KINETICS AND MECHANISM OF ALKYLATION OF STERICALLY HINDERED PHENOL SALTS BY FUNCTIONALLY SUBSTITUTED OLEFINS

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The alkylation of sterically hindered phenols (SHP) is an extremely interesting reaction, from both theoretical and practical viewpoints, that can be used to obtain the corresponding 4-alkyl-substituted phenols. The alkylation of SHPs by alkyl halides in an alkaline media, or by alcohols or olefins in acidic media is a wellknown reaction in many examples [1]. There has been less research on the alkylation of SHPs by functionally substituted olefins in the presence of bases.

Obviously, the alkylation of SHPs by alkyl halides and functionally substituted olefins in alkaline media have much in common. There is no doubt that in both cases, in order for the reaction to proceed successfully, the nucleophilicity of the original phenol must be increased. This is realized by formation of the corresponding phenolates in the alkaline medium. Since the acidities of SHPs are substantially lower than those of alcohol and water (for 2,6-di-tert-butylphenol, pKa = 11.7 [1]), the existence of phenolates, and hence the actual occurrence of alkylation, are possible only in aprotonic media.

Here we report on a kinetic and mechanistic study of the alkylation of the Li salt of 2,6-di-tert-butylphenol (I) by methyl acrylate (MA) (which was also used as a solvent) in DMFA medium. The reaction was carried out in a closed vessel equipped with a thermostatting device and a sampler. The Li phenolate used in this work was obtained by preliminary addition of 1 eq. of LiH to a solution of 2,6-di-tert-butylphenol in DMFA that had been dried and purified to remove amines. The alkylation process was investigated in the interval 100-140°C. In order to prevent oxidation reactions, the reaction vessel was purged with N_2 . With a small excess of MA (10%), the alkylation proceeds with high yield, giving the methyl ester of β -(4-hydroxy-3,5-di-tert-butylphenyl) propionic acid (II). The contribution of side reactions (dealkylation or isomerization of the original phenol and polymerization of the MA) is no greater than 3-5% under these particular conditions.

In Fig. 1 we show kinetic curves for the accumulation of the salt (II), and also a rectification of these curves on second-order reaction coordinates. It can be seen that satisfactory rectification is achieved up to rather high conversions of the original salt (I). The alkylation rate increases with increasing temperature. The Arrhenius relationship gives an activation energy of 19.7 kcal/mole (Fig. 2).

It can be concluded that in the present case we are dealing with a conventional bimolecular process of nucleophilic addition at an activated multiple bond.



The reaction evidently proceeds through the intermediate (III), which in a polar medium is rapidly isomerized to the salt (II).

It is known from the literature [1] that the acidity of 4-alkyl-2,6-di-tert-butylphenol is somewhat lower than that of 2,6-di-tert-butylphenol (for 4-methyl-2,6-di-tert-butylphenol, pKa = 12.23; for 2,6-di-tert-butyl-

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Fig. 1. Kinetic curves for accumulation of (II) (a), and anamorphoses of these curves (b), at the following reaction temperatures, °C: 1) 100; 2) 110; 3) 130. $[I]_0 = 1.59$, $[MA]_0 = 1.75$ moles/kg, DMFA.

$$Y = \frac{1}{[MA]_0 - [I]_0} \ln \frac{[I]_0 ([MA]_0 - [II])}{[MA]_0 ([I]_0 - [II])}$$

Fig. 2. Arrhenius relationship for alkylation of (I) with MA. $[I]_0 = 1.59$, $[MA]_0 = 1.75$ moles/kg, DMFA.

phenol, $pK_a = 11.7$, in water at 20°C). If this is also true in our case, then, if there is an excess of 2,6-di-tertbutylphenol (Ia) in the mixture, an exchange equilibrium reaction is possible:

$$(II) + (Ia) \rightleftharpoons (IV) + (I)$$

In theory, therefore, the process of alkylation of 2,6-di-tert-butylphenol by MA can be carried out in a "pseudocatalytic" regime, using small amounts of the salt (I) added to the reaction mixture. In general form, such an alkylation process is described by the following series of reactions:

PhOLi + MA
$$\stackrel{k_1}{\longrightarrow}$$
 Ph'OLi
Ph'OLi + PhOH $\stackrel{k_2}{\underset{k_{-2}}{\longrightarrow}}$ Ph'OH + PhOLi

Despite its simplicity, this scheme is not amenable to complete kinetic analysis, but such an analysis can be performed if certain assumptions are made. In fact, since the second stage of the process is a typical ion exchange reaction (replacement of a weak acid in a salt by a stronger acid), it is highly probable that the equilibrium is established rapidly, this equilibrium being shifted almost entirely to the right when there is a large excess of the original phenol (Ia). If this assumption is valid, then, in the initial stages of the process, with the condition [PhOH] > [PhOLi], the equality [PhOLi]₀ \simeq [PhOLi] should be observed. Whence, under the condition that $k_2 \gg k_1$, it follows that

$$\frac{d \,[\text{PhOLi}]}{dt} = -k_1 \,[\text{PhOLi}]\,[\text{MA}] + k_2 \,[\text{Ph'OLi}]\,[\text{PhOH}] = 0$$

 \mathbf{or}

$$[Ph'OLi] = \frac{k_1}{k_2} \frac{[PhOLi]_0[MA]}{[PhOH]}$$
(1)

For the consumption of MA, we have the following law:

$$[MA] = [MA]_0 e^{-k_1 [PhOLi]_0 t}$$
⁽²⁾

Taking Eqs. (1) and (2) into account, we have for the rate of accumulation of the final ester (IV):

$$\frac{d \left[\text{Ph'OH} \right]}{dt} = k_1 \left[\text{PhOLi} \right]_0 \left[\text{MA} \right]_0 e^{-k_1 \left[\text{PhOLi} \right]_0 t}$$

Integration of this expression in the interval from 0 to t gives the following dependence of the concentration of the final ester on the reaction time:



Fig. 3. Kinetic curve for accumulation of (IV) (a) and anamorphosis of this curve (b). $[Ia]_0 = 3.13$, $[I]_0 = 0.08$, $[MA]_0 = 4.12$ moles/kg, 130°C. Fig. 4. Dependence of k_{ef} on concentration of (I). $[Ia]_0 = 3.13$, $[MA]_0 = 4.12$ moles/kg, 130°C.

$$\ln\left(1 - \frac{[\text{Ph'OH}]}{[\text{MA}]_0}\right) = -k_1 [\text{PhOLi}]_0 k_1$$

An analysis of this expression provides grounds for the conclusion that if the conditions [PhOLi] > [PhOLi] and $k_2 \gg k_1$ are realized in the initial stages of the alkylation process, the accumulation of the final ester (IV) should follow an exponential law, and the effective alkylation rate constant should be linearly dependent on the concentration of the salt (I).

In Fig. 3 we show the kinetic curve for accumulation of the ester (IV) and the rectification of this curve on coordinates of $\ln(1 - [Ph'OH]/[Ma]_0)$ vs t $(130^{\circ}C, 40$ -fold excess of phenol with respect to the salt). It can be seen that for relatively high conversions (~50%) of the 2,6-di-tert-butylphenol, the accumulation of the ester (IV) follows the exponential law satisfactorily. The second consequence of our assumptions, linear dependence of the effective rate constant of the alkylation process on the concentration of the salt (I), is also fulfilled quite well (Fig. 4). As would be expected, the alkylation rate increases with increasing concentration of salt in the original mixture.

It is noteworthy that the exponential dependence of the accumulation of the ester (IV) in the initial stages of the process is observed even when the system contains only a fivefold excess of phenol in relation to the salt. This indicates that the equilibrium $Ph^{OLi} + PhOH \Rightarrow Ph^{OH} + PhOLi$ is strongly shifted toward formation of the salt of the original phenol.

When the "pseudocatalytic" regime of alkylation was realized at different temperatures (100-140°C), it was found that the process rate increased with increasing temperature; the effective activation energy is 18.5 kcal/mole. This value is extremely close to that obtained above for the activation energy of the bimolecular reaction of alkylation of the salt (I) by MA in DMFA solution. This indicates that here also, under conditions of the "pseudocatalytic" regime of alkylation with MA, it is the lithium phenolate that reacts.

Obviously, the relationships that we have described above for the alkylation of the Li salt of 2,6-di-tertbutylphenol with methyl acrylate can be extended to other alkali metal phenolates and any olefin with an ac-tivated double bond can be used as the alkylating reagent.

EXPERIMENTAL

The 2,6-di-tert-butylphenol was purified to chromatographic purity (Silufol UV-254, hexane) by fractional distillation, followed by low-temperature crystallization from hexane. The DMFA and MA were purified by standard procedures [2, 3].

The alkylation was performed in a 3-liter autoclave equipped with a stirrer, a device for metering in the MA, a thermostatting device, and a sampler. The salt (I) was prepared in the autoclave before the reaction, by dissolving LiH in phenol or in its solution in DMFA, at 100-110°C. The excess pressure was bled off, and the MA was introduced. After the process conditions had leveled out, samples (5-10 ml) were drawn at certain intervals. Each sample was diluted with 20 ml of hexane, and the mixture was treated with 5% HCl and water.

The hexane layer was drawn off and analyzed for contents of 2,6-di-tert-butylphenol and the ester (IV). The analyses were performed in a Tsvet-104 gas-liquid chromatograph with programmed heating (5% SE-30 by volume on Chromatone IV-W-AESD, column heating rate 11° C/min).

CONCLUSIONS

The alkylation of the lithium salt of 2,6-di-tert-butylphenol by methyl acrylate is a bimolecular process of nucleophilic addition at an activated double bond, which can be carried out in a "pseudocatalytic" regime by using a small excess of lithium phenolate.

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MECHANISM OF INTERACTION OF CYCLOHEXADIENONE

CARBENES WITH DEUTEROBENZENE AND BENZENE

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The interaction of electrophilic singlet carbenes with the aromatic ring usually begins with attack on the aromatic π -system by the carbene. The subsequent course of the reaction depends on the stability and the paths of conversion of the norcaradiene structure that is formed as an intermediate. Depending on the structure, two paths of norcaradiene transformation are possible: conversion to cycloheptatriene or aromatization to form products of formal implantation of the carbene in a C-H bond of the aromatic ring. The products of the latter type, arylphenols, are also formed by the interaction of cyclohexadienone carbenes with benzene derivatives [1]. It is natural to assume that cyclohexadienomylidenes will react with aromatic compounds in accordance with the generally accepted mechanism. In this case, however, attempts to register the formation of norcaradiene in-termediates by chemical or spectral methods have been unsuccessful [2].

The present work has been aimed at spectral and kinetic investigation of the mechanism through which cyclohexadienone carbenes interact with aromatic compounds. As the reaction to be studied, we selected the thermal and photochemical decomposition of 2,6-di-tert-butyl-1,4-benzoquinonediazide (I) in a medium of benzene or deuterobenzene.

Through IR and PMR spectroscopic analysis of the reaction mixtures obtained at various degrees of thermolysis and photolysis of (I) in a benzene medium, it was shown that only two substances are present – the original quinonediazide (I) and 4-phenyl-2,6-di-tert-butylphenol (III). Evidently, the intermediate norcaradiene structure that is formed by the interaction of 3,5-di-tert-butyl-2,5-cyclohexadien-4-onylidene (II) with benzene is thermally unstable, and even at 25°C (conditions of photolysis) it is rapidly converted to the phenol (III). This is consistent with literature data on the thermal lability of cyclopropane spirane systems having a vinyl substituent on the three-membered ring [3].



Here and subsequently, $R = C(CH_3)_3$.

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