nitrogen in the planar structure. The O1s core energy in 1-azabicyclo[3.3.1]nonan-2-one is higher than that in 1-*n*-butyl-2-pyrrolidone, consistent with resonance theory. While the O1s value in the aziridinone is especially high, there are no cyclopropanone data to compare it with. The low N1s core energy in 1-pyrrolidinecarboxaldehyde is only 0.08 eV lower than the model value—very close to the combined experimental and estimation uncertainties. While this is consistent with its experimentally-known distortion, the O1s value is 0.04 eV lower than its model value. However, there are significant uncertainties and gaps in the O1s data.

The relatively high carbonyl C1s ionization energy in ketones suggests important contributions from resonance contributors such as **13b** which have $C^+–O^-$ character. The relatively low carbonyl C1s ionization energy in amides suggests a much larger contribution from **1b**. The explanation of the reduced carbonyl C1s ionization energies in distorted lactams may rest with the electronegativity at nitrogen. However, it is clear that much more work must be done in order to observe the dependencies of experimental core ionization energies upon specific distortion modes and their relationships with different calculations of atomic charge.

Acknowledgment. We wish to acknowledge the donation of compounds to this study by and helpful discussions with Professor Robert S. Brown, University of Alberta, some assistance in syntheses from Mr. Quan-Sing Tu and Ms. Yeu-Yi Chiu, New Jersey Institute of Technology, and helpful discussions with Professor Joel F. Liebman, University of Maryland Baltimore County. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. The experimental measurements of core ionization energies were supported in part by the National Science Foundation.

Registry No. $HCONH_2$, 75-12-7; $HCON(CH_3)_2$, 68-12-2; $CH_3CON(CH_3)_2$, 127-19-5; $(CH_3)_2NH$, 124-40-3; $CH_3NHC_2H_5$, 624-78-2; $(C_2H_5)_2NH$, 109-89-7; $C_2H_5NH(n\text{-}C_3H_7)$, 20193-20-8; $(n\text{-}C_3H_7)_2NH$, 142-84-7; $HCONHCH_3$, 123-39-7; $CH_3cONHCH_3$, 79-16-3; $CH_3CON(C_2H_5)_2$, 685-91-6; $CH_3CONHC_2H_5$, 625-50-3; $CH_3CON(CH_3)C_2H_5$, 38806-26-7; CH_3NH_2, 74-89-5; $(CH_3)_3N$, 75-50-3; $(CH_3)_2NC_2H_5$, 598-56-1; $(C_2H_5)_3N$, 121-44-8; 1-pyrrolidinecarboxaldehyde, 3760-54-1; *N*,2′-dimethylacetanilide, 573-26-2; 1,3-di-*tert*-butylaziridinone, 14387-89-4; 2-azetidinone, 930-21-2; 2-pyrrolidone, 616-45-5; 1-methyl-2-pyrrolidone, 872-50-4; 1-*n*-butyl-2-pyrrolidone, 3470-98-2; 1-azabicyclo[3.3.1]nonan-2-one, 74331-49-0; azetidine, 503-29-7; propanone, 67-64-1; cyclobutanone, 1191-95-3; 2-butanone, 78-93-3; 2-pentanone, 107-87-9; 3-pentanone, 96-22-0; piperidine, 110-89-4; pyrrolidine, 123-75-1; 1-methyl-2-piperidone, 931-20-4; *N*-methylpyrrolidine, 120-94-5; *N*-methylpiperidine, 626-67-5.

Specific Activation by Microwaves: Myth or Reality?

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Ene reactions involving carbonyl enophiles have been carried out under microwave irradiation at controlled temperature and atmospheric pressure. The reactions of diethyl mesoxalate with 1-decene and β-pinene and the cyclization of (+)-citronellal under homogeneous (neat liquid) or heterogeneous (clay catalyst) conditions have been studied. In each case the dependence of reaction yield on time and the stereoisomer ratios of the products are unaffected by the heating mode.

In the last few years there have been a growing interest in the use of microwave heating in organic synthesis[1-10] ("MORE chemistry": microwave oven-induced reaction enhancement). The use of such nonconventional reaction conditions reveals several features: (i) a reduction in the usual thermal degradation and/or better selectivity,[1,6,7] and (ii) for some reactions, especially under heterogeneous conditions,[1,3-5] there seems to be a marked rate enhancement compared to conventional heating. It should be noted however, that in most cases the reaction conditions (temperature, pressure, etc.) were not monitored with accuracy. In this respect, it appeared that organic solvents under microwave irradiation superheat by 13–26 °C above their conventional bp's at atmospheric pressure.[11] Thus, at this time, it is unresolved whether the use of microwaves provides specific activation. Accurate studies comparing the use of microwave to conventional heating are needed.

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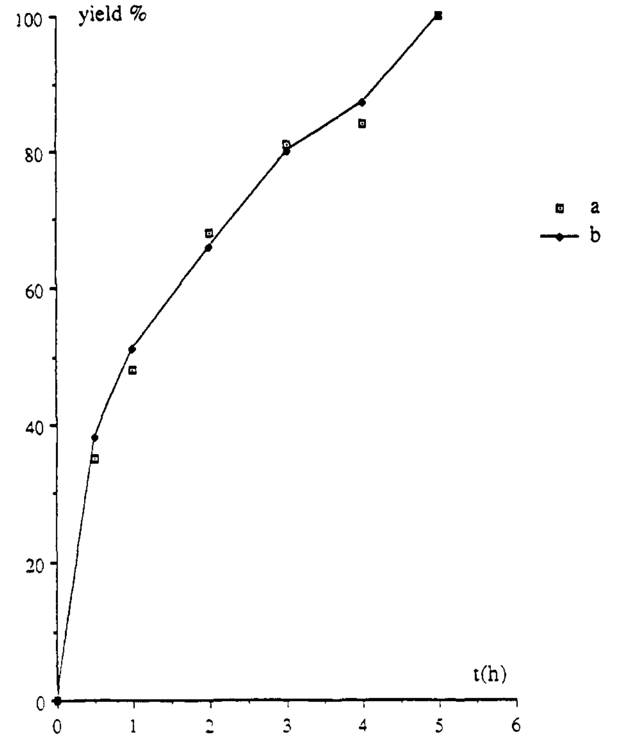

Figure 1. Yield in ene adduct 4 as a function of time for reaction 1: (a) conventional heating, 170 °C (±0.5°); (b) microwave irradiation, 170 °C (±2°).

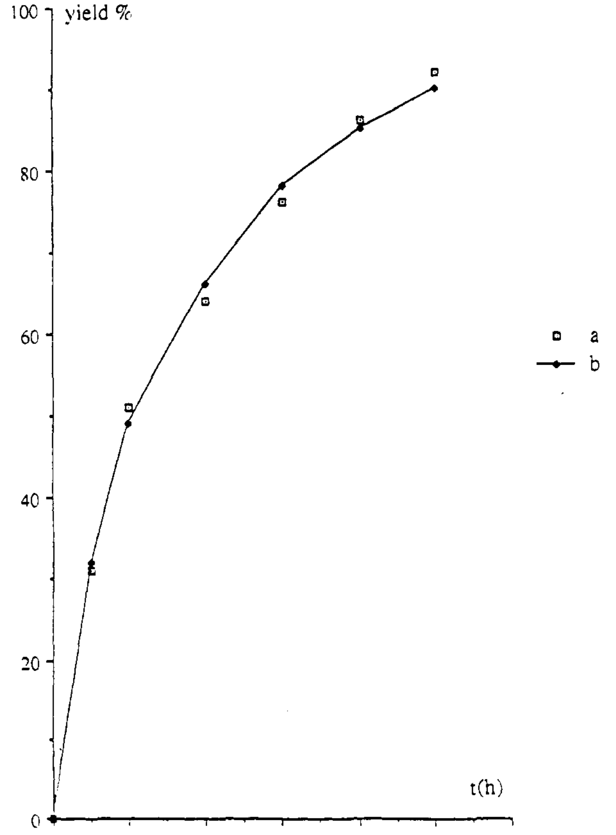

Figure 2. Yield in ene adduct 5 as a function of time for reaction 2 in CCl_4 as solvent: (a) conventional heating, 80 °C (±0.5°); (b) microwave irradiation, 80 °C (±2°).

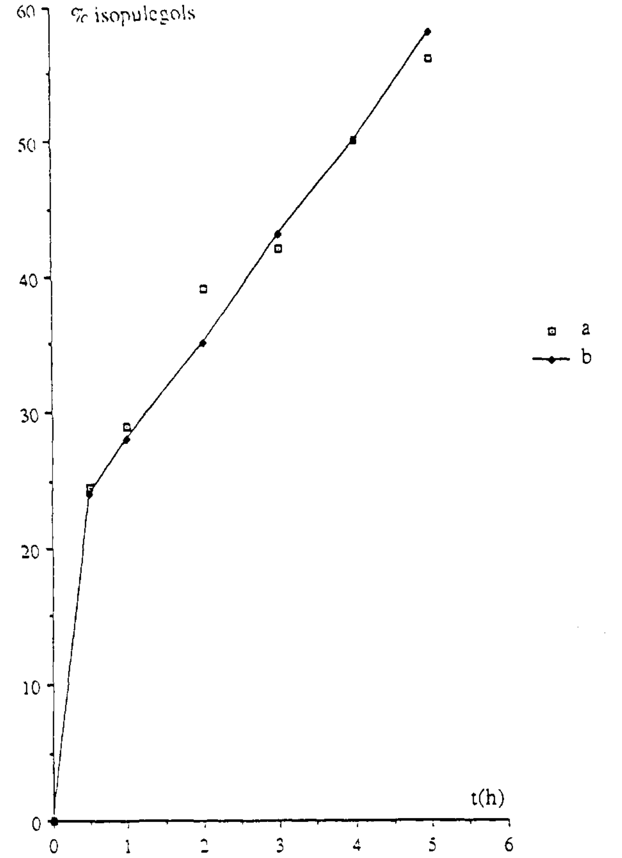

Figure 3. Yield in isopulegols 7 as a function of time for reaction 3 without solvent: (a) conventional heating, 180 °C (±0.5°); (b) microwave irradiation, 180 °C (±2°).

Recently, Bond et al. have shown that microwave irradiation has no effect on the rate of an esterification reaction when compared to conventional heating.[12] On the other hand, we have reported significant kinetic effects for some Diels–Alder reactions,[7a] together with selectivity and rate enhancements for the thermal cyclic trimerization of urea[7b] with microwave heating.

In the case of microwave heating it appears that, unlike conventional heating, the bulk temperature is no longer representative of the reaction conditions. A similar effect is observed with ultrasonic irradiation, and in this case the "hot spots" theory is now well established.[13] By analogy, although we acknowledge that sonic waves as mechanical vibrations differ from microwaves which are electromagnetic, we have suggested that microwave activation could also derive from "hot spots" generated by dielectric relaxation on the molecular scale.[7]

We have investigated this problem further with the ene reaction[14] using carbonyl enophiles. It appeared to us that

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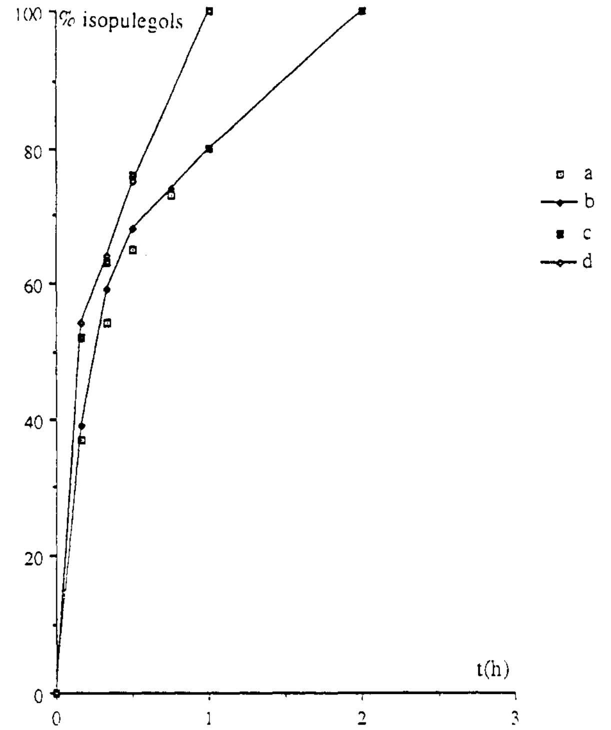
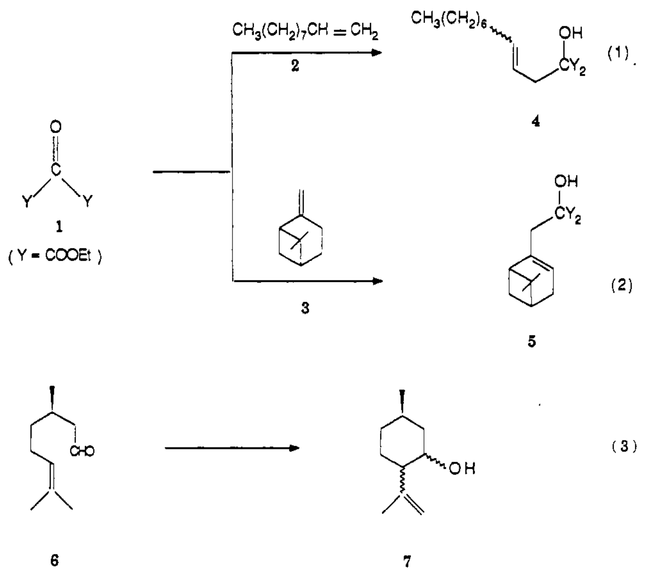


Figure 4. Yield in isopulegols 7 as a function of time for reaction 3 in CCl_4 as solvent: (a) montmorillonite KSF (5%) catalyst, conventional heating, 77 °C (±0.5°); (b) montmorillonite KSF (5%) catalyst, microwave irradition, 77 °C (±2°); (c) montmorillonite KSF (10%) catalyst, conventional heating, 77 °C (±0.5); (d) montmorillonite KSF (10%) catalyst, microwave irradiation, 77 °C (±2°).

this reaction would be a good model for several reasons: (i) the polar carbonyl group of the enophile moiety serves as a good "antenna group"; in other words, this group is at the same time directly involved in the reaction and in the molecular interaction with the waves; (ii) the experimental conditions required for this reaction permit a comparative kinetic study with conventional heating; and (iii) it is possible to carry out this reaction under either homogeneous or heterogeneous conditions with a solid catalyst.

We have studied three reactions: diethyl mesoxalate[15] with either 1-decene (eq 1) or β-pinene (eq 2) and the cyclization of citronellal (eq 3). This latter reaction has been studied under both homogeneous[16] (neat liquid) and heterogeneous (clay catalysis[17]) conditions. In each case we have plotted the dependence of reaction yield on time under conventional conditions and with microwave heating. In both cases the reactions were run at the same bulk temperature and at atmospheric pressure (Figures 1–4). The microwave system has been described previously.[7a]



It can be seen that, under homogeneous conditions, in all cases the reaction rate is not affected by microwave irradiation (compare Figures 1a–3a with 1b–3b). Furthermore, the product distribution from reaction 2 (an E/Z mixture) and that from reaction 3 (a mixture of four diastereoisomers isopulegols **7a–d**) is also unaffected by microwaves.

Due to the importance of isopulegol (**7a**) in the industrial synthesis of menthol, several groups have studied the catalyzed ring closure of citronellal.[17–20] It is thought that specific microwave activation is more likely to occur under heterogeneous conditions, since "hot spots" could be more specifically produced at the surface of the catalyst.[4,5,21] This prompted us to compare the clay-catalyzed cyclization of citronellal under conventional heating (Figure 4a,c) and microwave heating (Figure 4b,d) using KSF montmorillonite in CCl_4 suspension.

Clearly, the clay catalyst markedly enhances the reaction rate (compare Figure 3a with 4a,c) but, surprisingly, no particular effect of the microwave heating can be observed.

"MORE chemistry" is still in its infancy, and at this time it is difficult to say whether it is myth or reality as there are too many apparently contradictory results. It seems likely that the main problem arises from differences in experimental conditions resulting from imprecise monitoring and improper controls. In addition, microwave activation could also depend on the nature of the reagents, the value of the dielectric constant of the complex, and the reaction conditions (solution or "dry" conditions, nature of the added solid or catalyst, etc.). The nature of the reaction itself is also important, e.g., ionic, nonionic, nature of the transition state, etc. More studies are needed in which the reaction conditions are carefully controlled before the title question can be answered.

Experimental Section

Materials. Compounds **1**, **2**, **3**, and **6** were purchased from Aldrich or Fluka. The commercial (+)-citronellal, containing 10–15% of isopulegols, was purified via the bisulfite derivative.

Sampling and Conventional Heating. Reaction 1: **1** (0.52 g, 3 mmol), **2**, (4.20 g, 30 mmol); 170 °C (±0.5°). Reaction 2: **1** (0.70 g, 4 mmol), **3** (1.64 g, 12 mmol) in 10 mL of anhydrous carbon

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tetrachloride; 80 °C (±0.5°). Reaction 3: 6 (5 g, 32.5 mmol), neat liquid; 180 °C (±0.5). 6 (3 g, 19.5 mmol), KSF montmorillonite (0.15 g and 0.3 g), 15 mL of anhydrous CCl_4; 77 °C (±0.5°). Samples were heated in a 50-mL Pyrex flask under nitrogen atmosphere in an oil bath equipped with a thermostat.

Microwave Heating. The apparatus has already been described.[7a] It includes the following: a magnetron from a commercial microwave oven (2.45 GHz; adjustable power within the range 20–800 W), and a wave guide (monomode T_{01}) including (i) a circulator and a water load to absorb the reflected waves, (ii) a directional coupler (47,83 dB) connected to a power meter (Hewlett-Packard 438) through two sensors to measure the incident and reflected powers, and (iii) an E. H. tuner to minimize the reflected power.

The reactor, a quartz tube (25-mm internal diameter) fitted with a reflux condenser, temperature probe, and a septum for sampling are introduced in a cavity at a $\lambda/4$ distance of the short circuit located at the end of the wave guide.

Temperature measurement was carried out with a Luxtron optical fiber thermometer (755 Multichannel FLuoroptic Thermometer).

The reaction conditions under microwave irradiation were as follows: same amounts of reagents as conventional heating and absorbed power: reaction 1, from 270 to 150 W, 170 °C (±2°), reaction 2, from 141 to 23 W, 80 °C (±2°), reaction 3, neat cintronellal from 138 to 50 W, 180 °C (±2°), 5‰ KSF clay, from 301 to 247 W, 77 °C (±1°), and 10% KSF clay, from 278 to 223 W, 77 °C (±1°).

Analysis. The reaction mixtures were analyzed by ^{1}H NMR on Bruker AC 80 or AC 200 apparatus. Samples of isopulegols containing variable amounts of various diastereoisomers **7a–d** ((−)-isopulegol (**7a**), (+)-neoisopulegol (**7b**), (+)-isoisopulegol (**7c**), (+)-neoisoisopulegol (**7d**)) were prepared according to the methods previously described.[16,17]

These isomers were identified by ^{1}H NMR at 200 MHz, in particular from the proton CHO signals.[16,17] The reactions without catalyst (Figure 3a,b) led to the isomer ratios **7a**/**7b**/**7c** = 71/16/12 (trace of **7d**). In the case of KSF montmorillonite catalysis the ratios obtained were **7a**/**7b**/**7c** = 57/35/7 (trace of **7d**). These ratios have been found to be independent of the heating mode.

Adducts 4 and 5 were chromatographed on a silica column with hexane–ethyl acetate (9:1) as eluent and identified by comparison of the ^{1}H NMR with authentic samples.[14e] In the case of diethyl 2-hydroxy-2-(2-decenyl)propane-1,3-dioate (4) the trans isomer ($CY_2CH_2C{=}C$, $\delta = 2.70$ ppm, $J = 7.5$ Hz; $CH{=}CH$, 2 m, $\delta = 5.36$ and 5.52 ppm, $J = 15.3$ Hz) is the major isomer (74%); the cis isomer ($CY_2CH_2C{=}C$, $\delta = 2.79$, $J = 7.5$ Hz) is the minor one, regardless of the heating mode.

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Mesitylene-Derived 1,3-Alternate [1.1.1.1]Metacyclophanes

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Synthetic procedures to conformationally immobile 1,3-alternate [1.1.1.1]metacyclophanes based on mesitylene units are described. Coupling of mesitol (19) with bis(chloromethyl)mesitol (20) and bis(chloromethyl)mesitylene (21) in nitroethane in the presence of $SnCl_4$ affords metacyclophanes 6 and 7–10, respectively, possessing extra-annular hydroxyl groups. Metacyclophanes 12 and 14, which hold one or two pairs of carboxyl groups in the distal positions, have been obtained from the appropriate distal diol 8 and tetrol 6 by treatment with *tert*-butyl bromoacetate followed by basic hydrolysis. Functionalized molecular frameworks, such as 15 and 18, have been also prepared in high yield by direct methods. The ^{1}H NMR spectral characteristics of 1,3-alternate metacyclophanes synthesized are briefly discussed. The structures of mono-, tri-, and tetrahydroxy metacyclophanes 10, 7, and 6, respectively, have been determined by X-ray crystallography. All three macrocycles have very similar 1,3-alternate–biconic conformations with approximate $\bar{4}2m$ symmetry. Molecules 10 and 7 are isomorphous, and the lone hydroxyl group in 10 and the three hydroxyl groups in 7 are disordered over four possible sites. A toluene of solvation is docked against the molecular cavity in both 10 and 7. Compound 6 has crystallographic 2-fold symmetry and what would have been voids in the crystal lattice are occupied by disordered solvent molecules.

Introduction

During the last decade there has been growing interest in the search for new conformationally preorganized building blocks from which specific hosts with desired properties can be designed by appropriate functionalization. In this respect readily available calix[4]arenes 1 and calix[4]resorcinarenes 2 (Chart I), containing a cavity adorned with intra- or extra-annular hydroxyl groups, respectively, have been the focus of considerable attention.[1] A further interest in calix[4]arenes relies on the fact that upon functionalization these macrocycles may adopt four extreme conformations, i.e. cone, partial cone, 1,2-alternate, and 1,3-alternate, thus providing additional shapes for selective molecular recognition.

The 1,3-alternate conformation of *p-tert*-butylcalix[4]arene has been shown to be appropriate to afford molecular receptors presenting new and peculiar inherent symmetries. Examples of doubly-crowned calix[4]arenes 3[2,3] and double calixcrown 4,[3,4] showing special shapes associated with the 1,3-alternate calix[4]arene moieties connected by

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