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SOLVOLYSIS OF 2-(2-METHOXYETHYL)-3-METHYL-2-CYCLOHEXENYL p-NITROBENZOATE. A CASE OF NON-PARTICIPATION OF METHOXY GROUP

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

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

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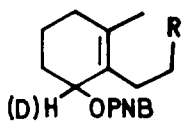
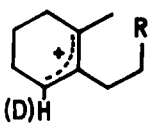
Abstract - In an attempt to study possible π-participation in allyl derivatives, 2-(2-methoxyethyl)-3-methyl-2-cyclohexenyl p-nitrobenzoate 4 was solvolyzed in various solvents including fluorinated alcohols. Its solvolysis rate is slower than that of the 2-butyl analog 3. This rate retardation can be explained by an electron-withdrawing inductive effect of methoxy group. The secondary α-deuterium isotope effect of ester 4 is normal in all the solvents investigated. These results show that the methoxy group does not assist the ionization of ester 4.

In our previous study[1] of possible π-participation in allyl derivatives, 2-alkenyl-3-methyl-2-cyclohexenyl p-nitrobenzoates 1 and 2 were solvolyzed in 97% trifluoroethanol and 80% ethanol. These esters show in both solvents a solvolysis rate retardation in comparison with the saturated analog 3, and normal values of secondary α-deuterium isotope effects (k_H/k_D = 1.17 to 1.22).



1, R = $CH{=}CH_2$
2, R = $CH{=}CMe_2$
3, R = CH_2CH_3
4, R = OCH_3



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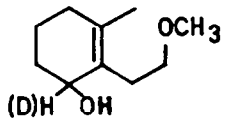
It was concluded that the side-chain double bond in esters 1 and 2 cannot participate in ionization due to its nucleophilicity which is low even in comparison with that of 97% trifluoroethanol as a solvent.[2] Consequently, these esters solvolyze via a stepwise mechanism involving the rate-determining formation of an allylic cation 5 (R = $CH{=}CH_2$ or $CH{=}CMe_2$) as reaction intermediate.

These results prompted us to investigate[3] possible n-participation in ester 4. The nucleophilicity of the methoxy group is significantly higher than that of the alkenyl group,[4] providing the opportunity for methoxy group to participate in ionization. The length of the side-chain in ester 4 was chosen in such a way that possible n-participation would involve formation of five-membered oxygen-containing ring (MeO-5) which is known[5-9] to be very favorable in various systems and often superior to the formation of oxonium ions with other ring sizes.

RESULTS AND DISCUSSION

The esters 4H and 4D were prepared from the corresponding alcohols 6H and 6D which were synthesized by reduction of ketone 7 with $LiAlH_4$ and $LiAlD_4$, respectively.



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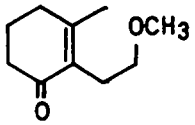

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The esters 4H and 4D, as well as the reference esters 3H and 3D, were solvolyzed in various solvents. Clear first-order kinetic behavior was observed in all solvolyses. The kinetic results are presented in Table 1.

Our results show that the neighboring methoxy group does not assist the ionization of ester 4. The solvolysis of this ester is slower than the solvolysis of reference ester 3 whatever the solvent. This result can be explained by electron-withdrawing inductive effect of methoxy group. The extent of rate-retardation, e.g. the ratio k(4)/k(3), is almost constant in various aqueous mixtures of acetone or ethanol, ranging from 0.716 to 0.897 at 20°C (Table 1). It is interesting to note that this ratio remains constant through the wide range of ionization power (Y_{OTs}) of these solvents (Figure 1). Esters 3 and 4 pre-

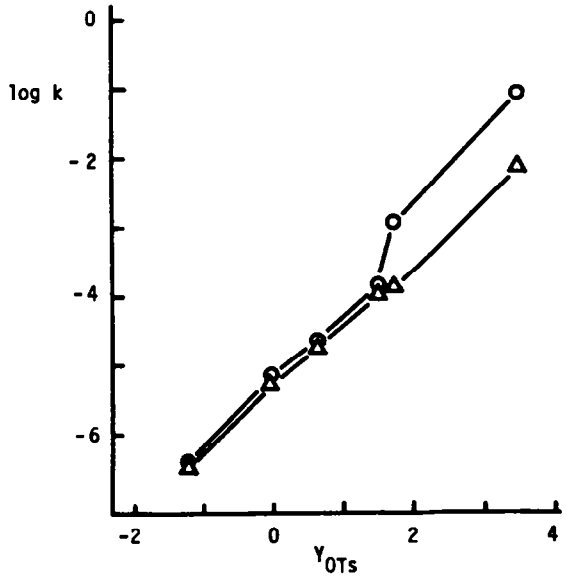

Figure 1. Plot of log k values for solvolysis of esters 3 (O) and 4 (Δ) in various solvents at 20°C against Y_{OTs}[10].

Table 1. Rates, Secondary α-Deuterium Kinetic Isotope Effects and Activation Parameters for Solvolyses of 2-Substituted-3-methyl-2-cyclohexenyl p-Nitrobenzoates 3 and 4

solvent[a]	temp. °C	k, s^{-1}	k_H/k_D	$\Delta H^{\ddagger}$ kJ mol^{-1}	$\Delta S^{\ddagger}$ J $mol^{-1}K^{-1}$	k(4)/k(3) at 20°C
		ester 3				
97 H	20	$(7.37 \pm 0.07)\times10^{-2}$				
	50	$(1.88 \pm 0.01)\times10^{-2}$				
97 T	25	$(1.879 \pm 0.006)\times10^{-3}$[b]	1.190 ± 0.008[b]	71.2 ± 0.2	-58.4 ± 0.6	
	20	1.13×10^{-3}[c]				
	50	$(3.59 \pm 0.01)\times10^{-3}$				
45 A	40	$(1.32 \pm 0.01)\times10^{-3}$		81.4 ± 1.0	-40.5 ± 3.2	
	20	1.46×10^{-4}[c]				
	50	$(7.79 \pm 0.03)\times10^{-4}$				
60 A	40	$(2.57 \pm 0.02)\times10^{-4}$		90.8 ± 0.6	-24.0 ± 2.0	
	20	2.24×10^{-5}[c]				
	65	$(1.49 \pm 0.01)\times10^{-3}$				
80 E	50	$(2.94 \pm 0.01)\times10^{-4}$[b]	1.19 ± 0.02[b]	95.7 ± 0.5	-17.1 ± 1.5	
	20	7.01×10^{-6}[c]				
	75	$(6.25 \pm 0.03)\times10^{-4}$				
96 E	60	$(1.07 \pm 0.01)\times10^{-4}$		111.4 ± 1.2	12.7 ± 3.6	
	20	4.05×10^{-7}				
		ester 4				
97 H	20	$(6.38 \pm 0.07)\times10^{-3}$	1.21			0.087
	50	$(3.35 \pm 0.01)\times10^{-3}$				
97 T	25	$(2.38 \pm 0.01)\times10^{-4}$[b]	1.218 ± 0.009[b]	81.9 ± 0.3	-39.5 ± 1.0	0.112
	20	1.33×10^{-4}[c]				
	50	$(2.83 \pm 0.02)\times10^{-3}$	1.20 ± 0.02			
45 A	40	$(1.01 \pm 0.01)\times10^{-3}$		83.9 ± 0.8	-34.7 ± 2.4	0.716
	20	1.05×10^{-4}[c]				
	50	$(6.51 \pm 0.05)\times10^{-4}$	1.21 ± 0.01			
60 A	40	$(2.09 \pm 0.04)\times10^{-4}$		93.0 ± 1.6	-18.7 ± 5.0	0.766
	20	1.71×10^{-5}[c]				
	65	$(1.20 \pm 0.01)\times10^{-3}$				
80 E	50	$(2.30 \pm 0.02)\times10^{-4}$[b]	1.20 ± 0.02	97.0 ± 0.9	-15.1 ± 2.6	0.732
	20	5.12×10^{-6}[c]				
	75	$(4.05 \pm 0.02)\times10^{-4}$	1.20 ± 0.01			
96 E	60	$(7.50 \pm 0.06)\times10^{-5}$		105.6 ± 0.6	-7.7 ± 1.8	0.897
	20	3.63×10^{-7}[c]				

[a] 97 H = 97:3 (w/w) 1,1,1,3,3,3-hexafluoro-2-propanol/water;
97 T = 97:3 (w/w) 2,2,2-trifluoroethanol/water;
45 A = 45:55 (v/v) acetone/water; 60 A similarly;
80 E = 80:20 (v/v) ethanol/water; 96 E similarly.

[b] Reference 3.

[c] Extrapolated from higher temperatures.

sumably solvolyze in all these solvents via the same mechanism which involves the formation of a solvent-separated ion pair (k_2 step[10-12]) as the rate-determining step.

On the other side, in the fluorinated solvents (97% TFE and 97% HFIP) the ratio k(4)/k(3) is considerably lower (0.118 and 0.087, respectively; Table 1). This result is peculiar because both fluorinated solvents have low nucleophilicity and high ionization power and could be expected to permit marked neighboring methoxy participation in the ionization step.[13] Two major effects can rationalize this observation. First, both these fluorinated solvents are notably more acidic[14,15] than the aqueous mixture of acetone or ethanol, and consequently they are extremely strong hydrogen-bonding donors which can form complexes with various bases.[14] Such intermolecular hydrogen-bonding of fluorinated alcohols with ethers as proton acceptors has been extensively studied by spectroscopic[14,16-22] and calorimetric methods.[14,23,24] In our case, TFE and HFIP can form strong hydrogen bonds with the side-chain methoxy group of ester 4, resulting in the increased electron-withdrawing inductive effect of methoxy group[25] and the pronounced solvolysis rate retardation of ester 4 relative to the solvolysis of ester 3. Second, the difference in solvation of esters 3 and 4 in the fluorinated solvents can be considerably larger than in the aqueous mixtures of acetone or ethanol.[26]

The obtained isotope effects are also in full agreement with the proposed mechanism of solvolysis. The ester 4 shows in all solvents a normal value of secondary α-deuterium isotope effects[27] (k_H/k_D = 1.20 to 1.22), proving the absence of even low degree of methoxy participation. With the weak neighboring group participation, anchimeric effect could be masked by a strong rate-retardating inductive effect[28], but in this case at least slightly reduced secondary α-deuterium isotope effects should be observed.

Finally, the activation parameters (Table 1) also show the similarity in solvolysis mechanisms of esters 3 and 4. Although the narrow temperature ranges in which these solvolyses were studied do not permit the precise calculation of these parameters, both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values are almost the same (within the limits of experimental error) for the solvolysis of esters 3 and 4.

In conclusion, the obtained results prove that ester 4 solvolyzes in all the solvents considered here via a stepwise mechanism which excludes the n-participation of methoxy group in ionization, but involves allylic cation 5 (R = OCH_3) as reaction intermediate.

EXPERIMENTAL

Infrared spectra of neat samples were recorder 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.

2-(2-Methoxyethyl)-3-methyl-2-cyclohexenone (7)

As described in the literature[1,29,30], ethyl 2-methyl-4-keto-2-cyclohexenecarboxylate[31] (7.28 g, 40 mmol) was alkylated by 1-bromo-2-methoxyethane (6.39 g, 46 mmol) in N,N-dimethylformamide (35 mL) with NaH (0.97 g, 40 mmol) as base. The ketoester obtained was hydrolyzed and decarboxylated with KOH (3.96 g, 71 mmol) in anhydrous ethanol (25 mL). The resulting crude product was purified on a silica gel column with benzene-ether (4:1) mixture as eluent to give ketone 7

(2.18 g, 32.4%) as a pale yellow oil: bp 54.5-56°C (0.070 mm Hg); IR 1665 (C=O), 1630 (C=C), 1110 cm^{-1} (C-O-C); ^1H NMR δ 3.19 (2H, t, J = 6.6 Hz, OCH_2), 3.18 (3H, s, OCH_3), 1.92 (3H, s, C=C-CH_3), 1.60-2.55 (8H).

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58.
Found: C, 71.45; H, 9.49.

2-(2-Methoxyethyl)-3-methyl-2-cyclohexenol (6H)

Ketone 7 (400 mg, 2.4 mmol) was reduced by $LiAlH_4$ (800 mg, 21 mmol) in anhydrous ether (20 mL) according to the previously described procedure[1,29] to give alcohol 6H (380 mg, 94%) as a colorless oil: IR 3400 (O-H), 1110 cm^{-1} (C-O-C); ^1H NMR δ 3.78 (1H, broad s, O-C-H), 3.32 (2H, t, J = 7.5 Hz, OCH_2; 3.30 (3H, s, OCH_3), 3.05 (1H, s, OH), 1.60 (3H, s, C=C-CH_3), 1.30-2.15 (8H).

1-Deuterio-2-(2-methoxyethyl)-3-methyl-2-cyclohexenol (6D)

Reduction of ketone 7 (400 mg, 2.4 mmol) with $LiAlD_4$ (800 mg, 19 mmol) in anhydrous ether (20 mL), by the same procedure as for the synthesis of the undeuterated analog, gave alcohol 6D (380 mg, 93%) as a colorless oil: IR 3390 (O-H), 2120 (C-D), 1115 cm^{-1} (C-O-C); ^1H NMR δ 3.36 (2H, t, J = 7.5 Hz, OCH_2), 3.32 (3H, s, OCH_3), 3.20 (1H, s, OH), 1.60 (3H, s, C=C-CH_3), 1.30-2.25 (8H); deuterium content >98% d_1 (by ^1H NMR).

2-(2-Methoxyethyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (4H)

Alcohol 6H (300 mg, 1.76 mmol) was esterified with p-nitrobenzoyl chloride (800 mg, 4.31 mmol) in dry pyridine (20 mL), according to our literature procedure[1]. The crude product was purified on a silica gel column with pentane as eluent to give pure (as indicated by TLC) p-nitrobenzoate 4H (545 mg, 97%): IR 3045 (Ar-H), 1718 (CO-O-C), 1607 (C=C), 1530 and 1345 (NO_2), 1116 and 1105 (C-O), 722 cm^{-1} (Ar-H); ^1H NMR δ 8.20 (4H, s, p-O_2N-C_6H_4), 5.57 (1H, s, O-C-H), 3.37 (2H, t, J = 7.0 Hz, OCH_2), 3.20 (3H, s, OCH_3), 1.77 (3H, s, C=C-CH_3), 1.45-2.45 (8H).

1-Deuterio-2-(2-methoxyethyl)-3-methyl-2-cyclohexenyl p-Nitrobenzoate (4D)

Esterification of alcohol 6D (300 mg, 1.75 mmol) with p-nitrobenzoyl chloride (800 mg, 4.31 mmol) in dry pyridine (20 mL) by the same procedure as for the synthesis of undeuterated analog, gave p-nitrobenzoate 4D (540 mg, 96%): IR 3045 (Ar-H), 1718 (CO-O-C), 1608 (C=C), 1530 and 1350 (NO_2), 1120 and 1106 (C-O), 723 cm^{-1} (Ar-H); ^1H NMR δ 8.17 (4H, s, p-O_2N-C_6H_4), 3.32 (2H, t, J = 7.0 Hz, OCH_2), 3.18 (3H, s, OCH_3), 1.77 (3H, s, C=C-CH_3), 1.45-2.45 (8H); deuterium content >98% d_1 (by ^1H NMR).

KINETIC MEASUREMENTS

Reaction rates were measured by continuous 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 mL of solvent and the released acid titrated with 0.025 M NaOH solution in the same solvent.

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REFERENCES

1. M. Ladika and D.E. Sunko, J. Org. Chem., in press.
2. W.S. Trahanovsky and M.P. Doyle, J. Am. Chem. Soc., 89, 4867 (1967): "Solvent nucleophilicity is a measure of the tendency of a solvent to attack as a nucleophile some electron-deficient center relative to the tendency of a standard nucleophile to undergo a standard nucleophilic reaction in that solvent", and "The internal olefin should be an excellent standard nucleophile since it is nonpolar and should thus not be highly solvated."
3. For a preliminary communication see: M. Ladika and D.E. Sunko, Croat. Chem. Acta, 57, 179 (1984).
4. For review see: B. Capon and S.P. McManus, Neighboring Group Participation, Vol. 1, Plenum Press, New York, 1976.
5. S. Winstein, E. Allred, R. Heck and R. Glick, Tetrahedron, 3, 1 (1968).
6. E.L. Allred and S. Winstein, J. Am. Chem. Soc., 89, 3991 (1967).
7. D.S. Noyce, B.R. Thomas and B.N. Bastian, J. Am. Chem. Soc., 82, 885 (1960).
8. G.T. Kwiatkowski, S.J. Kavarnos and W.D. Closson, J. Heterocycl. Chem., 2, 11 (1965).
9. P. Kocovsky and V. Cerny, Collect. Czech. Chem. Commun., 44, 226 (1979).
10. a) F.L. Schadt, T.W. Bentley and P.v.R. Schleyer, J. Am. Chem. Soc., 98, 7667 (1976).
    b) T.W. Bentley and G.E. Carter, J. Org. Chem., 48, 579 (1983).
11. a) P.v.R. Schleyer, J.L. Fry, L.K.M. Lam and C.J. Lancelot, J. Am. Chem. Soc., 92, 2542 (1970).
    b) V.J. Shiner, Jr., S.R. Hartshorn and P.C. Vogel, J. Org. Chem., 38, 3604 (1973).
12. a) F.G. Bordwell and T.G. Mecca, J. Am. Chem. Soc., 97, 123 (1975).
    b) F.G. Bordwell and T.G. Mecca, ibid., 97, 127 (1975).
    c) F.G. Bordwell, P.F. Wiley and T.G. Mecca, ibid., 97, 132 (1975).
13. D.J. Raber, W.C. Neal, Jr., M.D. Dukes, J.M. Harris and D.L. Mount, J. Am. Chem. Soc., 100, 8137 (1978).
14. W.J. Middleton and R.V. Lindsey, Jr., J. Am. Chem. Soc., 86, 4948 (1964).
15. B.L. Dyatkin, E.P. Mochalina and I.L. Knunyants, Tetrahedron, 21, 2991 (1965).
16. a) A. Kivinen, J. Murto and L. Kilpi, Suomen Kemi. B, 40, 301 (1967).
    b) A. Kivinen and J. Murto, ibid., 42, 190 (1969).
17. a) K.F. Purcell and S.T. Wilson, J. Mol. Spectry., 24, 468 (1967).
    b) K.F. Purcell, J.A. Stikeleather and S.D. Brunk, ibid., 32, 202 (1969).
18. A. Fratiello, R.E. Schuster, G.A. Vidulich, J. Bragin and D. Liu, J. Am. Chem. Soc., 95, 631 (1973).
19. A.A. Samoilenko, Zh. Strukt. Khim., 16, 568 (1975).
20. A.V. Iogansen, G.A. Kurkchi, V.M. Furman, V.P. Glazunov and S.E. Odinokov, Zh. Prikl. Spektr., 33, 460 (1980).
21. O. Schrems, H.M. Oberhoffer and W.A.P. Luck, J. Phys. Chem., 88, 4335 (1984).
22. B. Juršić, M. Ladika and D.E. Sunko, Tetrahedron Lett., in press.
23. A.D. Sherry and K.F. Purcell, J. Phys. Chem., 74, 3535 (1970).
24. R.M. Guidry and R.S. Drago, J. Am. Chem. Soc., 95, 759 (1973).
25. W.A. Sheppard and R.W. Taft, J. Am. Chem. Soc., 94, 1919 (1972). For OCH_3 and $O(Me)BCl_3$ substituents σ_I values are 0.23 and 0.54, respectively.
26. D. Lenoir and R.M. Frank, Chem. Ber., 118, 753 (1985).
27. 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.
28. P.v.R. Schleyer and C.J. Lancelot, J. Am. Chem. Soc., 91, 4297 (1969). These authors suggested that "the detection of any rate enhancement due to anchimeric assistance, no matter how small, is indicative of strong (not weak!) participation by the neighboring group."
29. W.S. Johnson, P.J. Neustaedter and K.K. Schmiegel, J. Am. Chem. Soc., 87, 5148 (1965).
30. J.A. Marshall, N. Cohen and A.R. Hochstetler, J. Am. Chem. Soc., 88, 3408 (1966).
31. L.I. Smith and G.F. Rouault, J. Am. Chem. Soc., 65, 631 (1943).