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Chemical Engineering at Supercritical Fluid Conditions,

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CHAPTER 26

THERMAL ORGANIC REACTIONS IN SUPERCRITICAL FLUIDS

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ABSTRACT

Intermolecular thermal reactions were studied in a flow-type system at pressures of up to 500 bar and temperatures of up to 500°C. Under these conditions alkanes are added to alkenes (e.g., n-alkenes, acrylonitrile, methyl acrylate, methyl vinyl ketone) as well as to 1,3-dienes and alkynes thus allowing functionalization of saturated hydrocarbons. Acrylic compounds such as methyl acrylate are dimerized thermally yielding dimethyl 2-methylene-glutarate. Benzene reacts with some alkynes in a Diels-Alder type reaction. A high pressure-high temperature flow apparatus ("HP-HT" apparatus) to perform these reactions is described.

INTRODUCTION

It is well known fact that organic reactions are accelerated at higher temperatures. This experience is widely applied in laboratory and industrial work, because thermal energy is cheap and everywhere available.

One therefore would expect that organic chemists use specifically all ranges of temperature to perform chemical reactions. Surprisingly there is a remarkable gap: intermolecular reactions are scarcely performed above 300°C. Pyrolysis reactions are dominating in this range of temperatures. Reactions

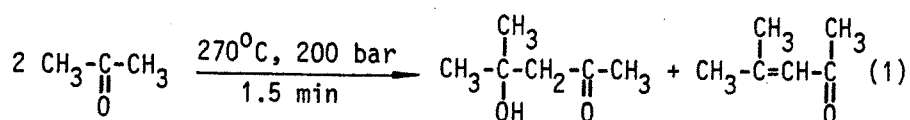
of this type are of high technical and economical importance e.g., the thermal cracking of hydrocarbons for olefin production. Some other pyrolytic reactions are also well known e.g., the pyrolysis of esters, the retro-Diels-Alder reaction, and the retro-ene reaction [1].

Organic chemists likewise apply this range of temperature to perform preparatively important reactions related with thermal rearrangements of molecules and formation of new bonds. All these reactions occurring in the gas phase are of intramolecular and monomolecular type, such as thermal cyclizations of unsaturated carbonyl compounds and intramolecular ene reactions. Temperatures of up to 600°C are often used in these cases [1]. These examples clearly demonstrate that application of high temperatures favours also preparatively important reactions with the formation of new bonds.

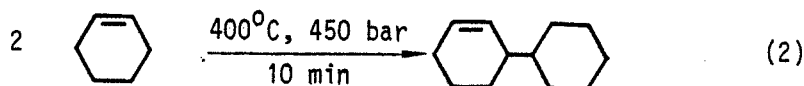
At temperatures above 300°C some processes of technical importance are of the intermolecular reaction type. First the high pressure polymerization of ethylene has to be mentioned which is carried out at pressures of up to 3500 bar and temperatures of up to 350°C. The production of biphenyl from benzene at 800°C is another example.

Fundamental research on this subject was performed in the thirties and forties of this century. The theoretical concept of pericyclic reactions for the guided search for thermal reactions have been developed mainly in the last two decades [2]. A sentence of HENDRICKSON refers to this fact: "Many presently unknown pericyclic reactions may have been overlooked simply because relatively simple and well-known potential substrates have not been deliberately heated above 300°C. Many others which do not appear to proceed may be pre-empted by competitive reactions of lower activation energy". [3]

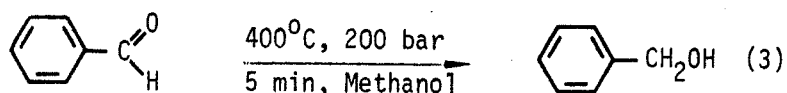
The use of organic solvents for supercritical extraction has stimulated the investigation of reactions at elevated temperatures and high pressures [4]. We observed condensation reactions of acetone during the extraction of biomass with supercritical acetone [5]. 2.1 % diacetone alcohol and 0.6 % mesityloxide are obtained from pure acetone formed apparently by a thermally induced aldol condensation (1)



Nonactivated alkenes show thermal dimerization [6] e.g., cyclohexene is dimerized to 3-cyclohexyl-cyclohexene (2).



These along with other observations stimulated us to start a systematical investigation of thermal intermolecular reactions at relatively high temperatures and pressures. Hitherto we have investigated addition reactions of C-H bonds to carbon-carbon double and triple bonds. Some preliminary experiments have been performed with some other systems e.g., addition reactions to C=O bonds. The results are promising. Benzaldehyde is reduced to benzylic alcohol, furfural to furfuryl alcohol by methanol (3).



EXPERIMENTAL

All experiments were performed in a high-pressure/high-temperature flow apparatus ("HP-HT" apparatus), which enables relatively unproblematical operation at pressures of up to ca. 500 bar and temperatures of up to 600°C. A schematic diagram of the apparatus is shown in Fig. 1.

The sample in reservoir 1 is pumped with a high pressure pump 3 into reactor 6. The reactor is made from commercial high-quality stainless steel tube (o.d. 1.6 mm, i.d. 0.7 mm). The length of the reactor can be changed from a few meters to 50 m and more depending on the reaction under investigation. This gives much flexibility with respect to the reactor size.

We used also fused silica capillaries as reactor (up to 400°C and 200 bar) to exclude possible transition metal catalysis.

The reactor is heated up to 450°C in GC-furnace 12, up to 600°C in tubular furnace respectively. The reaction mixture is quenched in heat exchanger 9. Reaction pressure is maintained with valve 8; pressure reduction is done in two steps

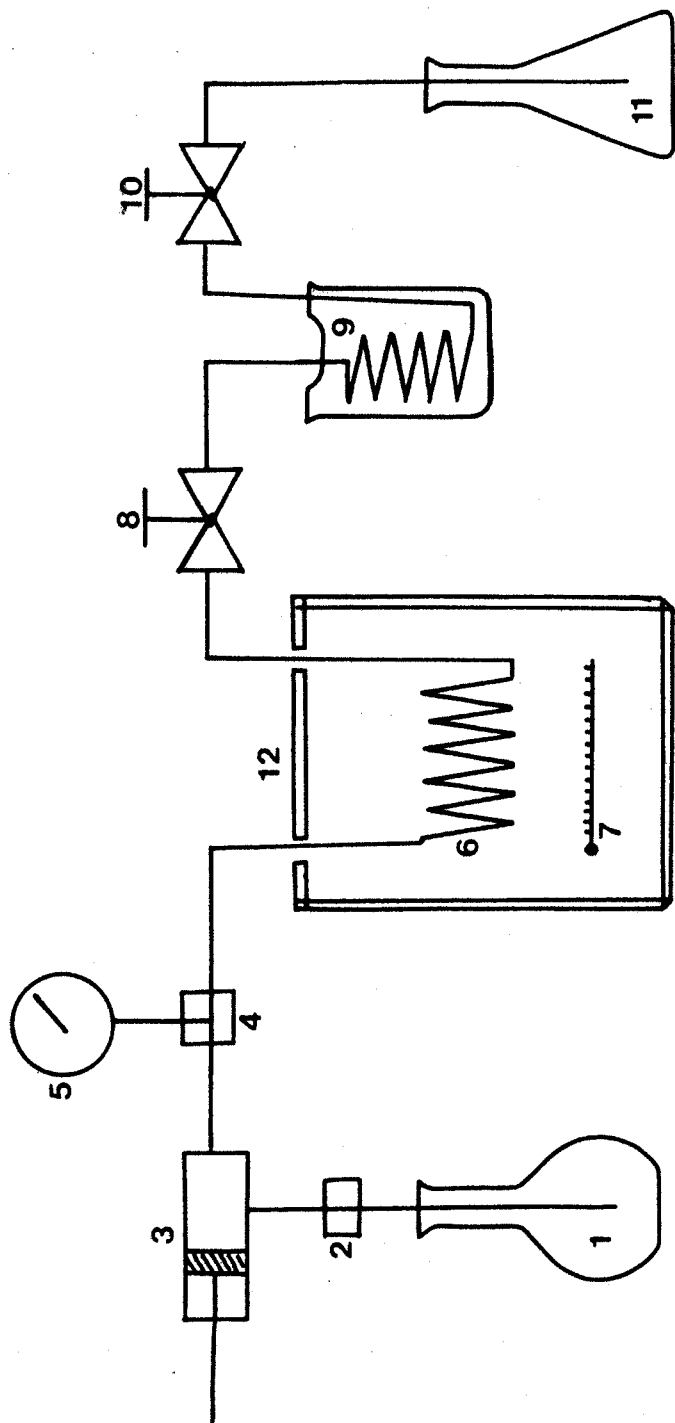


Figure 1. Schematic diagram of the HP-HT apparatus. 1) solvent reservoir; 2) filter; 3) high-pressure pump for up to 500 bar; 4) T-piece; 5) manometer for up to 600 bar; 6) reactor; 7) thermometer; 8) valve; 9) heat exchanger (1.6 mm-diameter capillary); 10) valve; 11) collector; 12) furnace.

with the valves 8 and 10. The same valves are used also to adjust the flow rate.

The HP-HT apparatus is started up as follows. First pure solvent is pumped through the reactor. When the parameters of the reaction (pressure, temperature, residence time) are adjusted, we change from pure solvent to the educt solution with a three-way valve on the low-pressure side. After the passage of four to five reactor volumina we take the first sample for analysis. Assuming that the reaction is already optimized, we can produce on a preparative scale. It is very important - and that is always true for a flow reactor - that for each reaction the parameters temperature, residence time, concentration and pressure are optimized. Due to the rapid adjustment of the reaction parameters the optimization is relatively fast with slightest consumption of reactants.

Analysis: The samples were analyzed qualitatively by GC-MS and quantitatively with internal standard by capillary GC with on-column injection (25 m fused silica capillary OV 101). The products were isolated by distillation or by preparative GC and characterized by NMR, IR, MS.

EXAMPLES

Synthesis of methyl 3-cyclohexyl-2-methyl propionate

10 g (0.1 mol) methyl methacrylate in 336 g (4 mol) cyclohexane were pumped through the HP-HT apparatus at 450°C and 300 bar, with a residence time of 2.5 min. Concentration of the product solution in vacuo gave 13.7 g of crude product. Spinning band distillation yielded 6.7 g = 37 % product (bp 56°C/0.2 torr, n_D^{20} 1.4491).

Synthesis of dimethyl 2-methyleneglutarate

86.1 g (1 mol) methyl acrylate solved in 1000 ml benzene were pumped through the HP-HT apparatus at 400°C, 200 bar, with a residence time of 5 min. Concentration of the product solution in vacuo yielded 73.5 g of crude product. Distillation with a 30 cm - Vigreux column yielded a) dimethyl 2-methyleneglutarate 25g = 29 % (bp 102-104°C/15 torr.) b) Trimethyl 1-hexane-2,4,6-tricarboxylate (trimer) 13.7 g = 17 %, bp 134-138°C/0.2 torr.

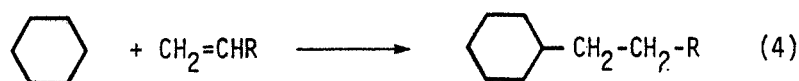
RESULTS

1. Thermal Addition of Alkanes to Alkenes - the "Ane Reaction".

We were able to demonstrate that alkanes are adding generally to alkenes at temperatures above 300°C, 200 - 500 bar and reaction times of 1 - 10 min [7].

Table I shows the results of the reaction of cyclohexane with a representative selection of activated, deactivated and normal alkenes.

Table I. Addition of Cyclohexane to Selected Alkenes



Alkene	Alkane/ Alkene	T[°C]	Residence time [min]	Yield [mol %]
Acrylonitrile	100	400	3.5	60
Methyl vinyl ketone	20	400	3	17
Vinyl acetate	20	450	0.5	19
Heptene-1	100	450	4	30

The addition of cyclohexane to methyl acrylate (5) has been investigated more in detail.

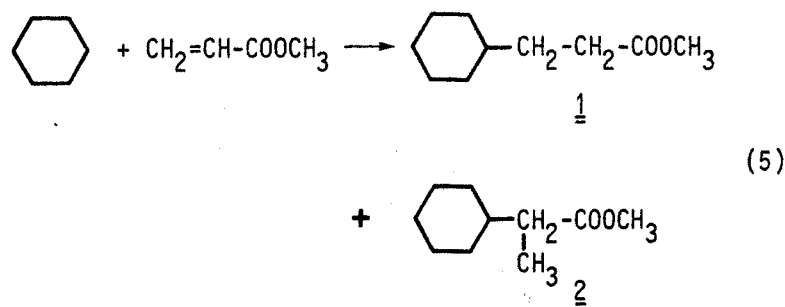


Figure 2a shows the yield of the anti-Markownikow addition product 1 increasing from 5 % at 250°C up to 45 % at 450°C.

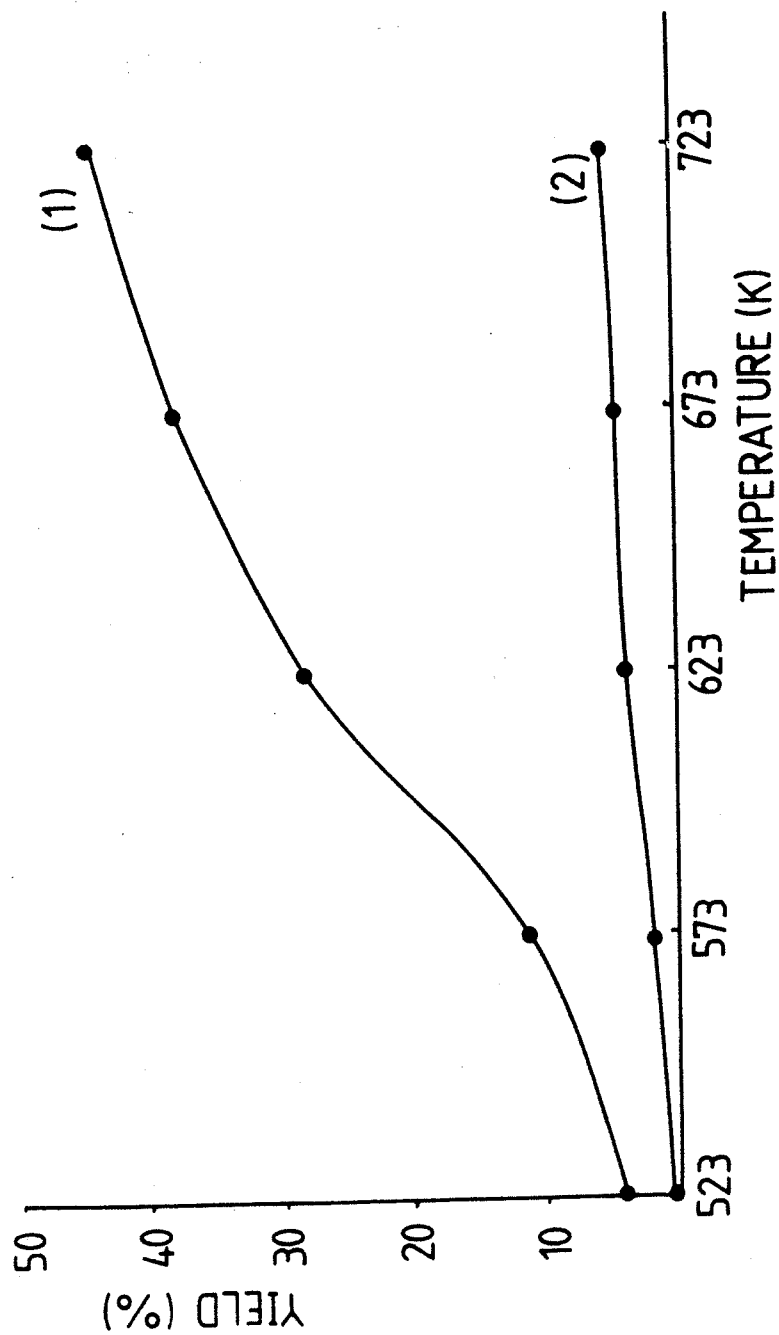


Figure 2a. Addition of cyclohexane to methyl acrylate. Effect of temperature on yield of methyl 3-cyclohexyl propionate 1 and methyl 2-cyclohexyl propionate 2. Reaction conditions: cyclohexane/methyl acrylate 25/1; residence time 10 min; pressure 450 bar; yield based on methyl acrylate charged.

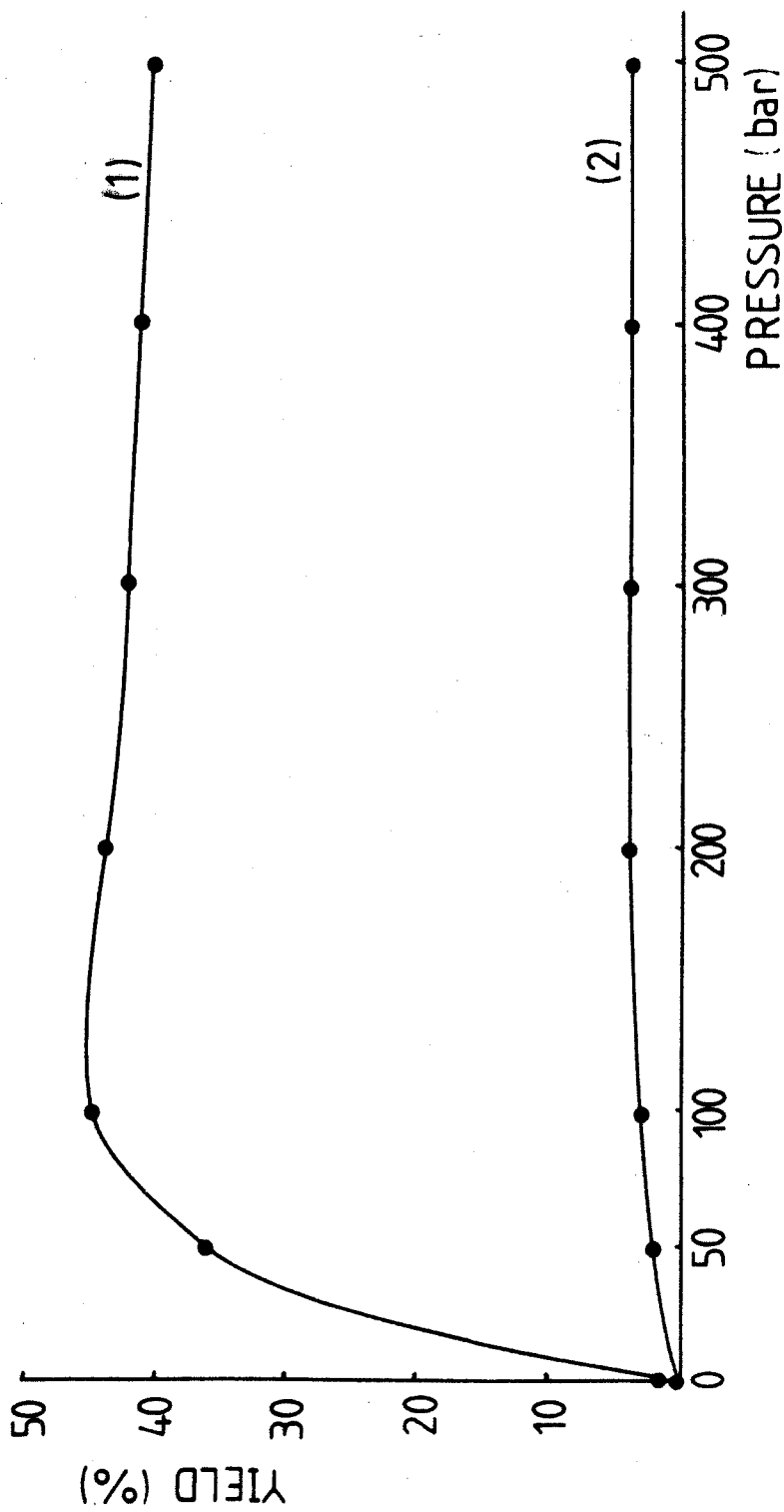


Figure 2b. Effect of pressure on yield of 1 and 2. Reaction condition: cyclohexane/methylacrylate 25/1; residence time 10 min; temperature 723 K.

The Markownikow product 2 is formed in minor amounts.

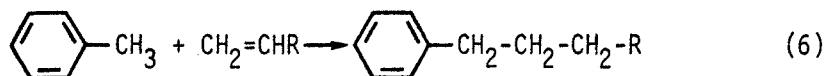
The influence of pressure shows Figure 2b. The yield is increasing significantly with pressure up to 100 bar. The critical data of cyclohexane are: $p_c=40$ bar, $T_c=280^\circ\text{C}$. The reaction mixture is supercritical. The essential influence of pressure can be explained by the increase of the density of the reactants allowing an intermolecular reaction with an appropriate rate.

Influence of residence time can be deduced from Figure 2c. At 450°C the reaction is complete after 3 min. At longer reaction times yield is reduced by consecutive reactions.

This example demonstrates unequivocally a remarkable advantage of reactions at elevated temperatures: they proceed extremely fast. On the other hand a rapid withdrawal of products from the reaction zone is necessary to avoid side reactions. This is possible only in a flow reactor.

Figure 2d shows the large effect of the concentration of either reactants. Apparently the concentration of cyclohexane is an important factor in the rate equation. High concentrations of methyl acrylate are favouring the oligomerization of acrylic ester (see section 5).

Table II. Addition of Toluene to Selected Alkenes.



Alkene	Toluene/ Alkene	T[$^\circ\text{C}$]	Residence time [min]	Yield [mol %]
Acrylonitrile	20	400	7	19.5
Methyl vinyl ketone	20	400	3	15
Vinyl acetate	20	380	2	4
Cyclohexene	50	410	10	2

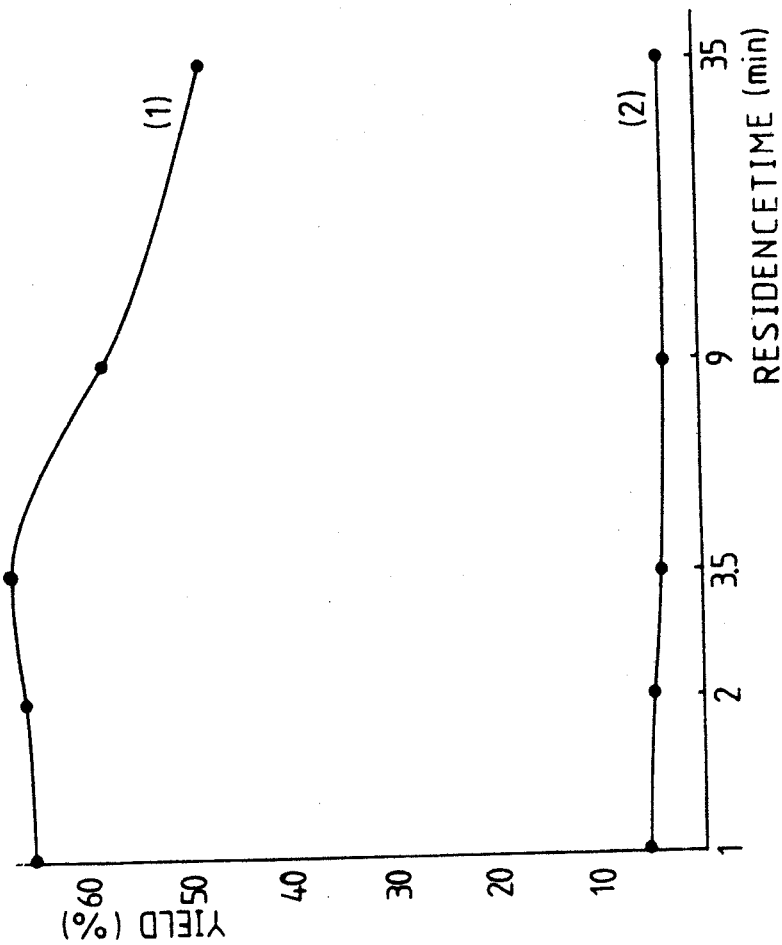


Figure 2c. Effect of residence time on yield of 1 and 2. Reaction conditions: cyclohexane/
methyl acrylate 50/1; pressure 200 bar; temperature 723 K.

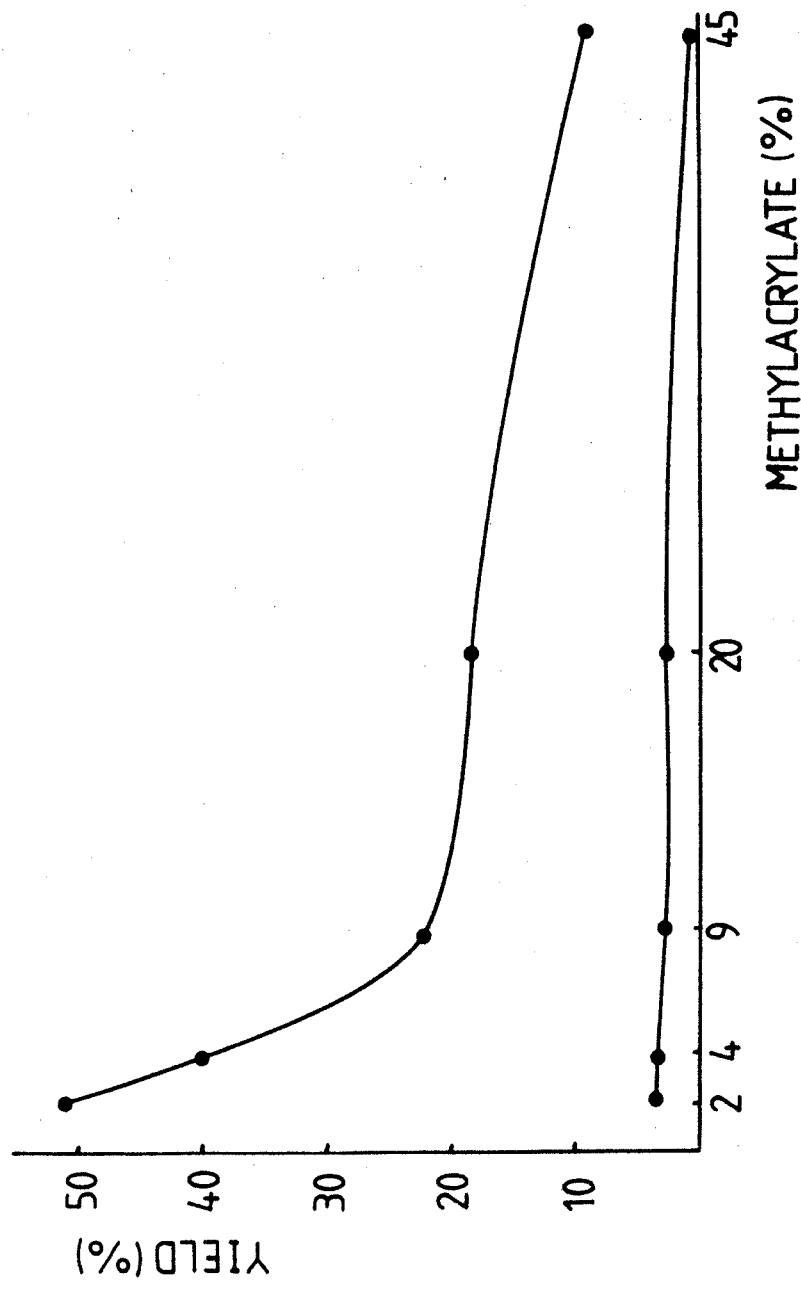


Figure 2d. Effect of concentration of methyl acrylate in cyclohexane on yield of 1 and 2.
 Reaction conditions: residence time 8 min; pressure 300 bar; temperature 723 K.

Besides cyclohexane we used other cycloalkanes such as cyclopentane and cycloheptane in order to obtain a simple product pattern. This is possible and observed also with alkylaromatics like toluene, xylene, cumene and analogous compounds (see Table II). A mixture of isomeric substitution products is obtained with n-alkanes. Our research with regard to alkane components is in progress. It may be mentioned that to our knowledge benzene is the only inert solvent for alkenes at elevated temperatures.

Currently we are trying to clarify the mechanism of this interesting reaction. Until now we can exclude catalysis of the transition metals of the reactor. The results obtained are identical in fused silica or stainless steel reactors (Figure 3). Addition of radical scavengers (hydroquinone, 2,6-di-tert-butyl-4-methyl-phenol) did not influence the yield of main reaction product.

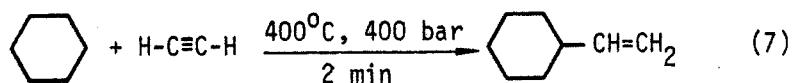
In the literature thermal addition of alkanes and alkylaromatics to alkenes has been described only for some special cases [8 - 12]. ALDER [10] compared this reaction with the Diels-Alder reaction and the ene reaction. We therefore proposed the term "ane-reaction" [7].

2. Thermal Addition of Alkanes to 1,3-Dienes.

Alkanes are adding thermally also to 1,3-dienes. Cyclohexane and 1,3-cyclohexadiene (400°C, 200 bar, 4 min, 1 mol % cyclohexadiene in cyclohexane) are yielding two isomeric cyclohexylcyclohexenes (12 % and 7 % respectively based on cyclohexadiene). The detailed structure analysis of these adducts is in progress. Comparable results are obtained with 1,3-butadiene and methyl 2,4-pentadienoate respectively as diene component in the reaction with cyclohexane. An addition product is not obtained with dimethyl 1,3-cyclohexadiene-1,4-dicarboxylate, but the dehydrogenation product dimethyl terephthalate is isolated.

3. Thermal Addition of Alkanes to Alkynes.

Alkanes are adding in a remarkably uniform reaction to alkynes to form alkenes [13]. For instance cyclohexane saturated with acetylene at 0.5 bar and pumped through the "HP-HT" apparatus yields 0.2 % (based on cyclohexane charged) vinylcyclohexane, a commercially interesting monomer.



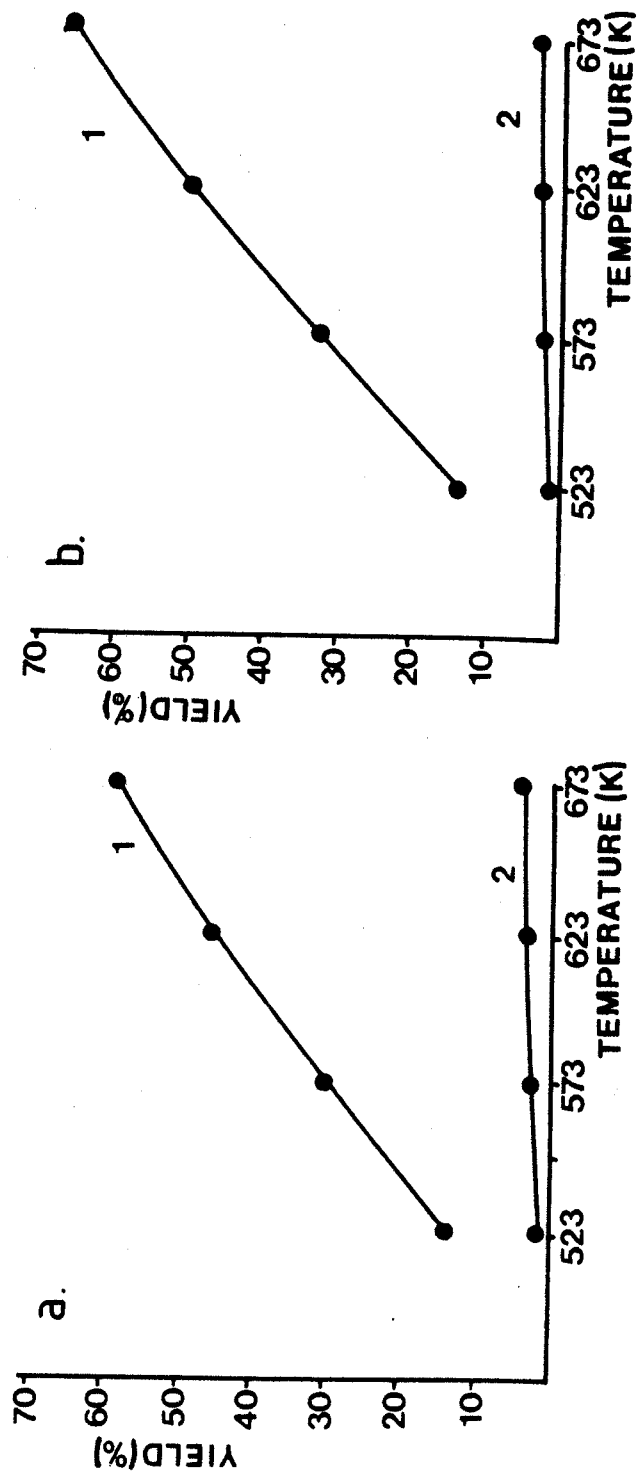


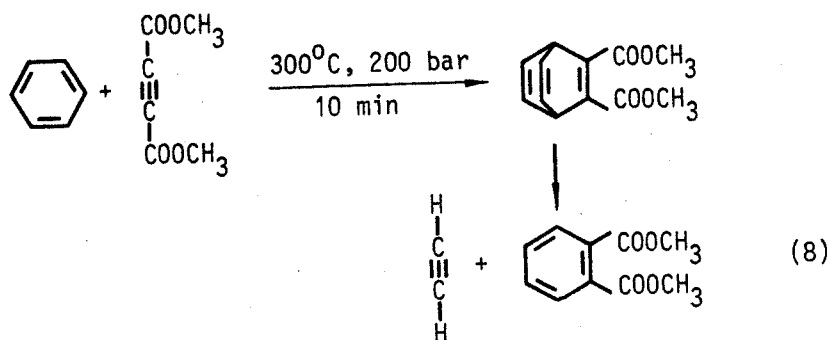
Figure 3. Comparison of the addition of cyclohexane to methyl acrylate in a) stainless steel reactor; b) fused silica reactor. Other reaction conditions are identical: residence time 1 min; pressure 200 bar; cyclohexane/methyl acrylate 100/1. 1: methyl 3-cyclohexyl propionate; 2: methyl 2-cyclohexyl propionate.

Recently KARPf and DREIDING published an intramolecular analogon of this reaction [14].

4. Reaction of Alkynes with Benzene.

In contrast to alkenes alkynes do react with benzene. A patent describes the synthesis of styrene from benzene and acetylene [15]. We could reproduce this result using our technique. Analogous experiments with methyl propiolate yielded methyl benzoate amongst other products. Dimethyl acetylenedicarboxylate gave dimethyl phthalate (8).

Apparently benzene is reacting as diene with an alkyne as dienophile to a barrelene derivative [16] followed by a retro-Diels-Alder-reaction. By GC/MS we could detect styrene in the reaction mixture, which should be formed from acetylene and benzene as mentioned above.



5. Thermal Dimerization of Acrylic Compounds.

There has been much interest in the catalytic dimerization of acrylic compounds yielding 2-methyleneglutarate derivatives, which represent trifunctional compounds and useful intermediates in organic synthesis [18]. Thermal dimerization has not been much investigated. DANUSSO [19] was able to isolate dimethyl 2-methylene-glutarate in connection with experiments of thermal polymerization of methyl acrylate at temperatures of 300°C to 400°C. No yield data were given.

We have carried out the thermal dimerization and oligomerization of methyl acrylate in the HP-HT apparatus (9).

This reaction corresponds to an addition of a vinylic C-H bond to an alkene.

Our results are compiled in Figures 7 and 8 respectively.

Apparently dimerization occurs as the first step of the thermal polymerization of methyl acrylate. At temperatures below 340°C higher oligomers are favoured. With temperature increasing the formation of higher oligomers is reduced in

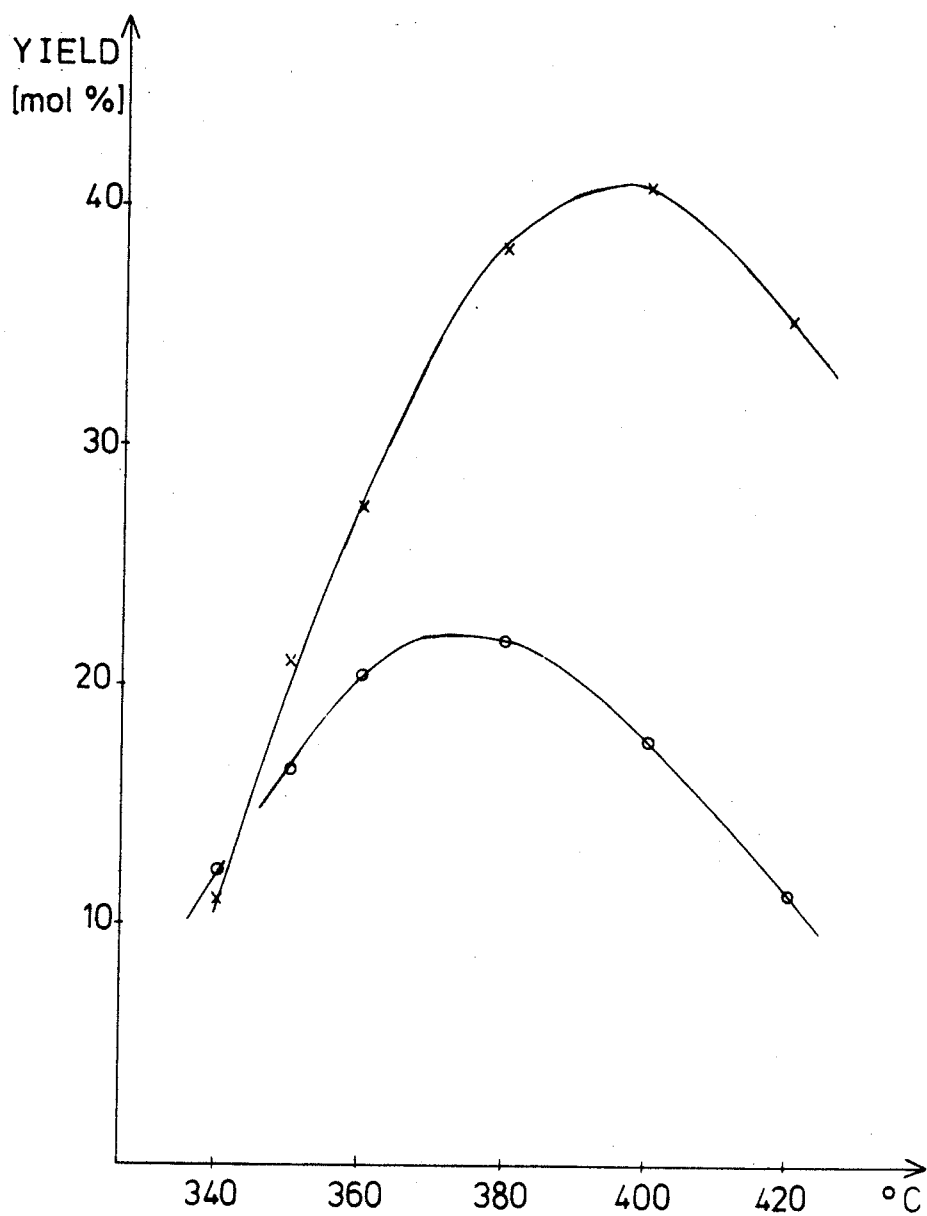


Figure 4. Dimerization of methyl acrylate. Effect of temperature on yield of dimer (xxx) and trimer (ooo). Reaction conditions: 1 mol/l methyl acrylate in benzene; residence time 5 min; pressure 200 bar.

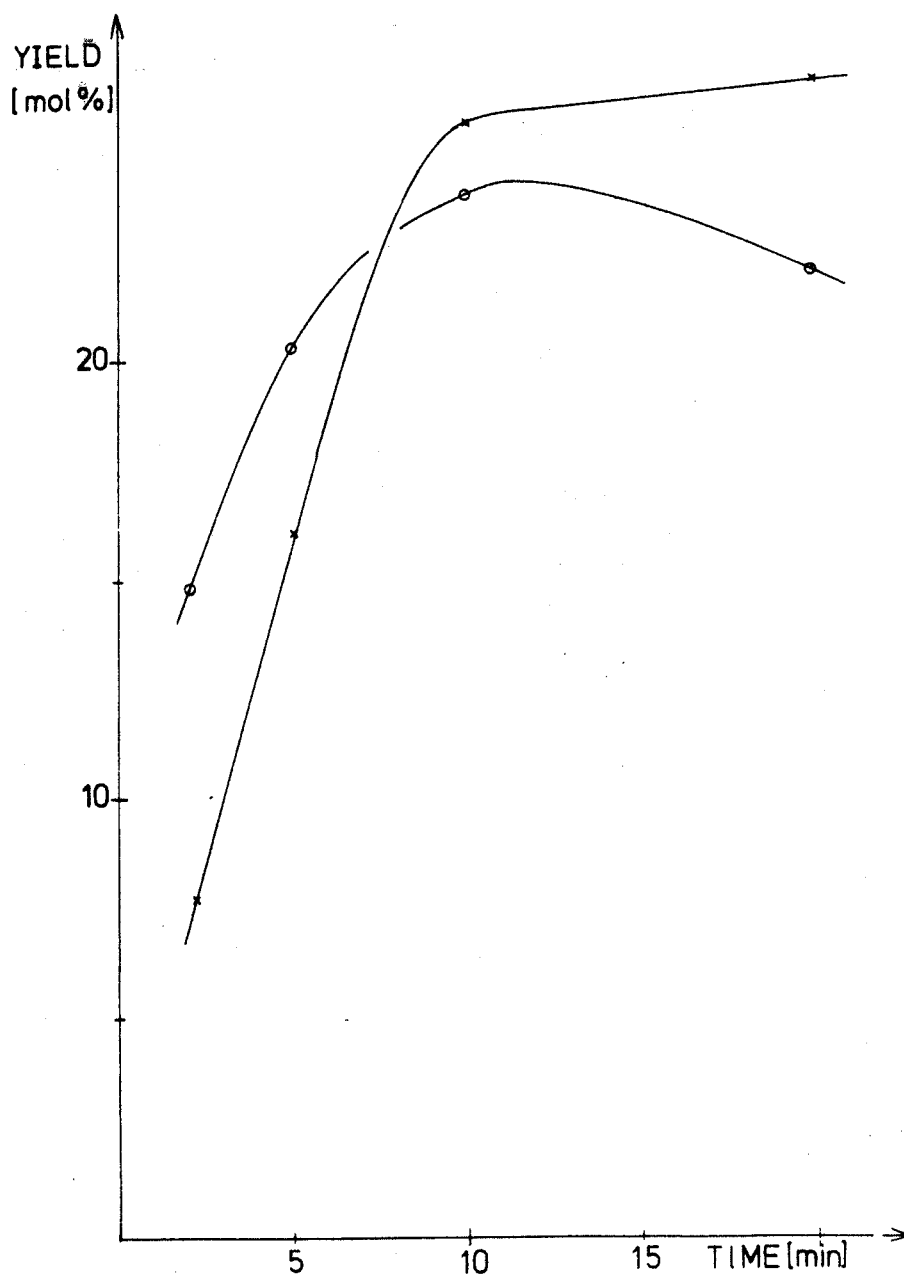
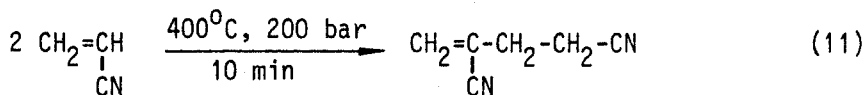
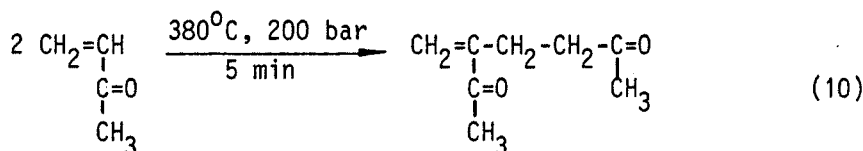
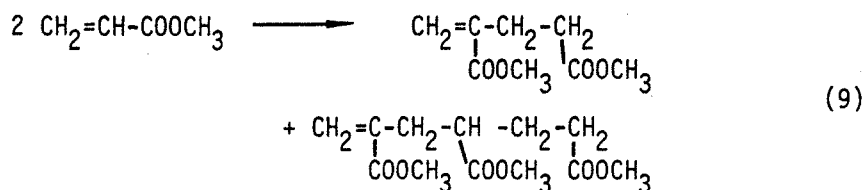


Figure 5. Dimerization of methyl acrylate. Effect of residence time on yield of dimer (x x x) and trimer (o o o). Reaction conditions: 2 mol/l methyl acrylate in benzene; temperature 350°C; pressure 200 bar.

favour of the dimer. Depolymerization reactions are dominating above 400°C.

Methyl vinyl ketone and acrylonitrile are able to dimerize analogously (10,11).



CONCLUSIONS

Experimental work of explorative nature has shown that intermolecular thermal reactions of hydrocarbons can proceed with high yields of components which have great potential for the synthetic organic chemist and industrial application. These C-C bond forming reactions proceed at temperatures of 300°C and up which is the range for thermal cracking of hydrocarbons. The high yield of addition products is enhanced by the density of the reactants.

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