

Thermolysis Improvements in Retro-Diels–Alder Reactions of Benzylamino Alcohols under Microwave Irradiation†

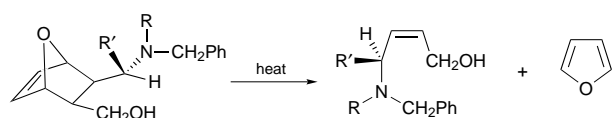
J. Chem. Research (S),
1998, 34–35†

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Microwave activation under solvent-free conditions is shown to be the best procedure for performing retro-Diels–Alder reactions.

Retro Diels–Alder reactions often require drastic conditions, high temperatures and even sometimes flash vacuum thermolysis (FVT).^{1–4} Such thermolytic procedures have been used to prepare unsaturated amino alcohols from a variety of amino alcohols (Scheme 1).



Scheme 1

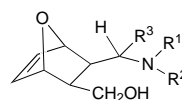
In the case of dibenzylamino alcohols ($R = \text{PhCH}_2$), satisfactory yields are obtained by refluxing in xylene solution for rather long times (6 h). However, these conditions prove unsuccessful in the case of monobenzylamino compounds ($R = \text{H}$) where only a solvent-free method (heating of the neat product for 6 h at 160 °C) leads to a mostly clean reaction. Owing to the lack of volatility of these compounds, FVT is not useful in this case, since decomposition occurs before evaporation in the hot tube. A dry technique, coupled with microwave activation, has been advocated in the case of high-temperature transformations^{6,7} and for the displacement of volatile polar molecules.⁸

Several reactions were therefore performed under microwave irradiation for a variety of neat liquid adducts **1** using a single mode reactor (Synthewave 402 apparatus from Pro-labo) in order to control precisely the experimental conditions (power and temperature). To check the possible specific effects (non-thermal) of microwaves, the results were compared with those obtained under conventional heating in a thermostatted oil bath, conditions elsewhere being equal.

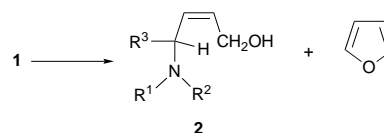
Yields were quantitative for all five desired products within very short times (10 or 15 min) and at relatively low temperatures (120–140 °C). A very important specific effect of microwaves is clearly exemplified, as on conventional heating under strictly otherwise identical conditions yields were less than 2%. Under classical thermal conditions, reaction times

of 6–10 h were necessary to obtain acceptable yields (however always lower than under microwaves) of less pure products. The specific effect of microwaves is here very important, although not always obvious under homogeneous conditions.¹⁰ It is interesting to note that such an intrinsic effect of microwaves occurs in the most difficult cases yet observed for other types of solvent-free reactions.¹¹ Such an observation is coherent with a remark of Lewis¹² who underlined a generalization which has recently become obvious, stating that the more important microwave effects are connected to the more difficult reactions.

Microwave activation coupled with solvent-free conditions is shown to be by far the most efficient method for performing these retro Diels–Alder reactions. The improvements are remarkable if we consider that both classical thermolysis and FVT (leading to decomposition) are poorly productive (or non-operative). Especially for monobenzylated amino compounds **1c–e**, solvent-free conditions plus microwave irradiation constitute the only method of giving fast and clean reactions.



- 1a** $R^1 = R^2 = \text{CH}_2\text{Ph}$, $R^3 = \text{Bu}^n$
1b $R^1 = R^2 = \text{CH}_2\text{Ph}$, $R^3 = [\text{CH}_2]_3\text{OCH}_2\text{Ph}$
1c $R^1 = \text{H}$, $R^2 = \text{CH}_2\text{Ph}$, $R^3 = \text{Bu}^n$
1d $R^1 = \text{H}$, $R^2 = \text{CH}_2$ -, $R^3 = [\text{CH}_2]_3\text{OCH}_2\text{Ph}$
1e $R^1 = \text{H}$, $R^2 = \text{CH}_2$ -, $R^3 = \text{Bu}^n$



Scheme 2

Table 1 Microwave-assisted thermolysis of neat benzylamino alcohols **1a–e**

Substrate	Microwave activation			Classical heating		
	$T/^\circ\text{C}$	Time (t/min)	Yield (%) ^a of 2	$T/^\circ\text{C}$	Time (t/min)	Yield (%) ^a
1a	120	15	66	140	180	70
	140	10	≥ 98	140	480	84
1b	140	10	≥ 98			
1c	120	15	≥ 98	160	360	74
1d	120	15	≥ 98			
1e	100	15	≥ 65	120	180	50
	120	15	≥ 98	120	600	84

^aIsolated yield of pure product.

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1997, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Experimental

Focused microwave irradiations were carried out with a Synthewave S402 single mode reactor from Pro-labo (2450 MHz, 300 W) with irradiation monitoring by PC, infrared⁹ measurement and continual feedback temperature control. Indicated temperatures

were reached in less than 1 min and maintained by power regulation. For sake of comparison, reactions were also conducted under classical heating in a thermostatted oil-bath.

Neat amino alcohols **1a–e** (10 mmol)⁵ were placed in a Pyrex open flask allowing the removal of furan. After microwave irradiation or conventional heating, the products were removed with methylene dichloride and analysed by ¹H NMR spectroscopy. Unsaturated amino alcohols **2** obtained under microwaves were highly pure and did not need further purification.

Products **2a–e** showed similarities in their ¹H NMR spectra: in particular the values of the coupling constants between the vicinal ethylenic protons ($J \sim 10$ Hz) were characteristic of *Z*-olefins. For example, the full ¹H NMR spectrum of compound **2a** was the following: δ_{H} (CDCl₃, 250 MHz) 0.89 (t, J 6.5 Hz, 3 H), 1.23–1.44 (m, 5 H), 1.77–1.85 (m, 1 H), 2.40 (bs, 1 H), 3.37 (dt, J 8.5, 6.1 Hz, 1 H), 3.5 (d, J 13.6 Hz, 2 H), 3.73 (d, J 13.6 Hz, 2 H), 3.9 (ddd, J 6.5, 5, 1 Hz, 1 H), 3.93 (ddd, J 6.5, 6, 1 Hz), 5.57 (ddt, J 9.8, 9.5, 1 Hz, 1 H), 5.91 (ddt, J 9.8, 6.6, 1 Hz, 1 H), 7.21–7.40 (m, 10 H).

Received, 26th June 1997; Accepted, 16th September 1997
Paper F/7/06839E

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