Review Commentary
Organic processes initiated by non-classical energy sources

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ABSTRACT: Non-classical energy sources such as microwave energy, ultrasound and mechanoenergy and their combination with UV–VIS radiation are new tools in synthetic chemistry and chemical processing. Here we describe the application of microwave treatment for selected organic reactions such as (i) enzymatic transesterification of optically active alcohols, (ii) mercury-sensitized gas-phase photolysis of hydrocarbons in the microwave field, (iii) environmentally benign oxidations of olefins and (iv) the application of mechanoenergy separately and in combination with microwave irradiation for special oxidation reactions. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: non-classical energy sources; organic reactions; chemical processing

INTRODUCTION

Population growth and rising living standards in industrial countries and the expansion of market economies, necessitate an increase in production and consumption. Natural resources for the production of goods are taken from the environment. Wastes and contaminants from production processes are discharged into the environment. As a result, the environment is exposed to global impact and is endangered: 'Sustainable development meets the needs of the present without compromising the ability of future generations to meet their own needs!' (Brundtland Commission).[1]

Sustainability in the economic sense means the efficient allocation of scarce goods and resources. Sustainability in the environmental sense means not exceeding the limits of environmental impact and maintaining the natural basis of life. Sustainability in the social sense means a maximum of equality of opportunity, social justice and freedom. All these three elements must be in equilibrium with each other.[2]

The chemical industry can contribute significantly to this guiding principle. Its contribution is based on the use of environmental protection technologies.

'Green Chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products'.[3] Special tools of this 'benign by design' are the following:

- alternative feedstocks;
- alternative reagents;
- alternative solvents;
- alternative products;
- alternative catalysts;
- alternative energy stimulants.

We have been dealing with these tools in research and development for 3 years. Here we report on alternative energy stimulants.

Alternative energy stimulants or non-classical energies[4] have been used for many years to increase the reaction rate and to enhance the yield of particular reaction products. We shall review the situation in the field of energies and report on our own illustrative examples.

Non-classical energies lead to innovative methods and techniques for chemical transformations and material separations. Some forms of non-classical energies are discussed here as follows.

Supercritical conditions

The application of high pressures and high temperatures (HP–HT)[5] results in new separation technologies, inorganic solvent processes, milder reaction regimes, improved transport phenomena, higher turnover numbers in heterogeneous catalytic systems, improved hazardous waste treatment processes and improved solubilities.

Ultrasonic

Based on the phenomenon of cavitation, sonic waves can accelerate chemical transformations, affect product

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**Table 1.** Microwave systems (MLS, Leutkirch, Germany), reactors and limiting conditions

Microwave system	Reactor	Limiting conditions and tools
ETHOS 1600	Ceramic reactor	300 °C, 5 bar, 300 ml MW plasma –UV Useable for batch or flow reactions, extraction processes, gas-phase reactions
ETHOS MR	Reflux apparatus	Boiling-point of the reaction mixture, normal pressure MW plasma –UV
	HPR 3000/1 K	250 °C, 30 bar, 250 ml
	HPR 1000/6	280 °C, 80 bar, 6 × 50 ml
	μCLAVE	300 °C, 60 bar, 500 ml or 6 × 20 ml or MW plasma –UV
ETHOS contFlow	Flow reactor	160 °C, 50 bar, max. 1.6 1 h^{-1}

distributions, initiate free radical formation and (de)poly-merization, induce mechanical cleavages of polymers and increase the catalytic activity of metal particles by factors as high as 10^5.[6] The sonication of organic solutions of metal carbonyls leads to the formation of micro- to nanoparticles of metals, alloys, oxides and semiconductors. Applications in the synthesis of orga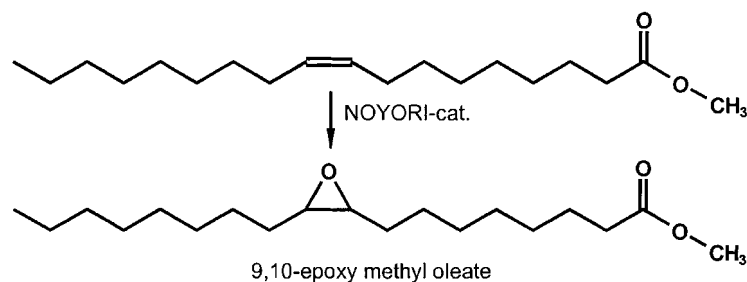nic fine chemicals are numerous, especially in free radical reactions. Polymer science also has a strong interest in this field.
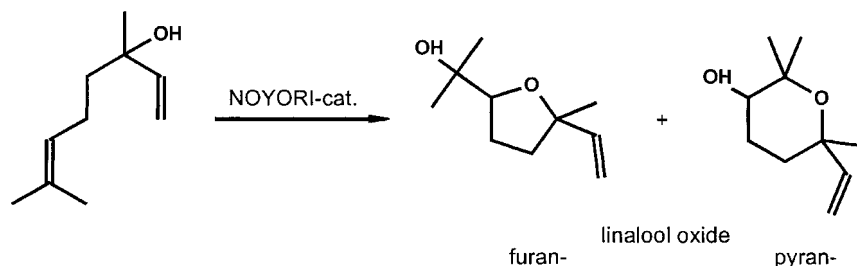
Microwaves

Microwaves activate the smallest degree of variance of polar molecules and ions, leading to molecular friction,
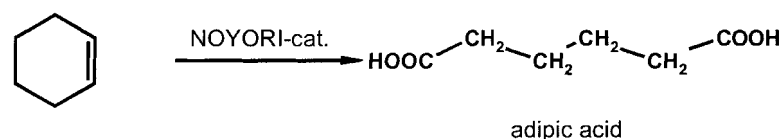
Figure 1. Oxidation of olefins with hydrogen peroxide on Noyori catalyst (sodium tungstate dihydrate + methyltrioctyl-ammonium hydrogensulfate, ratio 1:10)[12]
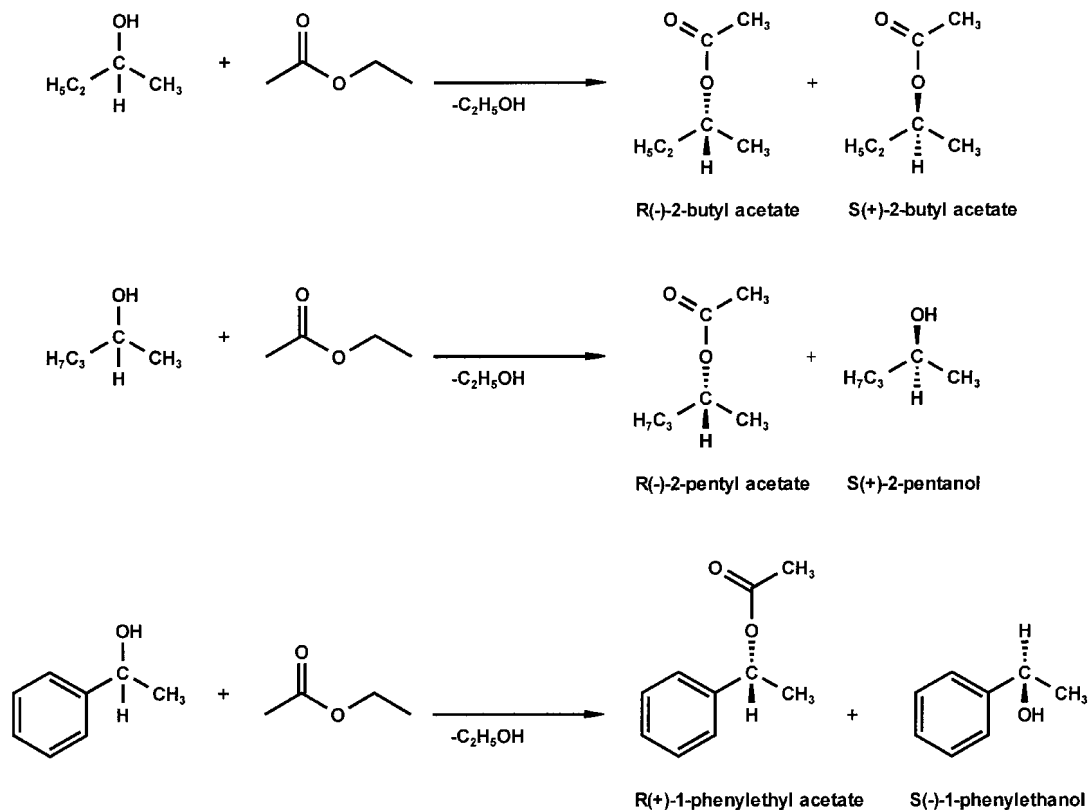
Figure 2. Microwave-assisted transesterification in presence of Novozym 435

and therefore the initiation of chemical reactions is possible. Chemical bonds cannot be cleaved by microwave energy.[7]

Microwave radiation can accelerate chemical transformations both in solution and in solid phases. High yields of highly pure products are reached within a short time.[8] The choice of solvent controls the dissipative energy transfer. Moreover, it is not always necessary to work in the presence of a solvent (dry synthesis), and this aspect is important for industry.

Plasma

The application of plasma discharges offers new

possibilities for the synthesis of new materials, the treatment of harzardous and toxic wastes and the acceleration of radical induced chemical transformations.[9]

Mechanochemistry

Mechanical activation is successfully used to carry out some inorganic and organic reactions. Naturally, the rates of the processes depend greatly on the conditions of mechanical load and hence on the design of mechanical activators. The best results are obtained using planetary centrifugal mills with acceleration factors of $50–100g$ using a $1–10^3$ g charge of the material to be treated.[10]

Table 2. Lipase-catalyzed transesterification of some optically active alcohols with ethyl acetate at different reaction temperature in a microwave field [MW 150 W, 60 min, yield in mass %; optical purity as enantiomeric excess (ee)]

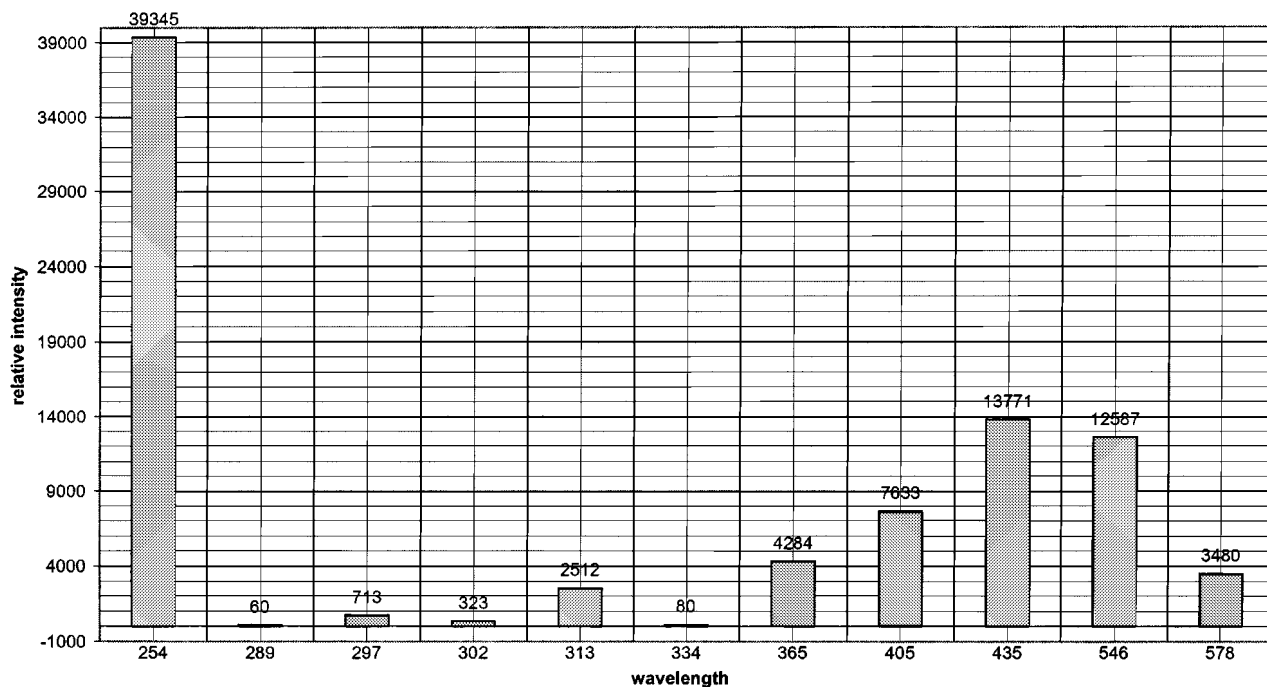|	37 °C		55 °C		65 °C		75 °C	
Product	Yield (%)	ee (%)	Yield (%)	ee (%)	Yield (%)	ee (%)	Yield (%)	ee (%)
$(R)(-)-+(S)(+)$-2-Butyl acetate	78	35	82	23	85	20	88	17
$(R)(-)$-2-Pentyl acetate	62	96	62	92	63	92	64	90
$(R)(+)$-1-Phenylethyl acetate	48	84	50	84	51	85	51	86

Figure 3. Spectral emission of an electrodeless mercury lamp. Wavelength scale in nm
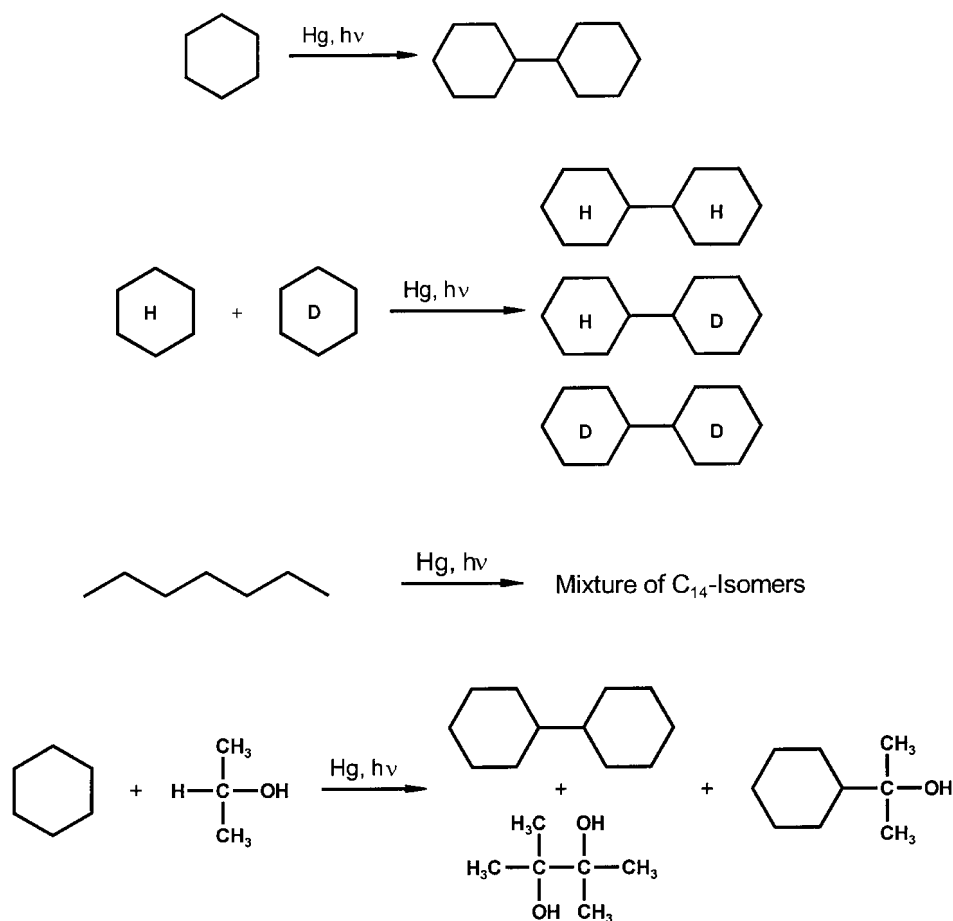

Figure 4. Examples of the dehydrodimerization of selected hydrocarbons and their derivatives with the MW–MWUV technique
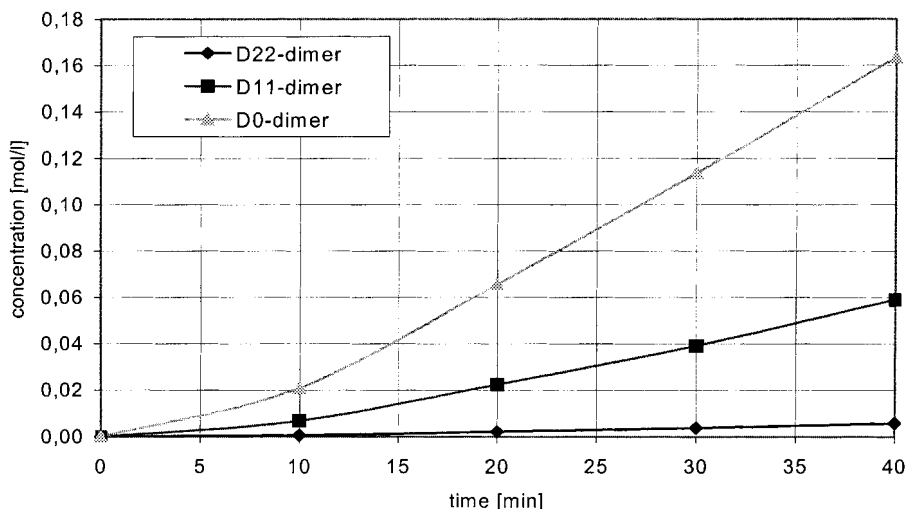
Figure 5. Cross-dehydrodimerization of cyclohexane-d_0 and cyclohexane-d_{12} in the MW–MWUV reactor system (molar ratio 1:1, reaction temperature about b.p.)

Combinations of non-classical condition

The combination of two of the energy forms mentioned above yields synergistic effects, so that the overall effect is more than the sum of the individual effects.[11] Combining innovative methods and techniques is a challenge that can lead to unexpected advances in chemical processing techniques.

EXPERIMENTAL AND DISCUSSION

All microwave-assisted reactions were carried out in systems from MLS (Leutkirch, Germany). Table 1 gives details of the microwave systems, reactors and boundary conditions.

The mechanoreaction (example 4) was carried out in a Pulverisette 7 planetars ball mill from Fritsch (Idar-Oberstein, Germany).

The first example deals with microwave-assisted oxidations. It illustrates how an applied electric field (2.45 GHz) can physically modify the catalyst and the reaction system, and thus modify the catalytic reaction. In the particular example, the Noyori oxidation,[12,13] we used a catalyst made of sodium tungstate dihydrate–methyltrioctylammonium hydrogensulfate and hydrogen peroxide as oxidant. The dielectric structure of this aqueous–organic biphasic system is not yet understood. We describe the effect of microwaves on the nature of the catalyst in terms of a new halide-free method of catalyst preparation. Selected results are given in Fig. 1 (M. Nüchter and B. Ondruschka, unpublished results, 1999).

The second example is that of microwave-promoted lipase-catalyzed reactions. The recent development of

Table 3. Oxidation of oxygen derivatives with potassium permanganate on alumina in presence of water[a]

No.	Educt (conversion, %, after mechanochemical reaction)	Product(s) after mechanochemical reaction (yield, %)	Products after (1) mechanochemical reaction + (2) microwave irradiation (yield, %)
1	Cyclohexanol (56)	Cyclohexanone (7) Cyclohexanedione (3) Adipic acid (46)	Cyclohexanone (7) Cyclohexanedione (8) Adipic acid (57)
2	Cyclohexanone (85)	Cyclohexanedione (19) Adipic acid (66)	Cyclohexanedione (12) Adipic acid (81)
3	Cycloheptanone (59)	Cycloheptanedione (14) Pimelic acid (45)	Cycloheptanedione (15) Pimelic acid (58,5)
4	Anthrone (96)	Anthraquinone (96)	Anthraquinone (79) Unknown product (21)
5	1-Phenylethanol (79)	Acetophenone (10) Benzoic acid (68)	Acetophenone (9) Benzoic acid (91)
6	Acetophenone (77)	Benzoic acid (77)	Benzoic acid (94)
7	Undecenoic acid (23)	Decanedicarboxylic acid (23)	Decanedicarboxylic acid (74)

[a] Mechanochemical reaction: Pulverisette 7 (Fritsch, Idar-Oberstein, Germany), 10 min, 400 rpm. Microwave irradiation: ETHOS MR (MLS, Leutkirch, Germany), 5 min, 300 W.
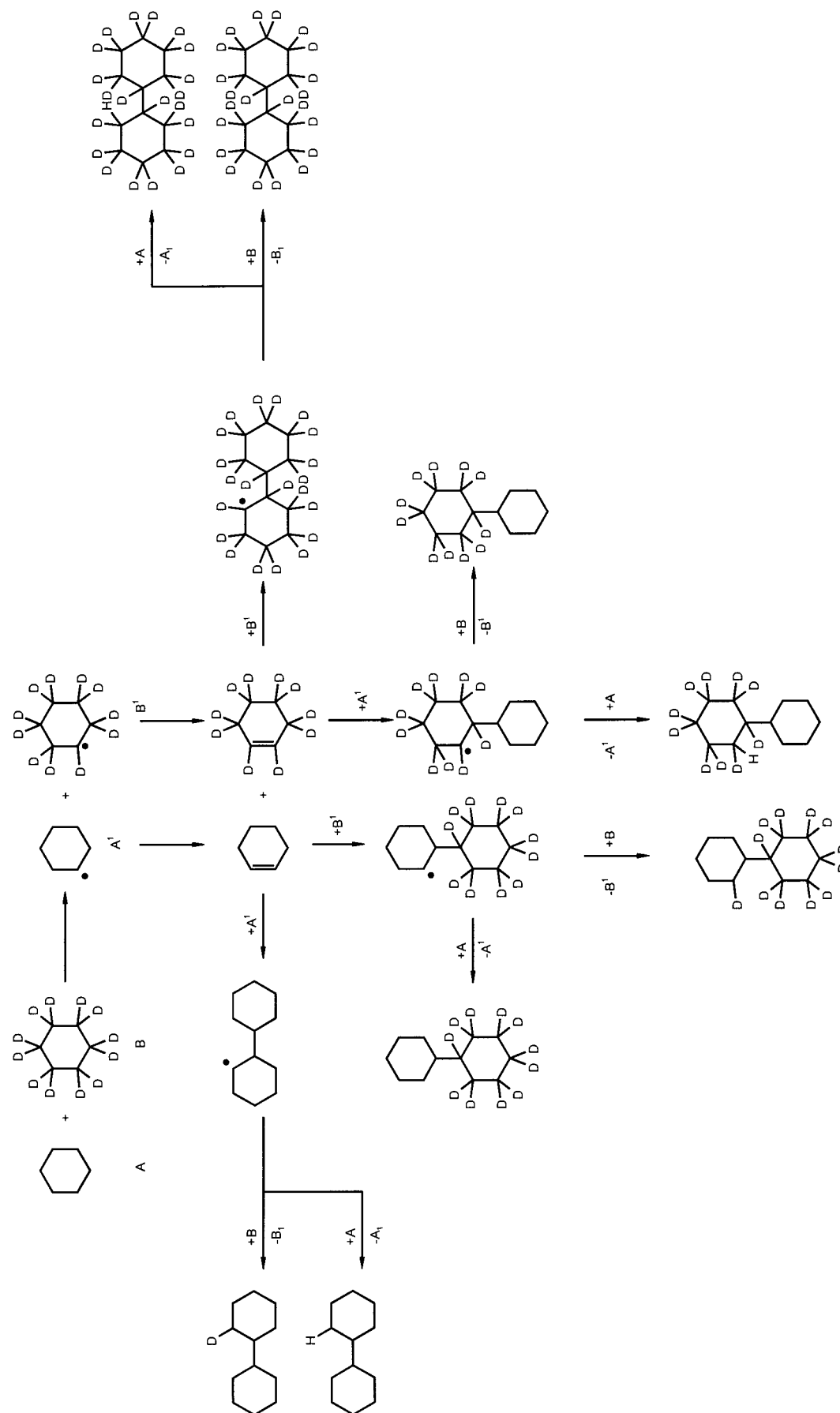
Figure 6. Mechanism of the photosensitized dehydrodimerization of a molar mixture of cyclohexane and perdeuterocyclohexane

with water >99 %
without water 81%

with water 97 %
without water 36 %

with water 96 %
without water 45 %

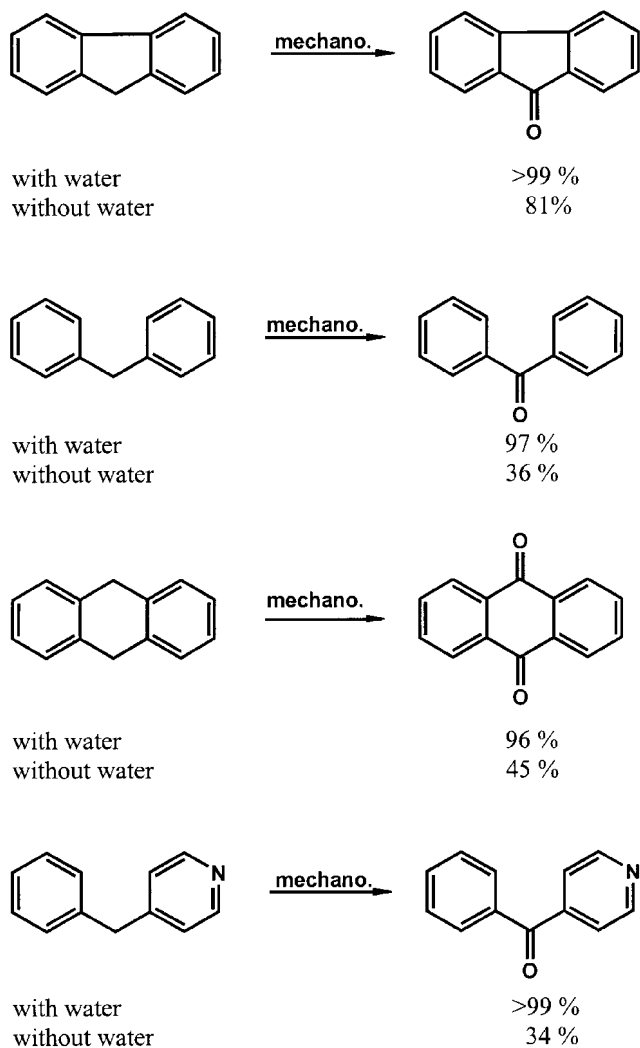with water >99 %
without water 34 %

Figure 7. Mechanochemical conversion of benzyl-type hydrocarbons (Pulverisette 7 planet mill, Fritsch, 400 r.p.m., 10 min)

enzyme catalysis in organic synthesis for the kinetic resolution of racemates has attracted the attention of organic chemists because of their synthetic utility.[14] Lipase-catalyzed transesterification has become a popular method in asymmetric synthesis. A major drawback of applying lipase-catalyzed reactions in organic synthesis is the low reaction rate. Immobilized *Candida antarctica* lipase (Novozym 435) catalyzed the reaction of some alcohols with ethyl acetate under multimode microwave irradiation and classical heating (Fig. 2). Some results are described relating to the dependence on temperature and on the substrate's structure (Table 2).[15]

The yields of acetate obtained at different temperatures are listed in Table 2. The lipase always converted preferentially the (*R*)-alcohol. However, the selectivity of the enzyme towards the substrate depends strongly on the molecular structure of the latter.

1-Phenylethyl acetate is produced with good optical

purity which is not changed upon increase in temperature. The conversion also remains almost unchanged. On the other hand, 2-butanol and 2-pentanol are converted to a larger extent and, consequently, the reaction is less selective. Here, the optical purity decreases at higher reaction temperature.

The third example concerns the first results with our new coupled microwave–microwave–ultraviolet (MW–MWUV) technique. In contrast to the 'microwave–ultraviolet combined reactor'[11] we combine the advantages of microwave heating with the properties of the MW-induced UV–VIS radiation in the same reactor system by use of electrodeless lamps. Photochemistry has been shown to exert a noticeable effect on many chemical reactions. This laboratory system is suitable for organic synthesis and for the degradation of water contaminants. In Fig. 3 the emission spectrum of an electrodeless mercury lamp is presented.

We demonstrate the productive power of the MW–MWUV method by the dehydrodimerizations of selected hydrocarbons and their derivatives and by comparison with well-known papers by Crabtree and co-workers on photochemical dimerization and functionalization of alkanes, ethers, primary alcohols and silanes.[16] Examples one presented in Figs 4 and 5. (B. Ondruschka, M. Nüchter and A. Jungnickel, presented at the 3rd Annual Green Chemistry and Engineering Conference, June 29–July 1, 1999, Washington, DC).

Crabtree and co-workers discussed a simple recombination mechanism for this reaction. However this model concept does not take into account the formation of side products, e.g. cyclohexene and cyclohexylcyclohexane, in the photolysis of cyclohexane. Likewise, the appearance of other than D_0-, D_{11}- and D_{22}- substituted cyclohexanes in the cross-dimerization of cyclohexane and perdeuterocyclohexane has not been elucidated. We discuss here a multi-step mechanism for this system (Fig. 6) The first step, kinetic control, is radical formation. Then the radicals can recombine but they can also disproportionate. Cyclohexene is the product of this disproportionation. A new radical now attacks the olefin and gives a dimeric radical, which reacts with another molecule of cyclohexane to the end product dicyclohexyl or disproportionates to saturated products and olefins. The dimeric products condense and so the reaction stops at the stage of dicyclohexyl.

The fourth example is concentrated on mechanochemical experiments. Numerous papers have reported on very successful MW-assisted dry syntheses,[7a,17] but blank tests after the sample preparation have not been described. Our interest was focused on the understanding of the overall procedure. Therefore, we repeated experiments in the literature and analyzed the prepared reaction mixture after mechanical stirring and also after the MW treatment. We found that in the case of oxidations with potassium permanganate relatively high yields were already achieved after the mechanochemical step. Some

results are given in Fig. 7 and Table 3 (M. Nüchter, B. Ondruschka and R. Trotzki, presented at the Symposium Umwelt- und ressourcenschonende Synthesen und Prozesse, Tübingen, August 1999).

The role of water in this reaction system is not well understood. It is possible that water reacts with the alumina surface, so the pH decreases, and the acidic conditions allow a fast reaction between potassium ions on the hydrated alumina surface. The free permanganic acid now reacts very rapidly with the organic educt. A second possibility is that the water forms a thin film on the alumina surface, where the permanganate is partially soluble. The organic educt is then oxidized in a liquid-phase reaction. The mechanoenergy activates the surface and affords in microscopic areas a high energy density to initiate the reaction.

CONCLUSION

The four examples presented illustrate the changes in microwave applications in chemistry. The diversity of possible microwave applications has been investigated, but the possible list is far from complete.

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