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NEIGHBORING SULFUR PARTICIPATION IN THE SOLVOLYSIS OF 2-(ω-ALKYLTHIOALKYL)-3-METHYL-2-CYCLOHEXENYL p-NITROBENZOATES

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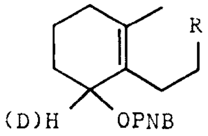
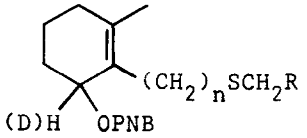
Summary: As shown by kinetic and product analysis, the solvolysis of 7 and 8 in 97% TFE includes several competitive reactions, one of them being neighboring sulfur participation and formation of intermediate cyclic sulfonium cation.

Recently we have demonstrated[1] the absence of π- or n-participation in solvolysis of esters 1-4.



1, R = $CH=CH_2$
2, R = $CH=C(CH_3)_2$
3, R = $C\equiv C-CH_3$
4, R = OCH_3
5, R = CH_2CH_3
6, R = $CH_2CH_2C_6H_5$

These compounds show in both 97% TFE and 80% EtOH a solvolysis rate retardation in comparison with the saturated analog 5, and normal values of secondary α-deuterium isotope effects (k_H/k_D = 1.17 to 1.22). These results prompted us to investigate possible neighboring sulfur participation in analogous allyl derivatives 7a-7c and 8a-8c.



7a, R = H; n = 2
7b, R = H; n = 3
7c, R = H; n = 6
8a, R = C_6H_5; n = 2
8b, R = C_6H_5; n = 3
8c, R = C_6H_5; n = 6

Bivalent sulfur was found[2] to be a better internal nucleophile than oxygen, due to its smaller inductive rate-retarding effect, higher ability to donate electron pairs, and larger size that increases the efficient overlap with the reacting center. A marked n-participation of thioethereal group was observed in cases where the formation of stable cyclic sulfonium cationic intermediates with a three-[3-5], five- or six-membered[6,7] ring was possible. Intermediates with a four-membered ring can also be favored[8], as well as the recently reported[9] CH_3S-17(!) participation.

Esters 7 and 8 were prepared according to the previously described procedure[1] and solvolyzed in 97% w/w 2,2,2-trifluoroethanol (97% TFE). Reaction rates were measured by continuous automatic potentiometric titration of the released p-nitrobenzoic acid and compared with rates of 5 and 6. In the solvolyses of 7c and 8c a clear first-order kinetic behavior was observed. On the other hand, the shape of the plot of base consumption vs. reaction time indicated that solvolysis of these compounds includes several competitive reactions. The kinetic data for these esters were collected by microcomputer and analyzed by a nonlinear least-squares computer program using various kinetic models[10]. The best description of data was obtained by model (1)[11] which is equivalent to model (2) assuming a steady-state approximation for I[10]

$$\text{Pdts} \xleftarrow{\quad k_1 \quad} A \xrightarrow{k_2} B \xrightarrow{k_3} \text{Pdts} \qquad (1)$$

$$\begin{tikzcd} \text{Pdts} & I \arrow[l] \arrow[r, shift left] & A \arrow[l, shift left] \arrow[r, "k_2"] \arrow[ll, bend right, "k_1"'] & B \arrow[r, "k_3"] & \text{Pdts} \end{tikzcd} \qquad (2)$$

The mechanism of solvolysis of esters 7 and 8 was rationalized using model (2) to give Scheme 1. The rate constants k_1, k_2, and k_3 were calculated and their values are listed in Table 1.

Path k_1 represents the formation of unrearranged products 11 and 12 via allyl cation 9, without sulfur participation. α-Deuterium isotope effects for this path in 97% TFE at 50°C are in the range of analogous effects for esters 1-6 in 97% TFE where k_Δ path is absent. The similarity of these isotope effects indicates that, likewise the solvolysis of esters 1-6, path k_1 is a stepwise process which includes an allyl cation 9 as a reaction intermediate[1] The k_1 rate constants of esters 7 and 8 are reduced in comparison with the rates of the reference esters 5 and 6, respectively, due to the electron-withdrawing inductive effect of thioethereal group. Log k_1 values for solvolyses of esters 7 and 8 in 97% TFE at 50°C show excellent linear correlation (correlation coefficients $r = 0.9992$ and 0.9925 for esters 7 and 8, respectively) with the logarithm of the number of C-atoms between the side-chain sulfur and the leaving group.

Path k_2 involves neighboring sulfur participation and the formation of an intermediate cyclic sulfonium cation 10. For esters 7c and 8c k_2 is negligible in comparison with k_1, so that first order kinetics is observed. Obviously, for these esters the formation of a cyclic sulfonium cation 10 with nine atoms in the ring is not favorable. On the other hand, compounds 7a and 8a, as well as 7b and 8b, solvolyze via the intermediate sulfonium cation 10 with five- and six-membered rings, respectively. For the solvolysis of these esters in 97% TFE at 50°C α-deuterium isotope effects for k_2 path (1.04-1.05) are in the normal range for k_Δ processes[12].

The intermediate sulfonium cation 10 collapses via path k_3 giving unrearranged monocyclic products 11 and 12 (which can also be formed via path k_1), rearranged products 13, and bicyclic products 14. The formation of these

Scheme 1. Mechanism of Solvolysis of 2-(ω-Alkylthioalkyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoates 7 and 8 in 97% TFE

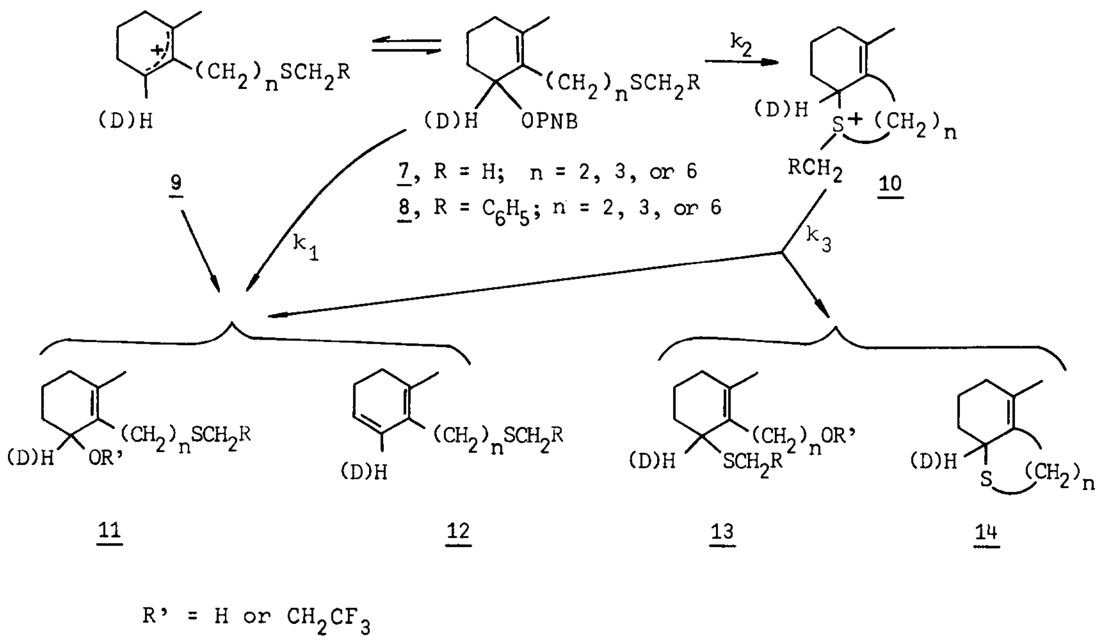
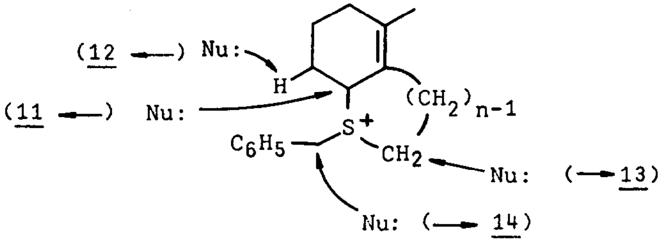


Table 1. Rate Constants for Solvolyses of 2-Substituted-3-methyl-2-cyclohexenyl p-Nitrobenzoates 5-8 in 97% TFE at 50°C

Ester	$k_1 \times 10^4$s	$k_2 \times 10^4$s	$k_3 \times 10^4$s
7a	30.2 ±0.8	29 ±1	6.43±0.09
7b	46.7 ±0.9	37.1±0.7	9.5 ±0.4
7c	138.6 ±0.7	-	-
5	188 ±1	-	-
8a	5.72±0.08	27.4±0.6	2.94±0.07
8b	9.6 ±0.4	31 ±2	4.3 ±0.3
8c	68.8 ±0.3	-	-
6	115.4 ±0.5	-	-

products can be explained by nucleophilic attack of solvent at various sites of the sulfonium cation 10:



Products 13 and 14 are formed only in the solvolysis of esters 7a, 7b, 8a, and 8b, and not in solvolysis of 7c and 8c where k_Δ path is negligible, confirming the proposed solvolysis mechanism. Solvolysis of ester 8b in 97% TFE at 50°C gives 12% of 11a (R = C_6H_5; R' = H; n = 3), 11% of 11b (R = C_6H_5; R' = CH_2CF_3; n = 3), 6% of 12 (R = C_6H_5; n = 3), 37% of 13a (R = C_6H_5; R' = H; n = 3), 26% of 13b (R = C_6H_5; R' = CH_2CF_3; n = 3), and 3% of 14 (n = 3); for ester 8a under the same reaction conditions a similar product composition was obtained. From the ratio k_2/k_1 for solvolysis of 8a and 8b in 97% TFE at 50°C (4.79 and 3.23, respectively) and from their product composition it can be deducted that 11 is formed via path k_1 in a much higher amount than via path k_3. From this we can conclude that product 11 is formed from 10 by an S_N2 mechanism, and not via S_N1 reaction which would include a reversible opening of 10 to allyl cation 9.

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