
2-Methoxy-6,7-dimethylnaphtalin


Ber. C 83,87 H 7,52,
Gef. C 83,86 H 7,39.


Substitut Effect on Reactivity of Alkyl Thiolacetates

F. DUTKA, A. F. MÁRTON, and P. VINKLER

Central Research Institute for Chemistry of the Hungarian Academy of Sciences, Budapest, Hungary
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Kinetics of catalyzed acyl group exchange between acetic-1-14C anhydride and alkyl thiolacetates was investigated. The exchange is not accompanied by chemical reaction and demonstrates the full equivalency of anhydride acyl groups in the process. The rate of exchange is lowered by increasing branching rather than lengthening in S-alkyl substituents. The role of catalyst and structures of possible intermediates are interpreted. Upon existing linear structure-reactivity relationship a common mechanism involving sulfur atom as the reaction site seems to be operative.

The effects of variations in structure upon rates of hydrolysis have been reported for a number of alkyl acetates and thiolacetates. Although these studies allow some generalization to be made, the comparative kinetics of ester and thiolester reactions are not well understood. There are also some differences in views on the effect of the S-alkyl group on thiolester reactivity. 1, 5

Independent of the thio component, alkyl thiolacetates tend to undergo acyl exchange with acetic-1-14C anhydride in nitromethane by the catalytic effect of Lewis acids. Under the same experimental conditions, primary and secondary alkyl acetates are unreactive towards acetic anhydride 4 while tertiary acetates suffer a chemical change simultaneously with the isotopic exchange 5. This finding shows a marked difference in acetate and thiolacetate reactivity and offers further possibility to obtain a better understanding of the chemical properties of thiolesters.

The present paper deals with studies on the kinetics and mechanism of acyl group exchange as well as on structure-reactivity relationship.


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Experimental section

Materials

All thiolacetates were prepared by acylation of the corresponding thiols. Purity of the esters was checked by analytical gaschromatograph. Nitromethane was a reagent grade Merck product and freshly sublimed before use.

Methods

All liquid scintillation counting was carried out using toluene scintillation solutions, prepared by dissolving 5.0 g of 2,5-diphenyloxazole ("PPO", REANAL, scintillation grade) and 0.5 g of 1,4-bis-(5-phenyl-oxazolyl) benzene (“POPO”, Packard scintillation grade) in 1.0 l of toluene.

Radioactivities were determined using the Packard TriCarb 574 Liquid Scintillation System.

IR spectra were recorded by means of an UR-10 spectrophotometer. In the spectrum of a typical reaction mixture (concentrations: 2 M ethyl thiolacetate, 1 M acetic anhydride and 0.33 M AICI₃) the carbonyl frequencies of the ACo·AICI₃ complex (1540 cm⁻¹ and 1707 cm⁻¹), of non-complexed acetic anhydride (1750 cm⁻¹ and 1819 cm⁻¹) and of ethyl thiolacetate (1688 cm⁻¹) were identified.

Gaschromatographic analyses and separations were carried out by using Carlo Erba models (Fractovap GV. and Fractovap P), resp.

Kinetics

The procedure is described here for one particular run and it is typical of that used throughout. AICI₃ (0.033 M) was dissolved in nitromethane (25 ml) and then acetic-1-¹⁴C anhydride (0.100 M) introduced into the yellow solution. The almost colorless solution obtained and a solution of alkyl thiolacetate (0.200 M) in nitromethane (30 ml) were thermostated separately at 45.0 ± 0.1°. At zero time the solutions were mixed rapidly and the total volume supplemented to 100 ml by addition of nitromethane kept also in the same thermostat. Stirring of the reaction mixture started without delay. Samples (10 ml) were removed at appropriate times (the first at zero time) with a syringe and injected quickly into a flask cooled by liquid air. After addition of freshly distilled aniline (0.1 ml) the mixture was allowed to stand for 10 min at room temperature. Acet-1-¹⁴C-anilide was crystallized by cooling in liquid air and separated by filtration. After repeated (usually three times) recrystallization from water its activity remained constant.

Specific activities of samples taken at zero time and separate experiments demonstrated no reaction of thiolacetates with aniline under these conditions. (In all cases aniline was used in amounts smaller than equivalent to ACO). In several experiments thiolacetates were also separated gaschromatographically from the mother liquor obtained after filtration of acetanilide and their activities measured.

Isotope exchange

Kinetics of acyl exchange was followed by measuring the decrease in the specific activity of labelled acetic anhydride in the form of acetanilide. Rates of exchange (Rₑ) were calculated from the equation suggested by McKay⁶, taking into consideration that the number of exchanging groups in acetic anhydride was two.

Results

The catalyzed acyl exchange reaction between alkyl thiolacetates and acetic-1-¹⁴C anhydride has the following characteristics:

1. The exchange is not accompanied by any chemical reaction as was shown by gaschromatographic analysis of the reacting system.

2. The specific activities of the equilibrated products are closely identical with the calculated values based on the assumption that both acetyl groups of acetic anhydride take part in the exchange.

3. The specific activities at equilibrium are determined exclusively by the concentrations and not affected by the sequence of mixing reactants.

4. The distribution of radiocarbon at equilibrium is unanimously determined by concentrations of acyl compounds, irrespective of whether acetic anhydride or thiolacetate is the originally labelled species.

5. Plotting log(1 − F) vs. time⁶ perfect linearity is obtained at 45°; at higher temperatures a slight deviation from linearity appears in the initial stages of the exchange (plots are not shown).

6. Increasing amounts of AICI₃ enhance the rate of exchange but do not affect the value of equilibrium specific activity.

7. The exchange rate (Rₑ) is first order with respect to each of the reactants as shown in Fig. 1.

![Fig. 1](image-url)
Table 1. Rate constants for acyl exchange of thiolacetates with acetic-1-14C anhydride in nitromethane at 45,0 ± 0,1°C.

<table>
<thead>
<tr>
<th>Substituent</th>
<th>10^5 k (Mol⁻¹ sec⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl</td>
<td>14.20</td>
</tr>
<tr>
<td>Ethyl</td>
<td>10.83</td>
</tr>
<tr>
<td>n-Propyl</td>
<td>2.53</td>
</tr>
<tr>
<td>i-Propyl</td>
<td>0.65</td>
</tr>
<tr>
<td>t-Butyl</td>
<td>0.16</td>
</tr>
</tbody>
</table>

The energy difference between the two structures is not large and the ion CH₃CO⁺ or the ion pair CH₃CO⁺ • AlCl₃OCOCH₃⁻ (b) rather than complex (a) is the species which takes part in the acylation. Supposing that ionization of the reactive complex occurs prior to acyl transfer, acyl exchange may take place through an oxonium (c) or sulphonium (d) intermediate:

\[
CH₃-C-SR → CH₃-CO⁺ \rightleftharpoons CH₃-C⁺SR \rightleftharpoons CH₃-C-S⁻R
\]

Catalytic cleavage of ethers and thioethers by acyl halides is explained by a similar mechanism.

There are two alternative mechanisms for decomposition of the intermediates yielding exchanged products: alkyl or acyl fission. Alkyl fission of the intermediates is hardly expected because it would imply real chemical reaction affording oxygen esters (by recombination of the alkyl cation with the acetate moiety of the complex) and thioacetic anhydride. Acyl exchange, however, was found not to be accompanied by any chemical change. On the other hand, acyl fission of the oxonium structure would lead to unchanged initial reactants.

Reasonably, a mechanism involving sulphonium intermediate (d) should probably be operative in the exchange. Sulphonium salts form more readily and are more stable than oxonium salts. Partitioning of the sulphonium intermediate to reactants and exchanged products by acyl fission takes place without producing new chemical species. Acyl fission in the exchange of t-butyl thiolacetate is not unexpected since, in sharp contrast to the behaviour of t-butyl acetate, the acid catalyzed hydrolysis of the sulfur analogue proceeds entirely by cleavage between the sulfur atom and the carbonyl group.

Radioactivity originally present in acetic anhydride, is equally devided into acetyl and acetoxy group of the complex. Transacylation through the above mechanism, however, involves only the acetyl group.

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group of the reactive complex. On the other hand, the value of specific activity at equilibrium is independent of the amount of AlCl₃ and demonstrates the participation of both acyl groups of acetic anhydride in the exchange. It can be concluded, therefore, that a complete acyl exchange also occurs between the complex and non-complexed anhydride. The precise pathway of this process has not been clarified as yet. Consequently, no detailed mechanism can be given for the over-all exchange reaction. At any rate, in this stage acetyl groups of the non-complexed acetic anhydride should be incorporated into the acetyl and acetoxyl group of the Lewis acid complex with equal chance. This can be realized by a dissociative equilibrium between the reactive complex and its constituents or by displacement of the complexed anhydride from the adduct by non-complexed acetic anhydride. In this manner the full equivalency of anhydride acyl groups in the over-all process which is unambiguously proved by exact linearity of log(1 - F) vs. time until the equilibrium isotope distribution can be explained. Difference in the reactivities of acyl groups would create a curvature in this plot as pointed out in complex exchange reactions ¹². Furthermore, it is quite evident that this step may not be rate determining because of the dependence of the observed exchange rate on the structure of thiolesters.

As can be seen from Table 1 the reaction rate decreases with the increasing +I effect of $S$-alkyl substituents. About the same sort of reactivities seems to be obtained in the cleavage of dialkyl ethers by acyl chlorides in the presence of ZnCl₂ ¹³. The question arises whether the rate of formation of the sulphonium intermediate or its rate of reaction is the kinetically important step. Apart from possible steric effects, a process with rate determining formation of the intermediate would produce the reversed reactivity sequence of thiolesters. Therefore the reaction rate is determined by the concentration of the intermediate and by its specific rate of reaction.

Rate constants $k$ for acyl exchange can be correlated with the Taft substituent constants (Fig. 2): In agreement with our experimental evidence, this

Fig. 2. Relationship between log $k$ and substituent constants in acyl exchange reaction of thiolacetates at 45°C. In Fig. 2 $Q = Q_e$.

linear free energy relationship supports a common mechanism in the series studied, the rate controlling step being governed solely by polar effects. The positive sign of the reaction constant $Q_e^*$ indicates that the exchange is facilitated by low electron density on the reaction site. Rate determining attack on the sulfur atom would result in a reaction constant with minus sign.

The same relationship was found to be effective in the hydrolyses of alkyl thiolacetates catalyzed by acids or bases ⁴. A comparison of the corresponding reaction constants ($Q_e^* = 6.5; Q_{H^+}^* = 1.46; Q_{HO^+}^* = 3.40$) exhibits remarkable differences. Although these processes were carried out under different experimental conditions, the greater value of $Q_e^*$ indicates a large sensitivity to the nature of substituent and is at least partly due to the fact that the reaction centre is nearer to the substituent ¹⁴ in exchange reactions than in hydrolyses.

Branching alkyl groups affect the rate of exchange to a greater extent than do substituents with non-branching chain (Table 1). Similar tendency appears in acylation reactions. Unfortunately, quantitative data on thiol acylations are fairly sparse. According to available results ¹⁵ the esterification constants markedly decrease with the increasing order of thiol. An estimated value of the reaction constant for esterification ($Q^* = 6$) shows a substituent sensitivity similar to acyl exchange. Thus the mechanism of acyl exchange resembles thiol acylation rather than thiolester hydrolysis.

The unreactivity of primary and secondary alcohol acetates towards acetic anhydride may partly

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14 R. W. TAFT and I. C. LEWIS, J. Amer. chem. Soc. 80, 2436 [1958].
be attributed to the importance of the resonance
form $\text{CH}_3-O^-$ as compared to thiolesters:

\[ \text{O}^- \text{C} \text{R} \]

this makes the alkyl oxygen more positive and prevents attack by the acyl cation. In this type of electron-releasing conjugation, sulfur is not as effective as oxygen, therefore, electron density on sulfur is decreased to a lesser extent. Binding of the electrophile derived from the reactive complex on the acyl oxygen of esters may result in exchange only by alkyl fission. It seems likely that the extraordinary behaviour of tertiary alkyl acetates can be interpreted by their tendency to suffer alkyl fission. The superiority of thiolacetates over oxygen analogues appears more unequivocally in acyl exchange than in catalyzed hydrolysies.


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The Nitrile Group as an Intraanular Substituent

Fritz Vögtle, Michael Zuber und Peter Neumann

Institut für Organische Chemie der Universität Heidelberg und Institut für Organische Chemie der Universität Würzburg


Cyclophane, Konformationsanalyse, Nitril-Gruppe, Protonenresonanz, Sterische Wechselwirkungen

The bridged aromatic compounds 1—3 with internally projecting nitrile groups have been prepared. The cyclophanes 1 and 3 are conformationally rigid due to steric hindrance of the inner cyano groups; 2 shows partial conformational mobility.


Sonderdruckanforde rungen an Dozent Dr. Fritz Vögtle, Institut für Organische Chemie der Universität Würzburg, D-8700 Würzburg, Landwehr.

Sonderdruckanforderungen an Dozent Dr. Fritz Vögtle, Institut für Organische Chemie der Universität Würzburg, D-8700 Würzburg, Landwehr.
