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A Search for Maximal Neighboring Group Participation in Solvolyses of Allylic Substrates. Ethanolysis of 2-(ω-Alkylthioalkyl)-3-methyl-2-cyclohexenyl *p*-Nitrobenzoates

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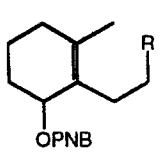
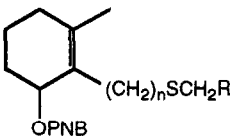
Abstract: The solvolysis of 2-(ω-methylthioalkyl)- and 2-(ω-benzylthioalkyl)-3-methyl-2-cyclohexenyl *p*-nitrobenzoates **5** and **6** in 80 vol % ethanol includes several competitive reactions. Path k_1 is a stepwise process (k_H/k_D = 1.18-1.20) which includes allylic cation **9** as a reaction intermediate, while path k_2 involves a neighboring sulfur participation (k_H/k_D = 1.01-1.03) and formation of an intermediate cyclic sulfonium cation **10**. Esters **5** and **6** solvolyze in 80% EtOH with a greater neighboring group participation than in 97% TFE It has been concluded that in solvolytic reactions of allylic substrates a pronounced neighboring group participation (k_2/k_1= 900) may occur only with very strong internal nucleophiles, and in solvents which can not form strong hydrogen bonds with these nucleophiles.

The participating ability of a neighboring group in solvolytic reactions depends on the type of substrate, nature and location (and orientation) of internal nucleophile, stability of a reaction intermediate formed upon participation, solvent, and some other factors.[2] During our previous study of neighboring group participation in the solvolysis of allylic substrates we have shown that alkenyl[3] and alkynyl groups[4], although properly juxtaposed for the possible closure of a five- or six-membered ring, do not participate in the ionization step of solvolysis of 2-cyclohexenyl esters **1** and **2** in 97% TFE and 80% EtOH as solvents.



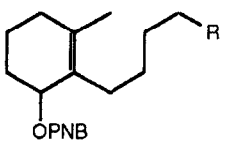
1a, R = $CH{=}CH_2$ **3a**, R = OCH_3
1b, R = $CH{=}C(CH_3)_2$ **3b**, R = $OCH_2C_6H_5$
2, R = $C{\equiv}C\text{-}CH_3$ **4a**, R = CH_2OCH_3
4b, R = $CH_2OCH_2C_6H_5$

In the solvolysis of *p*-nitrobenzoates **3** and **4** which each have an alkoxy group in the C-2 substituted side-chain, a weak neighboring group participation was observed only with esters **4** where the formation of a six-membered ring is possible, but not with esters **3** which would form a five-membered ring.[5] Furthermore, it was found that the ability of alkoxy groups to participate in the solvolysis of esters **4** was expressed only with 80% EtOH, and not with 97% TFE as a solvent. It was concluded that TFE can form strong hydrogen bonds with the side-chain ethereal group,[6] making it ineffective as an internal nucleophile. Bivalent sulfur is a better internal nucleophile than oxygen,[7] and therefore it is effective for participation in similar allylic systems even with 97% TFE as a solvent. When *p*-nitrobenzoates **5** and **6** were solvolyzed in 97% TFE, a marked n-participation of thioethereal group was observed with esters **5a**, **5b**, **6a**, and **6b** which can form the intermediate five- or six-membered cyclic sulfonium cation.[8] Similarly to the alkoxy group,



5a, R = H; n = 2 **6a**, R = C_6H_5; n = 2
5b, R = H; n = 3 **6b**, R = C_6H_5; n = 3
5c, R = H; n = 6 **6c**, R = C_6H_5; n = 6

the alkylthio group can form strong hydrogen bonds with TFE, but not with EtOH which is a weak proton donor.[6] Therefore, we predicted that the participating ability of thioethereal group in esters **5a**, **5b**, **6a**, and **6b**, which is expressed even in 97% TFE, should be much greater in 80% EtOH as a solvent. In order to investigate such a possibility, *p*-nitrobenzoates **5** and **6** were solvolyzed in 80% EtOH and their rate constants were compared with rates of esters **7** and **8**.

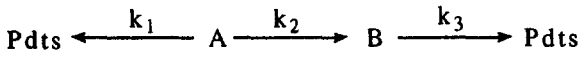


7, R = H
8, R = C_6H_5

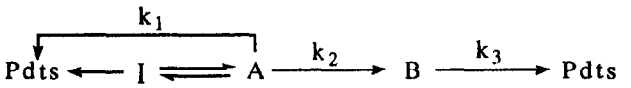
RESULTS AND DISCUSSION

Esters **5-8** were solvolyzed in 80 vol % EtOH at 50°C and their reaction rates were measured by continuous automatic potentiometric titration of the released *p*-nitrobenzoic acid. In the solvolysis of **5c** and **6c** a clear first-order kinetic behavior was observed, similarly to the ethanolysis of reference esters **7** and **8**, as well as to the solvolytic behavior of these four esters in 97% TFE.[8] For the solvolysis of esters **5a**, **5b**, **6a**, and **6b** in 80% EtOH the shape of the plot of base consumption vs. reaction time indicates that these solvolytic reactions, as with solvolyses of these esters in 97% TFE,[8] include several competitive reactions. The kinetic data for these esters were collected by a microcomputer and analyzed by a nonlinear least-squares computer program using various kinetic models. For esters **5a** and **5b** the best fit of kinetic data was obtained by

model (1)[9] which is equivalent to model (2) assuming a steady-state approximation for I.

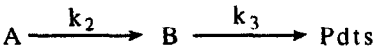


(1)



(2)

For esters **6a** and **6b** rate constants k_2 are almost 10^3 times larger than constants k_1, reducing model (2) to a simple model (3) for consecutive reactions.



(3)

The mechanism of solvolysis of esters **5** and **6** was rationalized using these kinetic models to give Scheme 1. The rate constants k_1, k_2 and k_3 were calculated (for more information see the Experimental Section) and their values are listed in Table 1.

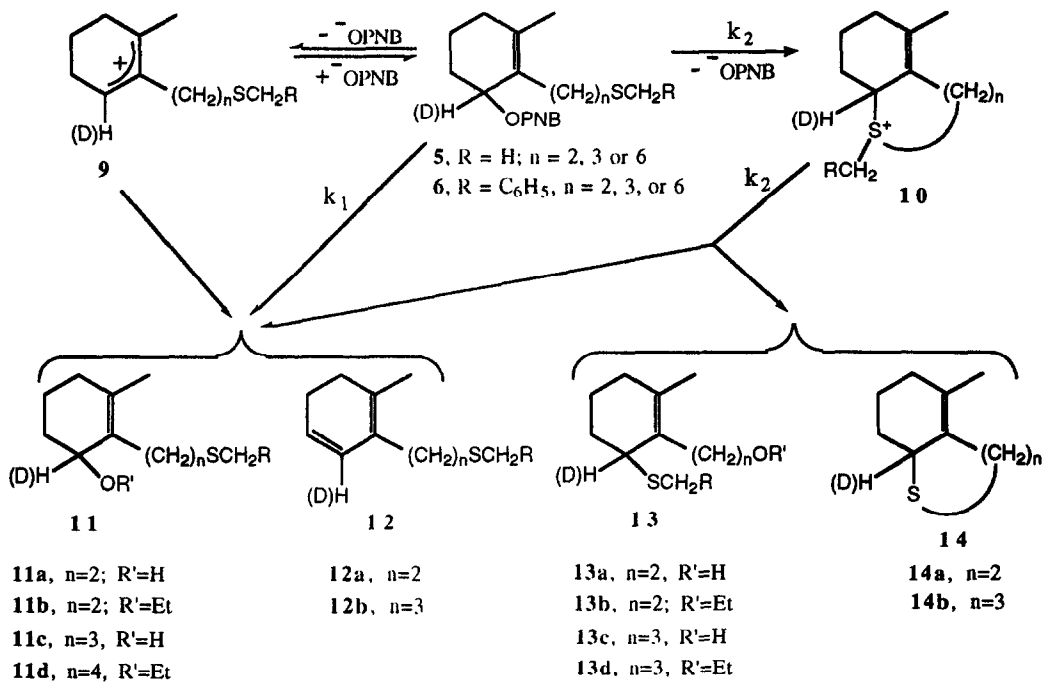
Table 1. Rate constants for solvolyses of 2-substituted 3-methyl-2-cyclohexenyl *p*-nitrobenzoates **5** and **6** in 80% EtOH at 50°C.

Ester	$k_1 \times 10^4$s	$k_2 \times 10^4$s	$k_3 \times 10^4$s	$(k_2/k_1)_{80E}$[a]	$(k_2/k_1)_{97T}$[b]
5a	1.104(5)[c]	12.5(6)	2.69(7)	11.3	1.0
5b	1.410(9)	42.4	2.32(2)	30.1	0.8
5c	2.74(2)	-	-	0	0
7	2.94(1)				
6a	0.39[d]	343(33)	1.875(8)	~900	4.8
6b	0.64[d]	454(56)	2.042(5)	~700	3.2
6c	1.792(7)	-	-	0	0
8	2.359(4)				

[a]Ratio of rate constants for solvolyses in 80% EtOH at 50°C.
[b]Ratio of rate constants for solvolyses in 97% TFE at 50°C; values from ref. 8.
[c]Numbers in parentheses are standard deviations of the mean.
[d]Estimated values; see text for explanation.

Path k_1 represents the formation of unrearranged products **11** and **12** via allyl cation **9**, without sulfur participation. For the solvolysis of esters **5a-5c**, **6c**, **7** and **8** in 80% EtOH at 50°C the α-deuterium isotope effects are 1.18-1.20. These values are in the range of analogous effects for the k_1 path of the same esters in 97% TFE, as well as of isotope effects for esters **1-3** in 80% EtOH and in 97% TFE where the neighboring group

participation is absent. The similarity of these isotope effects confirms that, likewise the solvolysis of esters **5** and **6** in 97% TFE, path k_1 is a stepwise process which includes the allyl cation **9** as a reaction intermediate.[8] The k_1 rate constants of esters **5** and **6** are reduced in comparison with the rates of the reference esters **7** and **8**, respectively, due to the electron-withdrawing inductive effect of a thioethereal group. Log k_1 values for solvolyses of esters **5** in 80% EtOH at 50°C show an excellent linear correlation (correlation coefficient r= 0.9983) with the logarithm of the number of carbon atoms between the side-chain sulfur and the leaving group. Similar linear correlations were observed for solvolysis of esters **5** and **6** in 97% TFE.[8,10] Assuming that such a linear correlation also exists for solvolyses of esters **6** in 80% EtOH at 50°C, and estimating that the slope of this correlation[10] is 2 20, it was calculated that k_1 constants for solvolysis of esters **6a** and **6b** in 80% EtOH at 50°C should have values around 0.39 x 10^{-4} and 0.64 x 10^{-4} s^{-1}, respectively (Table 1). These values are used in the discussion for the degree of sulfur participation in solvolysis of esters **5** and **6**.



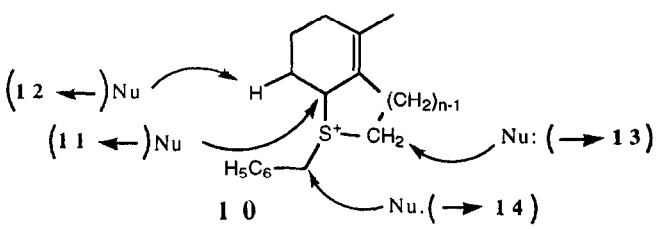
Scheme 1

Path k_2 involves neighboring sulfur participation and the formation of an intermediate cyclic sulfonium cation **10**. For the solvolysis of esters **5c** and **6c** in 80% EtOH, similarly

to their solvolysis in 97% TFE,[8] 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 in 97% TFE, nor in 80% EtOH. On the other hand, solvolyses of esters **5a** and **6a**, as well as **5b** and **6b**, include the advantageous intermediate sulfonium cation **10** with five- and six-membered rings, respectively. For the solvolysis of esters **5a** and **5b** in 80% EtOH at 50°C, α-deuterium isotope effects for the k_2 path are 1.03 and 1.01, respectively, falling in the normal range for k_Δ processes.[11]

Esters **5a**, **5b**, **6a**, and **6b** solvolyze in 80% EtOH with a far larger degree of neighboring sulfur participation than in 97% TFE. The k_2 rate constants for these esters in 97% TFE at 50°C are several times smaller than the solvolysis rates of reference esters **7** and **8**.[8] However, in 80% EtOH at 50°C the solvolysis of esters **5a** and **5b** via k_2 path is 4.3 and 14.4 times faster than the solvolysis of ester **7**, while the k_2 rate constants for esters **6a** and **6b** under the same conditions are 145 and 190 times faster than the rate constant for ester **8** (Table 1) Another parameter that reflects the degree of sulfur participation in these solvolytic reactions is the ratio of rate constants for the k_2 path (which involves sulfur participation) and the k_1 path (which is a stepwise process without participation). For all esters **5a**, **5b**, **6a**, and **6b** this ratio is much larger in 80% EtOH than in 97% TFE [ratios $(k_2/k_1)_{80E}$ and $(k_2/k_1)_{97T}$, respectively; Table 1], additionally confirming the pronounced sulfur participation in the former solvent. It is interesting to note that in both 80% EtOH and 97% TFE the k_2/k_1 ratios for esters **6a** and **6b** are larger than for **5a** and **5b**. This result can be explained by stabilization of a benzyl-sulfonium cation **10** by a phenyl group which acts as a π-electron donor.[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** (Scheme 1). The formation of these products can be explained by nucleophilic attack of a solvent at various sites on the sulfonium cation **10** (Scheme 2).



Scheme 2

Solvolysis of esters **5c** and **6c** in 80% EtOH at 50°C gives only unrearranged products **11** and **12**, and not the rearranged and bicyclic products **13** and **14**, confirming the proposed solvolysis mechanism On the other hand, in the solvolysis of esters **5a**, **5b**, **6a**,

and **6b** in 80% EtOH the k_Δ path is predominant, and all kinds of solvolysis product **11** - **14** were obtained. The product composition for the solvolysis of esters **6a**, and **6b** in 80% EtOH at 50°C is listed in Table 2. It is interesting to note the similarity in product composition for esters **6a** and **6b** in 97% TFE[8] and 80% EtOH. In all those cases the percentages of unrearranged, rearranged, and bicyclic products are about 30%, 67% and 3%, respectively.

Table 2. Solvolysis products of esters **6a** and **6b** in 80% EtOH at 50°C

	Product, % Yield					
Ester	Unrearranged Products[a]		Rearranged Products[a]		Bicyclic Products	
6a	**11a**, 12% **11b**, 9% **12a**, 7%	28%	**13a**, 48% **13b**, 21%	69%	**14a**, 3%	
6d	**11c**, 14% **11d**, 13% **12b**, 6%	33%	**13c**, 42% **13d**, 22%	64%	**14b**, 3%	

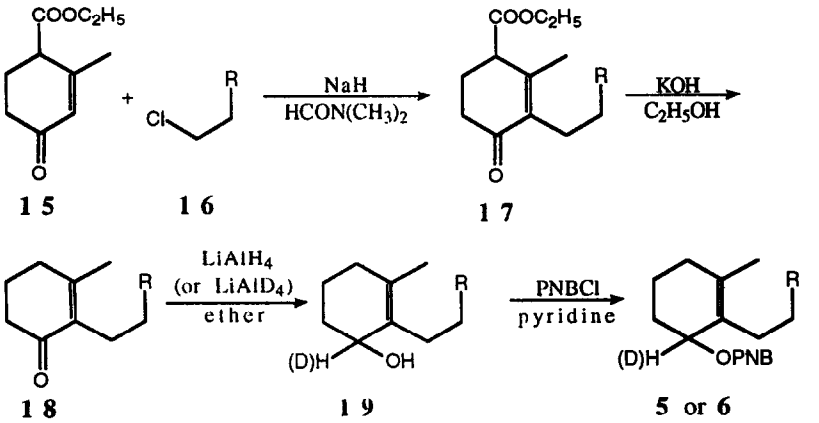
[a]R = C_6H_5 in all products.

Although the k_2/k_1 ratios for the solvolysis of these esters in 80% EtOH are about 200 times larger than in 97% TFE, indicating that the degree of sulfur participation in the former solvent is much larger, this difference does not reflect on the product composition. This result proves the known observation[13] that the percentage of cyclized and/or rearranged products in solvolytic reaction is not a reliable criterion for conclusions about a degree of neighboring group participation in the ionization step.

In conclusion, our results show that in solvolytic reactions of allylic substrates, pronounced neighboring group participation can occur, but only with very effective internal nucleophiles, and only in solvents which will not reduce the participating ability of these nucleophiles by protonation or formation of strong hydrogen bonds.

EXPERIMENTAL SECTION

All compounds were identified by IR, ^1H NMR, and in some cases by elemental analysis. Infrared spectra of neat samples were recorded on a Perkin-Elmer 257 spectrometer. ^1H NMR spectra of samples dissolved in tetrachloromethane were recorded on a Varian EM-360 or T-60 spectrometer, using tetramethylsilane as an internal standard. All reported yields are isolated yields. For ketones yields are from ethyl 2-methyl-4-keto-2-cyclohexenecarboxylate. All deuterated compounds have a deuterium content > 98% d_1 (by ^1H NMR).



16 - 19, 5, 6 **a**, R = SCH_3
b, R = CH_2SCH_3
c, R = $(CH_2)_4SCH_3$
d, R = $SCH_2C_6H_5$
e, R = $CH_2SCH_2C_6H_5$
f, R = $(CH_2)_4SCH_2C_6H_5$

Scheme 3

General Procedure for the Preparation of Ketones 18

These compounds were prepared according to slightly modified[14] literature procedures.[15,16] Ethyl 2-methyl-4-keto-2-cyclohexenecarboxylate (**15**)[17] (8 g, 43.9 mmol) was alkylated with chloride **16**[18] (45 mmol) in N,N-dimethylformamide (35 mL) using NaH (1.1 g, 46 mmol) as a base. The resulting ketoester was hydrolyzed and decarboxylated with KOH (4.48 g, 80 mmol) in anhydrous ethanol (30 mL), and the crude product was purified on a silica gel column with benzene-ether (4:1) as eluent to give ketone **18.**

2-(2-Methylthioethyl)-3-methyl-2-cyclohexenone (**18a**)

Yield 16%; IR 1655 (C=O) and 1628 cm^{-1} (C=C); ^1H NMR δ 2.07 (3H, s, SCH_3), 1.96 (3H, s, C=C-CH_3), 2.45-2.18 (10H).

2-(3-Methylthiopropyl)-3-methyl-2-cyclohexenone (**18b**)

Yield 18.1%; IR 1662 (C=O) and 1628 cm^{-1} (C=C); ^1H NMR δ 2.13 (3H, s, SCH_3) 1.94 (3H, s, C=C-CH_3), 2.50-2.17 and 1.73-1.23 (12H).

Anal. Calcd. for $C_{11}H_{18}SO$: C, 66.62; H, 9.15; S, 16.17
Found: C, 66.79; H, 9.37; S, 16.43

2-(6-Methylthiohexyl)-3-methyl-2-cyclohexenone (**18c**)

Yield 17.5%; IR 1660 (C=O) and 1625 cm^{-1} (C=C); ^1H NMR δ 1.98 (3H, s, SCH_3), 1.90 (3H, s, C=C-CH_3), 2.40-2.15 and 1.40-1.25 (18H).

Anal. Calcd. for $C_{14}H_{22}SO$: C, 69.95; H, 10.16; S, 13.34
Found: C, 70.07; H, 10.26; S, 13.32

2-(2-Benzylthioethyl)-3-methyl-2-cyclohexenone (**18d**)

Yield 18.6%; IR 3060, and 3020 (Ar-H), 1655 (C=O), 1630 (C=C), 770, and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.15 (5H, s, C_6H_5), 3.53 (2H, s, CH_2Ph), 1.85 (3H, s, C=C-CH_3), 2.40-2.05 and 1.70-1.10 (10H).

Anal. Calcd. for $C_{19}H_{20}SO$: C, 73.80; H, 7.74; S, 12.31
Found: C, 73.95; H, 7.69; S, 12.45

2-(3-Phenylthiopropyl)-3-methyl-2-cyclohexenone (**18e**)

Yield 15.9%; IR 3090, 3060, and 3030 (Ar-H), 1660 (C=O), 1640 (C=C), 760 and 705 cm^{-1} (Ar-H); ^1H NMR δ 7.10 (5H, s, C_6H_5), 3.57 (2H, s, CH_2Ph), 1,85 (3H, s, C=C-CH_3), 2.40-2.10 and 1.40-1.20 (12H).

Anal. Calcd. for $C_{17}H_{22}SO$: C, 74.40; H, 8.08; S, 11.68
Found: C, 74.29; H, 8.09; S, 11.58

2-(6-Phenylthiohexyl)-3-methyl-2-cyclohexenone (**18f**)

Yield 19.0%; IR 3080, 3060, and 3040 (Ar-H), 1670 (C=O), 1625 (C=C), 765 and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.04 (5H, s, C_6H_5), 3.56 (2H, s, CH_2Ph), 1.80 (3H, s, C=C-CH_3), 2.30-1.90 and 1.50-1.20 (18H).

General Procedure for the Preparation of Alcohols 19.

Ketones **18** (1.54 mmol) were reduced with $LiAlH_4$ (600 mg; 15.8 mmol) in dry ethyl ether (20 mL) by using a previously described procedure[15] to give alcohols **19.**

2-(2-Methylthioethyl)-3-methyl-2-cyclohexenol (**19aH**)

Yield 96.0 %; IR 3390 cm^{-1} (OH); ^1H NMR δ 3.97 (1H, br.s, CHOH), 2.50 (1H+2H+2H, m, $CH_2CH_2SCH_3$+OH), 2.10 (3H, s, SCH_3), 1.68 (3H, s, C=C-CH_3), 1.60-1.30 (6H).

1-Deuterio-2-(2-methylthioethyl)-3-methyl-2-cyclohexenol (**19aD**)

Yield 94.0%; IR 3380 (OH) and 2140 cm^{-1} (C-D); ^1H NMR δ 2.58 (1H, br.s, OH), 2.47 (4H, 2t, $CH_2CH_2SCH_3$), 2.08 (3H, s, SCH_3), 1.67 (3H, s, C=C-CH_3), 1.60-1.25 (6H).

2-(3-Methylthiopropyl)-3-methyl-2-cyclohexenol (**19bH**)

Yield 94.6%; IR 3360 cm^{-1} (O-H); ^1H NMR δ 3.90 (1H, br. s, CHOH), 2.03 (3H, s, SCH_3), 1.64 (3H, s, C=C-CH_3), 2.50-2 00 and 1.50-1.20 (12H).

1-Deuterio-2-(3-Methylthiopropyl)-3-methyl-2-cyclohexenol (**19bD**)

Yield 95.2%; IR 3360 (OH) and 2120 cm^{-1} (C-D); ^1H NMR δ 2.55 (1H, br. s, OH), 2.03 (3H, s, SCH_3), 1.63 (3H, s, C=C-CH_3), 2 45-2.10 and 1.50-1.20 (12H).

2-(6-Methylthioethyl)-3-methyl-3-cyclohexenol (**19cH**)

Yield 94.3%; IR 3360 cm^{-1} (OH); ^1H NMR δ 3.87 (1H, br. s, CHOH), 2.40 (2H, t, J=6Hz, CH_2SCH_3), 2.03 (3H, s, SCH_3), 1.65 (3H, s, C=C-CH_3), 1.50-0.90 (17H).

1-Deuterio-2-(6-methylthiohexyl)-3-methyl-2-cyclohexenol (**19cD**)

Yield 94.3%; IR 3390 (OH) and 2120 cm^{-1} (C-D); ^1H NMR δ 2.42 (2H, t, CH_2SCH_3), 2.03 (3H, s, SCH_3) 1.87 (1H, s, OH), 1.62 (3H, s, C=C-CH_3), 1.50-1.10 (16H).

2-(2-Benzylthioethyl)-3-methyl-2-cyclohexenol (**19dH**)

Yield 90.0%; IR 3360 (O-H), 3090, 3060, and 3030 (Ar-H), 1030 (C-O), 730 and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.13 (5H, s, C_6H_5). 3.80 (1H, br. s, CHOH), 3.60 (2H, s, CH_2Ph), 2.77 (1H, br. s, OH), 1.65 (3H, s, C=C-CH_3), 2.33-1.80 and 1.50-0.90 (10H).

2-(2-Benzylthioethyl)-1-deuterio-3-methyl-2-cyclohexenol (**19dD**)

Yield 97.5%; IR 3370 (OH), 3090, 360, and 3030 (Ar-H), 2120 (C-D), 705 cm^{-1}; ^1H NMR δ 7.12 (5H, s, C_6H_5), 3.60 (2H, s, CH_2Ph), 2.75 (1H, br. s, OH), 1.67 (3H, s, C=C-CH_3), 2.40-1.80 (10H).

2-(3-Benzylthiopropyl)-3-methyl-2-cyclohexenol (**19eH**)

Yield 96.7%; IR 3360 (OH), 3090, 3060, and 3030 (Ar-H), 740 and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.20 (5H, s, C_6H_5), 3.85 (1H, br. s, CHOH), 3.61 (2H, s, CH_2Ph), 2.73 (1H, br. s, OH), 1.65 (3H, s, C=C-CH_3), 2 30-1 80 and 1.50-1.10 (12H).

2-(3-Benzylthiopropyl)-1-deuterio-3-methyl-2-cyclohexenol (**19eD**)

Yield 93.2%; IR 3360 (OH), 3090, 3060, and 3030 (Ar-H), 2140 (C-D), 702 cm^{-1} (Ar-H); ^1H NMR δ 7.27 (5H, s, C_6H_5), 3.63 (2H, s, CH_2Ph), 2.32 (2H, t, J=7Hz, CH_2SBz), 1.65 (3H, s, C=C-CH_3), 2.10-1.80 and 1.40-0.90 (10 H).

2-(6-Benzylthiohexyl)-3-methyl-2-cyclohexenol (**19fH**)

Yield 94.0%; IR 3350 (OH), 3085, 3060, and 3020 (Ar-H), 725 and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.07 (5H, s, C_6H_5), 3 70 (1H, br.s, CHOH), 3.50 (2H, s, CH_2Ph), 2.47 (1H, br. s, OH), 1.67 (3H, s, C=C-CH_3), 2 20-1 80 and 1.50-1.10 (18H).

2-(-6-Benzylthiohexyl)-1-deutero-3-methyl-2-cyclohexenol (**19fD**)

Yield 93.0%; IR 3360 (OH), 3080, 3055, and 3020 (Ar-H, 2120 (C-D), and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.05 (5H, s, C_6H_5), 3.50 (2H, s, CH_2Ph), 1.67 (3H, s, C=C-CH_3), 2.20-1.75 and 1.50-1.10 (18H).

General Procedure for the Preparation of *p*-Nitrobenzoates 5 and 6.

Alcohol **19** (1.37 mmol) was dissolved in dry pyridine (20 mL) and the mixture was cooled (ice-water bath). *p*-Nitrobenzoyl chloride (800 mg, 4.31 mmol) was added in small portions over 5 min. and the reaction mixture was stirred at room temperature overnight. The reaction mixture was then poured on ice (500 g) and extracted with n-pentane (4x100 mL). The organic extracts were dried over anhydrous sodium sulfate and evaporated in a vacuum. The oily residue was purified on a silica gel column using a mixture of n-pentane and benzene (9:1) as an eluent to give ester **5** or **6** a yellow oil.

2-(2-Methylthioethyl)-3-methyl-2-cyclohexenyl *p*-Nitrobenzoate (**5aH**)

Yield 93.4%; IR 3110, 3080, and 3050 (Ar-H), 1720 (COO), 1530 and 1350 (NO_2), and 722 cm^{-1} (Ar-H); ^1H NMR δ 8.23 (4H, s, $C_6H_4NO_2$), 5.62 (1H, br.s, CHOPNB), 2.40 (4H, 2t, $CH_2CH_2SCH_3$), 2.03 (3H, s, SCH_3), 1 80 (2H, s, C=C-CH_3), 2.10-1.70 (6H).

1-Deuterio-2-(2-methylthioethyl)-3-methyl-2-cyclohexenyl *p*-Nitrobenzoate (**5aD**)
Yield 91.7%; IR 3110, 3080, and 3050 (Ar-H), 1720 (COO), 1530 and 1353 (NO_2), and 722 cm^{-1} (Ar-H); ^1H NMR δ 8.22 (4H, s, $C_6H_4NO_2$), 2.42 (4H, 2t, $CH_2CH_2SCH_3$), 2.02 (3H, s, SCH_3), 1.80 (3H, s, C=C-CH_3), 2.10-1.70 (6H).

2-(3-Methylthiopropyl)-3-methyl-2-cyclohexenyl *p*-Nitrobenzoate (**5bH**)
Yield 86.3%; IR 3105, 3070, and 3050 (Ar-H), 1730 (COO), 1525 and 1345 (NO_2), and 722 cm^{-1} (Ar-H); ^1H NMR δ 8.17 (4H, s, $C_6H_5NO_2$), 5.53 (1H, br.s, CHOPNB), 2.40 (2H, t, J=7Hz, CH_2SCH_3), 1.97 (3H, s, SCH_3), 1.78 (3H, s, C=C-CH_3), 2.20-2.00 and 1.70-1.20 (10H).

1-Deuterio-2-(3-methylthiopropyl)-3-methyl-2-cyclohexenyl *p*-Nitrobenzoate (**5bD**)
Yield 93.9%; IR 3110, 3080, and 3050 (Ar-H), 1705 (COO), 1525 and 1350 (NO_2) and 722 cm^{-1} (Ar-H); ^1H NMR δ 8.13 (4H, s, $C_6H_4NO_2$), 2.37 (2H, t, J=7Hz, CH_2SCH_3), 1.95 (3H, s, SCH_3), 1.77 (3H, s, C=C-CH_3), 2.20-2.00 and 1.70-1.40 (10H).

2-(6-Methylthiohexyl)-3-methyl-2-cyclohexenyl *p*-nitrobenzoate (**5cH**)
Yield 94.8%; IR 3100, 3080, and 3050 (Ar-H), 1715 (COO), and 722 cm^{-1} (Ar-H); ^1H NMR δ 8.10 (4H, s, $C_6H_4NO_2$), 5.49 (1H, br.s, CHOPNB), 2.33 (2H, t, J=6.5Hz, CH_2SCH_3), 1.98 (3H, s, SCH_3), 1.73 (3H, s, C=C-CH_3), 1.70-1.10 (16H).

1-Deuterio-2-(6-methylthiohexyl)-3-methyl-2-cyclohexenyl *p*-Nitrobenzoate (**5cD**)
Yield 91.2%; IR 31120, 3080, and 3050 (Ar-H), 1705 (COO), 1525 and 1350 (NO_2), and 722 cm^{-1} (Ar-H); ^1H NMR δ 8.07 (4H, s, $C_6H_4NO_2$), 2.38 (2H, t, J=6.5Hz), 2.02 (3H, s, SCH_3), 1.73 (3H, s, SCH_3), 1.73 (3H, s, C=C-CH_3), 1.57-1.20 (16H).

2-(2-Benzylthioethyl)-3-methyl-2-cyclohexenyl *p*-Nitrobenzoate (**6aH**):
Yield 90%; IR 3110, 3060, and 3030 (Ar-H), 1750 (COO), 1530 and 1350 (NO_2), 1120 (C-O), 722 and 702 cm^{-1} (Ar-H); ^1H NMR δ 8.08 (4H, s, *p*-$O_2NC_6H_4$), 7.10 (5H, s, C_6H_5), 5.47 (1H, s, CHOPNB), 3.58 (2H, S, CH_2Ph), 1.72 (3H, s, C=C-CH_3), 2.33-1.80 and 1.50-0.90 (10H).

Anal. Calcd. for $C_{23}H_{25}NO_4S$·	C, 67 13;	H, 6.02; N, 3.40; S, 7.79
Found:	C, 67.30;	H, 6.08; N, 3.31; S, 7.65

2-(2-Benzylthioethyl)-1-deuterio-3-methyl-2-cyclohexyl *p*-nitrobenzoate (**6aD**)
Yield 89.8%; IR 3105, 3080, 3060, and 3030 (Ar-H), 1720 (COO), 1525 and 1360 (NO_2), 722 and 704 cm^{-1} (Ar-H); ^1H NMR δ 8.08 (4H, s, $C_6H_4NO_2$), 7.08 (5H, s, C_6H_5), 3.60 (2H, s, CH_2Ph), 2.30 (4H, 2t, CH_2CH_2SBz), 1.68 (3H, s, C=C-CH_3), 2.20-1.80 (6H).

2-(3-Benzylthiopropyl)-3-methyl-2-cyclohexenyl *p*-nitrobenzoate (**6bH**)
Yield 92.3%; IR 3110, 3080, 3060, and 3025 (Ar-H), 1740 (COO), 1530 and 1350 (NO_2), 722 and 702 cm^{-1} (Ar-H); ^1H NMR δ 8.08 ($C_6H_4NO_2$), 7.12 (5H, s, C_6H_5), 5.45 (1H, s, CHOPNB), 3.55 (2H, s, CH_2Ph), 1.67 (3H, s, C=C-CH_3), 2.40-1.10 (8H).

2-(3-Benzylthiopropyl)-1-deuterio-3-methyl-2-cyclohexenyl *p*-nitrobenzoate (**6bD**)
Yield 89.6%; IR 3105, 3080, 3050, and 3020 (Ar-H), 1715 (COO), 1527 and 1350 (NO_2), 722 and 705 cm^{-1} (Ar-H); ^1H δ 8.19 (4H, s, $C_6H_4NO_2$), 7.20 (5H, s, C_6H_5), 3.57 (2H, s, CH_2Ph), 1.72 (3H, s, C=C-CH_3), 2.40-1.85 and 1.50-1.10 (8H).

2-(6-Benzylthiohexyl)-3-methyl-2-cyclohexenyl *p*-nitrobenzoate (**6cH**)
Yield 80.5%; IR 3085, 3060 and 3020 (Ar-H), 1715 (COO), 1525 and 1345 (NO_2),

750, 722, and 705 cm^{-1} (Ar-H); ^1H NMR δ 8.08 (4H, s, $C_6H_4NO_2$), 7.10 (5H, s, C_6H_5), 5.43 (1H, s, CHOPNB), 3.50 (2H, s, CH_2Ph), 1.70 (3H, s, C=C-CH_3), 2.28-1.80 and 1.50-1.00 (18H).

2-(6-Benzylthiohexyl)-1-deuterio-3-methyl-2-cyclohexenyl *p*-nitrobenzoate (**6cD**)

Yield 80.5%; IR 3105, 3080, 3055, and 3025 (Ar-H), 1715 (COO), 1525 and 1351 (NO_2), 722 and 702 cm^{-1} (Ar-H); ^1H NMR δ 8.10 (4H, s, $C_6H_4NO_2$); 7.12 (5H, s, C_6H_5), 3.49 (2H, s, CH_2Ph), 1.67 (3H, s, C=C-CH_3), 2 28-1.80 and 1.50-1.00 (18H).

Kinetic Measurements

Reaction rates were measured by a continuous automatic potentiometric titration of the liberated acid by means of a pH-stat (Radiometer, Copenhagen). In each measurement ca. 0.03 mmol of the substrate was dissolved in 15 mL of solvent and the liberated *p*-nitrobenzoic acid was titrated with 0.025 M NaOH solution in the same solvent. The data were directly collected with an on-line interface on memory of Apple-II+ computer. The solvolyses were followed up to a minimum of two half-lives of the slowest step in the reaction chain. In all cases at least a hundred points were collected.

The Evaluation of Kinetic Data

Kinetic data were analyzed by computer programs for Apple-II computers. Three kinetic models were applied in fitting all data obtained:

Model A:

$$A \xrightarrow{k} \text{products}$$

$$X = a\,(1 - e^{-k\,(t + b)}) \qquad (4)$$

Model B:

$$A \xrightarrow{k_2} B \xrightarrow{k_3} \text{products}$$

$$x = a\left[1 - \frac{k_2}{k_2 - k_3}\, e^{-k_3\,(t + b)} + \frac{k_3}{k_2 - k_3}\, e^{-k_2\,(t + b)}\right] \qquad (5)$$

Model C:

$$A \xrightarrow{k_2} B, \quad A \xrightarrow{k_1} \text{products}, \quad B \xrightarrow{k_3} \text{products}$$

$$x = a\left[1 - \frac{k_1 - k_2}{k_1 - k_3 + k_2}\, e^{-(k_1 + k_2)\,(t + b)} - \frac{k_2}{k_1 - k_3 + k_2}\, e^{-k_3\,(t + b)}\right] \qquad (6)$$

For kinetic data that follow equations (5) and (6), nonlinear least squared error curve fits were performed. Data were analyzed with available subprograms for curve fitting in "Passage", and "Kaleida Graph" programs for Macintosh and on 486 IBM PC with Math-Card. Uncertainties are standard deviations of the mean for five to ten separate runs.

Product Studies

Esters **6a** and **6b** (6.8 mmol) were solvolyzed in nitrogen atmosphere in 80% EtOH (220 mL) at 50.0 + 0.1°C under the same conditions as in our kinetic measurements, but for about 20 half-lives. The products were extracted with n-pentane (3 x 200 mL), the combined organic solvents were dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The product mixture was separated by column chromatography and thin-layer chromatography on silica gel. The structures of products were determined by IR and ^{1}H NMR, as well as by comparison with previously identified compounds.

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