

TO BETTER UNDERSTANDING OF ESTER AMINOLYSES IN APROTIC MEDIA

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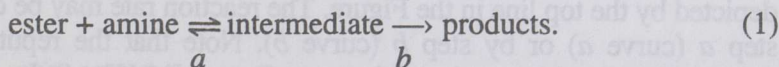
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Abstract. A zwitterionic intermediate cannot be responsible for negative activation energies of the reaction. A neutral tetrahedral intermediate is suggested.

Key words: aminolyses of esters, activation parameters, reaction mechanism.

The mechanism of ester aminolyses in aprotic media has been extensively studied ([1–3] and refs. therein). However, a number of conflicting conclusions have been published. It is generally believed that the third-order process, second-order in amine, includes the formation of an intermediate (Eq. 1):



The second molecule of the amine or any other catalyst is thought to be involved either in step *a* or in step *b* of the reaction. The nature of the intermediate has still remained an objective of discussions. The emergence of negative activation energies for ester aminolyses in aprotic solvents [4, 5] may shed light on the mechanism of the reaction. Activation parameters of aminolyses reactions as well as those of ester aminolyses have been determined in a few cases only. However, negative activation energies seem to be inherent to various aminolyses in aprotic media [6–8]. Some examples of activation parameters for aminolyses of esters and related compounds are presented in the Table.

Activation parameters for some aminolyses reactions

Substrate	Amine	Solvent	ΔH^\ddagger	ΔS^\ddagger	Refs.
<i>p</i> -Nitrophenyl trifluoroacetate	<i>n</i> -Butylamine	1,2-Dichloroethane	-11.5	-70.9	[4]
<i>p</i> -Nitrophenyl trifluoroacetate	<i>n</i> -Butylamine	Chlorobenzene	-10.5	-68.9	[4]
Isobutyl trichloroacetate	<i>n</i> -Hexylamine	<i>n</i> -Heptane	-6.2	-42	[5]
Butyl trifluoroacetate	<i>n</i> -Butylamine	<i>n</i> -Nonane	-8	...	^a
Butyl formiate	<i>n</i> -Butylamine	<i>n</i> -Nonane	~0	...	^a
<i>p</i> -Nitrophenyl <i>bis</i> (chloromethyl) phosphinate	<i>n</i> -Butylamine	Benzene	-5.1	...	[9]
Acetic anhydride	Aniline	Cyclohexane	-1.1	...	[10]
Acetic anhydride	Aniline	Chlorobenzene	~0	...	[10]

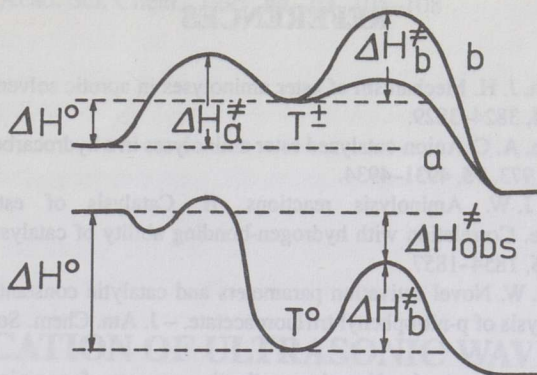
^a preliminary results from this laboratory. The enthalpies of activation are estimated from the temperature dependence of third-order rate constants obtained from the ester concentration determinations by means of g.l.c. Details of the experiment and further results will be published elsewhere.

Singh and Taft [4] supposed that the strong exothermicity of step *a* and the low activation energy of step *b* (Eq. 1) are responsible for the negative activation energy of the reaction.

Thus, $\Delta H_{\text{obs}}^\ddagger = \Delta H^\circ + \Delta H_b^\ddagger < 0$, since $-\Delta H^\circ > \Delta H_b^\ddagger$. All intermediates but the zwitterionic tetrahedral one were declined. A zwitterionic intermediate has also been suggested by other contributors [1-3]. Principally the same explanation of negative activation energy has been accepted for different aminolyses in aprotic media [6-8].

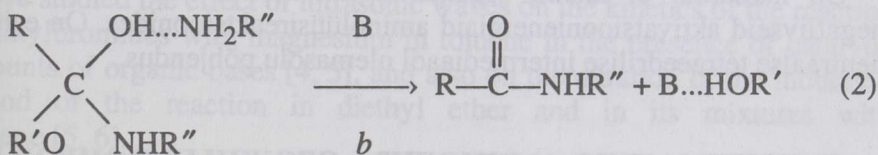
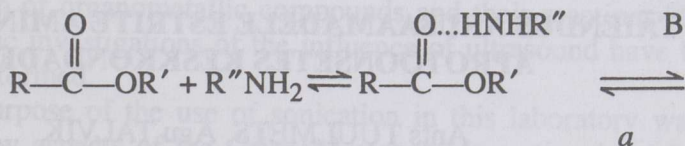
The purpose of our paper is to point at an inconsistency of the argumentations cited above.

A generally accepted reaction profile for nucleophilic substitution at carbonyl carbon, proceeding through a zwitterionic intermediate T^\pm , can be depicted by the top line in the Figure. The reaction rate may be determined by step *a* (curve *a*) or by step *b* (curve *b*). Note that the reputedly unstable intermediate lies higher above the reactants, and $\Delta H^\circ > 0$. In such cases no negative activation energy can be observed. The occurrence of negative activation energy requires a reaction profile like the bottom line in the Figure. As it has been shown [1, 4], step *b* is rate determining even in the case of good leaving groups. On the grounds of substituent effects in leaving groups of esters [1], the transition state is expected to be of ionic character. As the polar transition state in aprotic unpolar solvents is poorly stabilized, step *b* cannot be of low activation energy and thus the intermediate lies energetically considerably lower than the reactants, e.g. if $\Delta H_{\text{obs}}^\ddagger$ is about -10 kcal/mole, the stability of the intermediate must greatly exceed this value. A great value of activation entropy (see the first entries of the Table) cannot be explained merely by a translational entropy loss suggested by Singh and Taft [4]. It rather points at the polar transition state capable of arousing a noticeable structuring in the polarizable solvent.



Energetic profiles for aminolyses reactions (for notations see text).

Our reasonings can be expressed by Eq. 2. Preassociation of the ester with a proton-containing amine is highly plausible in aprotic solvents. Steps *a* and *b* may consist of several steps and very probably they do. This scheme does not exclude catalysis by bases or the occurrence of zwitterionic intermediates. The transition states in the reaction path can be either polar or cyclic, depending on reagents and reaction conditions. The essence of this scheme consists in (1) the process including more steps than Eq. 1, and (2) the most stable intermediate of the reaction that is an unpolar tetrahedral compound. The reaction scheme (Eq. 2) and its energetic profile (Figure, bottom line) are consistent with a more general conception of the preassociation with a consequent occurrence of a liberated intermediate introduced by Jencks [11] for nucleophilic reactions.



The unpolar intermediate T° can be revealed not only by the appearance of negative activation energy. Although Singh and Taft [4] were not able to detect the intermediate spectroscopically, its manifestation cannot be precluded in any other way. Our preliminary experiments are encouraging in this connection, because in some cases a little delay in the formation of alcohol with respect to the disappearance of the ester was observed. A further study is in progress.

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TÄIENDUS ARUSAAMADELE ESTRITE AMINOLÜÜSIST APROTOONSETES KESKKONDADES

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On näidatud, et laetud bipolaarne intermediaat ei saa põhjustada negatiivseid aktivatsioonienergiaid aminolüüsireaktsioonides. On esitatud neutraalse tetraeedrilise intermediaadi olemasolu põhjendus.

К ПОНИМАНИЮ АМИНОЛИЗА СЛОЖНЫХ ЭФИРОВ В АПРОТОННЫХ СРЕДАХ

Антс ТУУЛМЕТС, Агу ТАЛЬВИК

Показано, что заряженное биполярное промежуточное соединение не может обуславливать отрицательные энергии активации в указанных процессах. Приведены доводы в пользу существования нейтрального тетраэдрического интермедиата.