CHEMISTRY OF DI- AND TETRAHYDROPYRANS.

COMMUNICATION 2. AMINES OF DIHYDROPYRAN SERIES

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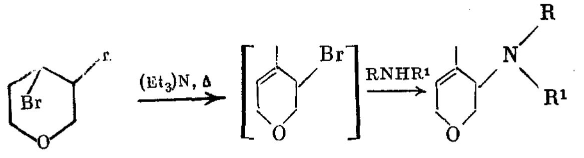
In the present work, we continued the study on the chemical properties of 5,6-dihydropyrans [1]. In the reaction of 3,4-dibromo-4-methyltetrahydropyran (I) with secondary aliphatic amines in benzene, β, γ-unsaturated derivatives of the pyran series are formed [2]. Also the reaction of (I) with certain primary amines (cyclohexyl- and benzylamines) proceeds under similar conditions [Table 1, (IIa, b)], but anilines did not react even on prolonged heating. The reaction of (I) with aromatic amines and also with γ-aminopyridine proceeded when triethylamine was used (see Table 1):

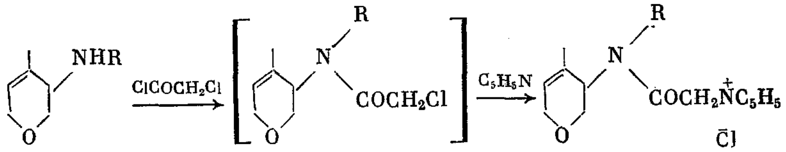


(I) (IIa–k)

R=H; $R^1=C_6H_{11}$ (a), $PhCH_2$ (b), Ph (c), $3\text{-}NO_2C_6H_4$ (d), $2\text{-}ClC_6H_4$ (e), $2\text{-}MeOC_6H_4$ (f), $3\text{-}MeC_6H_4$ (g), $2,6\text{-}Me_2C_6H_3$ (h) $4\text{-}NC_5H_4$ (i) (IIa-h); R^1=Ph; R=Me (j), Et (k) (IIj-k).

It is probable that 5-bromo-4-methyl-5,6-dihydropyran is formed as an intermediate product as the result of trans-diaxial elimination of a HBr molecule in the form of a salt with $(Et)_3N$. The subsequent nucleophilic substitution of the mobile Br atom leads to the amino derivatives (IIa-k). The structure of the amines synthesized was confirmed by the data of IR and PMR spectroscopy. Bands at 1678-1680 and 3300-3500 cm^{-1} were observed in the IR spectra that are characteristic of a trisubstituted double bond and the NH group [3]. The proton signals of the NH group in the PMR spectra were identified by means of CF_3COOH.

In the reaction with chloroacetyl chloride and pyridine, both cycloalkyl- and alkaryl- and aryl-substituted amines of the dihydropyran series convert into the corresponding pyridinium salts (see Table 1):



(IIIa—c)

$R = C_6H_{11}$ (a), $PhCH_2$ (b), Ph (c).

It is known that N-allyl-substituted anilines can rearrange into orthoderivatives by Claisen reaction [4]. Cycloolefins can also successfully take part in the reaction, for example, N-methyl-2-(2'-cyclohexenyl)aniline was obtained from N-methyl-N-(2'-cyclohexenyl) aniline [5].

The double bond in the 5,6-dihydropyrans synthesized (see Table 1) is in allyl position with respect to the nitrogen atom. Hence, the structure of N-substituted anilines is favorable for an amino-Claisen rearrangement, although no literature data on this reaction in the series of cyclic ethers are available. We succeeded in carrying out the rearrangement when amines (IIc, g, h, j, k) were heated in nitrobenzene in the presence of an equivalent amount of $ZnCl_2$:

Institute of Chemistry, Bashkir Branch, Academy of Sciences of the USSR, Ufa. Bashkir State University, Ufa. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 12, pp. 2753-2758, December, 1985. Original article submitted July 3, 1984.

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TABLE 1. Amines of Dihydropyran Series

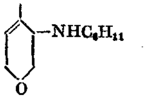
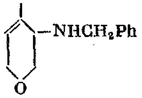
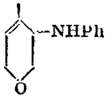
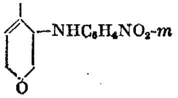
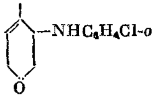
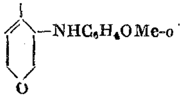
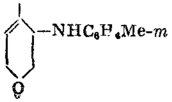
Compound		Yield, %	bp, °C (p, mm Hg), mp, °C n_D^{20}	Found/calculated				IR spectrum cm^{-1} (νNH, νNH_2)	PMR spectrum (δ, ppm)
				C	H	N	Cl		
 $-NHC_6H_{11}$	(IIa)	60	96–97 (7) 1,4956	74,10/73,79	10,25/10,84	7,89/7,17		3380	1,56 s (3H, CH_3), 1,4–2,0 m (11H, C_6H_{11}), 3,5–4,25 m (6H, NH, CH, CH_2OCH_2), 4,45 m (CH=C)
 $-NHCH_2Ph$	(IIb)	62	145–146 (16) 1,5448	77,42/76,85	9,05/8,37	7,13/6,89		3395	1,65 m (3H, CH_3), 2,5 m (NH), 3,30 m (CH_2Ph), 3,5–4,12 m (5H, CH, CH_2OCH_2), 4,5 m (CH=C), 7,32 m (5H, Ar)
 $-NHPh$	(IIc)	68	125–127 (3) 1,5741	76,98/76,20	8,56/7,93	7,99/7,40		3415	1,62 s (3H, CH_3), 3,12–4,00 m (6H, NH, CH, CH_2OCH_2), 5,3 m (CH=C), 6,12–7,1 m (5H, Ar)
 $-NHC_6H_4NO_2$-*m*	(IId)	48	84 *	62,43/61,56	6,47/5,98	12,37/11,96		3410	1,75 s (3H, CH_3), 3,05–4,25 m (6H, NH, CH, CH_2OCH_2), 5,15 m (CH=C), 6,75–7,25 m (4H, Ar)
 $-NHC_6H_4Cl$-*o*	(IIe)	55	144 (3) 1,5769	65,28/64,46	6,99/6,26	6,83/6,26		3415	1,71 s (3H, CH_3), 3,38–4,26 m (6H, NH, CH, CH_2OCH_2), 5,48 m (CH=C), 6,35–7,12 m (4H, Ar)
 $-NHC_6H_4OMe$-o	(IIf)	60	56 *	71,83/71,20	8,26/7,81	6,75/6,38		3420	1,65 s (3H, CH_3), 3,55 s (CH_3OAr), 3,2–4,1 m (6H, NH, CH, CH_2OCH_2), 5,45 m (CH=C), 6,36–6,6 m (4H, Ar)
 $-NHC_6H_4Me$-*m*	(IIg)	62	48 *	77,39/76,80	8,98/8,43	7,36/6,88		3410	1.56 s (CH_3), 2,12 s (3H, CH_3Ar), 3,25–4,01 m (NH, CH, CH_2OCH_2), 5,36 m (CH=C), 6,15–6,98 m (3H, Ar)

TABLE 1 (continued) ...

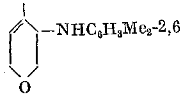
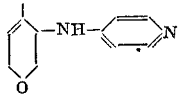
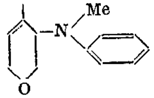
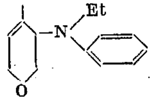
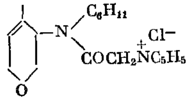
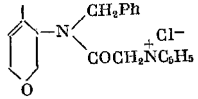
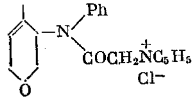
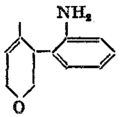
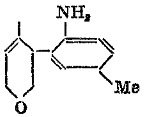
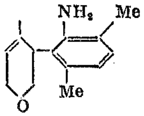
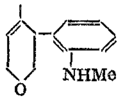
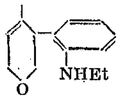
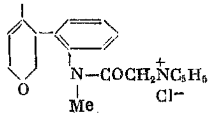
Compound		Yield, %	bp, °C (p, mm Hg), mp, °C, n_D^{20}	Found/Calculated				IR spectrum, cm^{-1} (νNH, νNH$_2$)	PMR spectrum (δ, ppm)
				C	H	N	Cl		
	(IIh)	65	125–127(1)	78,92/77,38	9,36/8,81	6,85/6,44		3420	1,65 s (CH_3), 1,32–2,25 s (6H, CH_3Ar), 3,25–4,00 m (NH, CH, CH_2OCH_2), 5,23 m (CH=C), 6,15–6,90 m (3H, Ar)
	(IIi)	50	79 *	70,89/69,45	6,85/7,42	15,39/14,72		3400	1,7 s (CH_3), 3,38–4,15 m (6H, NH, CH, CH_2OCH_2), 5,45 m (CH=C), 6,4–7,95 m (4H, C_6H_5)
	(IIj)	63	123–125(2)	77,39/76,81	8,95/8,43	7,10/6,89		–	1,52 s (CH), 2,8 s (NCH_3), 3,5–4,0 m (5H, CH, CH_2OCH_2), 5,5 m (CH=C), 6,4–7,1 m (5H, Ar)
	(IIk)	65	135–137(3–5) 1,5620	78,89/77,38	9,02/8,81	7,19/6,45		–	1,65 s (3H), 1,35 t (CH_3CH_2), 3,16–3,46 q ($\underline{CH_2}CH_3$), 3,64–4,08 m (5H, CH, CH_2OCH_2), 5,52 m (CH=C), 6,38–6,71 m (5H, Ar)
	(IIIa)	60	150	65,65/65,04	8,31/7,76	8,44/7,98	10,55/10,10	–	1,63 s (3H, CH_3), 1,45–2,00 m (11H, C_6H_{11}), 3,60–4,46 m (CH, CH_2OCH_2, $COCH_2N^+$), 5,52 m (CH=C), 8,00–9,50 m (5H, C_6H_5N)
	(IIIb)	65	145	67,35/66,94	6,98/6,47	8,35/7,80	9,21/9,83		1,59 s (3H, CH_3), 3,20–4,78 m (9H, CH_2Ph, CH, CH_2OCH_2, $COCH_2N^+$), 5,56 m (CH=C), 7,38 m (5H, Ar), 7,80–8,95 m (5H, C_5H_5N)
	(IIIc)	55	159	66,81/66,18	6,73/6,14	8,68/8,13	10,86/10,28		1,72 s (3H, CH_3), 3,65–4,96 m (CH, CH_2OCH_2, $COCH_2N^+$), 5,65 m (CH=C), 7,45 m (5H, Ar), 7,92–9,00 m (5H, C_5H_5N)

TABLE 1 (continued)

Compound		Yield, %	bp, °C (p, mm Hg), mp, °C, n_D^{20}	Found/Calculated				IR spectrum, cm^{-1} (νNH, νNH_2)	PMR spectrum (δ, ppm)
				C	H	N	Cl		
	(IVa)	49	119–120(1–3)** 39,5*	76,89/76,20	8,51/7,93	8,03/7,40		3450/3370	1,65 s (3H, CH_3), 4,65m (CH=C), 3,30–4,10m (NH_2, CH, CH_2OCH_2), 6,43–6,88m (4H, Ar)
	(IVb)	50	125–126(3–5)	77,33/76,81	9,19/8,43	7,23/6,89		3480/3385	1,70 s (3H, CH_3), 1,69s (CH_3Ar), 3,10–4,39 m (NH_2, CH, CH_2OCH_2), 5,5 m (CH=C), 6,50–6,75m (3H, Ar)
	(IVc)	58	130–132(3–5)	78,01/77,38	9,37/8,81	6,91/6,44		3480/3400	1,65 s (3H, CH_3), 1,65–2,00 s (6H, CH_3Ar), 3,20–4,15 (NH_2, CH, CH_2OCH_2), 5,56–6,90 m (2H, Ar)
	(IVd)	60	140(3–5)	77,36/76,81	9,21/8,43	7,35/6,89		3415	1,69s (3H), 2,75($\underline{CH_3}$–NH), 3,15–4,10 m (NH, CH, CH_2OCH_2), 6,35–7,11 m (4H, Ar)
	(IVe)	65	139–140(1–3)	77,92/77,38	9,24/8,81	6,99/6,45		3420	1,63 s (3H, CH_3), 0,9–1,21t ($\underline{CH_3}CH_2$), 3,2–3,5m (2H, $\underline{CH_2}CH_3$), 3,52–4,49m (NH, CH_2OCH_2, CH), 6,23–7,20 (4H, Ar)
	(V)	30	166*	67,53/66,96	7,01/6,46	8,00/7,80	10,14/9,88		

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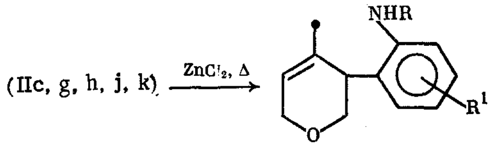
*Melting point.

†Refractive indexes were not determined because of formation of colored products.



(IVa-e)

$R = R^1 = H$ (a); $R = H$; $R^1 = 3\text{-Me}$ (b), $2,6\text{-Me}_2$ (c); $R^1 = H$; $R = Me$ (d); Et (e)

In the spectra of (IVa-c) there are two absorption bands of the primary amino group in each case, and in the spectra of (IVd, e) – one band in each case, characteristic of a secondary amino group. The presence of the NH group in (IVd) is unequivocally confirmed after treatment with $ClCH_2COCl$ and pyridine, when the corresponding pyridinium salt is formed [see Table 1 (V)].

In the case of N-alkyl-substituted anilines (IIj, k), the rearrangement proceeds into the ortho position of the benzene ring also, since in the PMR spectra of (IVd, e) the aromatic ring protons give a complex multiplet in the 6.30-7.10 ppm region. The latter is characteristic of a firmly bonded ABCD spin system, describing the ortho position of the substituents [3].

According to GLC data, besides the main product, a small amount of an unidentified compound is also present in the reaction mixture.

In [6] it was shown that a rearrangement can take place by the action of hydrochlorides of aromatic amines. It was found that hydrobromide salts also have a similar effect. Thus, when (I) is heated (150°C, 3 h) in a sealed ampule with a fivefold excess of aniline, products of N- and C-alkylation are formed in a ratio of 4:3 (GLC), which are 4-methyl-5-phenylamino-5,6-dihydropyran (IIb) and 4-methyl-5-(o-aminophenyl)-5,6-dihydropyran (IVa).

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrophotometer in a thin layer or in the form of a suspension in mineral oil and in a CCl_4 solution; the PMR spectra on a Tesla BS-487C spectrometer with a working frequency of 80 MHz in CCl_4 or DMSO solutions. The GLC was carried out on a LKhM-7A chromatograph, using a 3 m × 4 mm column with SE-30 on Chromaton N-AW-DMCS, in a He current (30 ml/min).

3,4-Dibromo-4-methyltetrahydropyran (I) was obtained by bromination of 4-methyl-5,6-dihydropyran [2].

4-Methyl-5-cyclohexylamino-5,6-dihydropyran (IIa). A mixture of 12.9 g (0.05 mole) of (I) and 14.88 g (0.15 mole) of cyclohexylamine in 90 ml of benzene was boiled for 24 h, and then cooled, and the precipitate was filtered and washed with ether. The combined filtrate was treated with a 20% solution of HCl, and extracted by ether. From the ether extract, 17% of the initial dibromide (I) was isolated. The aqueous layer was made alkaline with K_2CO_3, and extracted by ether. The ether was evaporated, and the residue was distilled in vacuo to yield 4.05 g of (IIa). Compound (IIb) was obtained in a similar way.

4-Methyl-5-phenylamino-5,6-dihydropyran (IIc). A mixture of 12.9 g (0.05 mole) of (I) and 4.6 g (0.05 mole) of aniline in 21.4 ml of Et_3N was heated for 18 h at 80°C. The mixture was then cooled, the precipitate was filtered, and washed by ether. The combined filtrate was evaporated, and the residue was distilled in vacuo to yield 3.2 g of (IIc). Compounds (IId-k) were synthesized in the same way as (IIc).

4-Methyl-5-(o-aminophenyl)-5,6-dihydropyran (IVa). A mixture of 2.27 g (0.012 mole) of (Ic) and 1.6 g (0.012 mole) of $ZnCl_2$ in 26 ml of nitrobenzene was held for 10 h at 120°C. The mixture was cooled, $ZnCl_2$ and nitrobenzene were removed, and the residue was distilled in vacuo. Yield, 1.12g of (IVa). Compounds (IVb-e) were obtained from compounds (IIg, h, j, k), respectively, in a similar way.

Pyridinium Chlorides (IIIa-c), (V). A 0.01-mole portion of $ClCH_2COCl$ was added to 0.01 mole of an amine of dihydropyran series and 2 g of K_2CO_3. The mixture was filtered, and ether was evaporated. To the residue 3 ml of dry pyridine were added. After 3 days, the precipitate was filtered and washed with acetone.

CONCLUSIONS

1. The reaction of 3,4-dibromo-4-methyltetrahydropyran with primary and secondary amines in triethylamine leads to 4-methyl-5-amino-5,6-dihydropyrans.

2. When 4-methyl-5-(R)-anilino-5,6-dihydropyrans are heated in the presence of zinc chloride, an amino-Claisen rearrangement takes place with the formation of ortho-substituted anilines.

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REACTION OF ETHYL DIAZOACETATE WITH N-2,7-OCTADIENYLANILINES CATALYZED BY COMPOUNDS OF COPPER

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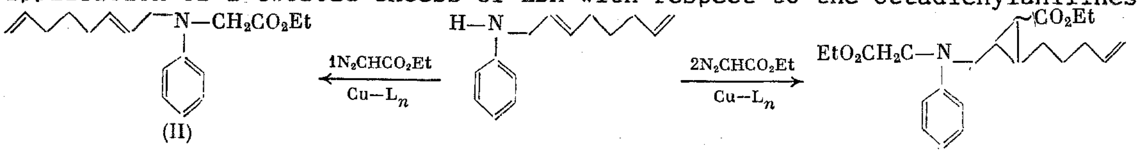
547.551

We recently established that the reaction of aliphatic allylamines with ethyl diazoacetate (EDA) in the presence of a copper compound is accomplished by the isomerization of the allyl substituent of the initial amine and the introduction of ethoxycarbonylcarbene (ECC) at the active C—H bond [1].

Continuing these investigations, we studied the reaction of EDA with the N-2,7-octadienyl derivatives of anilines of different structure in the presence of copper bis[N-(R,S)-α-phenylethylsalicylaldiminate], which is characterized by high activity and solubility in organic solvents [2].

Under these conditions, the reaction of N-2,7-octadienylaniline with excess EDA (molar ratio of 1:2) leads to the formation of N-carbethoxymethylanilino-N-methyl-2-(4-pentenyl)-3-carbethoxycyclopropane (I) — the product of the introduction of ECC at the active N—H bond and its addition to the disubstituted allyl double bond of octadienylaniline. By carrying out the reaction with the utilization of equimolar amounts of the unsaturated amine and EDA, N-carbethoxymethyl-N-2,7-octadienylaniline (II) is formed exclusively. The results obtained indicate that ECC is initially introduced at the N—H bond with the formation of (II); and the next molecule of ECC adds to the allylic disubstituted double bond with the formation of the cyclopropane derivative (I). The terminal vinyl group is not subjected to the cyclopropanation under the conditions of our experiments independently of the concentration of EDA. In connection with this, we performed all the subsequent experiments with the application of a twofold excess of EDA with respect to the octadienylanilines.



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