Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

Hydrolysis of Cyclopentenyl-*alkyl*-N-methyl Nicotinates in Micelles and Cyclodextrines

Renata Kobetić[a]; Dionis E. Sunko[b]
[a] Department of Organic Chemistry and Biochemistry, Rudjer Bošković Institute, Zagreb, Croatia [b] Department of Chemistry, Faculty of Science, University of Zagreb, Zagreb, Croatia

First published on: 13 September 2007

To cite this Article Kobetić, Renata and Sunko, Dionis E.(2008) 'Hydrolysis of Cyclopentenyl-*alkyl*-N-methyl Nicotinates in Micelles and Cyclodextrines', Supramolecular Chemistry, 20: 4, 369 — 377, First published on: 13 September 2007 (iFirst)
To link to this Article: DOI: 10.1080/10610270701268807
URL: http://dx.doi.org/10.1080/10610270701268807

Supramolecular Chemistry, June 2008 Vol. 20 (4), pp. 369–377

Taylor & Francis
Taylor & Francis Group

Hydrolysis of Cyclopentenyl-*alkyl*-N-methyl Nicotinates in Micelles and Cyclodextrines

RENATA KOBETIĆ[a,*] and DIONIS E. SUNKO[b]

[a]*Department of Organic Chemistry and Biochemistry, Rudjer Bošković Institute, P.O. Box 180, 10002 Zagreb, Croatia;* [b]*Department of Chemistry, Faculty of Science, University of Zagreb, Horvatovac 102 A, 10002 Zagreb, Croatia*

(Received 30 January 2007; Accepted 8 February 2007)

The formation, via superstructures of a high selectivity was obtained through the ionic interaction, electronic charge-transfer interaction, hydrophobic interaction, and van der Waals interaction in the hydrolysis of iodide-2-(Δ^3-cyclopentenyl)-ethyl-N-methyl-nicotinate, 12, and iodide-3-(Δ^3-cyclopenthenyl)-propyl-N-methyl-nicotinate, 14, in micelles and cyclodextrins. Hydrolysis was accomplished in the aqueous solutions of α- and β-cyclodextrins (CD) and in the aqueous solutions of cetyltrimethylammonium bromide (CTAB). The choice of the leaving group (nicotinate) and the reaction medium influence the reaction rate and the composition of the formed products. Contrary to published data, the hydrolysis of iodide-2-(Δ^3-cyclopenthenyl)-ethyl-N-methyl-nicotinate, 12, in the presence of α-CD yielded *endo*-2-norborneol.

Keywords: Hydrolysis; Cyclopentenyl-alkyl-nicotinates; Cyclodextrins; Micelles; Selectivity

INTRODUCTION

The activity of a carbon–carbon double bond as an internal reagent varies with geometry, substituents, and its position in the molecule. An example is the double bond in 2-(Δ^3-cyclopentenyl)ethyl-p-nitrobenzenesulfonate and tosylate [1,2] that participates directly in the solvolysis of these esters. This was confirmed through the formation of *exo*-2-norbornyl acetate from acetolysis in acetic acid. Lawton [3] showed that acetolysis of 2-(Δ^3-cyclopentenyl)ethyl-p-nitrobenzenesulfonates yielded mainly *exo*-2-norbornyl acetate, with about 3% unsaturated 2-(Δ^3-cyclopentenyl)ethyl-acetate being formed. The *endo*-product was not observed. 2-Bicyclo[2.2.1]-heptyl or 2-norbornyl cation formed as the intermediate in solvolysis of 2-(Δ^3-cyclopentenyl)ethyl-p-nitrobenzenesulfonate with the anchimeric assistance of double carbon–carbon bond from cyclopentenyl ring. Nonclassical, symmetric bridged cation is 24.8 kcal mol^{-1} more stabile than the isopropyl cation. The structure with the classical 2-norbornyl geometry does not correspond to the minimum of potential energy at the potential energy surface. In addition, the calculation showed that the nonclassical 2-norbornyl cation is 12–15 kcal mol^{-1} more stabile than classical structure [4].

Comparatively, one might expect an 2-bicyclo[3.2.1]-octyl cation to form in solvolysis of 3-(Δ^3-cyclopentenyl)propyl-p-nitrobenzenesulfonate [5]. Unfortunately, the double bond did not have any influence on the reaction and the open acetate was the product in the acetolysis.

The aim of this work was to study the hydrolysis reactions of the substrates which contained C=C bond as an internal nucleophile and which should be suitable models for the non enzymatic cationic cyclizations in model systems such as micelles and cyclodextrins. We believe that the best substrates for the water studies are the ones soluble in water. The RONicMeI type of the compounds are water soluble.

Therefore, we prepared iodide-2-(Δ^3-cyclopentenyl)-ethyl-N-methyl-nicotinate, **12**, and iodide-3-(Δ^3-cyclopenthenyl)-propyl-N-methyl-nicotinate, **14**, and explored if they form the inclusion complexes with cyclodextrins or the superstructures with CTAB and how that could influence the hydrolysis product formation. Our results confirmed our expectations. Namely, we report in this paper that the reactivity of the cyclopentyl C=C in the hydrolysis reaction

*Corresponding author. E-mail: rkobetic@irb.hr

ISSN 1061-0278 print/ISSN 1029-0478 online © 2008 Taylor & Francis
DOI: 10.1080/10610270701268807

of **12** as well as the product formation was influenced by an inclusion complex with α- or β-cyclodextrins, and also by the formation of a superstructure with CTAB micelle. The hydrolysis of iodide-3-(Δ^3-cyclopentenyl)propyl-N-methyl nicotinate, **14**, yielded 3-(Δ^3-cyclopentenyl)propanol, **10**, as the only product after hydrolysis regardless the medium used.

RESULTS

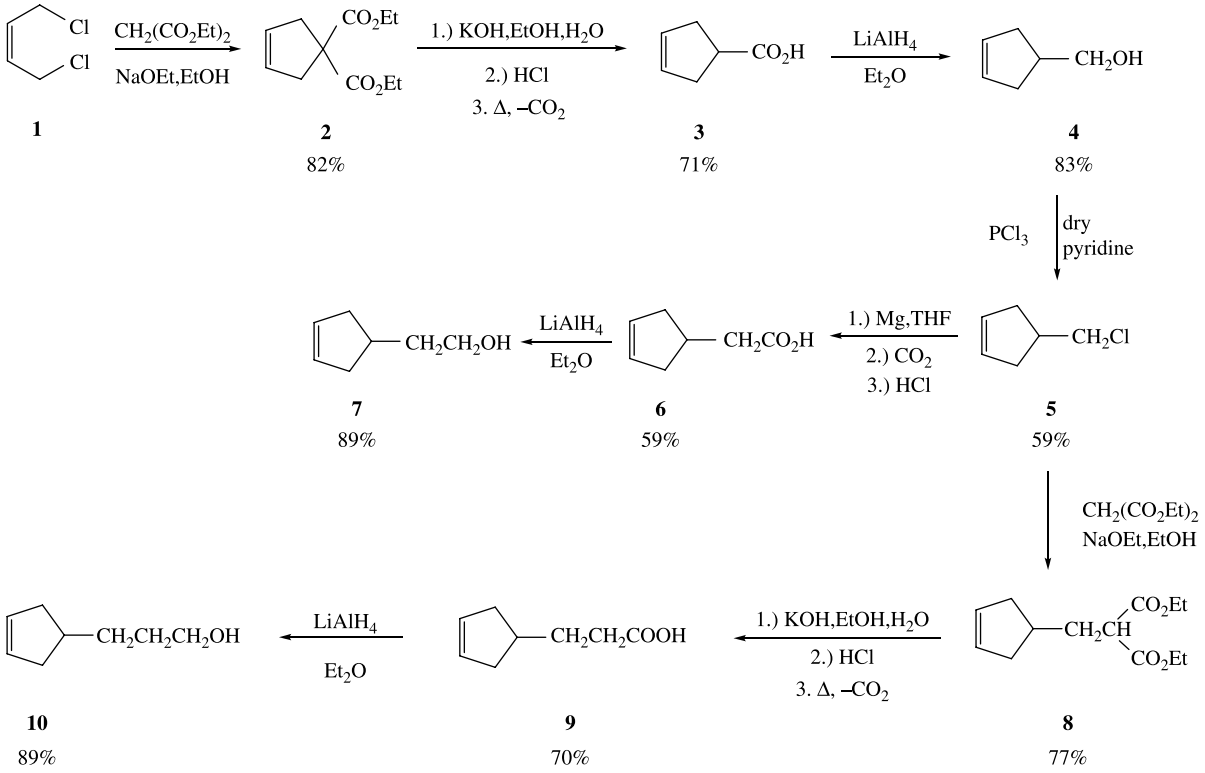
Synthesis

2-(Δ^3-Cyclopentenyl)ethanol, **7**, and 3-(Δ^3-cyclopentenyl)propanol, **10**, were synthesized with modified Sakurai's procedure [6], Scheme 1.

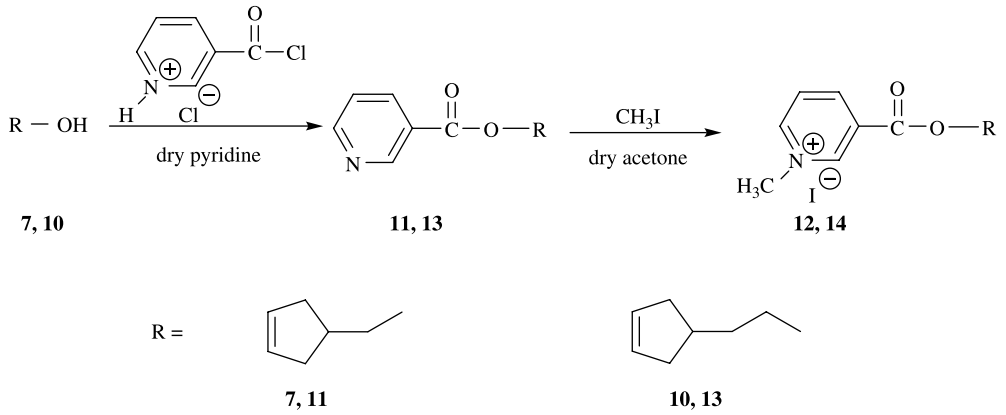
Esters **11** and **13** were prepared in dry pyridine from alcohols **7** and **10**, and nicotinoyl chloride hydrochloride followed by quaternization with iodomethane in acetone, Scheme 2.

Hydrolysis Products

The hydrolysis reactions of iodide-2-(Δ^3-cyclopentenyl)ethyl-N-methyl nicotinate, **12**, and iodide-3-(Δ^3-cyclopentenyl)propyl-N-methyl nicotinate, **14**, were studied in water, aqueous solutions of α-cyclodextrin, β-cyclodextrin and CTAB. The reactions were carried out at three different concentrations of CTAB in water: bellow cmc (9.2×10^{-5} mol dm^{-3}), at cmc (9.2×10^{-4} mol dm^{-3})

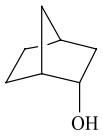
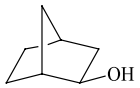
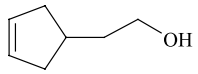


SCHEME 1 Synthesis of compounds **7** and **10**.



SCHEME 2 Synthesis of esters **11** and **13**.

TABLE I The product composition for hydrolysis of iodide-2-(Δ^3-cyclopentenyl)ethyl-N-methyl nicotinate (**12**) in different media at 60°C

Medium	*endo*-norborneol	*exo*-norborneol	2-(Δ^3-cyclopentenyl)ethanol	C/A[†]
				
	16	**15**	**7**	
α-CD	73	0	27	2.68
β-CD	0	0	100	0
CTAB (9.2×10^{-5} M)	<1	15	85	0.18
CTAB (9.2×10^{-4} M)	0	89	11	8.43
CTAB (9.2×10^{-3} M)	0	1	99	0.01
H_2O	24	0	76	0.31

[†] Ratio cyclic/acyclic products

and above cmc (9.2×10^{-3} mol dm^{-3}) [7]. Esters were hydrolyzed at 60°C. The hydrolysis products were separated with the gas chromatography and their structures were confirmed by NMR. The product distribution is summarized in the Table I.

The hydrolysis of iodide-3-(Δ^3-cyclopentenyl)propyl-N-methyl nicotinate, **14**, yielded 3-(Δ^3-cyclopentenyl)propanol, **10**, as the only product after hydrolysis regardless of the medium used.

DISSCUSION

From our earlier work [8] we know that RONicMeI type of the compound (structurally similar to cationic surfactants composed of the hydrophilic head (methylpyridinium iodide) and the hydrophobic tail (R)) are water soluble and display autoinhibition in hydrolysis reaction [9]. The nicotinate group as a leaving group gives the opportunity for three types of cleavage to occur, Fig. 1.

While in biological systems O-acyl cleavage is the most common mechanism (path *b*), N-alkyl fission has also been observed (path *c*). One could expect the O-alkyl fission to occur if the departing cationic fragment is stabile ion (path *a*). The benzylic and allylic esters with the same leaving group showed O-alkyl cleavage because they formed relatively stable allylic and benzylic cations.

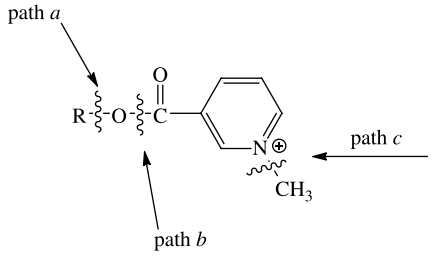


FIGURE 1 Schematic representation of the possible paths for the cleavage of the N-methyl-nicotinate group.

Our results showed that both *a* and *b* cleavages occurred in the hydrolysis of iodide-2-(Δ^3-cyclopentenyl)ethyl-N-methyl nicotinate, **12**, since the following three products **7**, **15**, and **16** were obtained, Scheme 3 and Table I.

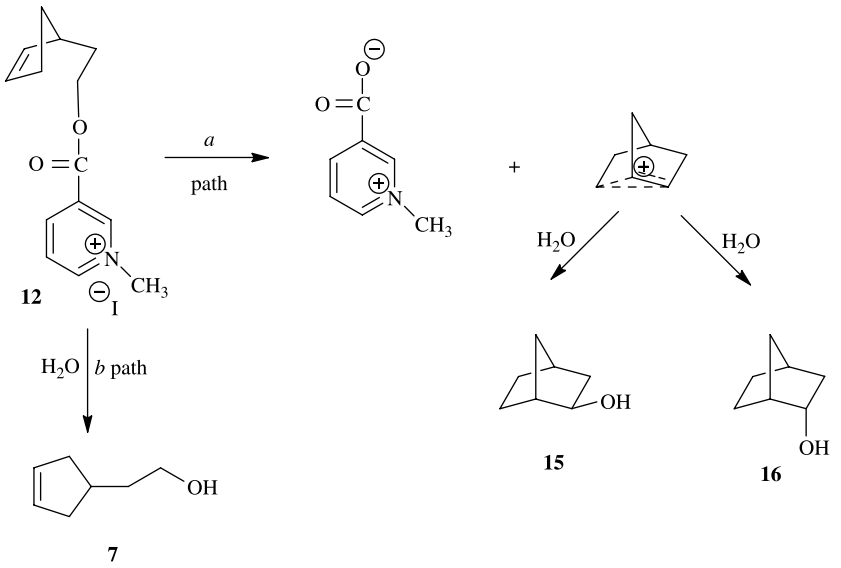
The hydrolysis of **12** in neat water yielded 76% of nonrearranged product **7** and 24% of cyclic product *endo*-2-norborneol **16**.

This is an unusually high percentage of nonrearranged product **7** that is formed via classical hydrolysis of esters, namely with O-acyl fission. Surprisingly, *endo*-2-norborneol **16** was formed as the second product. So far, the published results for the solvolysis of either 2-(Δ^3-cyclopentenyl)ethyl or norbornyl derivates [10–15] were mostly *exo*-2-norbornyl derivates, except in acetolysis in acetic acid where the formation of 3% of nonrearrangement product, 2-(Δ^3-cyclopentenyl)ethanol **7** was observed (see Table II with the literature data). The formation of the *endo* product was not reported.

The fission of the leaving group (N-methylnicotinate which is soluble in water) was supported by the anchimeric assistance of the carbon–carbon double bond from cyclopentenyl ring. The result of this participation should be the cyclization and the formation of an *exo*-2-norborneol **15** according to the literature (Table II).

But we confirmed the formation of *endo*-2-norborneol **16** with the internal standard by GC and ^{1}H NMR. As I mentioned earlier, we know that this type of compound (RONicMeI) behave like micelles, and therefore, iodide-2-(Δ^3-cyclopentenyl) ethyl-N-methyl nicotinate **12** could form a micelle. In this micelle the leaving group can be in a good position for the complexation with formed cation on the *exo* side, Scheme 4.

Endo-2-norborneol, **16** could be formed by the direct S_N2 decomplexation, very similar to an enzymatic cyclization (enzymes stabilize, with the internal nucleophyl the substrate and make possible the attack on the internal side).



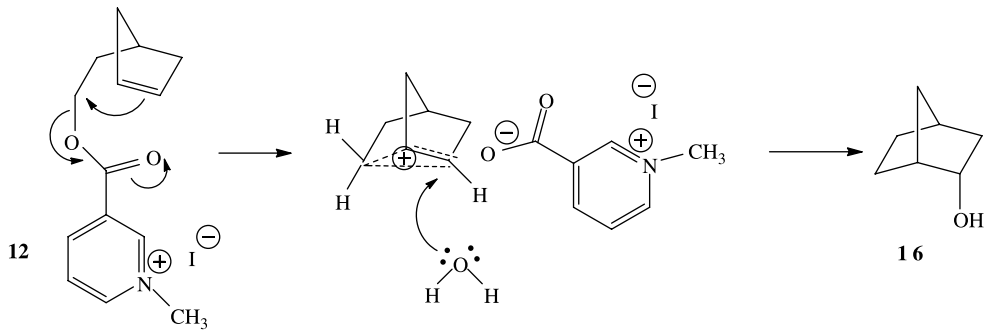
SCHEME 3 The hydrolysis of iodide-2-(Δ^3-cyclopentenyl)ethyl-N-methyl nicotinate, **12**.

The ratio of cyclic/acyclic products in water was 0.31 which is similar to Bartlett's results [16]. He obtained the ratio of cyclic/acyclic 2.6 in acetic acid, and after addition of sodium acetate (3 M) the ratio decreased to 0.59. Therefore, it is possible to compare the effect of the charged leaving group N-methylnicotinylcarboxylate with the effect of sodium acetate.

The hydrolysis of **12** in the CTAB micelles yielded mostly *exo*-2-norborneol, **15** and 2-(Δ^3-cyclopentenyl) ethanol, **7**, Table I. The product distribution was greatly influenced by the surfactant concentration. The similar effect was observed in the selective reduction of conjugated aldehydes and ketones in our laboratory [17]. We believe that the formation of the superstructures between the surfactant molecules and the substrate **12** is responsible for the observed product distribution, Fig. 2. First of all, the carbonyl group of the substrate and the ammonium cation of the surfactant molecules were attracted by the favorable Coulombic interactions and secondly, the alkyl chain of the substrate was associated

TABLE II Literature data for the solvolysis of different 2-(Δ^3-cyclopentenyl)ethyl derivates

Leaving group	Medium	Products			Temperature °C	Reaction rate s^{-1}	References
		exo-norbornil acetate	*exo*-norborneol	2-(Δ^3-cyclopentenyl) ethyl acetate			
ONs	0.04 M NaOAc/ HOAc	100	–	–	60	1.10×10^{-4}	3
OBz	HOAc	97	–	3	60		3
	0.02 M NaOAc/ HOAc				75.1	7.4×10^{-4}	15
OTs	50% EtOH				70.13	3.36×10^{-4}	1
	conc HCO_2H				59.85	8.8×10^{-4}	1
	50% HOAc	60	40		60	3.8×10^{-4}	2
OPNB	HOAc				55°C	0.83×10^{-4}	1



SCHEME 4 Schematic representation of the interaction between formed 2-norbornyl cation and the leaving N-methyl nicotinate group.

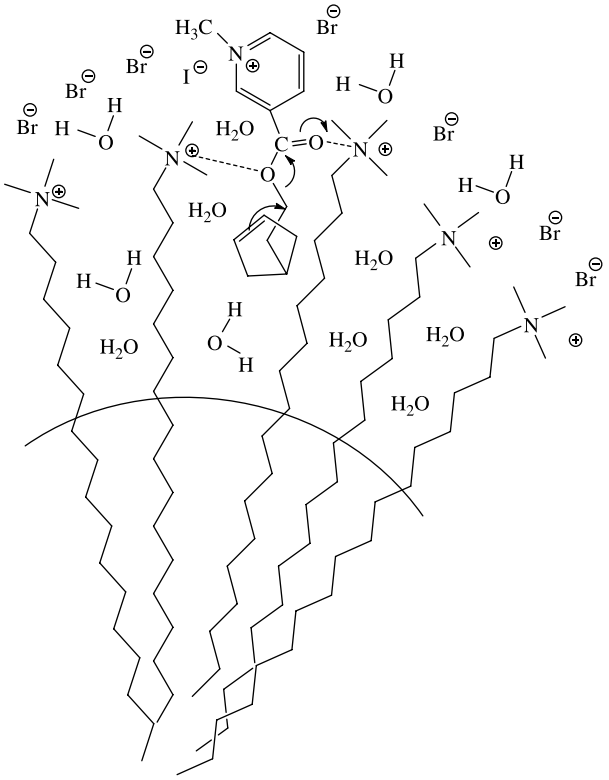


FIGURE 2 Schematic representation of the interaction of the CTAB micelle with the substrate iodide-2-(Δ^3-cyclopentenyl)-ethyl-N-methyl-nicotinate, **12**.

particularly with alkyl chain of CTAB minimizing the hydrophobic interactions with water.

Namely, below the critical micellar concentration (cmc) for CTAB ($c_{cmc} = 9.2 \times 10^{-4}$ M), micelles are not formed but rather partially associated the molecules of CTAB by themselves as well as with the substrate molecules, **12**. The major product was 2-(Δ^3-cyclopentenyl)ethanol, **7**, (85%), some of *exo*-2-norborneol, **15**, (15%) and the traces of *endo*-2-norborneol, **16**.

The results pointed out clearly that the cyclization just as π-participation is influenced by the intramolecular interactions.

At the cmc, micelles are formed with the most of the substrate packed within micelle. Due to the favorable interactions between the carbonyl group and the cationic micellar head, the majority of the pyridine ring could be in Sterns layer surrounded by Br^- and I^- ions. In the same time the hydrophobic part of the substrate molecule was not very deep in the core of the micelle. The water molecules were present [18] forcing the substrate to fold [19] e.g. pushing it to the favorable conformation for the C═C participation. The result of this interactions was the formation of 89% of *exo*-2-norborneol, **15**, product and only 11% of the open chain product, 2-(Δ^3-cyclopentenyl)ethanol, **7**.

It seemed that the reaction medium with the surfactant above cmc resulted in no favorable repulsion interaction between positive groups (the micellar head, the leaving group and the formed carbocation) if O-alkyl cleavage with the anchimeric assistance would occur. All of that was due to there being less water within the micelle and closer packing of the surfactant molecules and the substrate.

The hydrolysis of iodide-3-(Δ^3-cyclopentenyl)-propyl-N-methyl nicotinate, **14**, yielded 3-(Δ^3-cyclopentenyl)propanol, **10**, as the only product after hydrolysis. The changes in the surfactant concentration did not affect the composition of the formed product. It seemed that the propyl chain did not fold in the way to favor the C═C participation. The carbon–carbon double bond remained far from the reaction center and was unable to participate in the hydrolysis.

Very interesting results were obtained for the hydrolysis of the compounds **12** and **14** in cyclodextrins, Table I. Both compounds formed inclusion complexes with α- and β-cyclodextrins according to Bender [20–22] (the formation of an inclusion complex causes the UV_{max} shift). The formation of the inclusion complex between iodide-2-(Δ^3-cyclopentenyl)ethyl-N-methyl nicotinate, **12** and β-CD was confirmed with the shift of UV_{max} from 261 nm to 264 nm. Since α- and β-cyclodextrins consists of the different cavity size [23–25], the guest molecules could incorporate in different ways in the cavity and react differently. Our results confirmed out clearly the different hydrolysis rate and the product distribution [26] in each cyclodextrin.

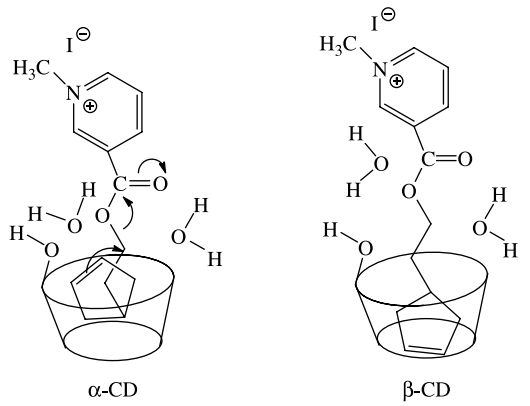


FIGURE 3 Schematic representation of the inclusion complexes between the substrate iodide-2-(Δ^3-cyclopentenyl)-ethyl-N-methyl-nicotinate, **12**, and α- and β-cyclodextrins.

α-CD cavity is smaller (diameter 4.7–5.3 Å) than β-CD cavity (diameter 6.0–6.5 Å) [27] and it is to expect that the substrate **12** packs more compactly within the α-CD cavity, leaving that part of the molecule probably even outside. The double bond was in a good position for the participation and the formation of cyclic product, Fig. 3. The formation of *endo*-2-norborneol, **16**, as a major product suggested that two possibilities by which that could occur: the water molecule approached only one side of the inclusion complex while the leaving group was departing, or a secondary hydroxyl group from α-CD attacked first followed by water. Which way was the preferential approach for the *endo*-2-norborneol formation, we can not say at this point.

β-CD cavity is a little wider and compound **12** could be packed in the inclusion complex in the way that C═C is deeper in the cavity and in an unfavorable position for the assistance yielding only the nonrearranged product 2-(Δ^3-cyclopentenyl) ethanol, **7**.

exo-2-Norborneol was not observed **15**, even in recordable traces in either cyclodextrin.

The hydrolysis of iodide-3-(Δ^3-cyclopentenyl)propyl-N-methyl nicotinate, **14**, in either cyclodextrin yielded 3-(Δ^3-cyclopentenyl)propanol, **10**, as the only product after hydrolysis.

CONCLUSION

We concluded that the choice of the leaving group (nicotinate) and the reaction medium influenced the reaction rate and the composition of the formed products. That was especially confirmed for the hydrolysis of the compound **12** where contrary to published data, the hydrolysis of iodide-2-(Δ^3-cyclopenthenyl)-ethyl-N-methyl-nicotinate, **12** in the presence of α-CD yielded *endo*-2-norborneol, **16**. Namely, in the literature data we could not find the case that cyclopenthenyl-ethyl derivatives hydrolyse to any *endo* product. The difference was the leaving group, nicotinate, and the reaction media. The importance is even greater knowing that the only one product, nonrearranged product 2-(Δ^3-cyclopentenyl)ethanol, **7**, was formed in β-cyclodextrin. The concentration of CTAB surfactant influenced the product formation also but the *endo*-2-norborneol, **16**, was formed in traces when CTAB was used bellow cmc.

MATERIALS AND METHODS

General

All chemicals were commercial products (Fluka and Aldrich) and used without further purification. The analysis and the characterization of the products has been done by: 1) GC-MS (GC Varian 3400 and MS Finningan MAT ITD 800, Column DB1, 30 m, Diameter 0.25, carrier gas He); 2) ^{1}H NMR (GEMINI 300 spectrometer; the chemical shifts of NMR are expressed in ppm from TMS as an internal standard, solvent $CDCl_3$); 3) IR (PERKIN ELMER FT-IR Spectrometer 1725 X); 4. UV/Vis (HITACHI 2000 and CARY 3 spectrometer). All boiling and melting points are uncorrected.

Synthetic Procedures for the Substrates 12 and 14

Diethyl Δ^3-Cyclopentenyl-1,1-Dicarboxylate, 2

Sodium ethoxide was prepared by dissolving 29.9 g (1.3 mol) of sodium in 536 cm^{-3} of absolute ethanol. To the mixture of 103 cm^{-3} of diethyl-1,3-propanedionate and 81 g (0.65 mol) *cis*-1,4-dichloro-2-butene heated at 60°C was added prepared sodium ethoxide dropwise. The reaction mixture was left to stir at 60°C over the night. Afterward, it was one hour on reflux and then 95% of the initial amount of ethanol was distilled out. To the cold reaction mixture was added 204 cm^{-3} of water and the layers were separated. The aqueous layer was washed three times with diethyl ether. The combined ether portions were dried over the anhydrous Na_2SO_4. The solvent was removed under the reduced pressure and it was obtained by the distillation 114.3 g (82%) of the oil, b.p. 120°C at 2.7×10^3 Pa. IR (film), $\tilde{\nu} = 3055, 2983, 2938, 1735, 1466, 1097\ cm^{-1}$.

3-Cyclopentenecarboxylic Acid 3

The mixture of 270 cm^3 of ethanol, 135 cm^3 water and 108 g (1.92 mol) KOH was added to 114 g (0.53 mol) of diethyl Δ^3-cyclopentenyl-1,1-dicarboxylate, **2**. The reaction mixture was refluxed for 4 h and than the ethanol was distilled off. To the crude product was added dil. HCl till the pH 2. The solution was extracted three times with diethyl ether.

The combined ether portions were dried over Na_2SO_4. The solvent was removed under the reduced pressure and the distillation of the remained crude product yielded 42.2 g (71%) of the colorless oil. IR (film), $\tilde{\upsilon} = 3310, 3055, 2926, 2848, 1726, 1616, 1442\,cm^{-1}$.

3-Cyclopentenemethanol 4

The suspension of 700 cm^3 of dry diethyl ether and 26.6 g (0.7 mol) of $LiAlH_4$ was prepared and 42 g (0.375 mol) of 3-cyclopenthenecarboxylic acid, **3**, dissolved in 10 cm^3 of dry diethyl ether was added dropwise. The reaction mixture was refluxed for 6 h. Water was added to the cold reaction mixture until the white precipitate was forming. Diethyl ether solution was filtrated off and the solvent was removed under the reduced pressure. It was obtained 30.7 g (83%) of the colorless oil b.p. 35°C at 270 Pa (lit. 98-99°C/7700 Pa) IR (film), $\tilde{\upsilon} = 3300, 3040, 2930, 2850, 1630, 1018\,cm^{-1}$. ^1H NMR ($CDCl_3$, 300 MHz) δ: 5.65 (2H, s); 3.54–3.47 (2H, d); 2.54–2.03 (5 H, m) [28].

Δ^3-Cyclopenthenylmethyl Chloride 5

To the mixture of 30 g (0.3 mol) of 3-cyclopentenemethanol, **4**, and 7 cm^3 of dry pyridine was added dropwise at 0°C, 14.4 cm^3 of PCl_3. The reaction mixture was heated at 60°C for 6 h. The cold reaction mixture was extracted with chloroform. The combined chloroform portions were dried over Na_2SO_4. After the removal of the solvent under reduced pressure and the distillation of the crude product, it was obtained 21 g (59%) of colorless oil, b.p. 87°C at 2700 Pa (lit. 70°C at 12 kPa [6] IR (film), $\tilde{\upsilon} = 3057, 2925, 2852, 1619, 1022, 797, 680\,cm^{-1}$.

Δ^3-Cyclopentenylacetic Acid 6 [29]

To the hot mixture of 30 cm^3 of dry tetrahydrofuran and 0.5 g (0.02 mol) of Mg in powder was added 2.5 g (0.02 mol) Δ^3-cyclopenteylmethyl chloride, **5**, and refluxed for 24 h. Afterward the solid CO_2 was added with the powerful stirring. Compact mixture was poured over the mixture of ice and 10 cm^3 of conc. HCl. After melting, the reaction mixture was extracted with diethyl ether. The combined ether portions were dried over the anhydrous Na_2SO_4. The solvent was removed under reduced pressure and it was obtained by the distillation of the crude product 1.5 g (50%) of colorless oil. IR (film), $\tilde{\upsilon} = 3309, 3055, 2926, 2848, 1726, 1616, 1442\,cm^{-1}$.

2-(Δ^3-Cyclopentenyl)ethanol 7 [30]

1.5 g (0.012 mol) of Δ^3-cyclopentenylacetic acid, **6**, dissolved in 10 cm^{-3} of dry diethyl ether was added dropwise to the suspension of 30 cm^3 dry diethyl ether and 0.5 g (0.0125 mol) of $LiAlH_4$. The reaction mixture was refluxed for 0.5 h. To the cold reaction mixture was added water until the formation of white precipitate formed. The diethyl ether solution was filtrated and the solvent was evaporated under the reduced pressure. It was obtained 1.2 g (89%) of colorless oil b.p. 35°C at 270 Pa (lit. 98–99°C/7700 Pa). IR (film), $\tilde{\upsilon} = 3350, 3040, 2960, 2840, 1620, 1040\,cm^{-1}$. ^1H NMR ($CDCl_3$, 300 MHz) δ: 5.66 (2H, s); 3.59–3.52 (2H, d); 2.64–2.03 (5 H, m) 1.61–1.26 (2H, m).

Diethyl[(Δ^3-Cyclopentenyl)-methyl]-1,3-Propanedionate 8

Sodium ethoxide was prepared by dissolving 2.3 g (0.1 mol) Na in 50 cm^3 of dry ethanol and added to 16 cm^3 (0.1 mol) of diethyl malonate. To the reaction mixture was added dropwise 11.6 g (0.1 mol) of Δ^3-cyclopenteylmethyl chloride, **5**, and the reaction mixture was refluxed for 2 h. From the reaction mixture was distilled the excess ethanol. Water was added to dissolve the precipitated NaCl. The reaction mixture was extracted three times with diethyl ether. The combined ether portions were dried over the anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and it was obtained by the distillation 5.5 g of colorless oil b.p. 130°C at 2 kPa. IR (film), $\tilde{\upsilon} = 3427, 3055, 2937, 2850, 1730, 1620, 1075, 1040\,cm^{-1}$.

3-(Δ^3-Cyclopentenyl)propionic Acid 9

The acid **9** was obtained from 5.5 g (0.023 mol) diethyl[(Δ^3-cyclopentenyl)-methyl]-1,3-propanedionate, **8**, 7.5 cm^3 of water and 4.5 g (0.08 mol) of KOH, using the procedure for the preparation of the compound **2**. It was obtained 2.25 g (70%) of colorless oil. IR (film), $\tilde{\upsilon} = 3309, 3055, 2926, 2848, 1726, 1616, 1442\,cm^{-1}$.

3-(Δ^3-Cyclopentenyl)propanol 10

The product was obtained from 2.25 g (0.016 mol) of 3-(Δ^3-cyclopentenyl)propionic acid, **9**, and 1 g of (0.026 mol) $LiAlH_4$ using the procedure for the preparation of the compound **3**. It was obtained 1.8 g (89%) of colorless oil b.p. 112°C at 3 kPa. IR (film), $\tilde{\upsilon} = 3340, 3030, 2960, 2850, 1615, 1050\,cm^{-1}$. ^1H NMR ($CDCl_3$, 300 MHz) δ: 5.66 (2H, s); 3.58–3.51 (2H, d); 2.564–2.14 (5 H, m) 2.04–0.94 (4H, m).

2-(Δ^3-Cyclopentenyl)ethyl Nicotinate 11 [9]

1.0 g (8.9 mmol) of 2-(Δ^3-cyclopentenyl)ethanol, 20 cm^3 of dry pyridine and excess of nicotinoyl chloride hydrochloride were stirred for 24 h. Afterward, the

reaction mixture was poured over the ice and extracted with diethyl ether. The combined ether portions were dried over the anhydrous Na_2SO_4. The solvent was removed under the reduced pressure, and the product was purified by column chromatography (silica gel G) benzene:diethyl ether = 1:1. It was obtained 1.7 g (87%) oil. IR (film), $\tilde{\upsilon} = 3050, 3010, 2960, 1730, 1175\,cm^{-1}$.

3-(Δ^3-Cyclopentenyl)propyl Nicotinate 13

The product was prepared from 1.0 g (7.9 mmol) of 3-(Δ^3-cyclopentenyl)propanol using the procedure for the preparation of compound **11**. It was obtained 1.65 g (90%) of oil. IR (film), $\tilde{\upsilon} = 3040, 3010, 2930, 1730, 1640, 1176\,cm^{-1}$.

Iodide-[2-(Δ^3-Cyclopentenyl)ethyl]-N-methyl Nicotinate 12

In 10 cm^3 dry acetone was dissolved 1.0 g (4.5 mmol) of 2-(Δ^3-cyclopentenyl)ethyl nicotinate and 10 cm^3 of iodomethane. The reaction mixture was stirred in the dark for 24 h. Acetone was distilled off under the reduced pressure. It was obtained 1.4 g (86%) of yellow crystals m.p. = 83–85°C. IR (film), $\tilde{\upsilon} = 3436, 3050, 3010, 2960, 2846, 1729, 1632, 1590, 1175\,cm^{-1}$. ^1H NMR ($CDCl_3$, 300 MHz) δ: 9.76–9.69 (1H, d); 9.45 (1H, s); 8.98–8.88 (1H, d); 8.45–8.29 (1H, t), 5.7 (2H,s) 4.81 (3H, s); 4.54–4.3 (2H, m); 2.76–1.97 (5 H, m) 1.54–1.25 (2H, m).

Iodide-[3-(Δ^3-Cyclopentenyl)propyl]-N-methyl Nicotinate 14

The product was prepared from 1.0 g (4.9 mmol) of 3-(Δ^3-cyclopentenyl)propyl nicotinate using the procedure for preparation of the compound **12**. It was obtained 1.5 g (90%) of yellow crystals m.p. 80–82°C. IR (film), $\tilde{\upsilon} = 3437, 3010, 2929, 2844, 1729, 1635, 1591, 1475, 1176\,cm^{-1}$. ^1H NMR ($CDCl_3$, 300 MHz) δ: 9.84–9.77 (1H, d); 9.35 (1H, s); 8.99–8.87 (1H, d); 8.42–8.33 (1H, t), 5.7 (2H,s) 4.81 (3H, s); 4.53–4.33 (2H, m); 2.77–2.14 (5 H, m) 1.82–0.91 (2H, m).

The Analysis of the Products from the Hydrolysis Reactions

Hydrolysis of Iodide-[2-(Δ^3-Cyclopentenyl)ethyl]-N-methyl Nicotinate, 12—in Water

It was hydrolyzed 0.1 g (0.29 mmol) of iodide-[2-(Δ^3-cyclopentenyl)ethyl]-N-methyl nicotinate, **12**, in 50 cm^3 of water. The reaction mixture was heated for 24 h at 60°C. Afterward the reaction mixture was extracted with diethyl ether. With GC, IR and ^1H NMR was confirmed the formation of 24% *endo*-norborneol and 76% 2-(Δ^3-cyclopentenyl)ethanol.

Hydrolysis of Iodide-[2-(Δ^3-Cyclopentenyl)ethyl]-N-methyl Nicotinate, 12—in α-Cyclodextrine

It was hydrolyzed 0.05 g (0.14 mmol) of iodide-[2-(Δ^3-cyclopentenyl)ethyl]-N-methyl nicotinate **12**, in 50 cm^3 of water and 0.25 g α-CD. The reaction mixture was heated for 24 h at 60°C. Afterward the reaction mixture was extracted with diethyl ether. With GC, IR and ^1H NMR was confirmed the formation of 73% *endo*-norborneol, **16**, and 27% 2-(Δ^3-cyclopentenyl)ethanol, **7**.

Hydrolysis of Iodide-[2-(Δ^3-Cyclopentenyl)ethyl]-N-methyl Nicotinate, 12—in β-Cyclodextrine

It was hydrolyzed 0.05 g (0.14 mmol) of iodide-[2-(Δ^3-cyclopentenyl)ethyl]-N-methyl nicotinate **12**, in 50 cm^3 of water and 0.27 g of β-CD. The reaction mixture was heated for 24 h at 60°C. The cold reaction mixture was extracted with diethyl ether. With GC, IR and ^1H NMR was confirmed the formation of only 2-(Δ^3-cyclopentenyl)ethanol **7**.

Hydrolysis of Iodide-[2-(Δ^3-Cyclopentenyl)ethyl]-N-methyl Nicotinate, 12—in CTAB

It was hydrolyzed 0.05 g (0.14 mmol) of iodide-[2-(Δ^3-cyclopentenyl)ethyl]-N-methyl nicotinate, **12**, in 50 cm^3 of aqueous solution of CTAB (below the cmc (9.2×10^{-5} mol dm^{-3}), on cmc (9.2×10^{-4} mol dm^{-3}) and above cmc (9.2×10^{-3} mol dm^{-3}). The reaction mixture was heated for 24 h at 60°C. Afterward the reaction mixture was extracted with diethyl ether. With GC, IR and ^1H NMR was confirmed the formation of; <1% *endo*-norborneol **16**, 15% *exo*-norborneol, **15** and 85% 2-(Δ^3-cyclopentenyl)ethanol, **7**, on 9.2×10^{-5} mol dm^{-3} CTAB, 89% *exo*-norborneol **16**, and 11% 2-(Δ^3-cyclopentenyl)ethanol, **7**, on 9.2×10^{-4} mol dm^{-3} CTAB and, 1% *exo*-norborneol **15** and 99% 2-(Δ^3-cyclopentenyl)ethanol, **7**, on 9.2×10^{-3} mol dm^{-3} CTAB.

Hydrolysis of Iodide-[3-(Δ^3-Cyclopentenyl)propyl]-N-methyl Nicotinate, 14

It was hydrolyzed 0.05 g (0.14 mmol) of iodide-[3-(Δ^3-cyclopentenyl)propyl]-N-methyl nicotinate, **14**, in water, in aqueous solution of α-cyclodextrin, in aqueous solution of β-cyclodextrin and in aqueous solution of CTAB (below cmc (9.2×10^{-5} mol dm^{-3}), on cmc (9.2×10^{-4} mol dm^{-3}) and above cmc (9.2×10^{-3} mol dm^{-3}). The conditions were the same as for iodide-[2-(Δ^3-cyclopentenyl)ethyl]-N-methyl nicotinate, **12**. With GC, IR and ^1H NMR was confirmed formation of only 3-(Δ^3-cyclopentenyl)propanol, **7**.

Acknowledgements

This work was supported by a grant from the Ministry of Science, Education and Sports No. 1-07-185.

References

[1] Bartlett, P. D.; Bank, S.; Crawford, R. J.; Schmid, G. H. *J. Am. Chem. Soc.* **1965**, *87*, 1288.
[2] Bartlett, P. D.; Bank, S. *J. Am. Chem. Soc.* **1961**, *83*, 2591.
[3] Lawton, R. G. *J. Am. Chem. Soc.* **1961**, *83*, 2399.
[4] Raghavachari, K.; Haddon, R. C.; Schleyer, P. v. R.; Schaefer, H. *J. Am. Chem. Soc.* **1983**, *105*, 5915.
[5] Bartlett, P. D.; Trahanovsky, W. S.; Bolon, D. A.; Schmid, G. H. *J. Am. Chem. Soc.* **1965**, *87*, 1314.
[6] Hosomi, A.; Makami, M.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2784.
[7] For the definition and the determination of the critical micelar concentration (cmc) see, for example:, Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*; John Wiley & Sons: Chichester, UK, 2000; p 690.
[8] Kobetić, R. *Doctoral Thesis*; University of Zagreb, 1993.
[9] Juršić, B.; Ladika, M.; Sunko, D. E. *Tetrahedron* **1987**, *43*, 1955.
[10] Winstein, S.; Trifan, D. *J. Am. Chem. Soc.* **1952**, *74*, 1154.
[11] Bartlett, P. D.; Sargent, G. D. *J. Am. Chem. Soc.* **1965**, *87*, 1297.
[12] Nordlander, J. E.; Greutzmacher, R. R.; Kelly, W. J.; Jindal, S. P. *J. Am. Chem. Soc.* **1974**, *96*, 181.
[13] Bentley, T. W.; Bowen, C. T. *J. Chem. Soc. Perkin II* **1978**, 557.
[14] Bentley, T. W.; Bowen, C. T. *J. Chem. Soc. Perkin II* **1980**, 1244.
[15] Winstein, S.; Carter, P. *J. Am. Chem. Soc.* **1961**, *83*, 4485.
[16] Bartlett, P. D.; Bank, S.; Crawford, R. J.; Schmid, G. H. *J. Am. Chem. Soc.* **1965**, *87*, 1288.
[17] Juršić, B.; Sunko, D. E. *J. Chem. Res. (S)* **1988**, 202.
[18] Juršić, B.; Sunko, D. E. *Bioorg. Chem.* **1988**, *16*, 1.
[19] Tamelen, E. E.; Curphey, T. J. *Tetrahedron Lett.* **1962**, 121.
[20] Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer Verlag: New York, 1978.
[21] Saenger, W. *Angew. Chem., Int. Engl.* **1980**, *19*, 344.
[22] Szejtli, J. *Cyclodextrins and Their Inclusion Complexes*; Akademiai Kiado: Budapest, 1982.
[23] Fornasier, R.; Reniero, F.; Scrimi, P.; Tonellato, U. *J. Org. Chem.* **1985**, *50*, 3209.
[24] Fornasier, R.; Lucchini, V.; Scrimi, P.; Tonellato, U. *J. Org. Chem.* **1986**, *51*, 1769.
[25] Ramamurthy, V.; Reddy, G. D. *J. Org. Chem.* **1987**, *52*, 3952.
[26] The hydrolysis rates differed too: $k_{\alpha\text{-CD}}/k_{\beta\text{-CD}} = 1.37$ for compound **12** at 60°C. Results from Kobetic, R., *Doctoral Thesis*;, University of Zagreb 1993.
[27] Hecht, S. M. *Bioorganic Chemistry: Carbohydrates*; Oxford University Press: New York, 1999.
[28] Meinwald, J.; Gassman, P. G.; Crandel, J. K. *J. Org. Chem.* **1962**, *27*, 3366.
[29] Lai, Y. -H. *Syntheses* **1981**, 585.
[30] Brown, H. C.; Muzzio, J. *J. Am. Chem. Soc.* **1966**, *88*, 2811.