

## BROMIDE-ION CATALYZED $S_E1$ SOLVOLYSIS OF ETHYL $\alpha$ -BROMO-MERCURY-*p*-NITROPHENYLACETATE IN ETHANOL \*

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### Summary

The single product of bromide-ion catalyzed solvolysis of ethyl  $\alpha$ -bromomercury-*p*-nitrophenylacetate in ethanol is shown to be ethyl *p*-nitrophenylacetate. This reaction does not occur without nucleophilic assistance. Anions as well as neutral nucleophilic molecules, such as  $I^-$ ,  $Br^-$ , Py and DMSO, which possess a significant affinity for mercury, can serve as the assistants. When performed in EtOD the reaction gives mainly dideuterated ethyl *p*-nitrophenylacetate and smaller amounts of mono- and trideuterated compounds. The occurrence of dissociation of ethyl  $\alpha$ -bromomercury-*p*-nitrophenylacetate producing the carbanion  $p\text{-NO}_2\text{C}_6\text{H}_4\text{-}\bar{\text{C}}\text{HCOOEt}$  in aprotic solvents such as DME, THF, HMPT, etc., in the presence of bromide ions was demonstrated using UV spectroscopy. The reverse reaction between the carbanion and  $\text{HgBr}_2$  was also shown to be possible. These and some other data are the reasons why the reaction considered is classified as an  $S_E1(N)$  type process.

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### I. Introduction

Alkyl  $\alpha$ -bromomercuryphenylacetates substituted in the benzene ring, which were first synthesised by Professor O.A. Reutov and his co-workers during 1951–1964 [1–5], have been intensively used in investigations of the kinetics and mechanism of electrophilic substitution reactions at a saturated carbon atom. It was these reactions which gave the first experimental evidence for the occurrence of organomercury reactions via a path of monomolecular electrophilic substitution,  $S_E1$  [6,7]. In this series of organomercury compounds the substitution occurs at the benzylic carbon atom.

The reactivity of organomercury substrates in  $S_E1$  reactions depends, first of all, on the relative stabilities of the carbanions produced by ionization of C–Hg bonds

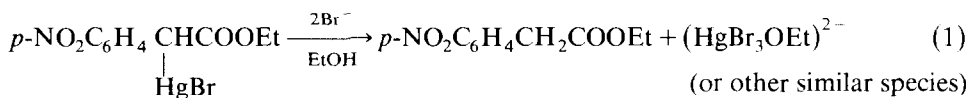
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\* Dedicated to Professor Oleg Reutov on the occasion of his 65th birthday on 5 September 1985.

in a given medium [8]. Among all the available organomercury compounds of the ethyl phenylacetate series, one of the most stable carbanions might be produced from ethyl  $\alpha$ -bromomercury-*p*-nitrophenylacetate because this benzylic carbanion is stabilised by ( $-M$ ) effects of the *p*-nitro and  $\alpha$ -COOEt groups. Hence  $S_E1$  reactions can be expected to be particularly inherent for this organomercury substrate. In this paper we report the results of our studies on the reaction of  $p$ -NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>-CH(HgBr)COOEt with ethanol, which is a very weak electrophile, in the presence of nucleophilic catalysts such as bromide ions. This reaction results in the rapid formation of  $p$ -NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>COOEt, the product of HgBr-for-H displacement.

## II. Results and discussion

Non-substituted ethyl  $\alpha$ -bromomercuryphenylacetate, PhCH(HgBr)COOEt, does not change under reflux in EtOH for many hours. In the presence of a double excess of Bu<sub>4</sub>NBr, extremely slow decomposition of this substrate producing ethyl phenylacetate, PhCH<sub>2</sub>COOEt, can be seen but the situation changes dramatically when a *p*-nitro substituent is introduced. Although the formation of  $p$ -NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>COOEt was not observed for at least 10 h in pure ethanol, small additions of halide salts, such as Bu<sub>4</sub>NBr, NaBr, Bu<sub>4</sub>NI, etc., resulted in a fast reaction. Thus, in EtOH solutions containing 10<sup>-2</sup> mol/l concentrations of  $p$ -NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CH(HgBr)COOEt and NaBr, the organomercury compound has completely disappeared in 5 min at 20°C, according to TLC data. Polarographic (Fig. 1) and GLC analyses showed this reaction to result in the formation of ethyl *p*-nitrophenylacetate, other organic products not being detected.



Thus, reaction 1, being very slow in pure ethanol and in ethanol containing Bu<sub>4</sub>NBF<sub>4</sub>, is dramatically accelerated by anions which possess a high affinity for mercury. Besides halide ions, neutral organic molecules capable of coordinating with the mercury atom of the organomercury compound, such as pyridine or DMSO, can also function as catalysts. Although these uncharged nucleophiles do not accelerate the reaction to such a high extent as Br<sup>-</sup> and I<sup>-</sup> ions, nevertheless it takes only 5 min in 2 mol/l solution of pyridine in EtOH while ca. 4 h in the presence of the same concentration of DMSO.

Reaction 1, when performed in EtOD, showed the final product, ethyl *p*-nitrophenylacetate, to consist of 96% of a mixture of mono-, di- and tri-deuterated esters. This means that the source of the hydrogen atom for the final ester was the hydroxyl group of ethanol. We believe that reaction 1 can be considered as an  $S_E1$ -type substitution because: (1) ethanol is a rather weak electrophile; (2) the reaction is strongly assisted by a nucleophile with a high affinity for mercury; and (3) the carbanion,  $p$ -NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub> $\bar{\text{C}}$ HCOOEt, is relatively stable in the EtOH medium.

The  $pK_a$  value for ethyl *p*-nitrophenylacetate, measured in dimethoxyethane, is 15.1 (counter-ion K<sup>+</sup>) [9]. Therefore, one may expect the carbanion to exist in an EtOH/EtO<sup>-</sup> solvent/base system in concentrations sufficient to be observed. Indeed,  $p$ -NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>COOEt dissolved in ethanolic 0.1 M EtONa gives a red-coloured solution, and in the electronic spectrum of the solution, in addition to the

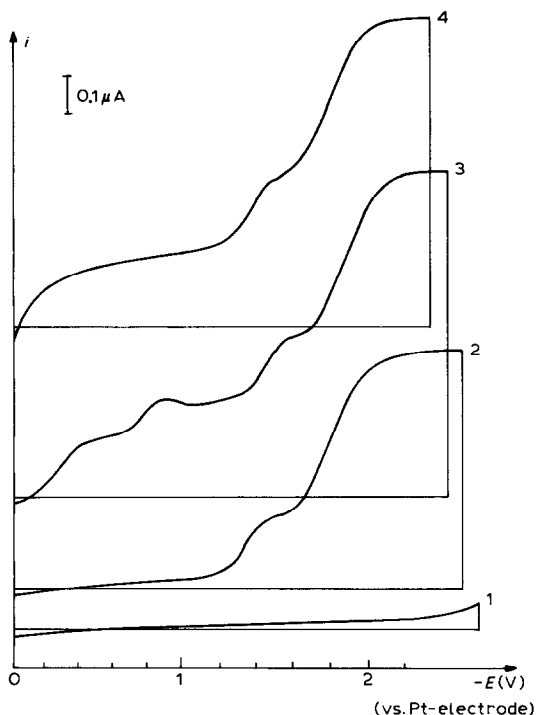


Fig. 1. Polarograms of  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}(\text{HgBr})\text{COOEt}$  in the absence and presence of bromide ions. Curves: 1, 0.05  $M$  solution of  $\text{Bu}_4\text{NBF}_4$  in EtOH; 2,  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{COOEt}$  ( $10^{-4}$  mol/l) in a 0.05  $M$  solution of  $\text{Bu}_4\text{NBF}_4$  in EtOH; 3,  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}(\text{HgBr})\text{COOEt}$  ( $10^{-4}$  mol/l) in the same solution; 4,  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}(\text{HgBr})\text{COOEt}$  ( $10^{-4}$  mol/l) and  $\text{Bu}_4\text{NBr}$  ( $4 \times 10^{-4}$  mol/l) in the same solution (5 min after the reactants had been mixed).

maximum corresponding to non-ionized  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{COOEt}$  ( $\lambda_{\text{max}}$  267 nm), another long-wave maximum appears, which corresponds to absorption of the carbanion ( $\lambda_{\text{max}}$  529 nm; for this carbanion in DMSO  $\lambda_{\text{max}}$  550 nm [9]).

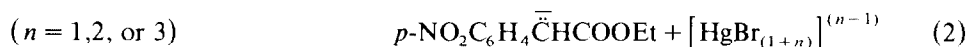
In the spectrum of the reaction mixture ( $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}(\text{HgBr})\text{COOEt} + \text{NaBr}$  in EtOH), the long-wave maximum was not observed. This is quite reasonable since the medium is weakly basic in this case because, on the one hand, the concentration of  $\text{EtO}^-$  cannot exceed the initial concentration of the organomercury substrate ( $10^{-2}$   $M$ ), and, on the other hand,  $\text{EtO}^-$  ions are associated with Lewis acids, such as  $\text{HgBr}_2$  and  $\text{HgBr}_3^-$ , in stable complexes. Displacement of the bromide ions from the coordination sphere of mercury(II) by ethoxide ion is also possible. In this case, mercury(II) ethoxide,  $\text{Hg}(\text{OEt})_2$ , is formed, which is a yellowish substance, poorly soluble in ethanol [10]. Indeed, in our polarographic experiments we observed the formation of small amounts of precipitates in the polarographic cell. This is the reason why the first, the least cathodic, wave on the polarograms of the reaction mixture at the end of reaction 1 is lower than it should be in accordance with the double-electron nature of mercury(II) salt reduction (Fig. 1, curve 4): part of the mercury(II) salts is in the precipitate. Thus, the concentration of the carbanions is very low under the experimental conditions of reaction 1 because of their rapid protonation by the solvent.

TABLE 1

DISTRIBUTION OF DEUTERATED PRODUCTS IN THE REACTIONS  $\text{RHgBr} + \text{NaBr} + \text{EtOD}$  AND  $\text{RH} + \text{EtONa} + \text{EtOD}$  ( $\text{R} = p\text{-NO}_2\text{C}_6\text{H}_4\text{CHCOOEt}$ )

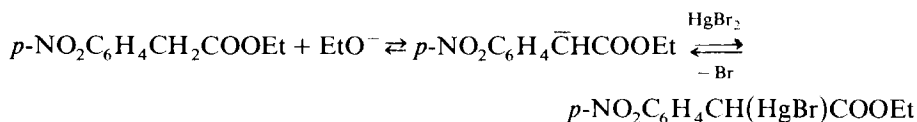
Reaction, 20°C	Yields (%) of RH with number of D atoms/molecule			
	$d_0$	$d_1$	$d_2$	$d_3$
$\text{RHgBr}(10^{-2} M) + \text{NaBr}(2 \times 10^{-2} M) + \text{EtOD (solv.)}$	3.7	22.1	66.1	8.2
$\text{RH}(3 \times 10^{-2} M) + \text{EtONa}(2 \times 10^{-2} M) + \text{EtOD (solv.)}$	–	5.9	91.3	2.9

However, in aprotic solvents one can succeed in observing the formation of the carbanions in appreciable concentrations immediately from the organomercury substrate. For instance, if an excess of  $\text{Bu}_4\text{NBr}$  is added to solutions of  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}(\text{HgBr})\text{COOEt}$  in hexamethylphosphortriamide (HMPT), dimethoxyethane (DME), pyridine (Py), or tetrahydrofuran (THF), the initial colourless solutions become intensively red\* ( $\lambda_{\text{max}}$  543; 571 nm in HMPT; 545 nm in DME; 542 nm in THF; 550; 579 nm in Py). Thus, bromide-assisted ionisation of the C–Hg bond takes place in these solvents.



The extent of the ionisation depends on the nature of the solvent. If the molar extinction coefficient for the carbanion is assumed to be  $\epsilon = 43,000$  (this value was obtained in DMSO [9]) independent of the solvent, one can calculate from the electronic spectra that the equilibrium of reaction 2 is shifted to the right approximately by 75% in HMPT, 37% in DME and 31% in Py.

If reaction 1 follows the  $S_{\text{E}}1$  mechanism, it must also be a reverse process, namely reaction of the carbanion with mercury(II) salts [11]. In other words, the addition of EtONa to the mixture of  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{COOEt}$  and  $\text{HgX}_2$  in ethanol must result in the formation of the organomercury compound.



Actually, as our experiments showed, the reverse reaction does take place. Thus, if a small excess of  $\text{HgBr}_2$  is added to a  $5 \times 10^{-2} M$  solution of  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{COOEt}$  in a  $7 \times 10^{-2} M$  solution of EtONa in ethanol, the initial red colour of the solution disappears and the organomercury compound can be isolated in an almost 30% yield. However, if instead of pure  $\text{HgBr}_2$  a mixture of  $\text{HgBr}_2 + \text{NaBr}$  (1/1) is added to the same solution of  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{COOEt}$  and EtONa in EtOH, the yield of

\* In HMPT, when the organomercury salt concentration was sufficiently high, a pale-pink colour of the solution could be observed, even in the absence of bromide ions.

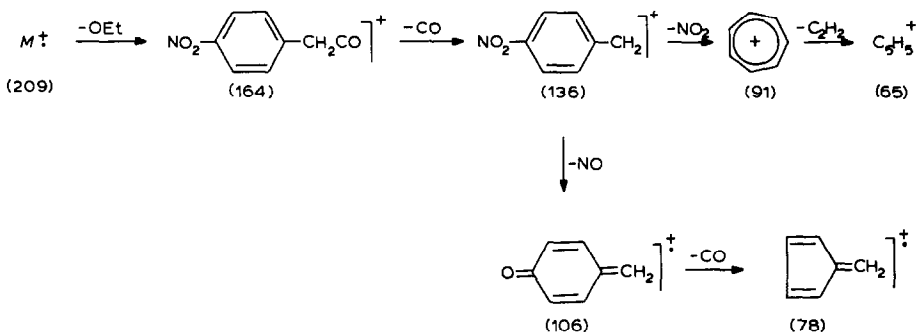
the organomercury compound decreases practically down to zero because bromide ions promote reaction 1.

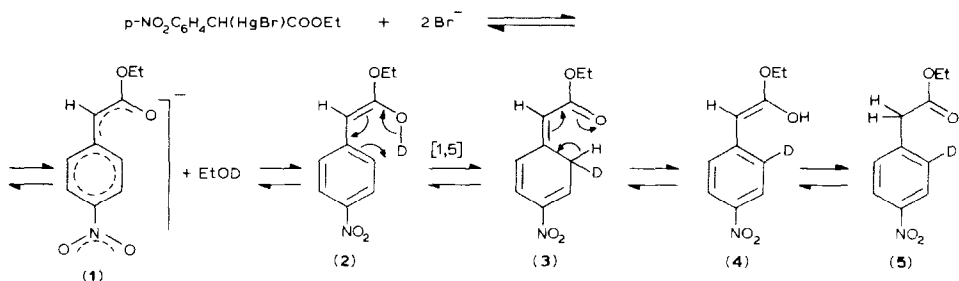
The distribution of the deuterated products for reaction 1 in EtOD is given in Table 1. The relative amounts of mono-, di- and tri-deuterated ethyl *p*-nitrophenylacetates were estimated, using mass spectroscopy, from the intensities of the peaks of the molecular ions with  $m/e$  209 ( $d_0$ ), 210 ( $d_1$ ), 211 ( $d_2$ ) and 212 ( $d_3$ ). As can be seen from Table 1, the deuterated esters are the major products in EtOD. The percentage of the products with different deuterium contents is also presented in Table 1 for the reaction of base-catalysed hydrogen exchange of ethyl *p*-nitrophenylacetate in the EtONa/EtOD system. In the latter reaction, H/D-exchange undoubtedly occurs via an intermediate carbanion,  $p\text{-NO}_2\text{C}_6\text{H}_4\text{C}^-\text{HCOOEt}$ , and, since the distribution of the deuterium label is qualitatively the same in protodemercurization of the organomercury compound and in hydrogen exchange of ethyl *p*-nitrophenylacetate ( $d_2 \gg d_1 > d_3$ ), the insertion of deuterium during the protodemercurization may be considered to occur as a step of the carbanionic intermediate.

We cannot draw any conclusions about the positions of deuterium in the molecules of mono-, di- and tri-deuterated esters from the mass spectral data. The calculations of the relative contents of  $d_1$ -,  $d_2$ - and  $d_3$ -products, which were carried out within the clusters with  $m/e$  209 and  $m/e$  78, gave the same results. This provides no more than good evidence that all the deuterium atoms of the  $d_1$ -,  $d_2$ - and  $d_3$ -esters are preserved in the fragment ion  $\text{C}_6\text{H}_6^{+\cdot}$  ( $m/e$  78)\*. Nevertheless, we can confirm that because the deuterium insertion reaction is undoubtedly an electrophilic process, deuterium atoms must enter into the benzylic position and/or in the position *ortho* to the benzylic carbon (i.e. in the *meta*-position to the nitro group). Therefore the  $d_1$ -product may be  $\alpha$ -*d* or *o*-*d* esters, the  $d_2$ -product may be  $\alpha,\alpha$ - $d_2$ ;  $\alpha,o$ - $d_2$ ; or *o,o*- $d_2$  esters; and the  $d_3$ -product may be  $\alpha,\alpha,o$ - $d_3$  or  $\alpha,o,o$ - $d_3$  esters.

It is worth considering the possible ways for deuterium to enter the *ortho*-position to the  $\text{CH}_2\text{COOEt}$  group. We suppose that a direct base ( $\text{EtO}^-$ )-catalysed exchange of aromatic hydrogen for deuterium is impossible during the reaction time (ca. 5 min) because the basicity of the medium is kept too low throughout reaction 1. For this reason, the mechanism which involves 1,5-sigmatropic shift of deuterium from oxygen to the *ortho*-carbon within the enol form of the carbanion seems to be more acceptable:

\* The mass-spectral fragmentation of  $p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{COOEt}$  is as follows:





Similar thermal rearrangement via enolization, allowed by orbital symmetry, were postulated, for instance, for the equilibrium  $\alpha,\beta$ -unsaturated carboxylic acid  $\rightleftharpoons$   $\beta,\gamma$ -unsaturated acid [12]. Low activation energies and negative activation entropies are characteristic of these isomerizations. One may suppose that the polydentate carbanion **1** which arises in the pre-equilibrium of the organomercury compound ionisation undergoes deuteration at the carbonyl oxygen of the carboxylate group, as is usual for enolate ions [13], and then thermal intramolecular rearrangement of enol **2** to the methylenecyclohexadiene structure **3** occurs. The reverse reaction **3**  $\rightarrow$  **4** and the following reaction **4**  $\rightarrow$  **5** (probably intermolecular) result in the final product, with deuterium in the *ortho*-position.

The data presented allow us to classify the reaction of ethyl  $\alpha$ -bromomercuro-*p*-nitrophenylacetate with ethanol as an  $S_E1(N)$ -type process where the symbol N indicates that the reaction occurs with nucleophilic assistance. In order to assist in the reaction, the nucleophiles must possess a relatively high affinity for mercury; the higher this affinity, the faster the reaction. This is confirmed by the sequence of promoting ability obtained in the present work:  $\text{I}^-$ ,  $\text{Br}^- > \text{Py} \gg \text{DMSO}$ .

### III. Experimental

**Materials.** Ethyl  $\alpha$ -bromomercuro-*p*-nitrophenylacetate was prepared as described in ref. 5, m.p.  $134^\circ\text{C}$  (lit. m.p.  $135^\circ\text{C}$ ). Purified 95% ethanol was converted to "absolute" solvent by refluxing it over freshly ignited CaO (250 g/l) for 6 h, standing overnight and by distillation, taking precautions to exclude moisture. Further dehydration was performed by refluxing it over  $\text{Mg}(\text{OEt})_2$  for 2 h and distillation. Commercially available  $\text{NaBr} \cdot 2\text{H}_2\text{O}$  was dehydrated by ignition at  $100^\circ\text{C}$  and cooling in a desiccator over anhydrous  $\text{CaCl}_2$ . Deuteroethanol,  $\text{C}_2\text{H}_5\text{OD}$ , was commercially available (deuterium content 98%).

**Apparatus.** Chromatography was carried out on an LHM-8md chromatograph, 5-th model, at  $155^\circ\text{C}$  (2 m  $\times$  3 mm column, 3% SP2100, adsorbent Chromaton N-super), carrier gas  $\text{N}_2$  (30 ml/min), flame ionisation detector. Mass spectra were obtained using an MS-30 instrument, ionising potential 70 V. UV spectra were recorded using a Hitachi-124 spectrophotometer. Polarographic experiments were carried out on a PA-2 instrument in ethanolic solutions with 0.05 M  $\text{Bu}_4\text{NBF}_4$  as the indifferent electrolyte; oxygen was removed by bubbling purified Ar through the cell.

**Straightforward reaction procedure.** 0.052 g ( $5 \times 10^{-4}$  mol) of NaBr was dissolved in 25 ml of EtOH with slight heating and 0.120 g ( $2 \times 10^{-4}$  mol) of ethyl  $\alpha$ -bromomercuro-*p*-nitrophenylacetate was added to the solution. The reaction was followed by TLC on silica gel; eluent  $\text{C}_6\text{H}_6/\text{MeOH}$ , 4/1. When the reaction was

over, the solvent was evaporated in vacuo and ethyl *p*-nitrophenylacetate was extracted with boiling hexane. Yield of pure product: 0.048 g (91%). The structure of the product was confirmed by the mass spectrum. The reaction with EtOD was carried out in the same way.

*Reverse reaction procedure.* 0.100 g ( $5 \times 10^{-4}$  mol) of ethyl *p*-nitrophenylacetate was added to a solution of 0.050 g ( $7 \times 10^{-4}$  mol) of NaOEt in 10 ml of ethanol. The solution became intensively red. Then 0.360 g ( $1 \times 10^{-3}$  mol) of HgBr<sub>2</sub> was introduced into the solution and the colour of the solution turned yellow. The solvent was evaporated in vacuo, the mixture of ethyl *p*-nitrophenylacetate and ethyl  $\alpha$ -bromomercury-*p*-nitrophenylacetate was extracted with hot benzene, and the extract was separated by TLC (Silpearl UV-254). 0.04 g of the initial *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>COOEt and 0.041 g of *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CH(HgBr)COOEt were isolated (eluent C<sub>6</sub>H<sub>6</sub>/MeOH, 4/1).

*H/D-exchange of p-nitrophenylacetate.* 5 ml of a  $2 \times 10^{-2}$  M solution of NaOEt was prepared, bubbled with argon, and added to 0.03 g ( $1.5 \times 10^{-4}$  mol) of ethyl *p*-nitrophenylacetate. The solution became intensely red. One hour later it was slowly neutralized with a  $3 \times 10^{-2}$  M solution of D<sub>2</sub>SO<sub>4</sub> in ethanol up to the neutral reaction. The colour of the solution turned pale-yellow. The solvent was evaporated in vacuo and the product was extracted with hot hexane. 0.025 g (84%) of a mixture of ethyl *p*-nitrophenylacetates with different deuterium contents was isolated. The qualitative and quantitative compositions of the mixture as determined by the mass spectra are given in Table 1.

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