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THE METHOD OF FLASH VACUUM PYROLYSIS, PREPARATIVE APPLICATIONS AND ANALYTICAL STUDIES

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SUMMARY

Flash vacuum pyrolysis has been used to prepare a variety of differently substituted derivatives of the benzocyclobutene ring system starting with simple precursors. An analytical gas flow reactor is described which simulates reaction conditions of flash vacuum pyrolysis experiments. This reactor allows to optimise reaction conditions and to obtain structure reactivity correlations for thermolytic gas phase reactions.

INTRODUCTION

Ever since chemistry has emerged as a science heat has been used to perform chemical change. The notion that heat treatment of organic chemicals leads frequently to complex mixtures coupled with the tremendous potential of homogenous and heterogenous catalysis for the enhancement of chemical selectivity had as a consequence that the systematic study of thermolytic reactions in the synthetic organic laboratory was neglected for a long time. In industrial chemistry however, gas phase thermolytic processes always have played an important role for large volume production of basic organic chemicals.

In recent years the method of flash vacuum pyrolysis has been used increasingly for the preparation of useful organic compounds of moderate complexity. In flash vacuum pyrolysis experiments the substrate to be submitted to heat is transported by distillation under reduced pressure or by an inert carrier gas through a hot reaction tube, the products formed being isolated after condensation at low temperature. A wide variety of products of theoretical and synthetical interest have been prepared by this method. Information about the potential of the thermolytic method can be found in a comprehensive monograph [1] and in several recent review articles [2].

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REACTION VARIABLES IN FLASH VACUUM THERMOLYSIS

The experimental variables of importance in thermolytic gas phase reactions can be divided in three groups (see table 1).

TABLE 1 Experimental parameters in gas phase reactions

variable	typical values	consequences
1. temperature T_r contact time t_c	300-800°C 0.001-1 s	$\Delta G^{\ddagger}$ of primary process (% conversion)
2. reactant pressure p_r carrier gas, p_c	0.01-15 Torr	participation of bimolecular processes
3. reactor surface catalyst	fused SiO_2 Al_2O_3, K_2CO_3 etc.	participation of catalysed reaction steps

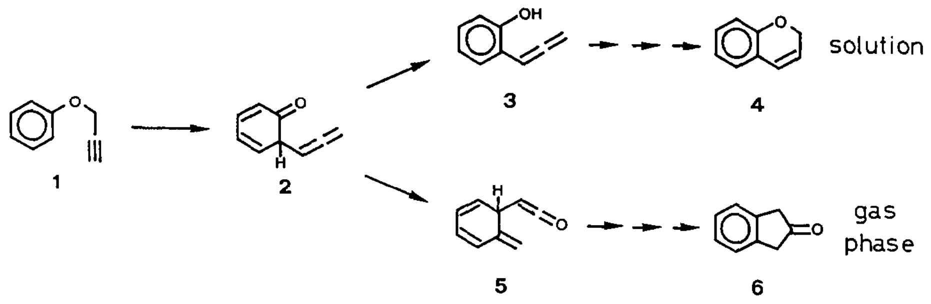
The reaction temperature T_r and the residence time t_c of the molecules in the hot reaction tube determine the upper limit of the free energy of activation, $\Delta G^{\ddagger}$, available for intramolecular primary processes.

The reactant partial pressure p_r and the nature of the carrier gas, if any, and its pressure p_c determine to which extent intermolecular processes can compete with intramolecular reactions.

The quality of the reactor surface and the nature of solid catalysts, if present, determine to which extent catalysed reaction steps compete with thermally induced intramolecular processes.

Typical reaction conditions of flash vacuum thermolysis experiments involve high reaction temperature (300-800°C), short contact time (0.001-1 s.), low reactant partial pressure (0.01-15 Torr) and inert reactor surface, fused silica frequently being the material of choice because of its inertness and its thermal stability. These reaction conditions are such that intramolecular processes are strongly favoured. Intermolecular or catalysed reaction steps often are suppressed in gas phase experiments to an extent which is never possible in reactions carried out in solution. Many thermolabile compounds therefore yield completely different products if submitted to heat treatment in the gas phase than in solution. One notable and useful example is the Claisen rearrangement of phenyl propargyl ether 1 (s. scheme 1).

Scheme 1

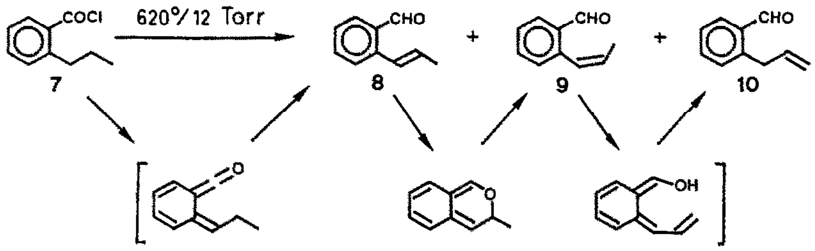


In solution a quantitative conversion of 1 to benzpyran 4 is observed [3] whereas in the gas phase indanone 6 is the only product formed [4]. The difference in the two reaction pathways is due to the fate of dienone 2, the primary reaction intermediate generated through 3,3-sigmatropic rearragement from 1. In solution aromatisation to 3 is rapid, followed by conversion to 4 through conventional sigmatropic and electrocyclic reaction steps. In the gas phase, however, aromatisation 2 → 3, formally a 1,3-hydrogen shift reaction, is precluded since a concerted, intramolecular-pathway is forbidden [5]. Instead, an alternate pathway via 5 to indanone is followed. In our laboratory we are using this reaction as a diagnostic test for the catalytic activity of the hot reactor surface. The absence of benzpyran 4 in the gas phase pyrolysis product of 1 is taken as evidence of no significant surface catalysis.

GENERATION OF BENZOCYCLOBUTENES THROUGH FLASH VACUUM PYROLYSIS

Thermolytic elimination of acid HX from suitable substrates is frequently carried out by the method of flash vacuum pyrolysis [6]. The formation of olefins through ester pyrolysis is a well documented example of this type of reactions [7].Some time ago we have found that ortho-alkylated benzoic acid chlorides can be induced to undergo similar uncatalysed 1,4-elimination of HCl across the aromatic ring [8]. An example is shown in Scheme 2.

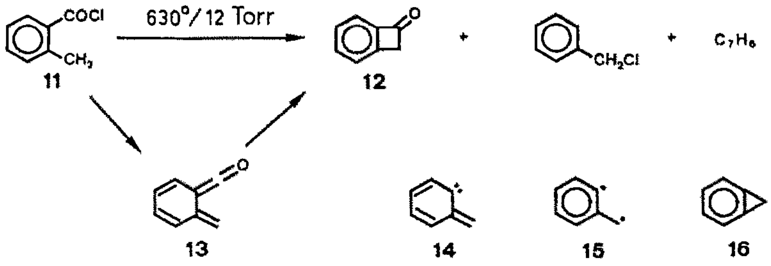
Scheme 2



The formation of 2-propenylbenzaldehydes 8, 9 & 10 from acid chloride 7, formally an intramolecular redox reaction, is the consequence of an uncatalised 1,4-elimination of HCl followed by an intramolecular 1,5-hydrogen shift reaction. As the three aldehydes 8 - 10 are formed as an equilibrium mixture, there must be concerted, low energy pathways available for their mutual interconversion.

Flash vacuum thermolysis of ortho-toluic acid chloride 11 leads to benzocyclobutenone 12 in fair yield[8]. Apparently stabilisation of the ortho-quinoid intermediate 14 in this case occurs through electrocyclic ring closure (see scheme 3). Benzocyclobutenone 12 is known to be thermolabile itself yielding ring contracted hydrocarbons C_7H_6 through loss of CO [9]. HCl-addition to the primary decarbonylation intermediate 14, 15 or 16 accounts for the benzylchloride which is found as a minor constituent in the pyrolysis product mixture obtained from 11.

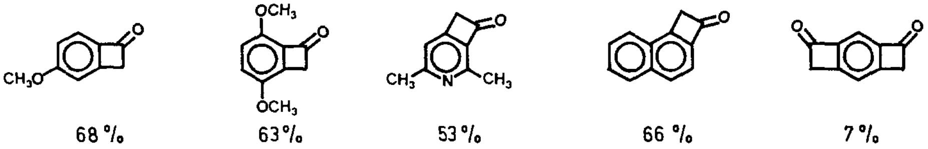
Scheme 3



The thermolytic generation of benzocyclobutenone 12 lends itself easily to scaleup . Pyrolysis experiments have been carried out in the laboratory on a 250 g-scale repeatedly. In preparative runs conversion is kept at or below 50% in order to prevent extensive decarbonylation. Unreacted starting material can readily be separated from ketone and recovered after hydrolysis.

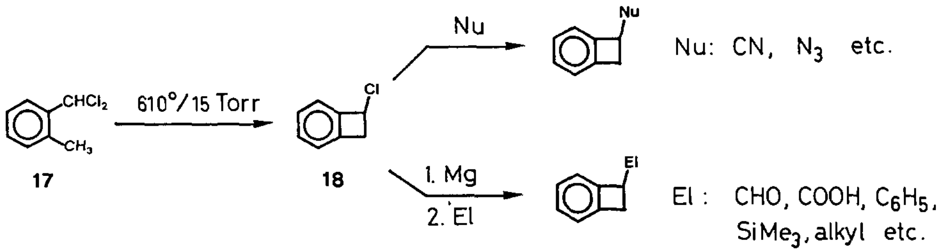
A wide variety of substituted benzocyclobutenones have been obtained from ortho-methylated aromatic acid chlorides by flash vacuum pyrolysis. Some examples are shown in scheme 4 with the yield reached in the pyrolytic step. Due to their ring strain these compounds are useful intermediates in organic synthesis [10], [11].

Scheme 4



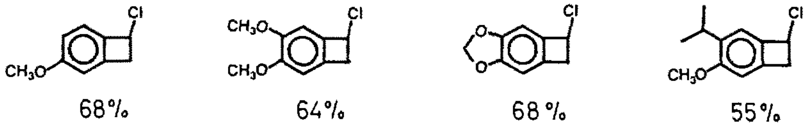
Upon flash vacuum pyrolysis 2-methyl benzalchloride 17, obtained quantitatively through PCl_5-treatment of 2-methyl benzaldehyde, is converted to α-chloro benzocyclobutene 18 in high yield (see scheme 5). The halogen in 18 can be replaced by substitution with nucleophiles and, via the Grignard reagent, through electrophiles [12]; thus an easy access to benzocyclobutenes carrying different substituents in the four-membered ring is opened.

Scheme 5



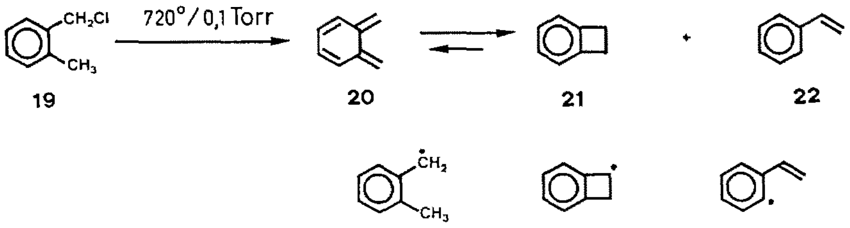
The reactions described in scheme 5 lend themselves readily to the preparation of benzocyclobutenes with ether or alkyl substituents in the aromatic ring. The required benzalchloride precursors are available from appropriate 2-methyl benzaldehydes by PCl_5-treatment in high yield. Many of these highly functionalized benzocyclobutenes, especially those carrying a cyano group in the four-membered ring, have found use as building blocks in the convergent synthesis of polycyclic natural products following the principle of intramolecular cycloaddition [13],[14]. Some examples of α-chlorobenzocyclobutenes obtained in this way are shown in scheme 6 together with the yield reached in the thermolytic HCl-elimination step.

Scheme 6



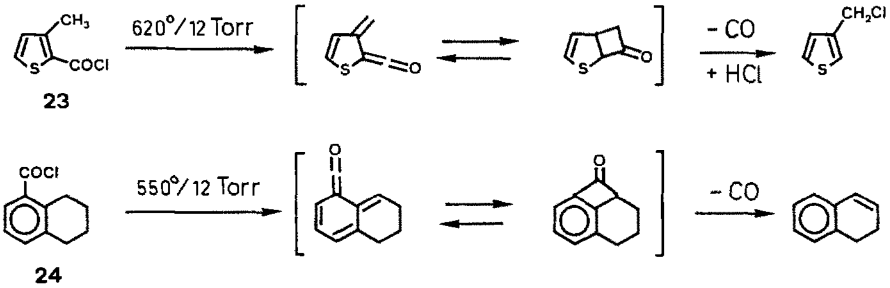
The thermolytic generation of benzocyclobutene <u>21</u> through 1,4-elimination of HCl from 2-methylbenzylchloride <u>19</u> has first been observed by Maccoll in 1969 in the course of a kinetic study of gas phase HCl-elimination reactions [15]. It took almost ten years for synthetic applications of this reaction to be realised. In 1978 both we in Basel [16] and Boekelheide in Oregon [17] reported about the preparation of benzocyclobutene <u>21</u> and substituted derivatives thereof through flash vacuum pyrolysis of appropriately substituted 2-methylbenzylchlorides. The value of this method has since been demonstrated elegantly through its use in the synthesis of polybridged paracyclophanes by the Oregon group [18].

Scheme 7



Benzocyclobutene 21 differs significantly from benzocyclobutenone 12 in its reactivity at high temperature. The ketone 12 is thermolabile losing CO under conditions very similar to its formation from the acid chloride 11. Decarbonylation seems to occur from the reactive orthoquinoid vinylketene intermediate 14. This is suggested by finding that acid chlorides such as 23 or 24 which would lead to highly strained arenocyclobutenones yield only decarbonylated products upon pyrolysis (see scheme 8).

Scheme 8



Benzocyclobutene 21 on the contrary is protected from unimolecular decomposition by high activation barriers. The intramolecular isomerisation to styrene recently described [19] being a high energy process not competing with the thermolytic formation of 21 from 19.

The critical property limiting the yield of benzocyclobutene 21 in its thermolytic generation from 19 is its high intermolecular reactivity and especially that of its reversibly formed valence isomer orthoquinodimethane 20. By carrying out thermolysis of 19 at moderate pressure (12-15 Torr) most of the benzocyclobutene 21 is consumed, styrene and polymer being formed in addition to dibenzocyclooctadiene and anthracene the known [20] high temperature dimerisation products of 20/21. Polymer formation and isomerisation to styrene seem to be radical induced chain processes; structures for initiator and possible chain carrier radicals are shown in scheme 7. As a practical consequence the preparation of intermolecularly reactive benzocyclobutenes such as the parent compound 21 through flash vacuum pyrolysis has to be carried out at very low pressure ($<$ 0.1 Torr).

RATE MEASUREMENTS OF HIGH TEMPERATURE GAS PHASE REACTIONS

Reaction conditions of flash vacuum pyrolysis experiments such as those described in the previous section frequently are ill defined. While the reaction temperature may be known more or less accurately, for many experiments reported in the literature there is little information about the residence time of the molecules in the hot reaction zone. An estimate of this reaction variable could be made if the reactor volume, the rate of reactant flow and its pressure in the reactor were known. However, this information is lacking in most reports about flash vacuum pyrolysis reactions in the literature. Frequently only the pressure read at the vacuum pump is reported. Obviously this value may differ significantly from the actual pressure in the reacting zone, especially if the experiment is carried out at low pressure.

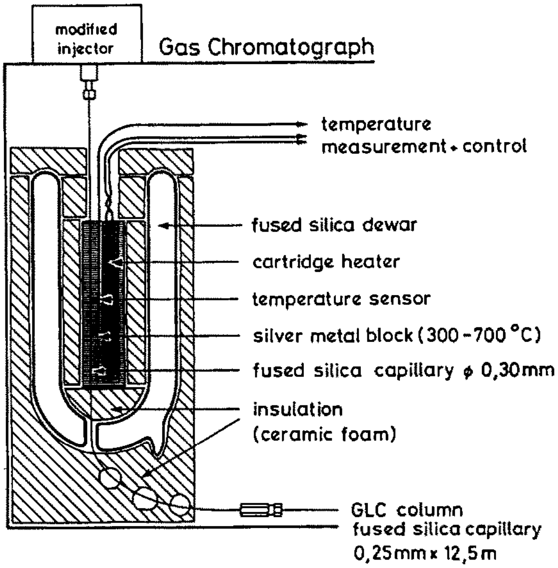
In our laboratory we are using for some time a simple analytical gas flow reactor [12]. In this reactor conditions typical of flash vacuum thermolysis prevail, i.e. high temperature, short contact time, low reactant partial pressure and inert reactor surface. A summary description of an improved version of this reactor and some recent results exemplifying its performance are given below.

Analytical gas flow reactor

The actual high temperature reactor consists of a fused silica capillary of 0.33 mm i.d. which is mounted in the oven of a gas chromatograph between the injector and the capillary separation column (fig. 1).

Fig. 1

high temperature analytical gas flow reactor

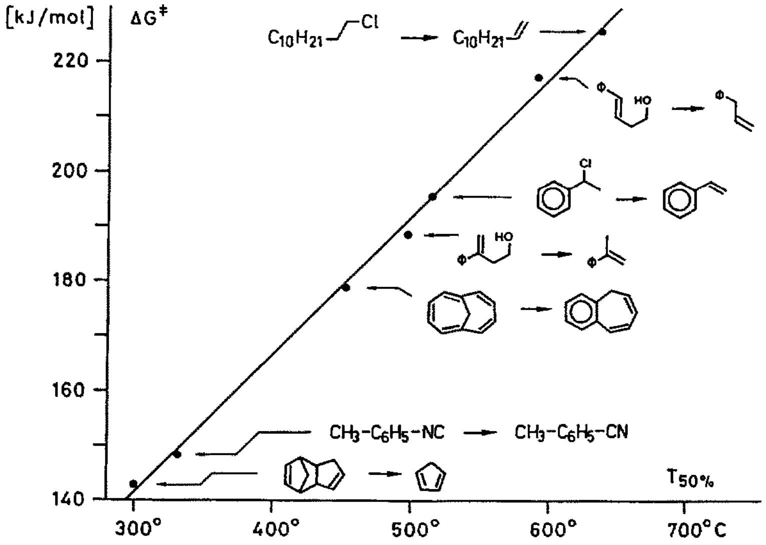


Uniform heat is applied to a 10 cm section of the untreated reactor capillary by means of insertion in an electrically heated silver block (2x10 cm) The hot reaction tube is carefully insulated in order to prevent interference with the independent oven temperature control of the gaschromatograph. The sample to be investigated is injected as a dilute solution in an appropriate solvent through the slightly modified VPC-injector and products are analysed on-line in the usual manner.

In principle the contact time t_c of the molecules in the hot reaction zone could be calculated from hydrogen carrier gas flow rate, volume and temperature of the reactor. However, we prefer to determine t_c indirectly by calibration under standard flow conditions with known intramolecular thermolytic reactions for which reliable gas phase kinetic data are available. At constant carrier gas flow rate (regulated at room temperature) the reactor temperature $T_{50\%}$ is determined at which exactly 50% conversion of reactant is observed. Assuming an intramolecular process for reactant consumption the residence time t_c at $T_{50\%}$ equals the half life $t_{1/2}$ of the thermally induced first order reaction. Keeping carrier gas flow rate constant throughout the experiment the $T_{50\%}$-value of a reaction is directly proportional to the free activation energy $\Delta G^{\ddagger}$ at that temperature ($T_{50\%}$). The calibration curve (fig. 2) shows that this proportionality holds over a wide range of temperatures.

Fig. 2

calibration curve for analytical gas flow reactor



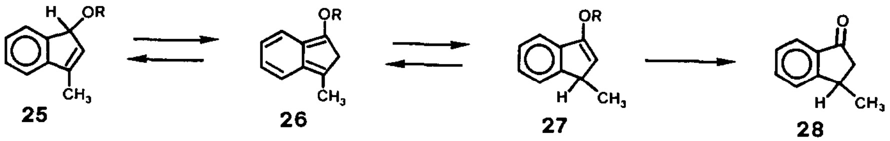
With the reactor described approximate rate data for high temperature gas phase reactions are obtained and complex pyrolysis mixtures can be analysed with little effort. This allows to map product composition of pyrolytic reaction mixtures as a function of pyrolysis temperature, to optimise reaction conditions for pyrolytic processes of preparative interest and to obtain structure-reactivity correlations with respect to elementary thermolytic reaction steps.

Surface catalysis

The isomerisation of indenes through uncatalysed sigmatropic 1,5(1,2)-hydrogen migration is a well established process [21]. The quantitative conversion of hydroxyindene 25 to indanone 28 at 230° in isoctane solution therefore is not unexpected, isomeric hydroxyindenes 26 and 27 being reasonable reaction intermediates.

Thermolysis of 25 in the gas flow reactor leads to 28 as in solution, however the conversion is not complete even at high temperature! Above 450°C 25 and 28 are obtained in a stationary ratio of 15:85. A sample of 28 submitted to the same thermolysis conditions is unchanged, indicating that the observed product ratio does not reflect a high temperature equilibrium between 25 and 28. We are forced to the conclusion that in the hot reaction zone only the uncatalysed hydrogen shift reactions occur leading to an equilibrium between allyl alcohol 25 and vinyl alcohol 27. The ketonisation 27 → 28, a formal 1,3-hydrogen shift reaction for which there is no allowed intramolecular, concerted pathway [5], apparently occurs only after condensation of the reactor effluent in the cool VPC-separation column. This conclusion is strongly supported by an equilibration experiment with methyl ethers 25b and 27b. Thermolysis in the gas flow reactor above 450°C leads to an equilibrium mixture of 25b and 27b (12:88) which is very similar in composition to the stationary mixture of 25a and 28 obtained from 25a (see scheme 9).

Scheme 9



a) R = H   b) R = CH_3

The apparent lack of conversion of vinylalcohol 27a to ketone 28 in the gas flow reactor is proof of the low catalytic activity of the hot reactor surface!

Structure-reactivity correlation

Acyl groups participate in sigmatropic 1,5-shift reactions with ease [22],[23]. An analytical study of the uncatalysed rearrangement of 1-acetyl-1-methyl indene (29a) carried out in our gas flow reactor yields the product temperature profile shown in figure 3. At 300°C the main reaction product is 1-acetyl-3-methylindene (31) indicating that the primary isoindene intermediate 30 formed through rate limiting sigmatropic 1,5(1,2)-acetyl migration from 29 reacts faster through a second acetyl than through hydrogen migration (see scheme 10). Only at higher temperature reversible hydrogen migration participates in product formation, an equilibrium mixture of isomers 29a (2%), 31 (18%), 33 (6%), 34 (58%) and 35 (16%) being formed above 450°C.

Scheme 10

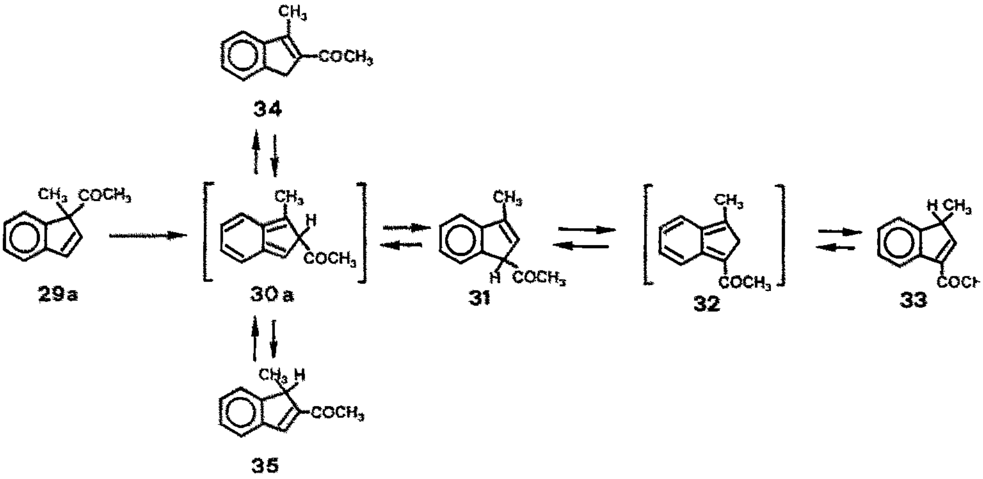
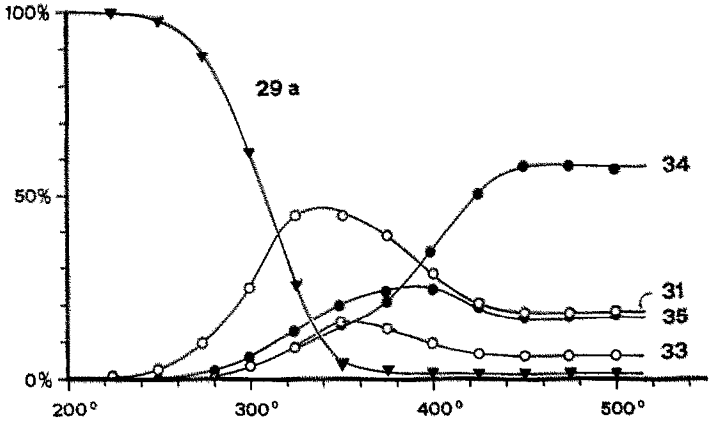


Fig. 3
Product-temperature profile for the isomerisation of 29a



Several other 1,1-disubstituted indenes of general structure 29 have been shown to behave similary yielding products through essentially irreversible 1,5(1,2)-migration of the functional group X in the primary reaction step (see scheme 11). $T_{50\%}$-values for the intramolecular isomerisations 29→30 as determined in our flow reactor are given in table 2 together with the corresponding $\Delta G^{\neq}$-values obtained from the calibration curve in fig. 2. The $\Delta G^{\neq}$-values are a measure for the migration tendency of the functional groups X in 1,5-sigmatropic rearrangement. Of special interest is the low reactivity of the cyano group.

Scheme 11

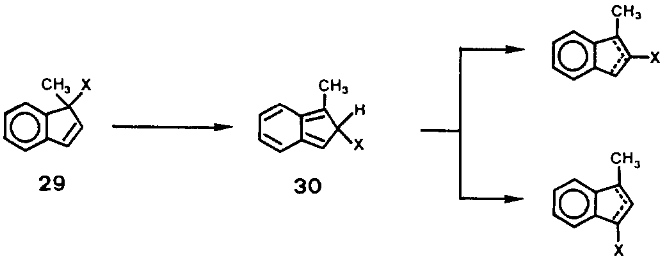


TABLE 2

Isomerisation of indenes 29 through sigmatropic shift reaction

	X	$T_{50\%}$ [°C]	$\Delta G^{\ddagger}$ [$kJmol^{-1}$]
29a	$COCH_3$	308°	144
29b	$COOCH_3$	460°	182
29c	C_6H_5	524°	198
29d	CN	535°	201

Reaction optimisation

Benzocyclobutenedione 37 for which several thermolytic formation pathways are known [24] is a useful building block in natural product synthesis [25]. One especially attractive access to 37 involves thermolytic 1,1-elimination of benzoic acid from readily available benzoyloxy phthalide 36a [26] (see scheme 12). In our hands, however, flash vacuum pyrolysis of 36a gave the diketone 37 in very low yield only, biphenylene 38 being formed instead through decarbonylation via dehydrobenzene. In our gas flow reactor a $T_{50\%}$-value of 540°C has been determined for the thermolytic decarbonylation of 37. In table 3 $T_{50\%}$-values for the decomposition of several phthalide derivatives carrying different leaving groups are given. It is clear that neither the benzoate 36a nor the chloride 36b are satisfactory precursors for the generation of 37 due to their insufficient reactivity. The acetate 36c and the formiate 36d are more reactive, however, they do not yield any 37 but only phthalic acid aldehyde 39, presumably reacting through six electron cyclic transition states (see scheme

12). The precursor of choice proved to be the trifluoroacetate 36e with a $T_{50\%}$-value well below 540°. In preparative flash vacuum pyrolysis experiments carried out at 540°/0.1 Torr conversion of 36e was kept at 50%. The diketone 37 could thus be obtained in a yield of 46% with respect to starting material consumed and not recovered after hydrolysis as 39.

Scheme 12

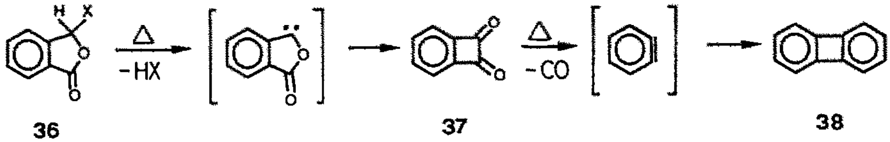
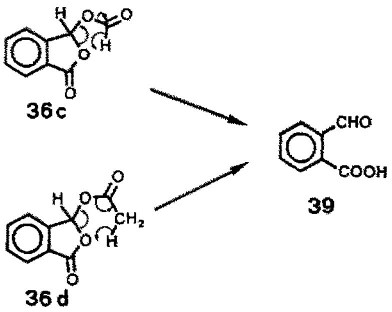


TABLE 3

$T_{50\%}$-values for phthalides 36

36	X	$T_{50\%}$ [°C]
a.	$OCOC_6H_5$	572°
b.	Cl	570°
c.	OCHO	460°
d.	$OCOCH_3$	500°
e.	$OCOCF_3$	512°

Scheme 13



CONCLUSION

We hope to have given a general idea of the method of flash vacuum pyrolysis and of its merits for the efficient generation of variously substituted derivatives of the benzocyclobutene ring system. Obtaining approximate rate constants for key gas phase reactions has helped a lot in elucidation of thermolytic decomposition pathways and in optimising reaction conditions for pyrolytic processes of synthetic interest. As thermolytic decomposition of organic chemicals gains importance in environmental chemistry, it is assumed that the analytical aspects of thermolysis reactions described in this paper may be of practical use in areas beyond synthetic and mechanistic organic chemistry.

ACKNOWLEDGEMENT

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