CONCLUSIONS

1. L zeolite exhibits weak selectivity for NH_4^+ cations which decreases as the degree of ion exchange increases in substitution of potassium cations with ammonia ions.

2. Only L zeolites with a degree of decationization above 50% exhibit catalytic activity in transformation of o-xylene.

3. Isomerization of xylenes on L zeolites primarily takes place by means of intramolecular transformations.

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REACTION OF ACETALS WITH ALIPHATIC NITRO COMPOUNDS. COMMUNICATION 4. REACTION OF ALIPHATIC AND ALICYCLIC KETALS WITH NITROACETIC ACID ESTER AND SYNTHESIS OF α,β-DEHYDRO-α-ACETYLAMINO ACID ESTERS

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α,β-Dehydro-α-amino acids (ΔAA) are necessary for the preparation of new antibiotics, phytotoxic peptides [1, 2], and other physiologically active compounds. ΔAA have also become increasingly important as substrates for asymmetric reduction to optically active α-amino acids (AA) [3].

The present article concerns the study of the alkoxyalkylation of nitroacetic acid ester (NAE) by open-chain ketals (I) as a possible means of synthesis of difficult-to-obtain β,β-disubstituted ΔAA.

It was previously shown that open-chain [4, 5] and cyclic [6] benzaldehyde acetals and some ring-substituted derivatives easily alkylate NAE in the presence of Ac_2O with formation of α-nitrocinnamic acid esters; the latter were then used for synthesis of AA from the phenylalanine series. Cyclic ketals did not react with NAE in the conditions studied [6]. In the present article, it is shown that ketals (I) in the presence of Ac_2O react with NAE during heating in an inert solvent with formation of β,β-disubstituted β-alkoxy-α-nitrocarboxylic acids (II) with high yields (Table 1). The best results were obtained with a twofold excess of (I) and Ac_2O with respect to the ratio to NAE. The reaction of (I) with NAE is more difficult than in the case of aromatic acetals

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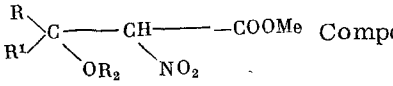
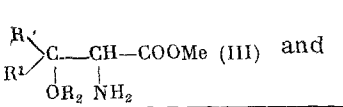
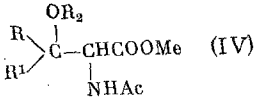
TABLE 1. Properties of  Compounds (II)

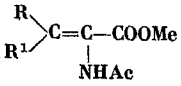
Compound	Time, h	Yield, %*	bp, °C (p, mm Hg)	IR spectrum (ν, cm^{-1} in a thin layer)	PMR spectrum (δ, ppm, CCl_4)	Empirical formula	Observed/Calculated, %		
							C	H	N
(IIa)	9	79	90—93(3)	1755, 1565, 1375	1,4 s (6H); 3,2 c (3H); 3,75 s (3H); 5,38 s (H)	$C_7H_{13}NO_5$	44,41 / 43,97	6,64 / 6,85	7,79 / 7,33
(IIb)	8	89	85–88(1)	1760, 1565, 1370	1,0 t (3H); 1,4 s (6H); 3,5 q (2H); 3,8 s (3H); 5,5 s (1H)	$C_8H_{15}NO_5$	46,92 / 46,82	7,33 / 7,37	7,05 / 6,83
(IIc)	10	68	95–103(1)	1750, 1560, 1365	0,85 t (3H); 1,0 t (3H, OR); 1,4 s (3H, CH_3); 1,8 q (2H); 3,45; 3,55 q (2H, OR); 3,8 s (3H); 5,45; 5,55 s (CH)	$C_9H_{17}NO_5$	49,13 / 49,30	7,74 / 7,82	6,06 / 6,39
(IId)	12	66	110–112(1)	1755, 1555, 1360	1,08 t (3H); 1,5 m(10H); 3,75 s (3H); 3,48 q (2H); 5,45 s (CH)	$C_{11}H_{19}NO_5$	53,90 / 53,86	7,68 / 7,81	5,35 / 5,71
(IIe)	10	56	104–106(1)	1770, 1570, 1380	1,1 t (3H); 1,5 m(8H); 3,75 s (3H); 3,5 q (2H); 5,4 s (CH)	$C_{10}H_{17}NO_5$	–	–	6,21 / 6,06

*After distillation, calculated for NAE.

TABLE 2. Properties of  (III) and  (IV)

Compound	Yield, % (after distillation)	bp, °C (p, mm Hg)	IR spectrum (in a thin layer), ν, cm^{-1}	PMR spectrum (δ, ppm, J, Hz; CCl_4)	Empirical formula	Observed/Calculated, %		
						C	H	N
(IIIa)	85	51 (1)	3360, 1735, 1600	1,07 (3H); 1,05 s (3H); 2,95 s (2H); 3,0 s (3H); 3,6 s (3H); 3,3 s (3H)	$C_7H_{15}NO_3$	51,99 / 52,15	9,48 / 9,38	8,99 / 8,69
(IVa)	65	124–125 (2)	3270, 1740, 1660	1,1 s (3H); 1,14 s (3H); 1,9 s (3H); 3,05 s (3H); 3,6 s (3H); 4,5 d (1H, J=7); 7,4 (NH, J=7)	$C_9H_{17}NO_4$	52,89 / 53,19	8,42 / 8,43	7,20 / 6,90
(IIIb)	80	100–101 (20)	3370, 1735, 1600	1,2 s (6H); 1,1 t (3H); 1,95 s (2H); 3,4 q (2H); 3,45 s (1H); 3,65 s (3H)	$C_8H_{17}NO_3$	54,90 / 54,83	9,80 / 9,78	8,27 / 7,99
(IVb)	77	130–131 (2)	3330, 1740, 1635	1,0 t (3H); 1,15 s (6H); 1,95 s (3H); 3,3 q (2H); 3,6 s (3H); 4,5 d (CH, J=8); 7,45 d (NH, J=8)	$C_{10}H_{19}NO_4$	55,69 / 55,28	8,76 / 8,82	6,91 / 6,45
(IIIc)	72	57–63 (2)	3350, 1735, 1620	0,85 t (3H); 0,95 t (3H); 1,15 s (3H), 1,55 q (2H); 2,55 br. s (2H); 3,5 m (2H); 3,65 s (3H); 3,7 s (1H)	$C_9H_{19}NO_3$	56,83 / 57,11	10,05 / 10,12	6,84 / 7,40
(IVc)	82	110–122 (1)	3270, 1740, 1655	0,9 t (3H); 1,05 t (3H); 1,15 s (3H); 1,7 m (2H); 3,3 m (2H); 1,95 s (3H, OAc); 3,65 s (3H); 4,55 m (CH); 7,45 m (NH)	$C_{11}H_{21}NO_4$	56,66 / 57,11	9,17 / 9,15	6,39 / 6,06
(IIId)	57	107–113 (1)	3300, 1740, 1600	0,95 t (3H); 1,3 m (10H); 1,7 br. s (2H); 3,3 q (2H); 3,55 s (3H); 3,35 s (1H)	$C_{11}H_{21}NO_3$	61,28 / 61,36	9,94 / 9,83	6,48 / 6,51
(IVd)	79	*	3250, 1730, 1650	1,05 t (3H); 1,4 m (10H); 2,0 s (3H); 3,3 q (2H); 3,6 s (3H); 4,7 d (CH, J=8); 7,5 d (NH, J=8)	$C_{13}H_{23}NO_4$	61,03 / 60,68	9,19 / 9,01	5,06 / 5,44

* Separated by chromatography in a column packed with SiO_2 (Merck, 70-230 mesh, eluent CCl_4).

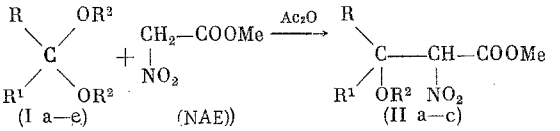
TABLE 3. Properties of  (V)

Compound	Yield, %	mp, °C	IR spectrum (in vaseline oil, ν, cm^{-1})	PMR spectrum (δ, ppm, $CDCl_3$)	Empirical formula	Observed/Calculated, %		
						C	H	N
(Va)	73 (27)	87–88 *	3250, 1725, 1640, 1530	1,73; 1,75 d (3H, OAc); 2,0 s (3H); 2,07 (3H); 3,65 s (3H); 7,2 b.s (NH)	$C_8H_{13}NO_3$	56,29 56,13	7,78 7,65	8,12 8,18
(Va)†	(31)	71–72	3250, 1720, 1645, 1520	1,2 t (3H); 1,75 s (3H); 1,95 s (3H); 2,05 s (3H); 4,1 q (2H); 7,4 b.s (NH)	–	–	–	–
(Vc)	56	–	3250, 1720, 1645, 1520	1,05 t (3H); 1,95; 1,97 s (3H, OAc); 1,95 s (3H); 2,25 q (2H); 3,6 s (3H); 8,7 b.s (NH)	$C_9H_{15}NO_3$	58,09 58,36	8,55 8,16	6,85 7,56
(Vd)	41	65–66	3270, 1710, 1645, 1530	1,4 m(10H); 2,0 s (3H, OAc); 3,75 s (3H); 7,65 s (NH)	$C_{11}H_{17}NO_3$	62,15 62,54	8,47 8,11	6,36 6,63

* Compare [11].

† Ethyl ether, yield in preparation by the method in [7].

and requires prolonged heating. The β-alkoxy derivatives (IIa-c) obtained are totally stable and are distilled without cleavage of the alcohol, in contrast to the aromatic analogs [4], which easily cleave alcohol with formation of a conjugated system:

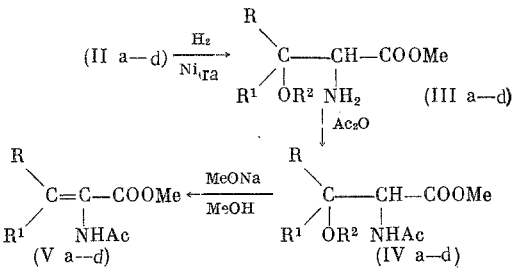


(I a–e) (NAE)) (II a–c)

R, R^1, R^2 = Me (a); R, R^1 = Me; R^2 = Et (b); R = Me; R^1, R^2 = Et (c); R, R^1 = = $(CH_2)_5$; R^2 = Et (d); R, R^1 = $(CH_2)_4$; R^2 = Et (e).

Two methods can be used for synthesis of β,β-disubstituted α,β-dehydroamino acids from (II): cleavage of alcohol with subsequent selective reduction of the nitro group, or reduction of the nitro group with subsequent cleavage of the alcohol. The second method was selected due to the difficulty of selective reduction [2].

Formation of ΔAA during its biosynthesis can be conducted by cleavage of the hydroxyl or mercapto groups in the β-position of AA [1, 2]. Catalytic reduction of nitro compounds (II) over Ni_{ra} with formation of β,β-disubstituted β-alkoxy-α-amino acid esters (III) was performed, and a method was developed for synthesis of β,β-disubstituted α-N-acetyl-ΔAA (V) by acetylation of (III) with production of N-acetyl derivatives of (III)-(IV) and cleavage of alcohol from (IV) by MeONa:



High yields of (III) were only obtained in an excess of Ni_{ra} (Table 2). With a smaller amount of catalyst, reduction stopped in an earlier stage (see the Experimental section). Acetylation of (III) was intended to increase the mobility of the α-hydrogen in the AA and to increase the stability of the ΔAA formed. It could also be conducted without preliminary separation and purification of (III).

Cleavage of the alkoxy group from the esters of (IV), as expected, is more difficult than cleavage of OTs, SH, $S-CH_2-C_6H_5$ and other easily detached groups [1,2], and is not observed in the presence of weak bases, Et_2NH, for example. Good yields of N-acetyl-ΔAA esters of (V) were only obtained in using Na methylate in alcohol (Table 3). The reaction is thus a convenient new method of synthesizing β,β-disubstituted N-acetyl-ΔAA esters which supplements the known azlactone and other methods [1, 2].

Compound (Va) was also obtained by reverse synthesis from α-nitro-β,β-dimethylacrylic acid by reduction on Ni_{ra} in a medium of Ac_2O similar to [7]. However, the yields of (Va) did not exceed 27-31%.

EXPERIMENTAL

The ESR spectra were taken on a Perkin-Elmer spectrometer (60 MHz, internal standard HMDS), and the IR spectra were taken on Hitachi ECI-S2 and UR-20 spectrometers.

Ketal (Ia) was prepared from acetone and MeOH at 27°C (catalyst: Dowex 50 in the H^+ form) similar to [8]. Ketals (Ib-e) were prepared from the corresponding ketones using ethyl o-formate under conditions of acid catalysis. Compounds (Ib and c) were preapred by the method in [9], and (Id and e) were prepared according to [10]. For (Ic), yield of 65%, bp of 135-136°C. IR spectrum (ν, cm^{-1}): 3000, 1180, 1140, 1100, 1075, 1055. PMR spectrum (δ, ppm): 0.75 t (3H); 1.05 t (6H); 1.15 s (3H); 1.55 q (2H); 3.4 q (4H). Observed: C 65.76; H 12.39%. $C_8H_{18}O_2$. Calculated: C 65.70; H 12.37%. The frequency of the ketals obtained was controlled by the IR spectra (absence of C=O absorption bands in the 1500-1800 cm^{-1} region) and by the ESR spectra.

Reaction of Ketals (Ia-e) with NAE. A solution (0.04 mole) of (I), 0.02 mole of NAE, and 0.041 mole of Ac_2O in 10 ml anhydrous benzene [for anhydrous $CH_3C_6H_5$ for (Id, e)] was boiled in a N_2 current for 8-12 h and evaporated. The residue was distilled in a vacuum or chromatographed in a column packed with SiO_2 (Merck, 70-230 mesh); CCl_4 was the eluent. The yields and properties of compounds (II) are reported in Table 1.

Reduction of (II) to (III). A mixture of 0.01 mole of (II), 10 g of activated Nira, and 50 ml of anhydrous MeOH was hydrogenated until absorption of a theoretical quantity of hydrogen (670 ml). After filtration, the solution was evaporated, and the residue was distilled in a vacuum; the yields and properties of amines (III) are reported in Table 2.

In conduction of hydrogenation with one-half the quantities of catalyst and in technical MeOH, products of incomplete reduction were primarily separated. For (IId), hygroscopic crystals with a mp of 147-148°C were separated and produced a vibration band in the IR spectrum in the 2870 cm^{-1} region, and a broad signal at 8.5 ppm in the PMR spectrum, which could be assigned to the methyl ester of the oxime of (1-ethoxycyclohexyl)-glyoxylic acid; this is in agreement with the findings of elemental analysis. Observed: C 51.41; H 8.88; N 5.48%. $C_{11}H_{19}O_4N \cdot 1.5H_2O$. Calculated: C 51.55; H 8.65; N 5.4%.

Preparation of β-Alkoxy-N-acetylamino Acid Esters (IVa-d). A mixture of 1-3 g of amine (III) and a twofold quantity (by weight) of Ac_2O was left for 3 h, evaporated, distilled in a vacuum or chromatographed in a column packed with SiO_2 in CCl_4. The yields and properties of N-acetylamines (IV) are reported in Table 2.

N-Acetyl-Δ-amino Acid Esters (Va-d). A solution of MeONa prepared from 0.01 g-atom of Na and 10 ml of MeOH was added to 0.01 mole of (IV) in 10 ml of MeOH, the mixture was boiled for 3 h, the MeOH was removed in a vacuum, the residue was extracted with $CHCl_3$, and the extract was rapidly washed with ice H_2O. It was dried with $MgSO_4$, evaporated, the residue in the case of (Va) was treated with petroleum ether, and the precipitated crystals were recrystallized from benzene with petroleum ether [11]. Compounds (Vc, d) were purified by chromatography on a column with SiO_2 in CCl_4. The yields and properties of (Va-d) are reported in Table 3.

Compounds (Va) and (Va') were also prepared by hydrogenation of the corresponding α-nitro-β,β-dimethylacrylic acid esters in Ac_2O over Nira in an autoclave at hydrogen pressure of 50-60 atm for 6 h similar to [7] (see Table 3).

CONCLUSIONS

1. Nitroacetic ester reacts with open-chain ketals of aliphatic and alicyclic ketones in Ac_2O medium with formation of esters of the corresponding β-alkoxy-α-nitrocarboxylic acids.

2. A series of β,β-disubstituted α,β-dehydro-α-acetylamino acid esters was prepared by catalytic reduction of the compounds obtained and subsequent acylation and cleavage of alcohol.

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