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Abstract

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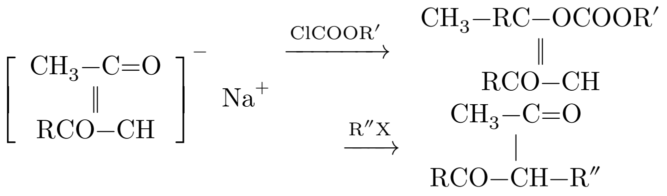
REACTIVITY OF AMBIDENT ANIONS

ALKYLATION OF SODIUM DERIVATIVES OF ACETOACETIC ESTER AND ACETYLACETONE WITH TRIETHYLOXONIUM FLUOROBORATE

A large literature is devoted to the dual reactivity of metallic derivatives of keto-enols. We refer to reviews and general articles of recent years (^{1}-^{3}).

Among the factors determining the direction of substitution reactions of sodium derivatives of keto-enols, attention has been given to the degree of electrophilicity of the attacking reagent. In reactions with ambident anions, strongly electrophilic reagents attack predominantly—or exclusively—oxygen, with formation of O-derivatives. This is how carbonyl chloride behaves in reaction with Na acetoacetic ester; in some cases chloromethyl ether and other strongly electrophilic reagents behave similarly. By contrast, alkyl halides, as well as esters of sulfuric and arylsulfonic acids, attack predominantly or exclusively carbon: the corresponding C-derivatives are formed:

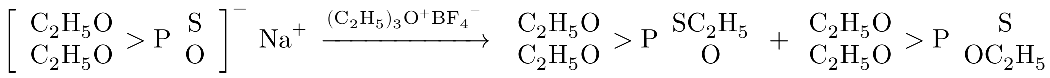


$$\left[\begin{array}{c}CH_3-C=O\\ \| \\ RCO-CH\end{array}\right]^- Na^+ \begin{array}{l}\xrightarrow{ClCOOR'} \begin{array}{c}CH_3-RC-OCOOR'\\ \| \\ RCO-CH\end{array}\\ \xrightarrow{R''X} \begin{array}{c}CH_3-C=O\\ | \\ RCO-CH-R''\end{array}\end{array}$$

It has recently been established that C-alkylation of keto-enols may be accompanied to one degree or another by O-alkylation if steric hindrance to C-alkylation is present (^{4}, ^{5}). However, in the absence of steric hindrance, the reaction of alkyl halides with Na acetoacetic ester gives only a negligible amount of O-ether; alkylation of sodium acetylacetonate in this case is also not accompanied by an O-reaction (^{5}).

Analogous relationships are also found in the alkylation of other ambident anions with alkyl halides.

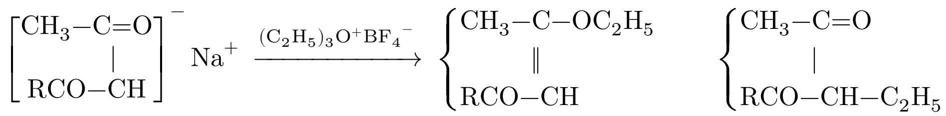
Different results have been observed when triethyloxonium fluoroborate is used as the alkylating agent. The literature contains information on O-alkylation of ambident anions of nitroparaffins by this reagent ([6], [7]). Recently we found that, on alkylation of potassium diethyl thiophosphate with triethyloxonium fluoroborate, along with the usual alkylation product—the S-derivative—appreciable amounts of the O-derivative are also formed ([8]):



$$\left[\begin{matrix}C_2H_5O\\C_2H_5O\end{matrix}>P\begin{matrix}S\\O\end{matrix}\right]^- Na^+ \xrightarrow{(C_2H_5)_3O^+BF_4^-} \begin{matrix}C_2H_5O\\C_2H_5O\end{matrix}>P\begin{matrix}SC_2H_5\\O\end{matrix} + \begin{matrix}C_2H_5O\\C_2H_5O\end{matrix}>P\begin{matrix}S\\OC_2H_5\end{matrix}$$

Considering that the principles governing the dual reactivity of ambident anions have general significance, we assumed that the use of triethyloxonium, i.e., a highly electrophilic reagent, as an alkylating agent should change the direction

alkylation of Na acetoacetic ester into sodium acetylacetonate toward the formation not only of the C derivative, as usual, but also of the corresponding O ether:



$$\left[\begin{array}{l}CH_3-C=O\\ \qquad\quad |\\ RCO-CH\end{array}\right]^- Na^+ \xrightarrow{(C_2H_5)_3O^+BF_4^-} \left\{\begin{array}{l}CH_3-C-OC_2H_5\\ \qquad\quad \|\\ RCO-CH\end{array}\right. \qquad \left\{\begin{array}{l}CH_3-C=O\\ \qquad\quad |\\ RCO-CH-C_2H_5\end{array}\right.$$

Experiment confirmed this assumption.

Alkylation of Na acetoacetic ester with triethyloxonium borofluoride was first carried out by Meerwein and co-workers (9); however, under the conditions of their experiments it was impossible to observe O-alkylation. We carried out the reaction in ether medium with an equimolar ratio of reagents. Because of the insolubility of the components, vigorous stirring and heating for 5 h to the boiling point of ether were used. The quantitatively formed sodium borofluoride was filtered off; after evaporation of the ether, the filtrate was distilled in vacuo, and the resulting reaction mixture was examined.

A chromatogram on a thin layer of aluminum oxide (activity IV according to Brockmann, eluent hexane-ethyl acetate, 13:1) contained 4 spots corresponding to the following substances: acetoacetic ester (on the start line), C-ethylacetoacetic ester (R_f 0.21; for a sample of a known substance R_f 0.20), C,C-diethylacetoacetic ester (R_f, respectively, 0.46 and 0.40), and O-ethylacetoacetic ester (R_f 0.61 and 0.58).

It is not possible to isolate the components of the mixture in pure form by fractional distillation because of the closeness of the boiling temperatures of the C- and O-ethylacetoacetic esters.

Gas-liquid chromatographic analysis (Willy-Giede instrument, GCH 18/2, thermal-conductivity detector, using fuel cow oil deposited on diatomaceous brick; temperature 150°, carrier gas—helium, 60-80 ml per 1 min) showed the following composition of the reaction mixture: acetoacetic ester 8.9%, C-ethylacetoacetic ester 73.8%, O-ethylacetoacetic ester 15.5%, and C,C-diethylacetoacetic ester 1.8% (the substances are listed in the order of elution from the chromatograph column). In identifying the peaks on the chromatogram by the method of adding a known substance to the mixture, acetoacetic ester, C-ethylacetoacetic ester, and C,C-diethylacetoacetic ester were proved. Upon addition of known O-ethylacetoacetic ester, the corresponding peak split. Assuming that the known crystalline β-ethoxycrotonic ester, obtained from β-chlorocrotonic ester and sodium ethoxide (10), and the liquid ether (for isolation see below), obtained in the alkylation of Na acetoacetic ester with triethyloxonium borofluoride, are geometric isomers, we synthesized O-ethylacetoacetic ester by ethylation of acetoacetic ester with diazoethane. Arndt and co-workers (11) showed that, in methylation of acetoacetic ester with diazomethane, a mixture of cis- and trans-β-methoxycrotonic esters is formed. In accordance with this, in our case O-ethylacetoacetic ester, obtained in the reaction of acetoacetic ester with diazoethane (b.p. 92–94° at 18 mm; yield 73%), gave, on the chromatogram under the same conditions, a split peak. Addition to this preparation, in turn, of O-ethylacetoacetic ester obtained from β-chlorocrotonic ester and that obtained by alkylation of acetoacetic ester with triethyloxonium led to an increase of first one, then the other component of the split peak. Thus, there is no doubt that, upon alkylation of Na acetoacetic ester with triethyloxonium borofluoride, one geometric isomer is formed, while in the reaction of sodium ethoxide with β-chlorocrotonic ester another is formed; in ethylation of acetoacetic ester with diazoethane, both stereoisomers are formed at once.

Since the reaction of sodium ethoxide with β-chlorocrotonic ester leads to crystalline β-ethoxycrotonic ester, which has, by analogy with the methylated derivatives, most probably the trans configuration (10), it must be assumed that ethylation of Na-acetoacetic ester with triethyloxonium fluoroborate gives liquid cis-β-ethoxycrotonic ester.

For the final identification of the reaction products, the reaction mixture obtained in the alkylation of sodium acetoacetic ester with triethyloxonium was treated, with cooling (below 5°), with 5% aqueous alkali, extracted with ether, and the alkaline extract was immediately neutralized. The ether extract remaining after repeated treatment with alkali contained, according to thin-layer chromatography, O-ethylacetoacetic ester and C,C-diethylacetoacetic ester. The extract was subjected to acid hydrolysis (HCl, 1 : 1; 4 h at room temperature), and the acetoacetic ester formed on hydrolysis of the O-ester was identified by the melting point of the 2,4-dinitrophenylmethylpyrazolone (from the reaction: m.p. 94—96°, authentic 96°, mixed sample: 94—96°; literature data: m.p. 96° (12)).

From the alkaline solution containing acetoacetic and C-ethylacetoacetic esters there were obtained: 1-(2,4-dinitrophenyl)-3-ethyl-4-methylpyrazolone-2 with m.p. 122° (from a mixture of ethyl acetate and alcohol; literature data: m.p. 122° (12); a mixed sample with an authentic specimen melted without depression) and 2,4-dinitrophenylmethylpyrazolone with m.p. 94—96° in the simple and mixed samples. C-Ethylacetoacetic ester was also identified by its copper salt: m.p. 186—188° (decomposition, rapid heating); literature data: m.p. 188—189° (decomposition, rapid heating (13)).

Thus, in the alkylation of Na-acetoacetic ester with triethyloxonium fluoroborate, along with the C-derivative, about 15% of the O-derivative is also formed, namely cis-ethoxycrotonic ester. If it is taken into account that the alkylation process was carried out under heterogeneous conditions, which, according to Kornblum (2), favor the formation of C-derivatives, then the fact of 15% O-alkylation becomes especially noteworthy.

Ethylation of sodium acetylacetonate with triethyloxonium fluoroborate was carried out under the same conditions with heating for 7 h. Examination of the reaction mixture gave the following results.

Thin-layer chromatograms (for conditions see above), obtained before and after distillation of the reaction mixture, were identical. The spots were identified as: acetylacetone (on the start line), C-ethylacetylacetone (R_f 0.22; for the authentic preparation R_f 0.22) and O-ethylacetylacetone (R_f 0.43 and, respectively, 0.42).

On alkaline separation, C-ethylacetylacetone and acetylacetone passed into the alkaline extract (according to thin-layer chromatography). The latter was precipitated as a copper complex and then identified as 1-carbamido-2,4-dimethylpyrazole (14) (m.p. 109°) and as the silicon chloroferrate $(C_5H_7O_2)_3SiFeCl_4$ (15) (m.p. 183—186°). After precipitation of the copper salt of acetylacetone, C-ethylacetylacetone was isolated, b.p. 68.5—70° at 13 mm, n_D^{20} 1.4356; d_4^{20} 0.9532; for an authentic sample of pure C-ethylacetylacetone, free from admixture of the O-ester: b.p. 76° at 20 mm; n_D^{20} 1.4419; d_4^{20} 0.9568 (5). C-Ethylacetylacetone was also identified as the silicon chloroferrate complex: $(C_7H_{11}O_2)_3SiFeCl_4$ (16), m.p. 162—163°.

The ether extract after alkaline extraction, as shown by thin-layer chromatography, contains, along with O-ethylacetylacetone, also traces of C-ethylacetylacetone. This mixture was subjected to acid hydrolysis, with conversion of the acetylacetone formed into the copper salt (yield based on O-ester 92%), and was then identified as described above. In the filtrate after precipitation of the copper salt, C-ethylacetylacetone was identified.

Gas-liquid chromatographic analysis of the reaction mixture gave the following results: acetylacetone 9.0%, C-ethylacetylacetone 62.5%, and O-ethylacetylacetone 28.5% (the substances are listed in the order in which they emerged from the chromatographic column). Identification of the peaks was carried out in the same way as in the experiments with acetoacetic ester. The O-ethylacetylacetone needed for identification was obtained by the reaction of diazoethane with acetylacetone. It was found that a known O-ethylacetylacetone, obtained in the reaction with diazoethane, was identical with the product obtained in the experiments with triethyloxonium. Whether it too is the cis isomer cannot yet be stated.*

Thus, O-alkylation of sodium acetylacetonate proceeds with an even higher yield than that of Na-acetoacetic ester. This is also under heterogeneous conditions.

As a result of the investigation, it has been established that, under the action of a strongly electrophilic alkylating agent such as triethyloxonium fluoroborate, the sodium derivatives of acetoacetic ester and acetylacetonate are alkylated not only at carbon, as is observed upon alkylation with alkyl halides, etc., but also at oxygen, which ordinarily (in the absence of steric hindrance to C-alkylation) does not occur.

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* It should be noted that, on the chromatogram of the reaction mixture obtained in the reaction with fluoroborate, a very small peak is observed near the peak of the O-derivative, which is possibly due to the presence of a second stereoisomer.

Note: Figure translations are in progress. See original paper for figures.

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