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HYDROLYSIS OF N-METHYLNICCTINYL AND N-METHYLISONICOTINYL ESTERS AND SOME n-PARTICIPATING DERIVATIVES UNDER MICELLAR CONDITIONS

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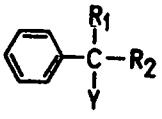
ABSTRACT. - Hydrolysis rate of two types of compounds, A and B were studied in the presence of variable concentrations of an anionic surfactant (sodium dodecylsulfate, SDS). Class A of compounds consists of substances which hydrolyze by the S_N1 mechanism and which are structurally related to cationic surfactants. The second class (B) contains an internal nucleophile and thus solvolyzes under anchimeric assistance. It was found that compounds of class A are forming an effective micelle and show a rate retardation relative to solvolysis in pure water. The hydrolysis rates of compounds of class B are relatively unaffected by the presence of the micelle forming surfactant. The merits of a N-methylnicotinoic and N-methylisonicotinoic esters as a new type of leaving groups are discussed.

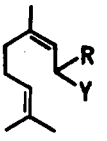
The reactivities of many compounds undergoing displacement reaction via S_N1 or S_N2 mechanism are strongly influenced by the choice of solvent. In the study of bioorganic reaction mechanisms, water would be the solvent of choice, but unfortunately many organic substrates of interest for such studies are insoluble in water. This pertains also to studies in aqueous micelles which are the probably simplest but quite suitable models for studies of biomimetic processes. It is generally accepted that aqueous micelles are approximately spherical but unfortunately no direct methods are as yet available for an unequivocal determination of their structure.[1,2] Two structurally different types of structure have been proposed and named by Menger the "fjord" and the "reef" model.[3] He studied ^{13}C NMR chemical shifts of the carbonyl carbon atom in different aldehydes and ketones in organic solvents, water and in water containing different amounts of a surfactant. From a correlation of these data with the E_T values it was concluded that the actual structure of the micelle is between the above named two

extremes and that it contains "deep water-filled groves".[3-6] In these as well as in other studies problems were encountered in obtaining good spectra of sparingly water soluble aldehydes and ketones in aqueous micellar media. However, all authors agree that a micelle contains liophilic parts in water "like organic islands in a see of water".

Bunton and others investigated the influence of surface active agents on the rate of hydrolysis of compounds reacting by a more or less limiting mechanisms.[7-9] In all cases a rate retardation was observed relative to the rate in pure water and a constant inhibition of the reaction was observed with the increasing concentration of the surfactant. However these data have to be taken with some caution. Rate constants for the hydrolysis in pure water were obtained by solvolyzing the given substrate in mixed solvent containing varying amounts of water (dioxane-water[7] or acetonitrile-water[8,9] mixtures) and extrapolating the obtained kinetic data to pure water (zero organic solvent). This kind of extrapolation contains a certain degree of uncertainty because of irregular trends in changes of reactivities when either of the extreme situation with respect to the solvent composition is approached. Furthermore, the low solubility in water of many substrates caused that rates of only few compounds could be directly measured below the critical micellar concentration (CMC). If a compound is only sparingly soluble in water in concentrations required for kinetic measurements, two processes became operative simultaneously, i.e. dissolution and hydrolysis. Thus, the concentration of the reacting substrate in the unit of time will remain constant regardless of the fact that the substrate is continuously being consumed. This can give the impression of the occurrence of mixed kinetics of complex order. In this paper we are describing the results of kinetic investigation of the hydrolysis reaction under micellar conditions of substrates containing N-methylnicotinyl and N-methylisonicotinyl leaving groups which makes them soluble in water thus avoiding the above mentioned complications. These new leaving groups show a reactivity similar to corresponding p-nitrobenzoates and can be also used in different organic solvolytic solvents.[10] In contrast to the mentioned kinetic behavior of quaternary nicotinyl esters, the hydrolysis rates of compounds containing an n-participating internal nucleophile are relatively unaffected by the presence of aqueous micelle.



2a; $R_1=R_2=H$, Y=ONicMeI
2b; $R_1=CH_3$, $R_2=H$, Y=ONicMeI
2c; $R_1=R_2=CH_3$, Y=ONicMeI
2d; $R_1=H$ $R_2=C_6H_5$, Y=ONicMeI
2e; $R_1=D$, $R_2=C_6H_5$, Y=ONicMeI



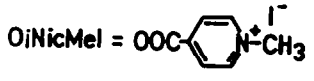
2f; R=H, Y=ONicMeI
2g; R=D, Y=ONicMeI
4f; R=H, Y=OiNicMeI
4g; R=D, Y=OiNicMeI

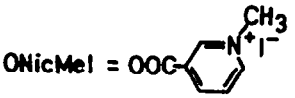
4a; $R_1=R_2=H$, Y=OiNicMe
4b; $R_1=CH_3$, $R_2=H$, Y=OiNicMeI
4c; $R_1=R_2=CH_3$, Y=OiNicMeI
4d; $R_1=H$, $R_2=C_6H_5$, Y=OiNicMeI
4e; $R_1=D$, $R_2=C_6H_5$, Y=OiNicMeI

$CH_3OCH_2CH_2OTf$ 5

$(CH_3)_2\overset{+}{N}HCH_2CH_2Cl\ Cl^-$ 6

$CH_3SCH_2CH_2Cl$ 7

OiNicMeI = 

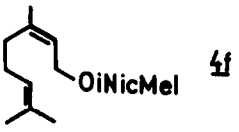
ONicMeI = 

Scheme 1

RESULTS AND DISCUSSION

Compounds 2 and 4 are structurally similar to cationic surfactants consisting of a hydrophilic head (methylpyridinium iodide) and hydrophobic tail. It was of interest to see how such compounds which could in principle also form micelles will affect their own hydrolysis. For this purpose compound 4f was chosen and the results are presented in Table 1. It is evident that with increasing concentration

Table 1. Hydrolysis Rate Constants of Ester 4f at 70°C



4f

Concentration of ester 4f mol dm^{-3}	$1x10^{-3}$	$5x10^{-3}$	$1x10^{-2}$	$5x10^{-2}$	$1x10^{-1}$
$kx10^3$ s^a	11.0(1)	11.0(1)	10.0(1)	1.87(4)	1.73(3)

[a]Numbers in parenthesis are standard deviations of the mean, e.g. 11.0(1) = 11.0±0.1.

of 4f in water an autoinhibition of the hydrolysis occurs. This is obviously caused by micellization (Figure 1). Possible π-participation by the neighboring

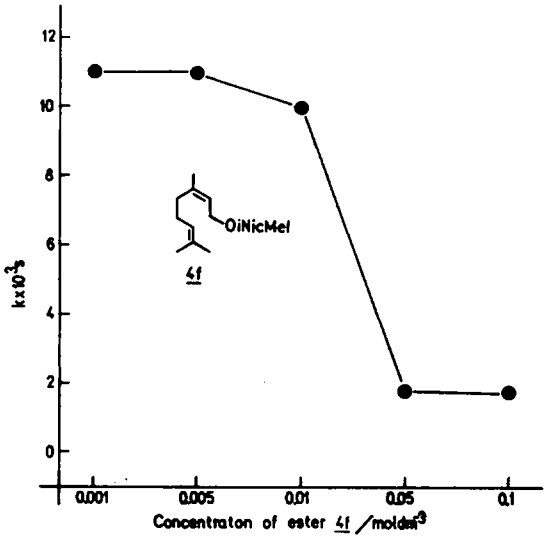
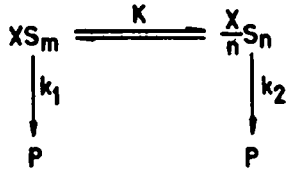


Figure 1. Plot of k values for hydrolysis of 1-methyl-4-(3,7-dimethyl-2,6-octadienyloxycarbonyl)pyridinium iodide (4f) vs. its concentration.

double bonds can be ruled out on the basis of the observed β-deuterium isotope effects which are of normal magnitude for rate determining formation of a solvent separated ion pair (k_H/k_D 1.21 and 1.23, resp.). The observed differences in the hydrolysis rates of ester 4f can be explained on the basis of Scheme 2.



Scheme 2

S_m is the concentration of the monomer unit of the surfactant, X the number of monomers, (ester 4f) in water, n the number of monomers in the micelle, and K the association constant of monomeric units in the micelle.

Before the micellization the monomer units are statistically distributed in the water (left part of the curve in Fig.1) and the compound solvolyzes with rate constant k_1. Reaching the critical micellization concentration (CMC), miceller associates are formed and they are in equilibrium with the monomeric units in water. At this point the hydrolysis rate is a combination of two rate constants, k_1 and k_2, which caused a drop in the reactivity with increasing concentration of 4f. These results are in agreement with previously discussed phenomena in NMR spectroscopy.[11]

Next we wanted to investigate the influence of added anionic surfactant on the hydrolysis rate. It was necessary to determine the mechanism of the hydrolysis of esters bearing the new leaving group. Theoretically three different fissions can occur (Fig. 2).

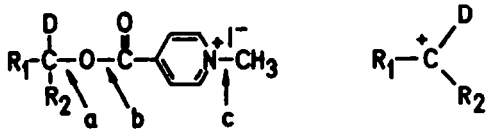


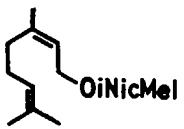
Figure 2

In biological systems O-acyl fission is the most common mechanism (b). It is also known that N-acyl fission can occur (c).[12] O-Alkyl fission can be expected to occur if the departing cationic fragment is a relatively stable ion(a). This problem was also encountered in the solvolysis of p-nitrobenzoyl esters, where the determination of α-secondary deuterium isotope effects was used as a probe of the mechanism.[13] We applied this test to our substrates and it was found that in all cases the observed α-effects are of normal magnitude (1.19-1.26) for reactions proceeding via rate determining formation of cationic intermediates. In our case, the cationic part is the benzyl and allyl cation, respectively. In all investigated cases (2, 4- 7) the addition of an anionic surfactant (SDS) resulted in an inhibition of the hydrolysis rates (Table 2). This inhibition is not the same in all cases. With esters 2 and 4 which are in a certain way also micelles and which solvolyze by S_N1 mechanism the inhibition is very pronounced. This is not the case with ccmpounds which react with neighboring group participation (5-7). Two explanations for this behavior can be given. Different polarities of the "head" part of SDS and substrates 2 and 4 form a compact mixed micelle decreasing the solvolytic reactivity.[11] Compounds 5-7 contain an internal nucelophile rendering the orientation within the micelle less important. The dependence of the hydrolysis rates on the concentration of SDS is shown in Tables 2 and 3. The behavior of compounds 2 and 4 cannot be explained only on the basis of a mixed micelle formation (Fig. 3). m-Values are also an important factor for defining the mechanism of the hydrolysis.[14] In a separate investigation we determined the Grunwald-Winstein m--values for compounds 4d, 5, 6, and 7 in different mixed aqueous organic solvents.[15] If these values are plotted against the logarithm of the ratio of hydrolysis rates in the presence of SDS and in pure water a straight line is obtained (corr. coeff. 0.9995, Fig. 5). The gradient of this plot shows the sensitivity of the investigated substrates to change in the polarities of the solvent.

Table 2. Hydrolysis Rate Constants for Compounds 2 and 4-7 in SDS Water Solution

Compound	t/°C	$k \times 10^4\ s^a$							$k_{H_2O}/k_{0.1M\,SDS}$	m
		H_2O	1×10^{-4}M SDS	5×10^{-4}M SDS	1×10^{-3}M SDS	5×10^{-3}M SDS	1×10^{-2}M SDS	1×10^{-1}M SDS		
$PhCH_2ONicMeI$ 2a	95	3.17(2)	3.00(3)	1.83(3)	0.540(2)	0.0543(7)	0.0549(7)	0.0535(7)	59.25	-
$PhCHCH_3$ ONicMeI 2b	95	22.99(5)	22.5(1)	21.9(1)	10.8(3)	0.767(7)	0.535(4)	0.496(1)	46.35	-
$PhC(CH_3)_2$ ONicMeI 2c	50	337(4)	328(2)	243(1)	154(1)	15.3(1)	6.00(3)	3.86(1)	87.31	-
PhCHPh ONicMeI 2d	80	451(2) 1.25(1)[b]	389(4) 1.24(2)[b]	328(2) 1.23(2)[b]	177(1) 1.22(1)[b]	25.0(3) 1.26(3)[b]	15.2(1) 1.24(1)[b]	1.50(1) 1.23(2)[b]	30.07	-
$PhCH_2OiNicMeI$ 4a	95	44.5(2)	36.1(2)	23.6(3)	19.7(2)	6.56(5)	3.66(6)	1.71(3)	26.02	-
$PhCHCH_3$ OiNicMeI 4b	90	51.8(3)	27.1(2)	25.1(3)	23.0(3)	5.97(2)	1.60(3)	7.9(2)	65.57	-
$PhC(CH_3)_2$ OiNicMeI 4c	30	337(3)	325(2)	118(1)	83.1(5)	4.53(4)	2.60(1)	2.51(1)	134.26	-
PhCHPh OiNicMeI 4d	60	123(1) 1.24(1)[b]	117(1)	70.2(4)	22.5(3)	2.28(2)	2.21(1)	2.08(1) 1.26(2)[b]	59.13	1

Table 2 - continued. Hydrolysis Rate Constants for Compounds 2 and 4-7 in SDS Water Solution

Compound	t/°C	k x 10^4 s^a							$k_{H_2O}/k_{0.1MSDS}$	m
		H_2O	$1x10^{-4}$M SDS	$5x10^{-4}$M SDS	$1x10^{-3}$M SDS	$5x10^{-3}$M SDS	$1x10^{-2}$M SDS	$1x10^{-1}$M SDS		
 **4f**	70	110(1) 1.21(2)[b]	99(1)	50.3(4)	15.4(2)	1.68(1)	1.51(1)	1.02(3) 1.26(4)[b]	106.86	-
$CH_3OCH_2CH_2OTf$ **5**	25	54.83(3)	52.0(2)	49.2(3)	27.1(3)	5.44(2)	5.43(2)	5.41(2)	10.03	0.548
$(CH_3)_2NH^+CH_2CH_2Cl$ Cl^- **6**	80	121(1)	109(1)	111(1)	106(1)	78.7(2)	46.5(3)	22.3(1)	5.43	0.399
$CH_3SCH_2CH_2Cl$ **7**	25	1.92(1)	1.84(1)	1.76(2)	1.70(1)	1.71(1)	1.71(2)	1.61(2)	1.20	0.066

[a] Numbers in parentheses are standard deviations of the mean, e.g. 3.17(2) = 3.07 ± 0.07.

[b] k_H/k_D values.

Table 3. Rates and Secondary α-Deuterium Kinetic Isotope Effects for the Hydrolysis of Ester 4f at 80°C in Different Concentrations of SDS in Water

Concentration of SDS in water mol dm^{-3}	0	10^{-4}	5×10^{-4}	10^{-3}	5×10^{-3}	10^{-2}	5×10^{-2}
$k \times 10^4$ s[a]	163(2)	143(1)	102(2)	55.1(1)	4.54(1)	2.34(1)	2.00(1)
k_H/k_D[a]	1.24(1)	1.23(2)	1.25(1)	1.26(3)	1.23(2)	1.22(1)	1.24(2)
Concentration of SDS in water mol dm^{-3}	10^{-1}	2×10^{-1}	3×10^{-1}	4×10^{-1}	5×10^{-1}	6×10^{-1}	2
$k \times 10^4$ s[a]	1.73(1)	1.65(1)	1.45(2)	1.37(1)	1.30(1)	1.26(1)	1.00(1)
k_H/k_D[a]	1.22(4)	1.23(3)	1.25(1)	1.26(1)	1.23(1)	1.25(2)	1.24(1)

[a]Numbers in parentheses are standard deviations of the mean, e.g. 136(2) = 136 ±2 and 1.24(1) = 1.24 ± 0.01.

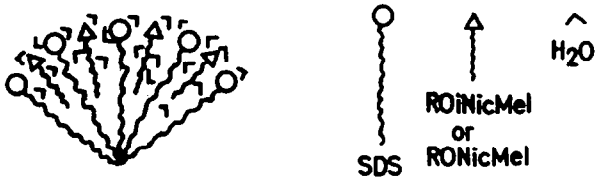


Figure 3

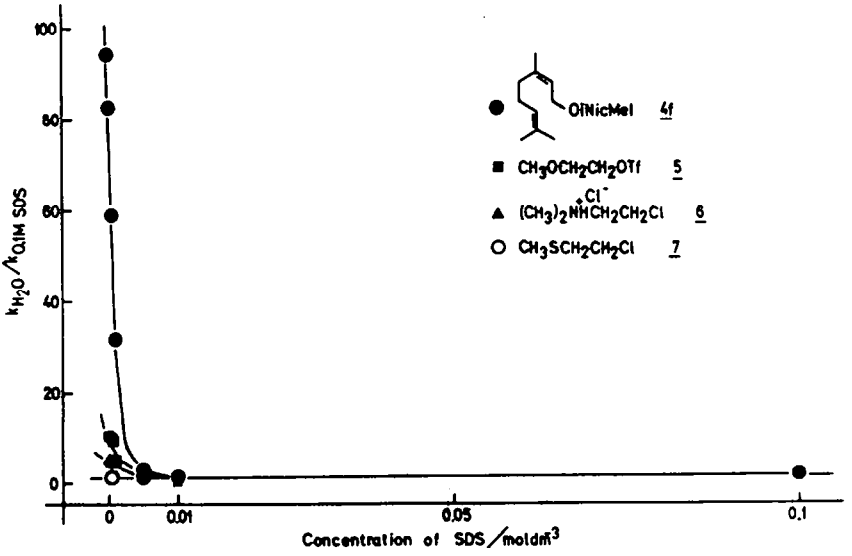


Figure 4. Plot of $k_{H_2O}/k_{0.1M\ SDS}$ for hodrolyses of compounds 4f, 5, 6 and 7 vs.SDS concentration in water.

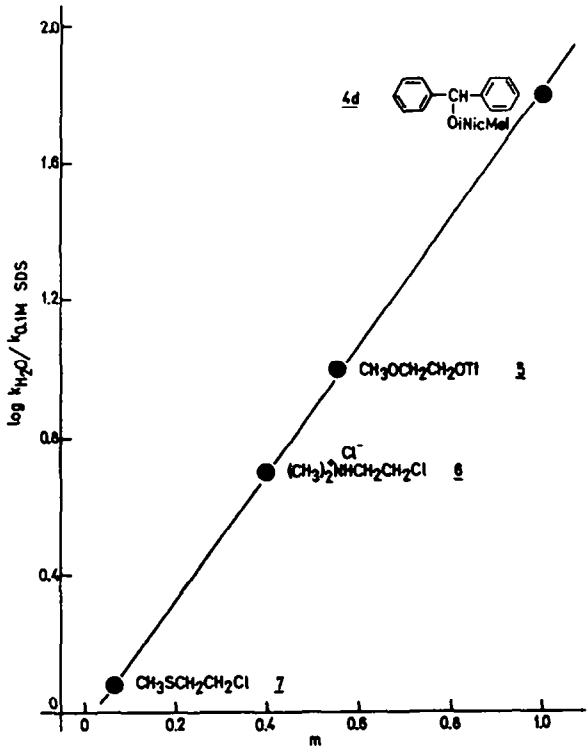
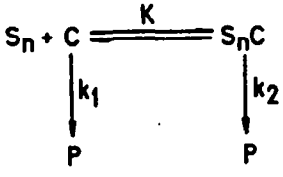


Figure 5. Linear correlation of log $k_{H_2O}/k_{0.1M\,SDS}$ of compounds 4d, 5, 6 and 7 with their m values.

Menger proposed the following scheme for the reaction of a substrate in a micellar solution:[15]



Scheme 3

By simple transformation equation (1)[7] was obtained which can be linearized by plotting $1/k_1-k_{obsd.}$ vs. $1/S_n$ ($S_n = (S_t-CMC)/n$); S_t is the total concentration of SDS. In this way the unknowns in equ. 1 can be evaluated:

$$\frac{1}{k_1 - k_{obsd.}} = \frac{1}{k_1 - k_2} + \frac{1}{(k_1 - k_2)KS_n} \qquad (1)$$

This approach cannot be applied in cases of 2 and 4 because they form mixed micelles with SDS and it would require the separate determination of CMC and n for each substrate. Therefore we propose a different form of linearization (equ. 2)

$$St = CMC + \frac{n}{K}\left(\frac{k_1 - k_{obsd.}}{k_{obsd.} - k_2}\right) \qquad (2)$$

which makes use only of known parameters from equation 1. The relation between S_t and $(k_1 - k_{obsd})/(k_{obsd}-k_2)$ is shown in Fig. 6 for 2f. Two lines can be drawn,

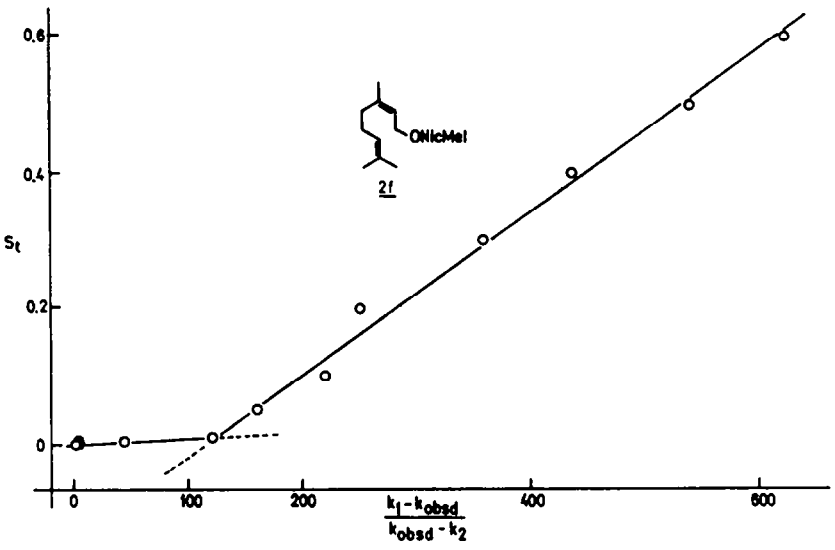


Figure 6. Plot of S_t vs. $k_1 - k_{obsd.}/k_{obsd.} - k_2$ for hydrolysis of ester 2f.

the left part pertains to the situation before micellization, and the right part with the steep line to the situation after micellization. The breaking point refers to a 1:1 ratio of substrate vs. SDS where the most stable micelle is formed.

Finally it is interesting to note that the products of the hydrolysis of substrates where a π-participation by the remote double bond was observed under different conditions, are only those resulting from direct displacement by water at the reacting center. This evidently shows that water must be present inside the mixed micelle which prevents due to its greater nucleophilicity the intramolecular attack by the double bond.

In conclusion, our results show that the two types of compounds used in the course of this work solvolyze in the micelle more slowly than in pure water. Two new leaving groups were introduced which match the reactivity of p-nitrobenzoates but enable rate studies of organic substrates in pure water.

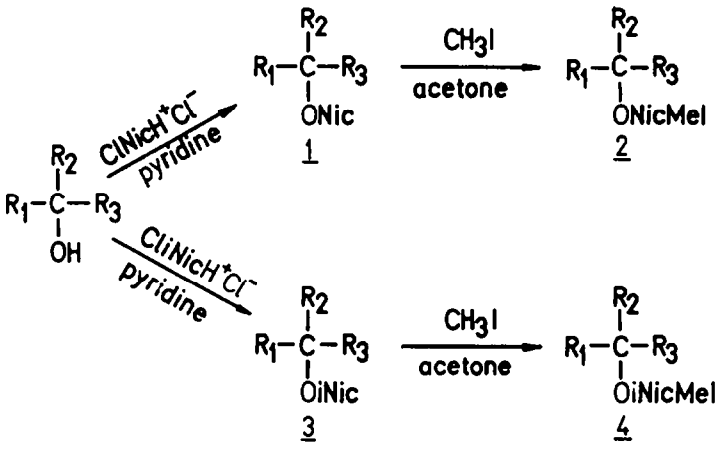
EXPERIMENTAL

Infrared spectra of samples in KBr were recorded on a Perkin-Elmer 257 spectrometer. ^{1}H NMR spectra were recorded on a JEOL FX-90Q spectrometer. Signal positions were given in δ units, with tetramethylsilane as the internal standard. All deuterated compounds have deuterium content >98% d_1 (by ^{1}H NMR). All new compounds were characterized by ^{1}H NMR and IR spectroscopy and in some cases also by elemental analysis.

The nicotinates 1a, 1b, and 1d[17,18], salt 2a[18] and chlorides 6[19] and 7[20] were prepared and characterized as previously described.

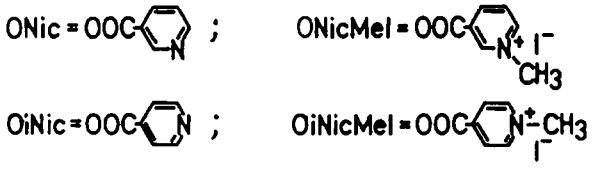
General Procedure for the Preparation of Nicotinates and Isonicotinates

Nicotinates 1c, 1e, 1f, and 1g and isonicotinates 3a-3g were prepared by a modified procedure for the synthesis of p-nitrobenzoates.[21] Solution of alcohol (0.71 mmol) and nicotinyl chloride hydrochloride or isonicotinyl chloride hydrochloride (410 mg, 2.5 mmol) respectively, in anhydrous pyridine (20 mL) was stirred for two days at room temperature. The mixture was then poured on ice and extracted with ether (5 x 30 mL). The dried (Na_2SO_4) ethereal solution was evaporated in vacuo and the residual crude product was purified on a silica gel column using mixture of benzene and ether (9:1) as eluent. By this procedure oily crystals of 1e, 1f, 1g, 3a, 3b, 3d, 3e, 3f, and 3g (90-96% yield) or 1c and 3c (38% and 40% yield, respectively) were obtained.



Compounds 1–4

a; $R_1 = C_6H_5, R_2 = R_3 = H$
b; $R_1 = C_6H_5, R_2 = CH_3, R_3 = H$
c; $R_1 = C_6H_5, R_2 = R_3 = CH_3$
d; $R_1 = R_2 = C_6H_5, R_3 = H$
e; $R_1 = R_2 = C_6H_5, R_3 = D$
f; $R_1 = (CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CH, R_2 = R_3 = H$
g; $R_1 = (CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CH, R_2 = H, R_3 = D$



Scheme 4

2-Phenyl-2-propyl Nicotinate (1c)

IR 3090, 3060, and 3030 (Ar-H), 1725 (CO-O-C), 1594 (C=C), 1293 and 1122 (C-O), 770, 750 and 705 cm^{-1} (Ar-H); ^1H NMR ($CDCl_3$) δ 9.27, 8.74, 8.32, and 8.23 (4H, four m, nicotinyl), 7.35 (5H, m, C_6H_5), 1.93 (6H, s, CH_3).

1-Deuteriodiphenylmethyl Nicotinate (1e)

IR 3090, 3060, and 3030 (Ar-H), 1712 (CO-O-C), 1590 (C=C), 1282 and 1115 (C-O), 761, 747, and 703 cm^{-1} (Ar-H); ^1H NMR ($CDCl_3$) δ 9.33, 8.79, 8.40, and 8.31 (4H, four m, nicotinyl), 7.37 (10H, m, $2 \times C_6H_5$).

3,7-Dimethyl-2,6-octadienyl Nicotinate (1f)

IR 3090, 3040, and 3030 (H-C=C), 1723 (CO-O-C), 1670 and 1595 (C=C), 1283 and 1115 (C-O), 749 and 710 cm^{-1} (Ar-H); ^1H NMR ($CDCl_3$) δ 9.24, 8.75, 8.33, and 8.23 (4H, four m, nicotinyl), 5.50 (1H, t, J = 8Hz, $\underline{CH}$-CH_2ONic), 5.11 (1H, m, $CH{=}C(CH_3)_2$), 4.84 (2H, d, J = 8Hz, CH_2ONic), 2.18 (4H, m, $2 \times CH_2$), 1.80 (3H, s, CH_3-C=C), 1.63 (6H, d, J = 6Hz, $(CH_3)_2C{=}C$).

Anal. Calcd. (%) for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40
Found (%): C, 74.16; H, 8.09; N, 5.38

1-Deuterio-3,7-dimethyl-2,6-octadienyl Nicotinate (1g)

IR 3090, 3040, and 3030 (H-C=C), 1727 (CO-O-C), 1670 and 1597 (C=C), 1280 and 1122 (C-O), 762, 702, and 682 cm^{-1} (Ar-H); ^1H NMR ($CDCl_3$) δ 9.24, 8.77, 8.32, and 8.25 (4H, four m, nicotinyl), 5.49 (1H, d, J = 7.6Hz, $\underline{CH}$=CHDONic), 5.12 (1H, m, $\underline{CH}$=C(CH_3)$_2$), 4.84 (1H, d, J = 7.5Hz, CHDONic), 2.17 (4H, m, 2xCH_2), 1.80 (3H, s, $\overline{CH_3}$-C=C), 1.64 (6H, d, J = 6Hz, (CH_3)$_2$C=C).

Benzyl Isonicotinate (3a)

IR 3090, 3070, and 3035 (Ar-H), 1728 (CO-O-C), 1600 (C=C), 1280 and 1122 (C-O), 762, 702, and 682 cm^{-1} (Ar-H); ^1H NMR (CD_3OD) δ 8.66 and 7.84 (4H, 2d, J = 6Hz, isonicotinyl), 7.38 (5H, m, C_6H_5 (2H, s, CH_2Ph).

1-Phenylethyl Isonicotinate (3b)

IR 3085, 3060, and 3030 (Ar-H), 1725 (CO-O-C), 1598 (C=C), 1282 and 1128 (C-O), 762, 702, and 685 cm^{-1} (Ar-H); ^1H NMR (CD_3OD) δ 8.68 and 7.88 (4H, 2d, J = 6Hz, isonicotinyl), 7.40 (5H, m, C_6H_5), 6.10 (1H, q, J = 6.7Hz), 1.65 (3H, d, J = 6.7Hz).

2-Phenyl-2-propyl Isonicotinate (3c)

IR 3085, 3060, and 3028 (Ar-H), 1727 (CO-O-C), 1600 (C=C), 1290 and 1125 (C-O), 763, 703, and 685 cm^{-1} (Ar-H); ^1H NMR (CD_3OD) δ 8.63 and 7.83 (4H, 2d, J = 6Hz, isonicotinyl), 7.30 (5H, m, C_6H_5), 1.87 (6H, s, 2xCH_3).

Diphenylmethyl Isonicotinate (3d)

IR 3083, 3060, and 3024 (Ar-H), 1728 (CO-O-C), 1600 (C=C), 1280 and 1126 (C-O), 765, 750, 705, and 684 cm^{-1} (Ar-H); ^1H NMR (CD_3OD) δ 8.73 and 7.85 (4H, 2d, J = 6Hz, isonicotinyl), 7.33 (10H, m, 2xC_6H_5), 7.70 (1H, s, $CHPh_2$).

1-Deuteriodiphenylmethyl Isonicotinate (3e)

IR 3080, 3060, and 3020 (Ar-H), 1720 (CO-O-C), 1598 (C=C), 1285 and 1128 (C-O), 765, 750, 703, and 682 cm^{-1} (Ar-H); ^1H NMR (CD_3OD) δ 8.65 and 7.86 (4H, 2d, J = 6Hz, isonicotinyl), 7.32 (10H, m, 2xC_6H_5).

3,7-Dimethyl-2,6-octadienyl Isonicotinate (3f)

IR 3090, 3040, and 3035 (H-C=C), 1730 (CO-O-C), 1670 and 1600 (C=C), 1282 and 1122 (C-O), 765, 715, and 685 cm^{-1} (Ar-H); ^1H NMR (CD_3OD) δ 8.71 and 7.89 (4H, 2d, J = 6Hz, isonicotinyl), 5.50 (1H, t, J = 8Hz, $\underline{CH}$-$\underline{CH_2}$OiNic), 5.11 (1H, m, $\underline{CH}$=C(CH_3)$_2$), 4.85 (2H, d, J = 8Hz, CH_2OiNic), 2.17 (4H, m, 2xCH_2), 1.80 (3H, s, $\overline{CH_3}$-C=C), 1.63 (6H, d, J = 6Hz, (CH_3)$_2$C=C).

Anal. Calcd. (%) for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40
Found (%): C, 74.08; H, 8.13; N, 5.37

1-Deuterio-3,7-dimethyl-2,6-octadienyl Isonicotinate (3g)

IR 3090, 3050, and 3030 (H-C=C), 1728 (CO-O-C), 1768 and 1600 (C=C), 1285 and 1125 (C-O), 765, 715, and 685 cm^{-1} (Ar-H); ^1H NMR (CD_3OH) δ 8.68 and 7.84 (4H, 2d, J = 6Hz, isonicotinyl), 5.48 (1H, d, J = 7Hz, $\underline{CH}$-CHDOiNic), 5.09 (1H, m, CH=C(CH_3)$_2$), 4.85 (1H, d, J = 7Hz, CHDOiNic), 2.15 (4H, m, $\overline{2}$xCH_2), 1.80 (3H, s, CH_3-C=C), 1.62 (6H, d, J = 6Hz, (CH_3)$_2$C=C).

General Procedure for the Preparation of 1-Methyl-3- and-4-Alkyloxy-carbonylpyridinium Iodides

These compcunds were prepared according to modified procedure for the synthesis of 1-methyl-3-benzyloxycarbonylpyridinium iodide (2a).[20] Solution of nicotinate or isonicotinate (0.5 mmol) and methyl iodide (280 mg, 2 mmol) in anhydrous acetone (20 mL) was kept for one day at room temperature. The semisolid mass which formed was finely ground, filtered and washed with little acetone. It was purified by solution in absolute alcohol and precipitation with dry mixture of ether--petroleum ether. The yields for all compounds were ~90%.

1-Methyl-3-(1-phenylethyloxycarbonyl)pyridinium Iodide (2b)

IR 3080, 3060, and 3030 (Ar-H), 1730 (CO-O-C), 1640 (C=$\overset{+}{N}$-CH_3), 1595 (C=C), 1295 and 1125 (C-O), 750 and 710 (phenyl), 775 and 670 cm-1 (pyridinium); ^1H NMR (DMSO-d_6) δ 9.56, 9.20, 9.05, and 8.27 (4H, s+d+d+2d, J = 6.5 Hz, pyridinium), 7.50 (5H, m, C_6H_5), 6.17 (2H, q, J = 6.5Hz, CHPh), 4.45 (3H, s, N-CH_3), 1.66 (3H, d, J = 6.5Hz, CH_3)

Anal. Calcd. (%) for $C_{15}H_{16}INO_2$: C, 48.80; H, 4.37; I, 34.37; N, 3.79
Found (%): C, 48.94; H, 4.42; I, 34.46; N, 3.68

1-Methyl-3-(2-phenyl-2-propyloxycarbonyl)pyridinium Iodide (2c)

IR 3080, 3060, and 3025 (Ar-H), 1729 (CO-O-C), 1635 ($C=\overset{+}{N}-CH_3$), 1595 (C=C), 1295 and 1123 (C-O), 751 and 708 (phenyl), 768 and 670 cm^{-1} (pyridinium); ^1H NMR (DMSO-d_6) δ 9.54, 9.20, 9,03, and 8.28 (4H, s+d+d+2d, J = 6.5Hz, pyridinium), 7.47 (5H, m, C_6H_5), 4.43 (3H, s, $\overset{+}{N}-CH_3$), 1.91 (6H, s, $2\times CH_3$)

Anal. Calcd. (%) for $C_{16}H_{18}INO_2$: C, 50.15; H, 4.73; I, 33.11; N, 3.65
Found (%): C, 49.98; H, 4.67; I, 33.31; N, 3.71

1-Methyl-3-diphenylmethyloxycarbonylpyridinium Iodide (2d)

IR 3085, 3055, and 3030 (Ar-H), 1730 (CO-O-C), 1635 ($C=\overset{+}{N}-CH_3$), 1595 (C=C), 1290 and 1120 (C-O), 750 and 710 (phenyl), 770 and 670 cm^{-1} (pyridinium); ^1H NMR (DMSO-d_6) δ 9.64, 9.18, and 8.26 (4H, s+2d+2d, J = 6.5Hz, pyridinium), 7.57 and 7.36 (4H+6H, 2m, $2\times C_6H_5$), 7.18 (1H, s, CHPh), 4.46 (3H, s, $^+N-CH_3$).

Anal. Calcd. (%) for $C_{20}H_{18}INO_2$: C, 55.70; H, 4.21; I, 29.43; N, 3.25
Found (%): C, 55.58; H, 4.30; I, 30.02; N, 3.24

1-Methyl-3-(1-deuteriodiphenylmethyloxycarbonyl)pyridinium Iodide (2e)

IR 3085, 3060, and 3030 (Ar-H), 1730 (CO-O-C), 1640 ($C=\overset{+}{N}-CH_3$), 1595 (C=C), 1298 and 1125 (C-O), 750 and 708 (phenyl), 770 and 670 cm^{-1} (pyridinium); ^1H NMR (DMSO-d_6) δ 9.63, 9.17, and 8.25 (4H, s+2d+2d, J = 6.5Hz, pyridinium), 7.55 and 7.33 (4H+6H, 2m, $2\times C_6H_5$), 4.47 (3H, s, $\overset{+}{N}-CH_3$).

1-Methyl-3-(3,7-dimethyl-2,6-octadienyloxycarbonyl)pyridinium Iodide (2f)

IR 3040 (H-C=C), 1732 (CO-O-C), 1642 ($C=\overset{+}{N}-CH_3$), 1595 (C=C), 1295 and 1122 (C-O), 755 and 672 cm^{-1} (pyridinium); ^1H NMR (DMSO-d_6) δ 9.50, 9.21, 8.96, and 8.26 (4H, s+d+d+2d, J = 7Hz, pyridinium), 5.48 (1H, t, J = 7Hz, $\underline{CH}CH_2ONicMeI$), 5.11 (1H, m, $\underline{CH}=C(CH_3)_2$), 4.91 (2H, d, J = 7Hz, $CH_2ONicMeI$), 4.44 (3H, s, $^+N-CH_3$), 2.16 (4H, m, $\overline{CH_2CH_2}$), 1.78 (3H, s, C=C-CH_3), 1.61 (6H, d, J = 5Hz, $C=C(CH_3)_2$).

Anal. Calcd. (%) for $C_{17}H_{24}INO_2$: C, 50.88; H, 6.03; I, 31.62; N, 3.49
Found (%): C, 50.70; H, 5.95; I, 30.99; N, 3.41

1-Methyl-3-(1-deuterio-3,7-dimethyl-2,6-octadienyloxycarbonyl)pyridinium Iodide (2g)

IR 3035 (H-C=C), 1732 (CO-O-C), 1643 ($C=\overset{+}{N}-CH_3$), 1596 (C=C), 1290 and 1128 (C-O), 755 and 673 cm^{-1} (pyridinium); ^1H NMR (DMSO-d_6) δ 9.54, 9.20, 8.95, and 8.25 (4H, s+d+d+2d, J = 7Hz, pyridinium), 5.45 (1H, d, J = 7Hz, $\underline{CHCHDONicMeI}$), 5.10 (1H, m, $\underline{CH}=C(CH_3)_2$), 4.90 (1H, d, J = 7Hz, CHDONicMeI), 4.44 (3H, s, $^+N-CH_3$), 2.15 (4H, m, $\overline{CH_2CH_2}$), 1.76 (3H, s, C=C-CH_3), 1.61 (6H, d, J = 5Hz, $C=C(CH_3)_2$).

1-Methyl-4-benzyloxycarbonylpyridinium Iodide (4a)

IR 3110, 3070, and 3040 (Ar-H), 1730 (CO-O-C), 1640 ($C=\overset{+}{N}-CH_3$), 1608 (C=C) 1290 and 1130 (C-O), 748 and 703 (phenyl), 770 and 682 cm^{-1} (pyridinium); ^1H NMR (DMSO-d_6) δ 9.21 and 8.54 (4H, 2d, J = 6.5Hz, pyridinium), 7.46 (5H, m, C_6H_5), 5.48 (2H, s, CH_2Ph), 4.48 (3H, s, $\overset{+}{N}-CH_3$).

Anal. Calcd. (%) for $C_{14}H_{14}INO_2$: C, 47.34; H, 3.97; I, 35.73; N, 3.94
Found (%): C, 47.20; H, 4.08; I, 35.47; N, 4.03

1-Methyl-4-(1-phenylethyloxycarbonyl)pyridinium Iodide (4b)

IR 3110, 3070, and 3030 (Ar-H), 1730 (CO-O-C), 1642 ($C=\overset{+}{N}-CH_3$), 1585 (C=C), 1283 and 1135 (C-O), 768, 708, and 683 cm^{-1} (Ar-H); ^1H NMR (DMSO-d_6) δ 9.22 and 8.56 (4H, 2d, J = 6Hz), 7.42 (5H, m, C_6H_5), 6.14 (1H, q, J = 6.5Hz), 4.47 (3H, s, $\overset{+}{N}-CH_3$), 1.68 (3H, d, J = 6 Hz, CH_3).

Anal. Calcd. (%) for $C_{15}H_{16}INO_2$: C, 48.80; H, 4.37; I, 34.37; N, 3.79
Found (%): C, 49.02; H, 4.41; I, 34.41; N, 3.65

1-Methyl-4-(2-phenyl-2-prcpyloxycarbonyl)pyridinium Iodide (4c)

IR 3110, 3060, and 3030 (Ar-H), 1718 (CO-O-C), 1640 ($C=\overset{+}{N}-CH_3$), 1585 (C=C), 1283 and 1135 (C-O), 768, 702, and 683 cm^{-1} (Ar-H); ^1H NMR (DMSO-d_6) δ 9.21 and 8.52 (4H, 2d, J = 6.5Hz, pyridinium), 7.44 (5H, m, C_6H_5), 4.47 (3H, s, $\overset{+}{N}-CH_3$), 1.91 (6H, s, $2\times CH_3$).

Anal. Calcd. (%) for $C_{16}H_{18}INO_2$: C, 50.15; H, 4.73; I, 33.11; N, 3.65
Found (%): C, 50.55; H, 4.82; I, 33.17; I, 3.73

1-Methyl-4-diphenylmethyloxycarbonylpyridinium Iodide (4d)

IR 3120, 3065, and 3035 (Ar-H), 1728 (CO-O-C), 1645 ($C=\overset{+}{N}-CH_3$), 1587 (C=C), 1290 and 1132 (C-O), 755 and 703 (phenyl), 767 and 688 cm-1(pyridinium); ^{1}H NMR (DMSO-d_6) δ 9.20 and 8.67 (4H, 2d, J = 7Hz), 7.55 and 7.36 (4H+6H, 2m, 2xC_6H_5), 7.14 (1H, s, $CHPh_2$), 4.46 (3H, s, $\overset{+}{N}-CH_3$).

Anal. Calcd. (%) for $C_{20}H_{18}INO_2$: C, 55.70; H, 4.21; I, 29.43; N, 3.25
Found (%): C, 55.51; H, 4.12; I, 29.66; N, 3.36

1-Methyl-4-(1-deuteriodiphenylmethyloxycarbonyl)pyridinium Iodide (4e)

IR 3110, 3060 and 3030 (Ar-H), 1730 (CO-O-C), 1644 ($C=\overset{+}{N}-CH_3$), 1587 (C=C), 1290 and 1130 (C-O), 750 and 700 (phenyl), 767 and 685 cm^{-1} (pyridinium); ^{1}H NMR (DMSO-d_6) δ 9.20 and 8.66 (4H, 2d, J = 7Hz), 7.55 and 7.34 (4H+6H,2m, 2xC_6H_5), 4.46 (3H, s, $\overset{+}{N}-CH_3$).

1-Methyl-4-(3,7-dimethyl-2,6-octadienyloxycarbonyl)pyridinium Iodide (4f)

IR 3140 and 3030 (H-C=C), 1730 (CO-O-C), 1670 and 1583 (C=C), 1643 ($C=\overset{+}{N}-CH_3$), 1285 and 1126 (C-O), 770 and 685 cm-1 (pyridinium); ^{1}H NMR (DMSO-d_6) δ 9.20 and 8.47 (4H, 2d, J = 6.5Hz, pyridinium), 5.44 (1H, t, J = 7Hz, $CHCH_2OINicMeI$), 5.11 (1H, m, $\underline{CH}=C(CH_3)_2$), 4.90 (2H, d, J = 7Hz, $CH_2OINicMeI$), 4.44 (3H, s, $\overset{+}{N}-CH_3$), 2.15 (4H, m, $\overline{CH_2CH_2}$), 1.78 (3H, s, $C=C-CH_3$), 1.61 (6H, d J = 5Hz, $C=C(CH_3)_2$).

Anal. Calcd. (%) for $C_{17}H_{24}INO_2$: C, 50.80; H, 6.03; I, 31.62; N, 3.49
Found (%): C, 50.26; H, 5.98; I, 31.63; N, 3.41

1-Methyl-4-(1-deuterio-3,7-dimethyl-2,6-octadienyloxycarbonyl)pyridinium Iodide (4g)

IR 3130 and 3030 (H-C=C), 1730 (CO-O-C), 1670 and 1582 (C=C), 1642 ($C=\overset{+}{N}-CH_3$), 1280 and 1125 (C-O), 770 and 680 cm^{-1} (pyridinium); ^{1}H NMR (DMSO-d_6) δ 9.20 and 8.52 (4H, 2d, J = 6.5Hz, pyridinium), 5.44 (1H, d, J = 7Hz, $\underline{CH}CHCOINicMeI$), 5.10 (1H, m, $\underline{CH}=C(CH_3)_2$), 4.88 (1H, d, J = 7Hz, $CHDOINicMeI$), 4.45 (3H, s, $\overset{+}{N}-CH_3$), 2.14 (4H, m, $\overline{CH_2CH_2}$), 1.75 (3H, s, $C=C-CH_3$), 1.61 (6H, d, J = 5Hz, $C=C(CH_3)_2$).

2-Methyloxyethyl tosylate (5) was prepared from 2-methyloxyethanol (380 mg, 5.0 mmol) and tosyl chloride (1.90 g, 10 mmol) in dry pyridine (20 mL) in a straightforward manner.[21] Yield = 83.2%.

IR (neat) 3080 and 3030 (Ar-H), 1598 (C=C), 1195 and 1180 (OSO_2) and 1100 cm^{-1} (C-O); ^{1}H NMR ($CDCl_3$) δ 2.42 (3H, s, $ArCH_3$), 3.22 (3H,s, OCH_3), 3.47 (2H, t, J = 7Hz, $\underline{CH_2}OCH_3$), 4.05 (2H, t, J = 7Hz, CH_2OTs), 7.25 and 7.67 (4H, AA'BB' pattern, $\overline{J}$ = 8Hz, C_6H_4).

Kinetic Measurements

Sodium dodecyl sulfate was of commericial quality (Fluka) and used without further purification. Reaction rates were measured by continuous automatic potentiometric titration of the liberated acid[22] by means of a pH-stat (Radiometer, Copenhagen) In each measurement, ca. 0.03 mmol of the ester was dissolved in 15 mL of solvent and the liberated acid titrated with 0.02M NaOH solution in the same solvent.

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REFERENCES

1. B. Svens and B. Rosenholm, J. Colloid Interface Sci., 44, 495 (1973).
2. D.Stigter, J. Phys. Chem., 78, 2480 (1974).
3. F.M. Menger, J.M. Jerkunica and J.C. Johnston, J. Am. Chem. Soc., 100, 4676 (1978).
4. F.M. Menger, Acc. Chem. Res., 12, 111 (1979).
5. F.M. Menger, J. Phys. Chem., 83, 893 (1979).
6. F.M. Menger and D.W. Doll,J. Am. Chem. Soc., 109, 1109 (1984).
7. F.M. Menger, H. Yoshinaga, K.S. Venkatasubban and A.R. Das, J. Org. Chem., 46, 415 (1981).
8. H. Al-Lohedan, C.A. Bunton and M.M. Mhala, J.Am. Chem. Soc., 104,6654 (1982).
9. C.A. Bunton and S. Ljunggren, J. Chem. Soc., Perkin Trans. II 1984, 355.
10. B. Juršić, M. Ladika and D.E. Sunko, to be published.
11. B. Juršić and D.E. Sunko, Bioorganic Chemistry (submitted for publication).
12. A.R. Katritzky and B. Brycki, J. Am. Chem. Soc., 108, 7295 (1986).

13. 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.
14. G.W. Klumpp, Reactivity in Organic Chemistry, John Wiley & Sons, New York--Chichester-Brisbane-Toronto-Singapore, 1982, pp. 196-203.
15. B. Juršić and D.E. Sunko, to be published.
16. F.M. Menger and C.E. Portnoy, J. Am. Chem. Soc., 89, 4698 (1967).
17. a) Z.J. Vejdelek and M. Protira, Chem. Listy, 45, 448 (1951); through C.A., 47, 8068 (1953); cf. Collection Czechoslov. Chem. Communs., 16, 344 (1951). b) R. Charonnat, J.V. Harispe and L. Chevilland, Bull. Soc. Chim. France, 1948, 1014.
18. Ed. Frommel, D. Vincent and Ph. Gold-Aubert, Therapie, 13, 508 (1958).
19. R.O. Hutchins and L. Rua, Jr., J. Org. Chem., 40, 2567 (1975).
20. W.R. Kirner and W. Windus, Org. Synth., Col. Vol. II, 136 (1943).
21. L. Fieser and M. Fieser, Reagents for Organic Synthesis, Wiley-Interscience, New York, 1967, Vol. 1, p. 1180.
22. For a detailed procedure see: S. Richter, I. Bregovec and D.E. Sunko, J. Org. Chem., 41, 785 (1976).