CONDENSATION OF ANILINE, o-PHENYLENEDIAMINE, AND THEIR SUBSTITUTED DERIVATIVES WITH SOME LACTONES

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The corresponding N-arylbutyrolactams and 2-benzimidazolylalkanols were obtained by the reaction of aniline, o-phenylenediamine, and their derivatives with some lactones.

Lactones can behave as alkylating or acylating agents [1-3]. Cleavage of the lactone ring at the ester group might have been assumed in reactions with amines. This sort of pattern is observed in the acylation of amines with pantolactone [4] and also in the reaction of aniline with β-trichloromethyl-β-propiolactone [5].

γ-Butyrolactone reacts stepwise with aniline: the anilide of γ-hydroxybutyric acid is formed initially and is then converted to N-phenylbutyrolactam. Electrophilic substituents in the m and p positions of the amine activate the formation of the reaction product (see Table 1). A methyl group in the o position hinders the condensation. 2-Naphthylamine is more reactive than 1-naphthylamine. m-Trifluoromethylaniline is considerably less active than m- and p-toluidines and m-bromoaniline. The acylation of aromatic amines by esters [6] proceeds similarly.

TABLE 1.

R	Mp, °C	Reaction time, h	Reaction mixture temp., °C	Empirical formula	N, % found	N, % calc.	Yield, %
C_6H_5	69*	48	185—225	$C_{10}H_{11}NO$	8,5 8,6	8,7	80
m-$CH_3C_6H_4$	58	50	190—280	$C_{11}H_{13}NO$	7,8 7,9	8,0	75
p-$CH_3C_6H_4$	88	60	130—235	$C_{11}H_{13}NO$	8,1 8,2	8,0	78
m-BrC_6H_4	70	30	180—185	$C_{10}H_{10}BrNO$	5,6 5,7	5,8	60
m-$CF_3C_6H_4$	60	30	180—190	$C_{11}H_{10}F_3NO$	6,4 6,4	6,1	19
p-ClC_6H_4	96—97	8	210—270	$C_{10}H_{10}ClNO$	7,0 7,1	7,2	77
α-$C_{10}H_7$	110—112	19	205—305	$C_{14}H_{13}NO$	6,4 6,5	6,6	14
β-$C_{10}H_7$	125	30	190—210	$C_{14}H_{13}NO$	6,7 6,5	6,6	62

*According to [9], this compound has mp 65-67°.

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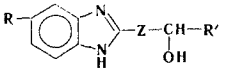
TABLE 2



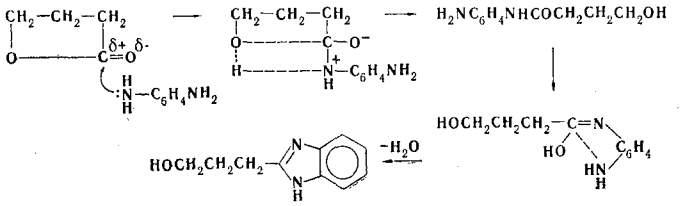
R	R′	Z	Mp, °C	Reaction time, h	Empirical formula	N, % found	N, % calc.	λ_{max}, nm (lg ε)*	Yield, %
H	CCl_3	$-CH_2-$	200 (dec.)	0,3	$C_{10}H_9Cl_3N_2O$	9,9 9,9	10,0	245 (3,93), 275 (3,96), 281 (4,00)	61
Cl	CCl_3	$-CH_2-$	181—182	0,3	$C_{18}H_8Cl_4N_2O$	8,7 8,8	8,9	250 (3,74), 284 (3,89), 291 (3,87)	85
CH_3	CCl_3	$-CH_2-$	175 (dec.)	0,3	$C_{11}H_{11}Cl_3N_2O$	9,3 9,1	9,5	248 (3,76), 281 (3,78), 288 (3,80)	87
H	H	$-CH_2CH_2-$	162—163 (163)†	1	$C_{10}H_{12}N_2O$	15,7 15,8	15,9	247 (3,84), 276 (3,91), 232 (3,97)	80
Cl	H	$-CH_2CH_2-$	167—168 (160—164)†	8	$C_{10}H_{11}ClN_2O$	13,7 13,5	13,3	248 (3,75), 283 (3,86), 291 (3,85)	24
CH_3	H	$-CH_2CH_2-$	137 (137)†	8	$C_{11}H_{14}N_2O$	14,5 14,6	14,7	250 (3,76), 282 (3,76), 289 (3,74)	31
H	CH_3	$-CH_2CH_2-$	115—116	4	$C_{11}H_{14}N_2O$	14,7 14,6	14,7	246 (3,61), 276 (3,68), 282 (3,74)	78
H	C_3H_7	$-CH_2CH_2-$	117—118	4	$C_{13}H_{18}N_2O$	12,6 12,7	12,8		78
Cl	C_3H_7	$-CH_2CH_2-$	123—124	1,5	$C_{13}H_{17}ClN_2O$	11,2 11,3	11,0		7
CH_3	C_3H_7	$-CH_2CH_2-$	124—125	1,5	$C_{14}H_{20}N_2O$	11,8 11,9	12,0		13
H‡	C_4H_9	$-CH_2CH_2-$	127—128	5	$C_{14}H_{20}N_2O$	12,3 12,4	12,0	246 (3,81), 275 (3,85), 281 (3,90)	75
Cl	C_4H_9	$-CH_2CH_2-$	113—114	13	$C_{14}H_{19}ClN_2O$	10,4 10,3	10,5		16.5
H	C_7H_{15}	$-CH_2CH_2-$	111—112	4	$C_{17}H_{26}N_2O$	9,9 10,1	10,2	246 (3,89), 275 (3,96), 281 (4,08)	66
H	H	$-CHC(CH_3)_2-$ OH	158—159	7	$C_{12}H_{16}N_2O_2$	12,4 12,4	12,7	247 (3,64), 276 (3,75), 282 (3,80)	50
H	H	$-CHCH_2-$ $COCH_3$	214—215	4	$C_{12}H_{14}N_2O_2$	12,7 12,8	12,8	253 (3,87), 276 (3,79), 282 (3,84)	40
Cl	H	$-CHCH_2-$ $COCH_3$	201—202	7	$C_{12}H_{13}ClN_2O_2$	10,9 10,9	11,0		16

*In alcohol (c 0.01 mg/liter).

† The melting points from [3, 7] are given in parentheses.

‡ The reaction was carried out in the presence of HCl.

Only the reaction of o-phenylenediamine with γ-butyrolactone in the presence of hydrochloric acid has been described in the literature [3, 7]. It seemed of interest to study the reaction of o-phenylenediamine with other γ-lactones and with β-trichloromethyl-β-propiolactone. γ-Alkyl-γ-butyrolactones readily react with o-phenylenediamine and its derivatives in the presence of hydrochloric acid to give 2-benzimidazolylalkanols. We accompanied this reaction in the absence of hydrochloric acid by refluxing equimolecular amounts of the diamine and γ-lactone (Table 2). o-Phenylenediamine reacts with γ-butyrolactone to form 3-(2-benzimidazolyl)-1-propanol, probably via the following scheme.



The maximum yield is achieved when the reaction mixture is heated at 220° for 1 h. Increasing the reaction time and raising the temperature decrease the yield because of the formation of a side product [3].

γ-Alkyl-γ-lactones do not differ in reactivity from γ-butyrolactone; the inductive effect of the alkyl groups is apparently not transmitted to the reaction center.

It might have been expected that the presence of a group with a negative inductive effect in the α position should increase the positive charge on the carbon atom of the carbonyl group and thereby promote the formation of a benzimidazole derivative in high yields. However, we found that α-aceto-d,l-α-hydroxy-β,β-dimethyl-γ-butyrolactone reacts with o-phenylenediamine to a considerably lesser extent than γ-substituted butyrolactones, probably as a result of blocking of the C=O group of the lactone by substituents in the α-position relative to the carbonyl group.

As compared with γ-lactones, β-trichloromethyl-β-propiolactone reacts readily with o-phenylenediamine and its 4-chloro- and 4-methyl-substituted derivatives. The high reactivity of β-trichloromethyl-β-propiolactone is explained by the fact that the formation of a dipolar $^{-}OCH(CCl_3)CH_2\overset{+}{C}=O$ ion and cleavage of the O–C bond are facilitated by the presence of a trichloromethyl group.

EXPERIMENTAL

N-Arylbutyrolactams (Table 1). An equimolecular mixture of an aromatic amine and γ-butryrolactone was heated at 130-305° for 19-50 h. The reaction usually ceased when the water that was isolated in the water separator was close to the calculated amount. The reaction mixture was fractionated, and the product was recrystallized. The IR spectra of the arylbutyrolactams contain an absorption band at 1690-1700 cm^{-1} (C=O in five-membered lactams), but there is no band at 3600 cm^{-1} (O–H).

3-(2-Benzimidazolyl)-1-alkanols (Table 2). Equimolecular amounts of o-phenylenediamine and γ-substituted γ-butyrolactones were heated in a flask equipped with a Dean–Stark adapter at 220° for 0.25-8 h. Two methods were used to isolate the reaction product.

A. The reaction mixture was dissolved in alcohol, the solution was decolorized with activated charcoal, and the product was precipitated by the addition of water and recrystallized.

B. The reaction mixture was extracted with dilute hydrochloric acid, and the extract was treated with activated charcoal. The solution was neutralized with ammonia, and the precipitate was removed by filtration and recrystallized.

3-(5-Methyl- and 5-Chloro-2-benzimidazolyl)-1-alkanols. Equimolecular amounts of the substituted diamine and γ-butyrolactone in xylene were refluxed for 4-13 h. The solvent was partially removed, and the precipitated crystals were washed with a small amount of xylene and recrystallized.

3-(2-Benzimidazolyl)-1,1,1-trichloro-2-propanols (Table 2). A mixture of 0.01 mole of β-trichloromethyl-β-propiolactone and 0.01 mole of o-phenylenediamine in 15 ml of xylene was heated for 20 min. The precipitated crystals were removed by filtration, washed with xylene, purified with activated charcoal, and recrystallized from aqueous alcohol.

The IR spectra of the 2-benzimidazolylalkanols contain absorption bands at 760-800 cm^{-1} (imidazole ring), 1500-1620 cm^{-1} (aromatic C–C and C–N bonds), 2200-3600 cm^{-1} (associated N–H bonds), and 1050-1150 cm^{-1} (hydroxyl C–O bonds).

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