Tetrahedron Vol. 43, No. 1, pp. 179 to 189, 1987
Printed in Great Britain

0040-4020/87 $5.00+.00
Pergamon Journals Ltd.

SOLVOLYSIS OF 2-(ω-ALKOXYALKYL)-3-METHYL-2-CYCLOHEXENYL p-NITROBENZOATES. SEARCH FOR NEIGHBORING OXYGEN PARTICIPATION

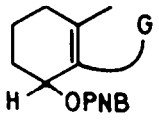
MLADEN LADIKA, BRANKO JURŠIĆ, AND DIONIS E. SUNKO*

Laboratory of Organic Chemistry, Faculty of Science,
University of Zagreb, Strossmayerov trg 14,
41000 Zagreb, Yugoslavia

(*Received in UK* 3 *November* 1986)

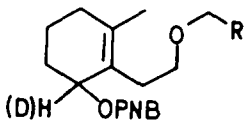
ABSTRACT. - The degree of alkoxy group participation in the solvolysis of allylic p-nitrobenzoates with an ω-alkoxyalkyl side-chain at C-2 center was studied. In 80% EtOH the solvolysis rates, secondary α-deuterium isotope effects, and the product composition show that, contrary to π-participation, neighboring oxygen interacts to a certain degree in the rate-determining step of solvolysis when a six-membered oxygen-containing ring can be formed. In all other cases, and also when 97% CF_3CH_2OH was used as a solvent, no oxygen participation could be detected.

In our previous investigations[1] of possible neighboring group participation in allyl derivatives, various 3-methyl-2-cyclohexenyl p-nitrobenzoates 1 with an internal nucleophile G in the 2-substituted side chain were studied.

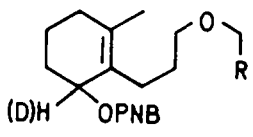


1

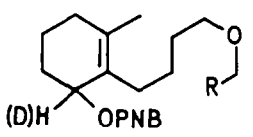
In case where G is weakly nucleophilic double[1a] or triple bond,[1b] the absence of π-participation was demonstrated. However, with an alkylthio group as a strong nucleophile and with the proper length of the 2-substituted side chain to enable the closure of a five- or six-membered ring, neighboring sulfur participation was observed.[1c] It is reflected in the formation of rearranged and cyclic products, and in complex kinetics which includes formation of an intermediate cyclyc sulfonium cation. For substrates with dialkylamino group G similar results were obtained.[1d] Between these groups which represent extremes in nucleophilic strength lies the alkoxy group as a moderate nucleophile.[2] Our recent study[1e] of the solvolysis of ester 2a showed that the methoxy group does not assist the ionization. In this work the solvolyses of 2-(ω-alkoxyalkyl) derivatives 2 - 4 and the reference esters 5 were studied in order to investigate the possible n-participation of an alkoxy group in more details.



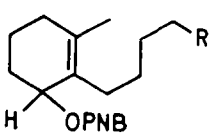
2a, R = H
b, R = C_6H_5



3a, R = H
b, R = C_6H_5



4a, R = H
b, R = C_6H_5



5a, R = H
b, R = C_6H_5

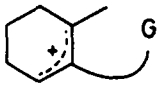
RESULTS

p-Nitrobenzoates 2 - 5 were prepared by appropriate modification[1a,e] of published procedures (see Experimental section).[3,4] Solvolyses of these esters were accomplished in 97 wt % 2,2,2-trifluoroethanol (TFE) at 25°C and 80 vol % ethanol at 50°C. The rates were measured potentiometrically at a constant pH. Clear first-order kinetic behavior was observed in all cases. The kinetic results are presented in Table I.

For product studies esters 2b and 3b were also solvolyzed under identical conditions as for the kinetic runs. The results are summarized in Table II.

DISCUSSION

The solvolyses of p-nitrobenzoates 2 - 4 in 97% TFE at 25°C show solvolysis rate retardation in comparison with the solvolyses of reference esters 5, due to the electron-withdrawing inductive effect of the ethereal group. Log k values for solvolyses of esters 2a - 4a, as well as 2b - 4b in 97% TFE at 25°C show good linear correlation (correlation coefficients are 0.977 and 0.987, respectively) with the logarithm of the number of C-atoms between the side-chain oxygen and the leaving group. The observed regularity in solvolytic behavior confirms that all of these esters solvolyze in 97% TFE via allyl cation 9 (G = OCH_3 or $OCH_2C_6H_5$), which was found[1] to be the reaction intermediate in the solvolysis of esters with various other nucleophiles G.



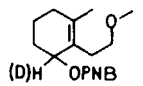
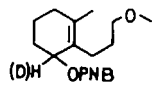
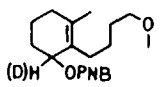
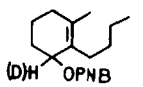
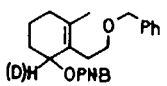
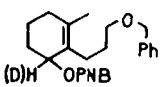
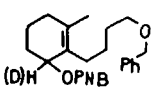
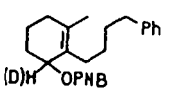
9

The observed difference in reactivity of the reference esters 5a and 5b in 97% TFE is probably due to the retardative electron-withdrawing inductive effect of phenyl group in the side chain of ester 5b, similarly to the effect of the side--chain double or triple CC bond in esters 1[1a,b]

The normal values of secondary α-deuterium isotope effects[5-7] for the solvolysis of p-nitrobenzoates 2 - 4 in 97% TFE (1.20-1.25; Table I) are also keeping with the proposed mechanism according to which n-participation is not revealed in ionization of these esters.

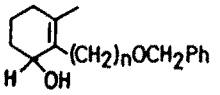
For the solvolysis of p-nitrobenzoates 2 - 4 in 80% EtOH at 50°C, the diversity of solvolytic mechanisms was observed. The esters 2a and 2b show again solvolysis rate retardation in comparison with the rates of the reference esters 5a and 5b, respectively, but these retardations are not so pronounced as in 97% TFE[1a].

Table I. Rates and Secondary α-Deuterium Kinetic Isotope Effects in Solvolysis of 2-(-Alkyloxyalkyl)-3-methyl-2--cyclohexenyl p-Nitrobenzoates

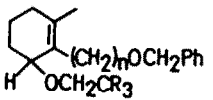
Ester		97% TFE; 25°C			80% EtOH; 50°C		
		10^4 k, s^{-1}[a]	k_{rel}	k_H/k_D	10^4 k, s^{-1}[a]	k_{rel}	k_H/k_D
2a		2.21 ± 0.01	0.118	1.218 ± 0.009[c]	2.30 ± 0.02[c]	0.782	1.20 ± 0.02[c]
3a		4.145 ± 0.007	0.220	1.216 ± 0.003	2.956 ± 0.007	1.007	1.185 ± 0.005
4a		7.56 ± 0.02	0.400	1.214 ± 0.005	2.78 ± 0.01	0.946	1.217 ± 0.005
5a		18.79 ± 0.06[b]	1.000	1.190 ± 0.008	2.94 ± 0.01[b]	1.000	1.19 ± 0.02[b]
2b		2.51 ± 0.02	0.247	1.25 ± 0.01	1.86 ± 0.02	0.788	1.24 ± 0.02
3b		4.72 ± 0.02	0.465	1.23 ± 0.02	2.68 ± 0.02	1.136	1.164 ± 0.008
4b		7.88 ± 0.01	0.775	1.198 ± 0.005	2.59 ± 0.02	1.055	1.21 ± 0.02
5b		10.16 ± 0.06	1.000	1.229 ± 0.007	2.359 ± 0.004	1.000	1.194 ± 0.002

[a]The rate constants correspond to undeuterated esters. [b]Reference 1a. [c]Reference 1e.

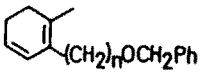
Table II. Solvolysis Products of 2-(2-Benzyloxyethyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (2b) and 2-(3-Benzyloxypropyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (3b)



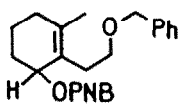
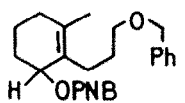
6bH, n=2
dH, n=3



7a, n=2, R=F
b, n=3, R=F
c, n=2, R=H
d, n=3, R=H



8a, n=2
b, n=3

Ester	Reaction Conditions[a]	Products, %		
		6	7	8
2b 	97T; 25°C	48[b]	47[b,d]	4[b]
	80E; 50°C	48[b]	45[b,e]	5[b]
3b 	97T; 25°C	46[c]	49[c,d]	4[c]
	80E; 50°C	58[c]	30[c,e]	11[c]

[a] 97T is 97 wt % aqueous 2,2,2-trifluoroethanol and 80E is 80 vol % aqueous ethanol. [b] n = 2. [c] n = 3. [d] R = F. [e] R = H.

The normal values of α-deuterium effects[5-7] of esters 2a and 2b in 80% EtOH (1.20 and 1.24, respectively; Table I) confirm that the neighboring ethereal group does not participate in ionization of these esters

However, ester 3b solvolyzes in 80% EtOH at 50°C significantly faster than the reference ester 5b, whereas p-nitrobenzoates 3a and 4b under the same conditions solvolyze slightly faster than the reference esters 5a and 5b, respectively. As in various other cases[5,7], secondary α-deuterium isotope effects were shown to be valuable mechanistic probes in determining whether in these solvolyses neighboring group participation is present or not. The p-nitrobenzoate 3a shows in 80% EtOH at 50°C slightly reduced value of α-deuterium isotope effect (1.185), whereas the effect for ester 3b is even significantly reduced (1.164). This is a strong indication of oxygen participation in the ionization step of esters 3a and 3b.

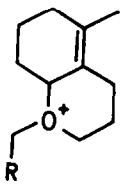
For solvolyses of esters 4a and 4b in 80% EtOH at 50°C the normal values of secondary α-deuterium isotope effects were observed (Table I), confirming that n-participation is not revealed in ionization of these esters. The slightly increased reactivity of ester 4b relative to 5b is probably due to the inadequate choice of reference ester for comparison of solvolytic data.

If the log k values for solvolyses of esters 2a - 4a, as well as 2b - 4b in 80% EtOH at 50°C are plotted against the logarithm of the number of C-atoms between the side-chain oxygen and the leaving group, deviations from linearity were observed. Presuming that esters 2a, 2b, 4a, and 4b solvolyze without any oxygen participation, the k_s constants (i.e. the rate constants for the hypothetical process which excludes n-participation)for esters 3a and 3b were calculated to be $2.48 \times 10^{-4} s^{-1}$ and $2.17 \times 10^{-4} s^{-1}$, respectively. The percentage of participation can be calculated from the relation (1)

$$k = k_s + k_\Delta \qquad (1)$$

where k is the observed rate constant, and k_Δ is the fraction of solvolytic process which includes participation.[8] Using this relation the approximative percentage of n-participation in the solvolyses of esters 3a and 3b in 80% EtOH were calculated to be 16% and 19%, respectively.

It is interesting to note that this participation is reflected only in the kinetic behavior, and not in the product composition (Table II). Esters 2b and 3b in either 97% TFE or 80% EtOH give only products of direct substitution or elimination, whereas rearranged products or bicyclic ethers were not detected. These results, as well as the fact that for solvolyses of esters 3a and 3b in 80% EtOH clear first-order kinetic behavior was observed, indicate that the cyclic oxonium cation 10 (R = H or C_6H_5) is not an intermediate in these solvolyses.



10

Esters 3a and 3b solvolyze in 80% EtOH via a single pathway which probably includes weak participation of a side-chain ethereal groups in the transition state leading to intermediate allyl cation 9. In these solvolyses ethereal groups compete with the allylic double bond for the participation in the ionization step. Such behavior was observed only in the case of esters 3 were a six-membered cyclic transition state is formed by oxygen participation, but not in the case of

esters 2 and 4 which would give a five- and seven-membered cyclic transition state, respectively. This result is peculiar because in various systems n-participation od alkoxy groups which leads to the formation of a five-membered oxygen-containing ring (RO-5) is very favorable and often superior to the formation of oxonium ions of other ring sizes.[6-13] In partly-planar rigid systems, six-membered rings seem to be favored relative to five-membered ones.

It seems that in the solvolysis of ester 2 the oxygen participation and formation of a five-membered cyclic transition state is prevented by the fact that placing the side-chain oxygen in a position which enables effective directionality of oxygen orbitals for participation causes a prohibitive strain due to severe structural deformations.[14] In the case of esters 3 the side chain is sifficiently long to enable the low-strained conformation of the transition state with oxygen orbitals in a favorable orientation for participation. These results are in contrast to the observed neighboring sulfur participation and formation of a five--membered cyclic sulfonium ion as the intermediate in the solvolysis of substrates 1 with the 2-alkylthioethyl side chain.[1c] Sulfur with its large size and polarizable electrons seems to be better able than oxygen to accommodate a bent trajectory necessary for formation of a five-membered cyclic structures.[15]

It is known[16] that benzyloxy substrates are prone to cleavage of $C_6H_5CH_2$-O bond in oxonium cations. Therefore, in the case that esters 2b - 4b solvolyze with the neighboring oxygen participation via cyclic oxonium cation as the intermediate, these esters should be expected to give a considerable amount of bicyclic ethers as solvolytic products, and to solvolyze significantly faster than their methoxy counterparts 2a - 4a. However, not only for 2b but also for 3b which solvolyze with some degree of n-participation, the formation of such bicyclic ethers was not observed (Table II). This result, as well as the similarity in kinetic data of substrates 2a - 4a and 2b - 4b with the methoxy and benzyloxy group in the side chain, respectively (Table I), additionally confirm that the cyclic oxonium cation is not included in these solvolyses as reaction intermediate.*

Finally, it is important to discuss the difference in solvolytic behavior of esters 2 - 4 in 97% TFE with that in 80% EtOH, which was also observed in our previous investigations.[1e] TFE can form strong hydrogen bonds with the side chain ethereal group,[17] making it ineffective for participation as internal nucleophile. On the contrary, EtOH is a weak proton donor which cannot form strong hydrogen bonding with the ethereal group, thus leaving the lone-pair electrons on the side--chain oxygen in esters 3a and 3b effective for n-participation.

EXPERIMENTAL

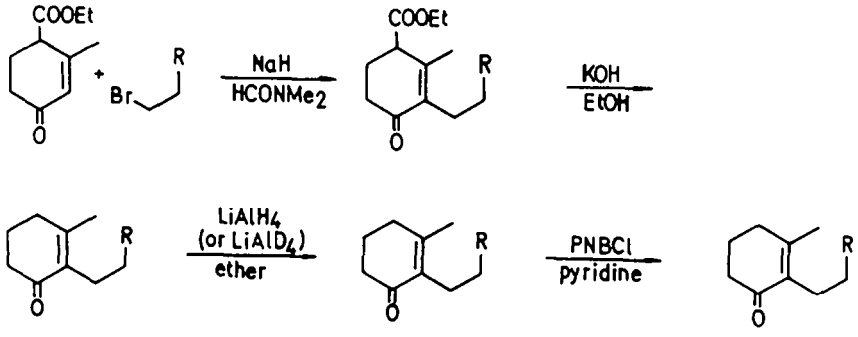
Infrared spectra of neat samples were recorded on a Perkin-Elmer 257 spectrometer. ^{1}H NMR spectra of samples dissolved in tetrachloromethane were recorded on Varian EM-360 or T-60 spectrometers, with tetramethylsilane as internal standard. All reported yields are isolated yields. For ketones 11 yields are from ethyl 2--methyl-4-keto-2-cyclohexenecarboxylate. All deuterated compounds have deuterium content >98% d_{11} (by ^{1}H NMR). All new compounds were oily liquids and were characterized by ^{1}H NMR and IR spectroscopy and in some cases also by elemental analysis.

Synthesis of Compounds

Following the published procedures[1a,e,3,4] p-nitrobenzoates 2 - 5 were prepared according to Scheme 1.

*We agree with the comment of a referee who suggested that the loss of $PhCH_2^+$ from BzO^+R_2 is expected if R is an ordinary alkyl group. Here one R is a tetraalkylated allyl group, which might well be lost more easily.

The synthesis and spectral identification of 2-(2-methoxyethyl)-3-methyl-2-cyclohexenone (11a), 2-butyl-3-methyl-2-cyclohexenone (11g), 2-(2-methoxyethyl)-3-methyl-2-cyclohexenol (6aH), 1-deuterio-2-(2-methoxyethyl)-3-methyl-2-cyclohexenol (6aD), 2-butyl-3-methyl-2-cyclohexenol (6gH), 2-butyl-1-deuterio-3-methyl-2-cyclohexenol (6gD), 2-(2-methoxyethyl)-3-methyl-2-cyclohexenyl p-nitrobenzoate (2aH), 1-deuterio-2-(2-methoxyethyl)-3-methyl-2-cyclohexenyl p-nitrobenzoate (2aD), 2-butyl-3-methyl-2-cyclohexenyl p-nitrobenzoate (5aH), and 2-butyl-1-deuterio-3-methyl-2-cyclohexenyl p-nitrobenzoate (5aD) were reported previously.[1a,e]



11a, R=OCH_3	6a, R=OCH_3	2a, R=OCH_3
b, R=$OCH_2C_6H_5$	b, R=$OCH_2C_6H_5$	b, R=$OCH_2C_6H_5$
c, R=CH_2OCH_3	c, R=CH_2OCH_3	c, R=CH_2OCH_3
d, R=$CH_2OCH_2C_6H_5$	d, R=$CH_2OCH_2C_6H_5$	d, R=$CH_2OCH_2C_6H_5$
e, R=$(CH_2)_2OCH_3$	e, R=$(CH_2)_2OCH_3$	e, R=$(CH_2)_2OCH_3$
f, R=$(CH_2)_2OCH_2C_6H_5$	f, R=$(CH_2)_2OCH_2C_6H_5$	f, R=$(CH_2)_2OCH_2C_6H_5$
g, R=CH_2CH_3	g, R=CH_2CH_3	g, R=CH_2CH_3
h, R=$(CH_2)_2C_6H_5$	h, R=$(CH_2)_2C_6H_5$	h, R=$(CH_2)_2C_6H_5$

PNB = p-nitrobenzoyl

Scheme 1

2-(2-Benzyloxyethyl)-3-methyl-2-cyclohexenone (11b)

Yield = 25.7%; IR 3090, 3060, and 3030 (Ar-H), 1662 (C=O), 1630 (C=C), 1105 (C-O-C), 742 and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.24 (5H, s, C_6H_5), 4.43 (2H, s, $ArCH_2$), 3.40 (2H, t, J = 6.5 Hz, OCH_2CH_2), 2.55 (2H, t, J = 6.5 Hz, OCH_2CH_2), 1.92 (3H, s, $C=C-CH_3$), 1.40-2.27 (6H).

2-(3-Methoxypropyl)-3-methyl-2-cyclohexenone (11c)

Yield = 30.0%; IR 1665 (C=O), 1630 (C=C), 1120 cm^{-1} (C-O-C); ^1H NMR δ 3.25 (2H, t, J = 6.5 Hz, OCH_2), 3.22 (3H, s, OCH_3), 1.92 (3H, s, $C=C-CH_3$), 1.20-2.40 (10H).

Anal. Calcd. (%) for $C_{11}H_{18}O_8$: C, 72.49; H, 9.95.
Found (%): C, 72.71; H, 9.99.

2-(3-Benzyloxypropyl)-3-methyl-2-cyclohexenone (11d)

Yield = 32.3%; IR 3090, 3060, and 3030 (Ar-H), 1665 (C=O), 1630 (C=C), 1105 (C-O-C), 742 and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.23 (5H, s, C_6H_5), 4.38 (2H, s, $ArCH_2$), 3.37 (2H, t, J = 6.5 Hz, OCH_2CH_2), 1.87 (3H, s, C=C-CH), 1.28-2.45 (10H).

Anal. Calcd. (%) for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58.
Found (%): C, 79.08; H, 8.79.

2-(4-Methoxybutyl)-3-methyl-2-cyclohexenone (11e)

Yield = 17.0%; IR 1.665 (C=O), 1630 (C=C), 1120 cm^{-1} (C-O-C); ^1H NMR δ 3.25 (2H, t, J = 6.5 Hz, OCH_2), 3.22 (3H, s, OCH_3), 1.90 (3H, s, $C=C-CH_3$), 1.25-2.33 (12H).

Anal. Calcd. (%) for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27.
Found (%): C, 73.41; H, 10.05.

2-(4-Benzyloxybutyl)-3-methyl-2-cyclohexenone (11f)

Yield = 20.3%; IR 3090, 3060, and 3030 (Ar-H), 1665 (C=O), 1630 (C=C), 1110 (C-O-C), 742 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.13 (5H, s, C_6H_5), 4.37 (2H, s, $ArCH_2$), 3.37 (2H, t, J = 6.5 Hz, OCH_2CH_2), 1.85 (3H, s, C=C-CH_3), 1.25-2.30 (12H).
Anal. Calcd. (%) for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88.
Found (%): C, 79.39; H, 8.74.

3-Methyl-2-(4-phenylbutyl)-2-cyclohexenone (11h)

Yield = 28.1%; IR 3080, 3055, and 3025 (Ar-H), 1660 (C=O), 1630 (C=C), 748 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.07 (5H, s, C_6H_5), 2.57 (2H, t, J = 7.0 Hz, $ArCH_2$), 1.83 (3H, s, C=C-CH_3), 0.93-2.32 (11H).
Anal. Calcd. (%) for $C_{17}H_{22}O$: C, 84.25; H, 9.15.
Found (%): C, 84.19; H, 9.24.

2-(2-Benzyloxyethyl)-3-methyl-2-cyclohexenol (6bH)

Yield = 93.9%; IR 3400 (O-H), 3090, 3060, and 3030 (Ar-H), 1105 and 1080 (C-O), 742 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.17 (5H, s, C_6H_5), 4.45 (2H, s, $ArCH_2$), 3.75-3.95 (1H, broad s, O-CH), 3.41 (2H, t, OCH_2CH_2), 3.30-3.35 (1H, broad s, OH), 1.57 (3H, s, C=C-CH_3), 1.60-2,60 (8H).

2-(2-Benzyloxyethyl)-1-deuterio-3-methyl-2-cyclohexenol (6bD)

Yield = 92.7%; IR 3400 (O-H), 3090, 3060, and 3030 (Ar-H) 2130 (C-D), 1105 and 1080 (C-O), 745 and 705 cm^{-1} (Ar-H); ^{1}H NMR δ 7.17 (5H, s, C_6H_5), 4.41 (2H, s, $ArCH_2$), 3.41 (2H, t, OCH_2CH_2), 3.30-3.35 (1H, broad s, OH), 1.54 (3H, s, C=C-CH_3), 1.83-2.60 (8H).

2-(3-Methoxypropyl)-2-cyclohexenol (6cH)

Yield = 90.4%; IR 3400 (O-H), 1120 and 1080 cm^{-1} (C-O); ^{1}H NMR δ 3.77-4.05 (1H, broad s, O-CH), 3.28 (2H, t, J = 6.0 Hz, OCH_2), 3.25 (3H, s, OCH_3), 2.43 (1H, broad s, OH), 1.60 (3H, s, C=C-CH_3), 1.15-2,17 (10H).

1-Deuterio-2-(3-methoxypropyl)-3-methyl-2-cyclohexenol (6cD)

Yield = 93.3%; IR 3400 (O-H), 2120 (C-D), 1120 and 1080 cm^{-1}(C-O); ^{1}H NMR δ 3.31 (2H, t, J = 6.0 Hz, OCH_2), 3.27 (3H, s, OCH_3), 2.47 (1H, broad s, OH), 1.60 (3H, s, C=C-CH_3), 1.15-2,23 (10H).

2-(3-Benzyloxypropyl)-3-methyl-2-cyclohexenol (6dH)

Yield = 93.3%; IR 3390 (O-H), 3090, 3060, and 3030 (Ar-H), 1105 and 1080 (C-O), 740 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.07 (5H, s, C_6H_5), 4.38 (2H, s, $ARCH_2$), 3.75-4.00 (1H, broad s, O-CH), 3.39 (2H, t, J = 6.0 Hz, OCH_2CH_2), 3.00 (1H, broad s, OH), 1.58 (3H, s, C=C-CH_3), 1.20-2.30 (10H).

2-(3-Benzyloxypropyl)-1-deuterio-3-methyl-2-cyclohexenol (6dD)

Yield = 92.6%; IR 3390 (O-H), 3090, 3060, and 3030 (Ar-H), 2130 (C-D), 1105 and 1080 (C-O), 740 and 700 cm^{-1} (Ar-H); ^{1}H NMR δ 7.13 (5H, s, C_6H_5), 4.38 (2H, s, $ArCH_2$), 3.38 (2H, t, J = 6.0 Hz, OCH_2CH_2), 2.70 (1H, broad s, OH), 1.58 (3H, s, C=C-CH_3), 1.20-2.30 (10H).

2-(4-Methoxybutyl)-3-methyl-2-cyclohexenol (6eH)

Yield = 92.9%; IR 3390 (O-H), 1120 and 1080 cm^{-1} (C-O); ^{1}H NMR δ 3.74-4.03 (1H, broad s, O-CH), 3.29 (2H, t, J = 6.0 Hz, OCH_2), 3.25 (3H, s, OCH_3), 2.40 (1H, broad s, OH), 1.60 (3H, s, C=C-CH_3), 0.90-2.20 (12H).

1-Deuterio-2-(4-methoxybutyl)-3-methyl-2-cyclohexenol (6eD)

Yield = 91.4%; IR 3390 (O-H), 2130 (C-D), 1120 and 1080 cm^{-1} (C-O); ^{1}H NMR δ 3.30 (2H, t, J = 6.0 Hz, OCH_2), 3.25 (3H, s, OCH_3), 2.34 (1H, broad s, OH), 1.60 (3H, s, C=C-CH_3), 0.90-2.13 (12H).

2-(4-Benzyloxybutyl)-3-methyl-2-cyclohexenol (6fH)

Yield = 96.7%; IR 3400 (O-H), 3090, 3060, and 3030 (Ar-H), 1108 and 1080 (C-O), 742 and 700 cm^{-1} (Ar-H); ^{1}H NMR δ 7.13 (5H, s, C_6H_5), 4.38 (2H, s, $ArCH_2$), 3.70-3.93 (1H, broad s, O-CH), 3.37 (2H, t, J = 6.0 Hz, OCH_2CH_2), 3.24 (1H, broad s, OH), 1.57 (3H, s, C=C-CH_3), 1.10-2.30 (12H).

2-(4-Benzyloxybutyl)-1-deuterio-3-methyl-2-cyclohexenol (6fD)

Yield = 87.6%; IR 3400 (O-H), 3090, 3060, and 3030 (Ar-H), 2120 (C-D), 1105 and 1080 (C-O), 742 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.13 (5H, s, C_6H_5), 4.38 (2H, s, $ArCH_2$), 3.38 (2H, t, J = 6.0 Hz, OCH_2CH_2), 3.27 (1H, broad s, OH), 1.57 (3H, s, C=C-CH_3), 1.10-2.30 (12H).

3-Methyl-2-(4-phenylbutyl)-2-cyclohexenol (6hH)

Yield = 95.5%; IR 3350 (O-H), 3080, 3060, and 3030 (Ar-H), 1080 (C-O), 745 and 702 cm^{-1} (Ar-H); ^1H NMR δ 7.15 (5H, s, C_6H_5), 3.77-4.05 (1H, broad s, O-CH), 2.60 (2H, t, J = 6.5 Hz, $ArCH_2$), 2.48 (1H, broad s, OH), 1.60 (3H, s, $C=C-CH_3$), 1.10-2.25 (12H).

1-Deuterio-3-methyl-2-(4-phenylbutyl)-2-cyclohexenol (6hD)

Yield = 90.0%; IR 3350 (O-H), 3080, 3060, and 3030 (Ar-H), 2110 (C-D), 1080 (C-O), 745 and 700 cm^{-1} (Ar-H); ^1H NMR δ 7.15 (5H, s, C_6H_5), 2.57 (2H, t, J = 6.5 Hz, $ArCH_2$), 2.47 (1H, broad s, OH), 1.60 (3H, s, $C=C-CH_3$), 1.10-2.25 (12H).

2-(2-Benzyloxyethyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (2bH)

Yield = 94.6%; IR 3105, 3090, 3060, and 3030 (Ar-H), 1715 (CO-O-C), 1608 (C=C), 1528 and 1348 (NO_2), 1272, 1118, and 1103 (C-O), 735 and 700 (Ar-H, Benzyl), 722 cm^{-1} (Ar-H, p-nitrobenzoyl); ^1H NMR δ 8.06 (4H, s, $p-O_2N-C_6H_4$), 7.08 (5H, s, C_6H_5), 5.37-5.67 (1H, broad s, O-CH), 4.37 (2H, s, $ArCH_2$), 3.44 (2H, t, J = 6.0 Hz, OCH_2CH_2), 2.37 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.73 (3H, s, $C=C-CH_3$), 1.45-2.20 (6H).

Anal. Calcd. (%) for $C_{23}H_{25}NO_5$: C, 69.86; H, 6.37; N, 3.54.
Found (%): C, 69.84; H, 6.56; N, 3.54.

2-(2-Benzyloxyethyl)-1-deuterio-3-methyl-2-cyclohexenyl p-Nitrobenzoate (2bD)

Yield = 92.5%; IR 3110, 3090, 3060, and 3030 (Ar-H), 1720 (CO-O-C), 1608 (C=C), 1530 and 1353 (NO_2), 1290, 1108, and 1103 (C-O), 740 and 702 (Ar-H, benzyl), 722 cm^{-1} (Ar-H, p-nitrobenzoyl): ^1H NMR δ 8.07 (4H, s, $p-O_2N-C_6H_4$), 7.12 (5H, s, C_6H_5), 4.37 (2H, s, $ArCH_2$), 3.42 (2H, t, J = 6.0 Hz, OCH_2CH_2), 2.35 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.75 (3H, s, $C=C-CH_3$), 1.45-2.20 (6H).

2-(3-Methoxypropyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (3aH)

Yield = 85.5%; IR 3105, 3080, and 3050 (Ar-H), 1715 (CO-O-C), 1608 (C=C), 1530 and 1350 (NO_2), 1275, 1120, and 1105 (C-O), 722 cm^{-1} (Ar-H); ^1H NMR δ 8.10 (4H, s, $p-O_2N-C_6H_4$), 5.37-5.67 (1H, broad s, O-CH), 3.25 (2H, t, J = 6.0 Hz, OCH_2), 3.20 (3H, s, OCH_3), 1.76 (3H, s, $C=C-CH_3$), 1.42-2.45 (10H).

1-Deuterio-2-(3-methoxyprcpyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (3aD)

Yield = 89.8%; IR 3105, 3075, and 3050 (Ar-H), 1715 (CO-O-C), 1608 (C=C), 1530 and 1350 (NO_2), 1285, 1118, and 1105 (C-O), 722 cm-1 (Ar-H); ^1H NMR δ 3.12 (4H, s, $p-O_2N-C_6H_4$), 3.25 (2H, t, OCH_2), 3.20 (3H, s, OCH_3), 1.75 (3H, s, $C=C-CH_3$), 1.40-2.45 (10H).

2-(3-Benzyloxypropyl)-3-methyl-2-cyclohexenyl p-nitrobenzoate (3bH)

Yield = 91.7%; IR 3105, 3090, 3060, and 3030 (Ar-H), 1717 (CO-O-C), 1610 (C=C), 1530 and 1350 (NO_2), 1270, 1117, and 1103 (C-O), 740 and 700 (Ar-H, benzyl), 722 cm^{-1} (Ar-H, p-nitrobenzoyl); ^1H NMR δ 8.07 (4H, s, $p-O_2N-C_6H_4$), 7.12 (5H, s, C_6H_5), 5.37-5.65 (1H, broad s, O-CH), 4.35 (2H, s, $ArCH_2$), 3.37 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.73 (3H, s, $C=C-CH_3$), 1.40-2.25 (10H).

Anal. Calcd. (%) for $C_{24}H_{27}NO_5$: C, 70.40; H, 6.65; N, 3.41 .
Found (%): C, 70.16; H, 6.69; N, 3.61.

2-(3-Benzoylpropyl)-1-deuterio-3-methyl-2-cyclohexenyl p-Nitrobenzoate (3bD)

Yield = 91.7%; IR 3110,3090, 3060, and 3030 (Ar-H), 1715 (CO-O-C), 1608 (C=C), 1530 and 0350 (NO_2), 1275, 1118, and 1105 (C-O), 740 and 700 (Ar-H, benzoyl), 722 cm-1 (Ar-H, p-nitrobenzoyl); ^1H NMR δ 8.10 (4H, s, $p-O_2N-C_6H_4$), 7.12 (5H, s, C_6H_5), 4.37 (2H, s, $ArCH_2$), 3.40 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.75 (3H, s, $C=C-CH_3$), 1.40-2.35 (10H).

2-(4-Methoxybutyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (4aH)

Yield = 85.8%; IR 3105, 3080, and 3050 (Ar-H), 1720 (CO-O-C), 1608 (C=C), 1530 and 1350 (NO_2), 1275, 1120, and 1105 (C-O), 722 cm^{-1} (Ar-H); ^1H NMR δ 8.10 (4H, s, $p-O_2N-C_6H_4$), 5.34-5.65 (1H, broad s, O-CH), 3.23 (2H, t, J = 6.0 Hz, COH_2CH_2), 3.08 (3H, s, OCH_3). 1.75 (3H, s, $C=C-CH_3$), 1.23-2,30 (12H).

1-Deuterio-2-(4-methoxybutyl)-3-methyl-2-cyclohexenyl p-Nitrobenzaote (4aD)

Yield = 88.7%; IR 3105, 3080, and 3050 (Ar-H), 1717 (CO-O-C), 1610 (C=C), 1530 and 1350 (NO_2), 1285, 1120, and 1105 (C-O), 722 cm-1 (Ar-H); ^1H NMR δ 8.13 (4H, s, $p-O_2N-C_6H_4$), 3.23 (2H, t, J = 6.0 Hz, OCH_2CH_2), 3.19 (3H, s, OCH_3), 1.74 (3H, s, $C=C-CH_3$), 1.20-2.30 (12H).

2-(4-Benzyloxybutyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (4bH)

Yield = 90.8%; IR 3110, 3090, 3060, and 3030 (Ar-H), 1720 (CO-O-C), 1610 (C=C), 1530 and 1350 (NO_2), 1268, 1120, and 1105 (C-O), 740 and 702 (Ar-H, Benzoyl),

723 cm^{-1} (Ar-H), p-nitrobenzoyl); ^{1}H NMR δ 8.08 (4H, s, p-O_2N-C_6H_4), 7.10 (5H, s, C_6H_5), 5.40-5.67 (1H, broad s, O-CH), 4.37 (2H, s, ArCH_2), 3.42 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.73 (3H, s, C=C-CH_3), 1.27-2.35 (12H).

2-(4-Benzyloxybutyl)-1-deuterio-3-methyl-2-cyclohexenyl p-Nitrobenzoate (4bD)

Yield = 96.4%; IR 3110, 3090, 3060, and 3030 (Ar-H), 1720 (CO-O-C), 1610 (C=C), 1530 and 1353 (NO_2), 1285, 1120, and 1108 (C-O), 742 and 702 (Ar-H), benzoyl), 723 cm-1 (Ar-H, p-nitrobenzoyl); 1H NMR δ 8.08 (4H, s, p-O_2N-C_6H_4), 7.12 (5H, s, C_6H_5), 4.33 (2H, s, ArCH_2), 3.38 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.73 (3H, s, C=C-CH_3), 1.24-2.30 (12H).

3-Methyl-2-(4-phenylbutyl)-2-cyclohexenyl p-Nitrobenzoate (5bH)

Yield = 92.0%; IR 3105, 3080, 3060, and 3030 (Ar-H), 1713 (CO-O-C), 1605 (C=C), 1527 and 1345 (NO_2), 1270, 1118, and 1105 (C-O), 750 and 702 (Ar-H, phenyl), 722 cm-1 (Ar-H, p-nitrobenzoyl); 1H NMR δ 8.10 (4H, s, p-O_2N-C_6H_4), 7.05 (5H, s, C_6H_5), 5.37-5.67 (1H, broad s, O-CH), 2.53 (2H, t, J = 6.0 Hz, ArCH_2), 1.72 (3H, s, C=C-CH_3), 1.15-2.27 (12H).

1-Deuterio-3-methyl-2-(4-phenylbutyl)-2-cyclohexenyl p-Nitrobenzoate (5bD)

Yield = 83.0%; IR 3105, 3080, 3060, and 3030 (Ar-H), 1703 (CO-O-C), 1603 (C=C), 1526 and 1350 (NO_2), 1275, 1118, and 1105 (C-O), 750 and 703 (Ar-H, phenyl), 722 cm-1 (Ar-H, p-nitrobenzoyl); 1H NMR δ 8.08 (4H, s, p-O_2N-C_6H_4), 7.03 (5H, s, C_6H_5), 2.52 (2H, t, J = 6.0 Hz, ArCH_2), 1.70 (3H, s, C=C-CH_3), 1.20-2.20 (12H).

Kinetic Measurements

Reaction rates were measured by c ntinuous automatic potentiometric titration of the released p-nitrobenzoic acid by means of a pH-stat (Radiometer, Copenhagen). In each measurement, ca. 0.03 mmol of the p-nitrobenzoate was dissolved in 15 cm3 of solvent and the released acid titrated with 0.025 M NaOH solution in the same solvent.[18]

Product Studies

Esters 2b and 3b were solvolyzed for product studies according to the published procedure[1a] and the products were separated by chromatography on silica gel.[19] The structures of products were determined by IR and ^{1}H NMR, as well as by comparison with previously identified compounds.

2-(2-Benzyloxyethyl)-1-methyl-3-(2,2,2-trifluoroethoxy)-cyclohexene (7a).

IR 3090, 3060, and 3030 (Ar-H), 1280, 1160, and 1110 (C-F), 740 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.22 (5H, s, C_6H_5), 4.42 (2H, s, OCH_2Ar), 3.75 (2H, q, J = 7.0 Hz, OCH_2CF_3), 3.40 (2H, t, J = 6.0 Hz, OCH_2CH_2), 2.50-2.75 (1H, broad s, O-CH), 2.40 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.63 (3H, s, C=C-CH_3), 1.15-2.15 (6H).

2-(3-Benzyloxypropyl)-1-methyl-3-(2,2,2-trifluoroethoxy)-cyclohexene (7b)

IR 3090, 3060, and 3030 (Ar-H), 1282, 1160, and 1110 (C-F), 740 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.23 (5H, s, C_6H_5), 4.40 (2H, s, OCH_2Ar), 3.75 (2H, q, J = 7.0 Hz, OCH_2CF_3), 3.40 (2H, t, J = 6.0 Hz, OCH_2CH_2), 2.57-2.75 (1H, broad s, O-CH), 1.62 (3H, s, C=C-CH_3), 1.20-2.60 (10H).

2-(2-Benzyloxyethyl)-3-ethoxy-1-methylcyclohexene (7c)

IR 3090, 3060, and 3030 (Ar-H), 1105 (C-O-C), 740 and 702 cm^{-1}(Ar-H); ^{1}H NMR δ 7.22 (5H, s, C_6H_5), 4.40 (2H, s, OCH_2Ar), 3.44 (2H, q, J = 7.5 Hz, OCH_2CH_3), 3.41 (2H, t, J = 6.0 Hz, OCH_2CH_2), 3.35-3.65 (1H, m, O-CH), 2.33 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.63 (3H, s, C=C-CH_3), 1.40-1.92 (6H), 1.12 (3H, t, J = 7.5 Hz, CH_2CH_3).

2-(3-Benzyloxypropyl)-3-ethoxy-1-methylcyclohexene (7d)

IR 3090, 3060, and 3030 (Ar-H), 1105 (C-O-C), 740 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.24 (5H, s, C_6H_5), 4.45 (2H, s, OCH_2Ar), 3.44 (2H, q, J = 7.5 Hz, OCH_2CH_3), 3.40 (2H, t, J = 6.0 Hz, OCH_2CH_2), 3.35-3,65 (1H, m, O-CH), 1.64 (3H,, s, C=C-CH_3), 1.41-2.20 (10H), 1.15 (3H, t, J = 7.5 Hz, CH_2CH_3).

2-(2-Benzyloxyethyl)-1-methyl-1,3-cyclohexadiene (8a)

IR 3088, 3060, and 3028 (Ar-H), 1638 and 1608 (C=C), 1105 (C-O-C), 810 (C=C-H), 740 and 702 cm-1 (Ar-H); 1H NMR δ 7.21 (5H, s, C_6H_5), 5.43-5.80 (2H, m, HC=CH), 4.45 (2H, s, OCH_2Ar), 3.50 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.77 (3H, s, C=C-CH_3), 1.25-2.68 (6H).

2-(3-Benzyloxypropyl)-1-methyl-1,3-cyclohexadiene (8b)

IR 3090, 3060, and 3030 (Ar-H), 1640 and 1605 (C=C), 1105 (C-O-C), 810 (C=C-H), 740 and 702 cm^{-1} (Ar-H); ^{1}H NMR δ 7.24 (5H, s, C_6H_5), 5.40-5.82 (2H, m, HC=CH), 4,46 (2H, s, OCH_2Ar), 3.43 (2H, t, J = 6.0 Hz, OCH_2CH_2), 1.78 (3H, s, $C=C-CH_3$), 1.33-2.67 (8H).

Acknowledgement . This work was supported by Grant JFP 545 from the National Science Foundation (U.S.) and by Grant II-21/0119 from the Research Council of Croatia (SIZ-II).

REFERENCES

1. a) M. Ladika and D.E. Sunko, J. Org. Chem., 50, 4544 (1985).
   b) M. Ladika, S. Borčić and D.E. Sunko, Croat. Chem. Acta, 57, 311 (1984).
   c) M. Ladika, B. Juršić, Z. Mihalić and D.E. Sunko, Tetrahedron Lett., 27, 1703 (1986).
   d) B. Juršić, M. Ladika, Z. Mihalić and D.E. Sunko, to be published.
   e) B. Juršić, M. Ladika and D.E. Sunko, Tetrahedron, 42, 911 (1986).
2. P. Wilder, Jr. and C.V.A. Drinnan, J. Org. Chem., 39, 414 (1974): "Oxygen is less effective than sulfur as a neighboring group owing to its greater inductive rate-retarding effect, lower ability to donate electron pairs, and smaller size that decreases overlap at a remote carbonium ion center".
3. W.S. Johnson, P.J. Neustaedter and K.K. Schmiegel, J. Am. Chem. Soc., 87, 5148 (1965).
4. J.A. Marshall, N. Cohen and A.R. Hochstetler, J. Am. Chem. Soc., 88, 3408 (1966).
5. D.E. Sunko and S. Borčić, "Isotope Effects in Chemical Reactions", ed. by C.J. Collins and N.S. Bowman, American Chemical Society, Washington, D.C., 1970, ACS Monograph No. 167, pp. 160-209.
6. R. Eliason, S. Borčić and D.E. Sunko, Croat. Chem. Acta, 51, 203 (1978).
7. I. Mihel, J. Šistek, S. Borčić, K. Humski and D.E. Sunko, J. Org. Chem., 44, 4091 (1979).
8. S. Winstein, E. Allred, R. Heck and R. Glick, Tetrahedron, 3, 1 (1958).
9. D.S. Noyce, B.R. Thomas and B.N. Bastian, J. Am. Chem. Soc., 82, 885 (1960).
10. G.T. Kwiatkowski, S.J. Kavarnos and W.D. Closson, J. Heterocycl. Chem., 2, 11 (1965).
11. E.L. Allred and S. Winstein, J. Am. Chem. Soc., 89, 3991 (1967).
12. P. Kocovsky and V. Cerny, Collect. Czech. Chem. Commun., 44, 226 (1979).
13. A.G. Constable, C.R. Langrick, B. Shabanzadeh and B.L. Shaw, Inorg. Chim. Acta, 65, L 151 (1982).
14. For an excellent discussion of the directionality of organic reactions, see: F.M. Menger, Tetrahedron, 39, 1013 (1983).
15. J.E. Baldwin, J. Cutting, W. Dupont, L. Kruse, L. Silberman and R.C. Thomas, J. Chem. Soc., Chem. Commun., 736, 1976.
16. a) G.R. Gray, F.C. Hartman and R. Barker, J. Org. Chem., 30, 2020 (1965).
   b) B. Capon, Chem. Rev., 69, 407 (1969), and references cited therein.
17. B. Juršić, M. Ladika and D.E. Sunko, Tetrahedron lett., 26, 5323 (1985).
18. For a detailed procedure see: S. Richter, I. Bregovec and D.E. Sunko, J. Org. Chem., 41, 785 (1976).
19. Products of this type are known[3] to be unstable under conditions for separation by gas chromatography.