CATALYTIC HYDROAMINATION OF FURFURYL AND TETRAHYDROFURFURYL ALCOHOLS WITH NITRILES

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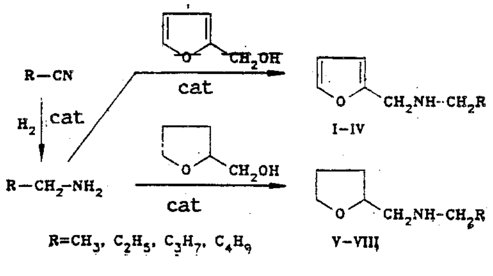
Reaction of furfuryl and tetrahydrofurfuryl alcohols with nitriles over copper oxide catalysts under a hydrogen pressure of 15 atm at a temperature of 230°C gives N-alkylfurfuryl- (yield 46-50%) and N-alkyl-tetrahydrofurfurylamines (49-53%), and N-alkylpiperidines (28-41%). A reaction mechanism is proposed.

Catalytic hydroamination is currently used extensively in the synthesis of organic compounds, but it has been little used for the synthesis of heterocycles. In particular, the reaction has received little attention with compounds of the furan series. A few methods have been reported for the preparation of furfurylamine by amination of furfuryl alcohol with ammonia [1, 2], and of aminofuran from furan ketones [3]. We have shown for the first time that nitriles may be used as aminating agents for the hydroamination of furans [4].

Continuing studies of the reactivity of furans in the hydroamination reaction, we have now examined the reactions of furfuryl (FA) and tetrahydrofurfuryl alcohols (TFA) with aliphatic nitriles under hydroamination conditions. The catalyzed reaction of TFA with ammonia is known to give piperidine [5, 6]. There are two views as to the possible mechanism of the reaction of TFA with ammonia. Yurev [7] considers that the formation of piperidine proceeds via the formation of dihydropyran, tetrahydropyridine, and disproportionation of the latter to pyridine and piperidine. Bashkirov et al., from a study of the kinetics of the amination of TFA with ammonia, propose that the conversion of TFA into piperidine proceeds via the formation of 5-aminopentan-1-ol [8]. It has been shown that treatment of FA with ammonia in the presence of alumina at elevated temperatures affords a mixture of high-boiling condensation products [7].

As these studies have shown, hydroamination of FA and TFA affords as principal products the N-alkylfurfuryl- or N-alkyltetrahydrofurfurylamines and N-alkylpiperidines. We assume that reductive amination of these alcohols follows two independent routes: at the alcohol grouping with conservation of the furan ring, and at the bridge oxygen of the five-membered ring with fission of the furan nucleus. As a result of reaction at the hydroxyl group, the amine formed by reduction of the nitrile undergoes intermoleclar dehydration with the alcohol group of the furan to give the secondary amine:



The possible conversion of N-alkylfurfuryl- and N-alkyltetrahydrofurfurylamines into piperidines has not been confirmed experimentally. Both amines remained unchanged when passed over the catalyst under the conditions of the reaction. FA and TFA under these conditions also remained unchanged in the absence of a nitrile. It is likely that the second route of formation of N-alkylpiperidines involves reaction of the amine with the bridge oxygen of the furan ring, followed by cyclization of the amino-alcohol. Also possible is simultaneous reaction of two molecules of the amine with the alcohol group and the bridge oxygen

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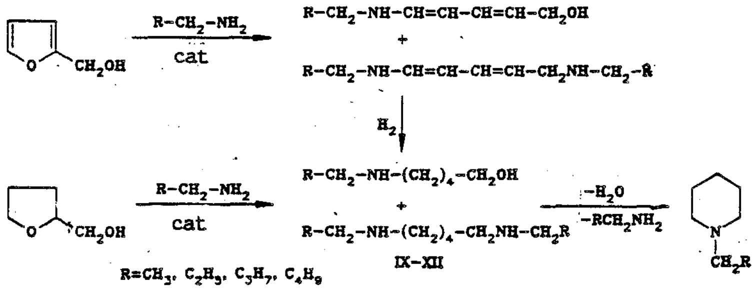
TABLE 1. Physicochemical Properties of Compounds Obtained

Compound	Name	BP, °C (760 mm)	d_4^{20}	n_D^{20}	Found, %			Empirical formula	Calculated, %		
					C	H	N		C	H	N
I	N-Ethylfurfurylamine	170—171	0,9505	1,4689	67,06	8,97	11,82	$C_7H_{11}NO$	67,17	8,86	11,19
II	N-Propylfurfurylamine	184—185	0,9403	1,4679	69,00	9,39	10,04	$C_8H_{13}NO$	69,06	9,35	10,07
III	N-Butylfurfurylamine	198—200	0,9205	1,4669	70.65	9,71	9,17	$C_9H_{15}NO$	70,58	9,80	9,15
IV	N-Pentylfurfurylamine	214—216	0,9149	1,4668	71,80	10,12	8,32	$C_{10}H_{17}NO$	71,86	10,18	8,38
V	N-Ethyltetrahydrofurfurylamine	172—173	0,9239	1,4442	65,10	11,60	10,40	$C_7H_{15}NO$	65,12	11,63	10,55
VI	N-Propyltetrahydrofurfurylamine	187—189	0,9128	1,4338	67,02	11,94	9,72	$C_8H_{17}NO$	67,13	11,89	9,79
VII	N-Butyltetrahydrofurfurylamine	200—201	0,9114	1,4253	68,84	12,13	8,85	$C_9H_{19}NO$	68,79	12,10	8,92
VIII	N-Pentyltetrahydrofurfurylamine	215—216	0,9008	1,4227	70,08	12,22	8,17	$C_{10}H_{21}NO$	70,17	12,28	8,19

TABLE 2. Products of the Hydroamination of FA and TFA with Aliphatic Nitriles (catalyst 36% Cu/MgO, T = 230°C, P = 15 atm, $\nu = 0.3\ h^{-1}$)

Aminating agent	Yield of amination products of FA, %			Yield of amination products of TFA, %		
	N-alkylfurfurylamine	N-alkylpiperidine	high-boiling products	N-alkyltetrahydrofurfurylamine	N-alkylpiperidine	high-boiling products
Acetonitrile	50	32	18	53	41	6
Propionitrile	49	31	20	51	40	9
Butyronitrile	47	29	24	50	40	10
Valeronitrile	46	28	26	49	38	13

to give an intermediate aliphatic diamine. As we have already shown [9], such diamines cyclize under hydroamination conditions with the loss of an amino group and the formation of the heterocycle:



The proposed mechanism provides an explanation of the formation of N-alkylpiperidines from FA, since the intermediate unsaturated straight-chain compounds are readily hydrogenated under the conditions of reductive amination. However, the conversion of furfuryl alcohol into N-alkylpiperidines via the intermediate formation of tetrahydropyran must be regarded as unlikely.

Aceto-, propio-, butyro-, and valeronitriles were employed in the hydroamination of FA and TFA. The length of the hydrocarbon radical of the nitrile group has little effect on the yields of product (Table 2). In the hydroamination of TFA, the yield of N-alkylpiperidine is slightly higher than with FA, since no condensation products of the intermediate unsaturated diamines and aminoalcohols are formed. Varying the reaction temperature, hydrogen pressure, and rate of addition of the reactants showed that the optimum conditions for the synthesis of amines are as follows: $T = 230°C$, $\nu = 0.3\ H^{-1}$, $P_{H_2} = 15$ atm. The copper-alumina catalyst (copper content 15%), probably as a result of the high acidity of the catalyst, caused considerable resinification (as high as 60%), with consequent low yields of the required products. For example, reductive amination of FA and TFA with acetonitrile gave 22 and 30% respectively of N-ethylfurfuryl- and N-ethyltetrahydrofurfurylamines, and 10-15% of N-ethylpiperidine. Addition of 8-10% of lithium hydroxide to this catalyst largely suppressed the formation of by-products, to give N-alkylpiperidines in yields of up to 30%, and secondary furan amines up to 40%. The amounts of condensation products decreased by 30%. Over an industrial copper-magnesium catalyst (copper content 36%), the yields of amines were increased by 15-20%.

The purity and structures of the products were proved by ^1H PMR and IR spectroscopy, and elemental analysis. The ^1H PMR spectra of the N-alkylfurfurylamines contained signals for the three separate protons of the furan ring at low field, with δ 7.12, 6.13, and 5.87, corresponding respectively to fifth, third, and fourth protons. A broadened singlet with δ 2.43 ppm is due to the proton of the amino group. The ^1H PMR spectra of the tetrahydrofurfurylamines contained three unresolved multiplets centered at δ 2.10, 1.20, and 0.88 ppm, assigned respectively to the protons of the methylene groups attached to nitrogen, the methylene protons, and the methyl protons. In the ^1H PMR spectra of the N-alkylpiperidines, unresolved multiplets are present at high field, centered at δ 2.71, 1.53, and 0.82 ppm, attributed to the methylene groups attached to nitrogen, the methylene groups of the hydrocarbon chain, and the methyl group of the alkyl. In the IR spectra of the furfurylamines, absorption is present at 1145 cm^{-1}, characteristic of the ether group in unsaturated oxygen heterocycles. In the IR spectra of the tetrahydrofurfurylamines, these bands are absent. The narrow absorption at 880 cm^{-1} is most characteristic of furans. The presence of the secondary amino group is confirmed by the absorption at 3330 cm^{-1}. The IR spectra of the N-alkylpiperidines contain no absorption for antisymmetric vibrations of the carbon—carbon double bonds in the ring at 1480-1650 cm^{-1} which are characteristic of pyridines.

EXPERIMENTAL

The catalysts used were copper on magnesia and alumina, and copper on alumina promoted with alkali to reduce the acidity of the carrier. The 36% copper/MgO catalyst was a commercial sample, and 15% Cu/Al_2O_3 and 8-10% LiOH/15% Cu/Al_2O_3 catalysts were obtained by impregnation.

The reactions of FA and TFA with nitriles were carried out in a flow reactor in hydrogen. A 1:1 mixture of the alcohol and nitrile was passed at 220-240°C and a hydrogen pressure of 7-15 atm, flow rate 0.2-0.4 h^{-1}. The catalyzate was analyzed by GC on an LKhM-8MD chromatograph, catharometer detector, column length 2 m, packed with 15% PEG-2000 and 5% KOH on Chromosorb W (60-80 mesh). The column temperature was programmed from 50 to 220°C at a rate of 6°C/min. The carrier gas (helium) flow rate was 40 ml/min.

The pure products were isolated by vacuum fractionation of the catalyzate following separation of the aqueous layer and drying over potassium hydroxide. The physicochemical properties of the N-alkylfurfuryl- (I-IV) and N-alkyltetrahydrofurfurylamines (V-VIII) are given in Table 1. The properties of the N-alkylpiperidines (IX-XII) were in accordance with those given in [10]. ^{1}H PMR spectra were recorded on a BS-487C80 spectrometer (80 MHz) for 10% solutions in CCl_4, internal standard TMS. IR spectra were obtained on a UR-20 spectrometer.

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STRUCTURES AND PROPERTIES OF FURAN-2-CARBOXYLIC ACID ESTERS.

2.* THERMODYNAMICS OF SORPTION PROCESSES UNDER GLC CONDITIONS

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The interrelationship between the thermodynamic characteristics of the dissolving of furan-2-carboxylic acid esters in a nonpolar stationary liquid phase and the structures of the esters was investigated by GLC. Additivity of the contributions of the structural elements of 2-furoate molecules to the molar energy of dissolving was demonstrated. The existence of a compensating effect was noted, and the isokinetic temperatures of the process were calculated.

The use of GLC to study the physicochemical properties of organic compounds has undergone extensive development [2-4]; however, data on the use of this method in the investigation of furan-2-carboxylic acid esters are scanty and have analytical character in the overwhelming majority of cases [5-7].

In a continuation of investigations of the physicochemical properties of 2-furoates and their interrelationship with their structures [8-10], in the present paper we present the

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*See [1] for Communication 1.

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