

ESTRONE SYNTHESIS UNDER SUPERCRITICAL FLUID CONDITIONS USING SHOCK HEATING BY COMPRESSED CARBON DIOXIDE

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ABSTRACT: A novel type of supercritical (sc) fluid-phase reaction is described in which a very hot fluid material is used to instantaneously heat a reaction mixture to high-temperature sc conditions. The method applies to processes which exhibit favorable reactivity and selectivity at high T . The fluid-phase pyrolysis of ADD to estrone is one example. Rapid (shock-) heating is performed with pre-heated fluid CO_2 . Reaction temperatures of 550 °C and above may be reached on a sub-second time scale.

INTRODUCTION

Carrying out chemical processes in sc fluid phase may be highly advantageous for one or more of the following reasons: With an extended, continuously tunable temperature and pressure range being available, optimum reactivity and selectivity conditions may be chosen. Tunability of the reaction medium provides the potential of establishing suitable combinations of solvent and of transport properties. Separation steps after reaction may be less difficult with a sc solvent medium. A disadvantage of reaction in supercritical fluid phase relates to the requirement of applying elevated or even high pressures. Thus mostly several advantages of reaction in sc fluid phase need to be combined in order to induce technical applications.

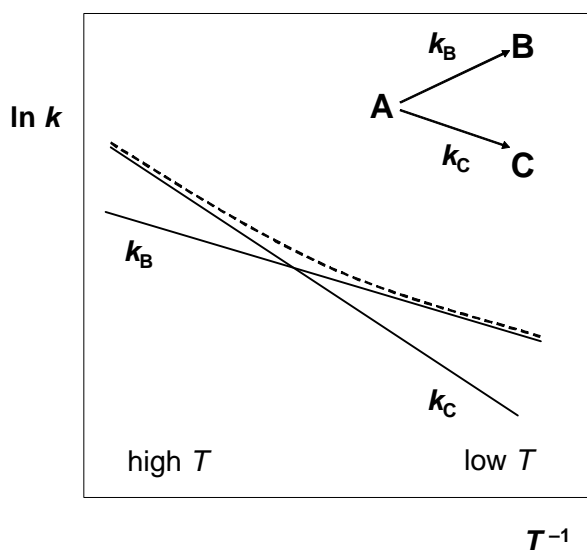
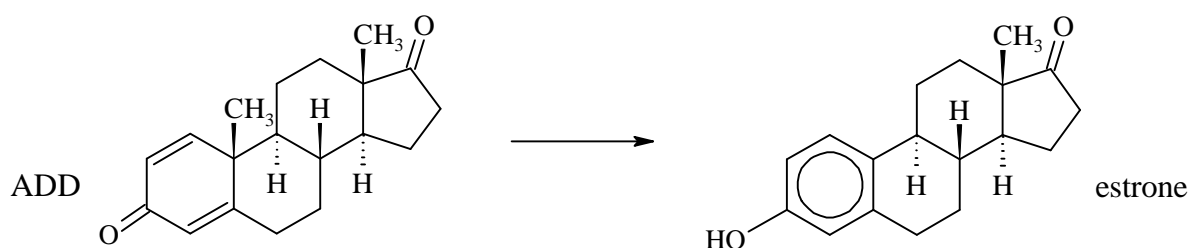


Figure 1: Temperature dependence of the overall rate coefficient k (dashed line) for two parallel reactions of component **A**, to **B** and to **C**, respectively.

The present paper illustrates a novel type of sc fluid-phase processing to be applied with reactions that exhibit favorable selectivity at high temperatures. A typical situation is illustrated in Figure 1. The starting material **A** may react via two parallel reactions to components **B** and **C** with the associated rate coefficients k_B and k_C , respectively, and with k being the overall rate coefficient for consumption of **A**. As is indicated by the two Arrhenius lines, reaction to **B** is favored at lower temperature whereas **C** constitutes the dominant product at high temperature. If **B** is the desired product, the reaction should be carried out at fairly low temperature and no interference by significant production of **C** is to be expected. On the other hand, with **C** being the desired product, the temperature range of unsatisfactory selectivity, this is where k_B exceeds k_C , needs to be passed very rapidly in order to keep the amount of starting material that reacts under conditions of inadequate selectivity as low as possible. A very effective means of rapidly heating a reaction mixture is by extremely fast addition of a very hot sc fluid medium. In order to reach high T , the pre-heat temperature of the sc fluid should be substantial which requires a thermally very stable material to be used. Carbon dioxide perfectly meets this requirement. The process is preferably carried out continuously by rapid mixing of hot supercritical carbon dioxide with the material (**A**) to be reacted. The ADD-to-estrone aromatization is presented as an example for the novel type of process.

RESULTS

Given in Scheme 1 are the formulae of the starting material 1,4-androstadiene-3,17-dione (ADD), which is available from natural sources in sufficient amounts, and of estrone which is an important pharmaceutical.

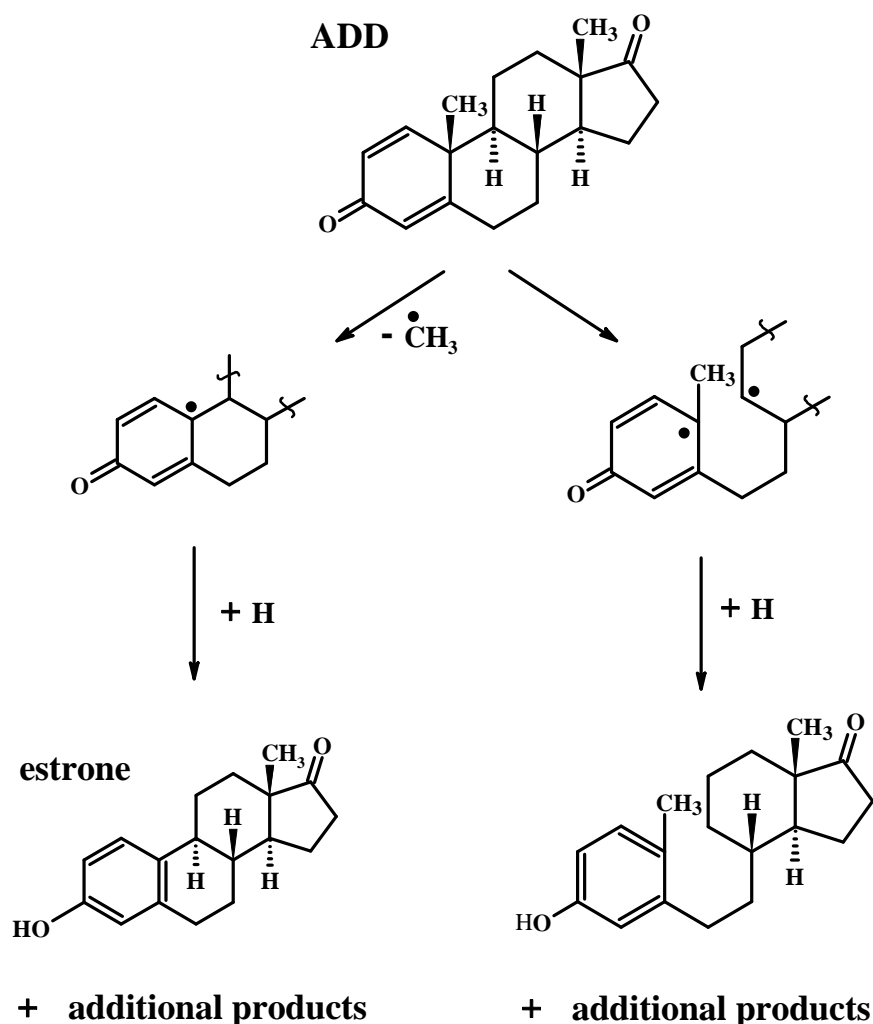


Scheme 1

The reaction appears to be rather simple, consisting just of the removal of the methyl group positioned at the bridging atom between the two six-membered rings and of subsequent addition of a hydrogen atom to form the phenolic structure. Tetralin has been used as a hydrogen donor. Actually, ADD is introduced into the reaction system in solution of tetralin. That the kinetic situation is not as simple as Scheme 1 suggests, is illustrated by the slightly extended kinetic Scheme 2 which still is an oversimplification of the actual kinetic situation, but catches a very essential aspect of ADD-to-estrone pyrolysis. Figure 2 demonstrates that, in addition to the removal of the methyl group, an alternative reaction may take place at the same carbon atom. This second reaction leads to ring-opened products and thus obviously constitutes an undesired reaction pathway with respect to estrone synthesis.

The kinetic situation depicted in Scheme 2 corresponds to what has been shown in Figure 1. The intermediate radicals illustrate the two types of bond scission at the bridged carbon atom between the two six-membered rings. The decomposition rate coefficients for reaction to the two intermediates are almost identical at about 400 °C. Toward higher temperature, the rate

coefficient for the desired pathway (to the intermediate on the way to estrone) becomes larger than the rate coefficient for the competing reaction (which leads to an opening of the steroidal structure). Estrone selectivity is significantly enhanced toward higher temperatures, e.g., of 500 °C and above [1,2]. ScCO₂ may effectively and very rapidly transfer the reaction medium into a high-temperature fluid state. CO₂ is thermally stable up to at least 1000 °C which allows for a very efficient action as heat-transfer agent. Moreover, the addition of pre-selected amounts of hot CO₂ allows to turn the reaction system into a sc fluid medium and thus to take advantage of the above-mentioned benefits of carrying out processes in the supercritical fluid state. Further advantages of using CO₂ are due to the fact that this material is cheap, inflammable, non-toxic, and is easily removed from the product mixture.



Scheme 2

Figure 2 shows a simplified schematic view of the setup. An ADD-in-tetralin solution is mixed with pre-heated CO₂ at the entrance to the tubular reactor. The mass ratios of the solution and of CO₂ may be significantly varied as may be the pre-heat temperature of CO₂. The mass ratio and also the pre-heat temperature, which typically is 700 °C or even higher, are chosen such that, after mixing of CO₂ with ADD/tetralin, reaction temperatures between 500 and 580 °C may be reached. The tubular reactor residence times are of the order of one second with larger times being chosen at the lower reactor temperatures. As is characteristic of sc fluid-phase reactions, process conditions may be continuously tuned in wide ranges of pressure and

temperature. The majority of experiments has been carried out at a reaction pressure of 100 bar. In these experiments, Vögele and Nguyen [3] reached estrone yields of 70 %.

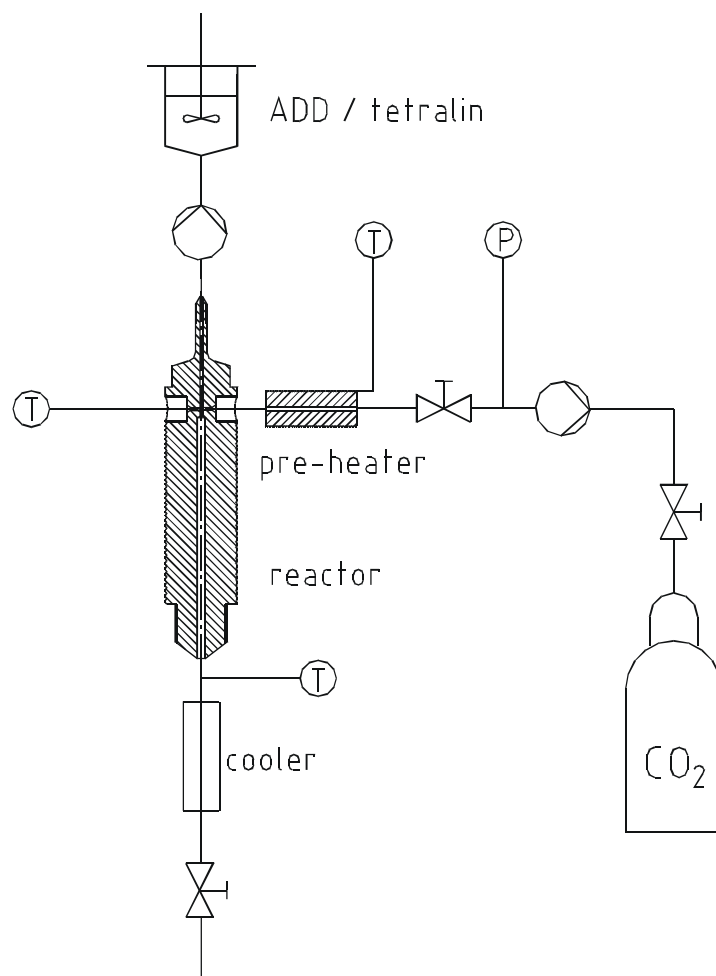


Figure 2: Schematic view of the experimental set-up for carrying out reactions in supercritical fluid phase after shock-heating with compressed hot CO₂.

CONCLUSIONS

The important pharmaceutical estrone may be produced via a sc fluid-phase process in high yield from readily available ADD. The basic idea behind the novel procedure consists of shock-heating reaction systems to fluid-phase conditions via a pre-heated, thermally stable material and of taking advantage of the benefits of reaction in sc fluid phase.

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