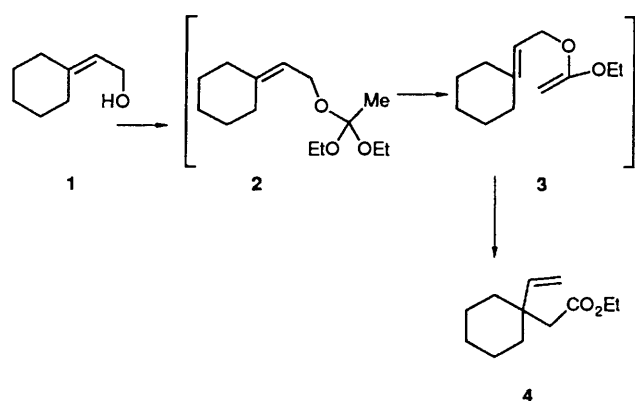
Table 1 Microwave accelerated ortho ester Claisen rearrangement^a (E = CO₂Et)

Entry	Alcohol	Product ^b	Time, (t/min)	Yield (%) ^c	Entry	Alcohol	Product ^b	Time (t/min)	Yield (%)
a			10	83	i			14	87
b			12	63 ^d	j			14	79
c			12	69 ^d	k			12	55 (67)
d			12	87	l			12	43 (78)
e			12	84	m			12	60 ^d
f			12	82	n			15	82 ^e
g			12	81					
h			14	59 (76)					

^a All reactions were carried out on 1–3 mmol scale. ^b All the compounds exhibited spectral data (IR and ¹H NMR) consistent with their structures.

^c Yields (unoptimised) refer to isolated and chromatographically pure compounds. Yields in parenthesis are based on recovered starting material.

^d Lower yields are probably due to the volatility of starting alcohols and/or product esters. ^e In addition 12% of mono Claisen product, ethyl 3-hydroxymethylpenta-3,4-dienoate, was also obtained.



Claisen rearrangement¹ of allyl and propynyl alcohols in dry dimethylformamide (DMF) in an open Erlenmeyer flask by a commercial microwave oven.

Irradiation of a solution of the alcohol 1, triethyl orthoacetate (TEOA) and a catalytic amount of propanoic acid in dry DMF by microwaves for 10 min using a commercial microwave oven* furnished the ester 4 in 83% yield.³ Whereas the same reaction under conventional conditions, *i.e.* heating 1, TEOA and propanoic acid in a sealed tube at 180 °C, took 48 h representing a reduction in the reaction time of more than 250 times using a microwave oven. To test the generality of this procedure, a wide variety of allyl and propynyl alcohols were used as starting materials and the results are summarised in Table 1.† The reactions carried out using the microwave oven were found to be cleaner and faster with the same or better efficiency, *e.g.*, but-2-yne-1,4-diol furnished the bis-Claisen product (Table 1, entry n), in 82% yield, in 15 min as against the

* Carried out in a Microwin MX1100 microwave oven using 100% power (650 W, microwave frequency 2450 MHz). Carrying out the irradiation for varying times changed the yield of 4, *e.g.*, 12% in 2 min, 20% in 3 min, 42% in 4 min; 56% in 6 min; 72% in 7 min and 74% in 8 min in a sealed tube. In the presence of either solid particles or boiling chips, we have noticed substantial evaporation of DMF within 2 min and lower yields of products were realised.

† Under these conditions normal Claisen rearrangement using either ethyl vinyl ether or methoxypropene in the presence of either mercuric acetate or propionic acid failed to give the products, probably due to the fast evaporation of enol ethers.

51% reported earlier using a conventional procedure.⁴ The synthetic potential of many of these Claisen esters is already well recognised, *e.g.* entries i,⁵ j.⁶

Typical Experimental Procedure.—A solution of the alcohol 1 (190 mg, 1.5 mmol), TEOA (1.5 cm³) and propanoic acid (catalytic) in dry DMF (5 cm³) in a clean Erlenmeyer flask (25 cm³ capacity without any boiling chips) was placed in a microwave oven³ and irradiated for 10 min. After irradiation the reaction mixture was cooled, taken up in ether (20 cm³), washed with dilute HCl followed by brine and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue over silica gel column using hexane as eluent furnished the ester 4 (245 mg, 83%) as a liquid; $\nu_{\max}(\text{neat})/\text{cm}^{-1}$ 1737 and 915; $\delta_{\text{H}}(90 \text{ MHz}; \text{CDCl}_3)$ 5.78 (1 H, dd, *J* 18, 11), ‡ 5.1 (1 H, dd, *J* 11, 1.5) and 5.0 (1 H, dd, *J* 18, 1.5) (olefinic), 4.08 (2 H, q, *J* 7.5, OCH₂CH₃), 2.32 (2 H, s, COCH₂), 1.1–1.9 (10 H, m, ring CH₂) and 1.24 (3 H, t, *J* 7.5, OCH₂CH₃).

‡ *J* Values are given in Hz.

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References

- W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner and M. R. Petersen, *J. Am. Chem. Soc.*, 1970, **92**, 741.
- J. Ipaktschi and M. Bruck, *Chem. Ber.*, 1990, **123**, 1591; D. Villemin, M. Lalaoui and A. B. Alloum, *Chem. Ind.*, 1991, 176; A. B. Alloum, B. Labiad and D. Villemin, *J. Chem. Soc., Chem. Commun.*, 1989, 386; G. Bram, A. Loupy, M. Majdoub and A. Petit, *Chem. Ind.*, 1991, 396 and refs. cited therein.
- R. Pitteloud and M. Petrzilka, *Helv. Chim. Acta*, 1979, **62**, 1319.
- Y. Ishino, I. Nishiguchi, M. Kim and T. Hirashima, *Synthesis*, 1982, 740.
- A. Srikrishna and S. Nagaraju, *J. Chem. Soc., Perkin Trans. 1*, 1991, 658.
- G. Mehta, N. Krishnamurthy and S. R. Karra, *J. Am. Chem. Soc.*, 1991, **113**, 5765.

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