ESTERS OF HETEROCYCLIC γ-AMINO ALCOHOLS

VI.* SYNTHESIS OF SUBSTITUTED cis-3-AMINOMETHYL-4-HYDROXYPIPERIDINES AND THEIR ACYL DERIVATIVES

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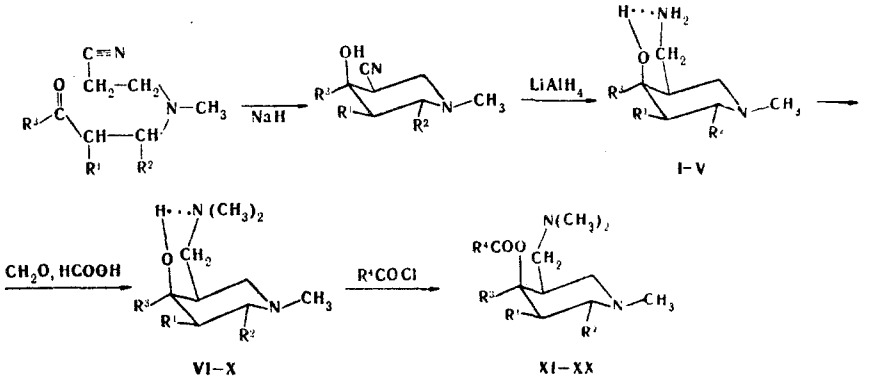
UDC 547.823.07:541.634

Reduction of cis-3-cyano-4-hydroxypiperidines with lithium aluminum hydride (LAH) gave cis-3-aminomethyl-4-hydroxypiperidines, which were converted to cis-3-dimethylaminomethyl-4-hydroxypiperidines by methylation with formaldehyde and formic acid. Acylation of the methylated compounds with benzoyl and cinnamoyl chlorides gave the corresponding esters. Condensation of cis-3-aminomethyl-4-hydroxypiperidines with formaldehyde gave perhydropyrido[3,4-e][1,3]oxazines, which were converted to 3-methylaminomethyl-4-hydroxypiperidines by means of LAH. The cis isomers of the corresponding O,N-diacyl derivatives of these amino alcohols were obtained by acylation with acetic anhydride and benzoyl and cinnamoyl chlorides.

Substances that have high anesthetizing activity have been found among esters of 1,2,5-trimethyl-4-phenyl-5-aminomethyl-4-hydroxypiperidines (for example, see [2]). However, the method previously used for their synthesis leads to the formation of mixtures of structural and spatial isomers, the separation of which presents great difficulties. In this connection it has become necessary to develop a stereospecific method for the preparation of compounds of this type.



$R^1, R^2 = H, CH_3$; $R^3 = CH_3, C_6H_5$; $R^4 = C_6H_5$, $CH{=}CHC_6H_5$

The above method for the synthesis of esters of γ-amino alcohols of the piperidine series (XI-XX) includes as the initial step the cyclization of methyl-β-acylalkyl-β-cyanoethylamines, which are readily obtained by the addition of β-methylaminopropionitrile to α,β-unsaturated ketones [3]. It was found that the cyclization of β-keto amino nitriles proceeds regiospecifically and stereospecifically to give, in up to 90% yields, substituted 1-methyl-3-cyano-4-hydroxypiperidines in only one cis configuration and a predominant conformation in solution with an axial hydroxy group and equatorial cyano group [4]. This makes it possible to accomplish the synthetic conversion from relatively simple and accessible starting compounds to piperidine derivatives with functional groups in the 3 and 4 positions.

*See [1] for communication V.

M. V. Lomonosov Moscow Institute of Fine Chemical Technology, Moscow 119831. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1363-1368, October, 1978. Original article submitted June 17, 1977; revision submitted February 8, 1978.

TABLE 1. cis-3-Aminomethyl-4-hydroxypiperidines

Compound	R¹	R²	R³	Synthetic meth.	Reaction conditions: amt. of $LiAlH_4$, moles[a]	Reaction conditions: time, h	mp, °C[b]	R_f[c]	ν_{OH}, cm^{-1}	ν_{NH}, cm^{-1}	Found, %: C	Found, %: H	Found, %: N	Empirical formula	Calc., %: C	Calc., %: H	Calc., %: N	Yield,[d] %
I	H	H	C_6H_5	A	3,5	6		0,24 (1 : 10)	3305	3410	71,2	9,1	12,5	$C_{13}H_{20}N_2O$	70,9	9,2	12,7	54
				B	3,5	6	108—110				71,0	8,9	12,4					68
II	CH_3	H	C_6H_5	A	3,5	6		0,28			71,7	9,6	12,0	$C_{14}H_{22}N_2O$	71,8	9,45	12,0	74
				B	3,5	8	128—130	(1 : 10)	3265	3398	71,8	9,3	12,1					79
III[e]	H	H	CH_3	A	2,5	10		0,41			60,8	11,6	17,8	$C_8H_{18}N_2O$	60,7	11,4	17,7	57
				B	2,5	6		(1 : 15)	3330	3400	60,7	11,4	17,7					61
IV	CH_3	H	CH_3	A	2,5	10		0,43			62,5	11,7	16,2	$C_9H_{20}N_2O$	62,8	11,7	16,3	59
				B	2,5	8	69—71	(1 : 15)	3330	3400	62,6	11,6	16,2					63
V	H	CH_3	CH_3	A	3	10	68—70	0,39 (1 : 10)	3336	3405	62,4 62,6	11,6 11,5	16,4 16,5	$C_9H_{20}N_2O$	62,8	11,7	16,3	75

[a]Per mole of the nitrile. [b]From benzene—hexane (1:2). [c]On KSK silica gel in 25% ammonia—96% ethanol systems (their ratios are given in parentheses). [d]Based on the cyanopiperidol. [e]This compound had bp 105-106°C (0.5 mm).

TABLE 2. cis-3-Dimethylaminomethyl- and cis-3-Methylaminomethyl-4-hydroxypiperidines

Compound	R¹	R²	R³	mp, °C[a]	R_f[b]	ν_{OH}, cm^{-1}	Found, %: C	Found, %: H	Found, %: N	Empirical formula	Calc., %: C	Calc., %: H	Calc., %: N	Yield, %
VI	H	H	C_6H_5	117—118	0,54	3180	72,4	9,5	11,5	$C_{15}H_{24}N_2O$	72,5	9,7	11,3	87
VII	CH_3	H	C_6H_5	162—163	0,56	3190	73,3	9,8	10,8	$C_{16}H_{26}N_2O$	73,2	10,0	10,7	86
VIII	H	H	CH_3	73—75	0,40	3170	64,4	11,9	14,9	$C_{10}H_{22}N_2O$	64,5	11,9	15,0	85
IX	CH_3	H	CH_3	79—80	0,44	3235	65,9	12,1	14,2	$C_{11}H_{24}N_2O$	66,0	12,1	14,0	85
X	H	CH_3	CH_3	76—78	0,54	3260	65,7	11,9	14,1	$C_{11}H_{24}N_2O$	66,0	12,1	14,0	81
XXVI	H	H	C_6H_5	110—112	0,50	3200	72,1	9,3	11,7	$C_{14}H_{22}N_2O$	71,8	9,5	12,0	92
XXVII	CH_3	H	C_6H_5	111—113	0,51	3185	72,3	9,8	11,0	$C_{15}H_{24}N_2O$	72,5	9,7	11,3	70
XXVIII	H	H	CH_3	71—73	0,29	3295	62,9	11,9	16,4	$C_9H_{20}N_2O$	62,8	11,8	16,3	81
XXIX	CH_3	H	CH_3	78—80	0,45	3250	64,5	12,0	15,1	$C_{10}H_{22}N_2O$	64,5	11,9	15,0	54
XXX	H	CH_3	CH_3	75—76	0,45	3210	64,2	11,8	15,3	$C_{10}H_{22}N_2O$	64,5	11,9	15,0	66

[a]Compounds VI-X were recrystallized from benzene—hexane (1:1), and XXVI-XXX were recrystallized from hexane. [b]On KSK silica gel in a 25% ammonia—96% ethanol system (1:1).

TABLE 3. Benzoates and Cinnamates of cis-3-Dimethylaminomethyl-4-hydroxypiperidines

Compound	R¹	R²	R³	R⁴	R_f[a]	Dihydrochloride						Yield, %
						mp, °C[b]	found, % Cl	found, % N	empirical formula	calc., % Cl	calc., % N	
XI	H	H	C_6H_5	C_6H_5	0,57	210—211	16,5	6,5	$C_{22}H_{28}N_2O_2 \cdot 2HCl$	16,7	6,6	77
XII	CH_3	H	C_6H_5	C_6H_5	0,55	227—228	16,0	6,5	$C_{23}H_{30}N_2O_2 \cdot 2HCl$	16,1	6,3	84
XIII	H	H	CH_3	C_6H_5	0,45	135—137	19,7	7,9	$C_{17}H_{26}N_2O_2 \cdot 2HCl$	19,5	7,7	60
XIV	CH_3	H	CH_3	C_6H_5	0,49	146—147	18,8	7,2	$C_{18}H_{28}N_2O_2 \cdot 2HCl$	18,8	7,4	54
XV	H	CH_3	CH_3	C_6H_5	0,51	224—226	18,7	7,3	$C_{18}H_{28}N_2O_2 \cdot 2HCl$	18,8	7,4	79
XVI	H	H	C_6H_5	$CH{=}CHC_6H_5$	0,57	220—222	15,5	6,4	$C_{24}H_{30}N_2O_2 \cdot 2HCl$	15,7	6,2	75
XVII	CH_3	H	C_6H_5	$CH{=}CHC_6H_5$	0,57	235—237	15,0	6,1	$C_{25}H_{32}N_2O_2 \cdot 2HCl$	15,2	6,0	90
XVIII	H	H	CH_3	$CH{=}CHC_6H_5$	0,37	150—151	18,4	7,3	$C_{19}H_{28}N_2O_2 \cdot 2HCl$	18,2	7,2	66
XIX	CH_3	H	CH_3	$CH{=}CHC_6H_5$	0,41	140—141	17,7	6,7	$C_{20}H_{30}N_2O_2 \cdot 2HCl$	17,6	6,9	38
XX	H	CH_3	CH_3	$CH{=}CHC_6H_5$	0,46	173—175	17,5	7,0	$C_{20}H_{30}N_2O_2 \cdot 2HCl$	17,6	6,9	41

[a]On KSK silica gel in a 25% ammonia—96% ethanol system (1:10). [b]From ethanol—ethyl acetate.

The corresponding substituted cis-3-aminomethyl-4-hydroxypiperidines (I-V) were obtained in 60-80% yields by reduction of cyanopiperidols (method A) or their acetates (method B) with lithium aluminum hydride (LAH) in ether (Table 1). It is apparent from Table 1 that the reduction of the cyanopiperidols themselves proceeds somewhat less efficiently than the reduction of their acetates and depends on a molar excess of the hydride. A threefold excess of the hydride and refluxing for 6-8 h can be considered as optimum conditions. Amino alcohols I-V are individual substances and have the same cis configuration of the functional groups as the starting cyanopiperidols and a predominant conformation in solution with an axial hydroxy group and an equatorial aminomethyl group. The IR spectra of dilute solutions of amino alcohols I-V contain broad symmetrical absorption bands of a hydroxy group linked by a hydrogen bond with the nitrogen atom of the amino group (ν 3265-3336 cm^{-1}). The IR spectra also contain absorption bands of stretching vibrations of the N—H bond of a primary amino group (ν 3398-3410 cm^{-1}). Absorption bands of a free hydroxy group are absent. The primary amino group in amino alcohols I-V was converted to a tertiary group by methylation with formaldehyde and formic acid. cis-3-Dimethylaminomethyl-4-hydroxypiperidines (VI-X, Table 2) are formed in 80-85% yields in this case. The corresponding esters (XI-XX) were obtained by acylation of amino alcohols VI-X with benzoyl and cinnamoyl chlorides (Table 3).

To obtain γ-amino alcohols with a secondary amino group, amino alcohols I-V were converted to perhydropyrido[3,4-e][1,3]oxazines XXI-XXV in 58-76% yields by reaction with formaldehyde (Table 4). A characteristic absorption band of stretching vibrations of a C—O—C bond at 1100 cm^{-1} is observed in the IR spectra of XXI-XXV. Cyclization with aldehydes and ketones to tetrahydro-1,3-oxazines is one of the convenient methods for the investigation of the configurations of aliphatic γ-amino alcohols [5, 6]. In the case of piperidooxazines XXI-XXV their configurations follow from the three-dimensional structures of starting amino alcohols I-V, which contain axial hydroxy and equatorial aminomethyl groups and in the cyclization of which cis fusion of the piperidine and tetrahydrooxazine rings occurs. Under the influence of LAH the C—O bond of the tetrahydrooxazine ring in the 1 and 2 positions in cis-piperidooxazines XXI-XXV is cleaved to give the corresponding cis-3-methylaminomethyl-4-hydroxypiperidines in up to 90% yields (XXVI-XXX, Table 2). Amino alcohols XXVI-XXX have the same configuration and primary conformation as amino alcohols I-V from which they were obtained. This is confirmed by the presence of absorption bands of a hydroxy group linked by an intramolecular hydrogen bond with the nitrogen atom of the side amino group at 3185-3295 cm^{-1} in the IR spectra of dilute solutions of amino alcohols XXVI-XXX.

TABLE 4. cis-Perhydropyrido[3,4-e][1,3]oxazines

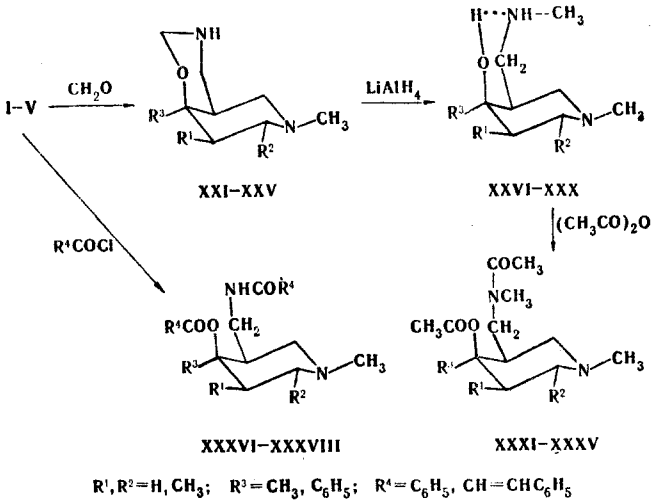
Compound	R^1	R^2	R^3	R_f[a]	Dihydrochloride: mp, °C[b]	found, % Cl	found, % N	empirical formula	calc., % Cl	calc., % N	Yield, %
XXI	H	H	C_6H_5	0,28	258—260	23,8	9,4	$C_{14}H_{20}N_2O \cdot 2HCl$	23,2	9,2	58
XXII	CH_3	H	C_6H_5	0,30	261—263	22,5	8,3	$C_{15}H_{22}N_2O \cdot 2HCl$	22,2	8,8	70
XXIII	H	H	CH_3	0,15	221—222	29,6	11,2	$C_9H_{18}N_2O \cdot 2HCl$	29,2	11,6	71
XXIV	CH_3	H	CH_3	0,31	228—230	28,0	10,5	$C_{10}H_{20}N_2O \cdot 2HCl$	27,6	10,9	76
XXV	H	CH_3	CH_3	0,31	232—234	28,2	10,5	$C_{10}H_{20}N_2O \cdot 2HCl$	27,6	10,9	62

[a]On KSK silica gel in a 25% ammonia—96% ethanol system (1:10). [b]From ethanol—acetone.

TABLE 5. cis-3-Acylaminomethyl-4-acyloxypiperidines

Compound	R^1	R^2	R^3	R^4	mp, °C[a]	R_f[b]	Found, % C	Found, % H	Found, % N	Empirical formula	Calc., % C	Calc., % H	Calc., % N	Yield, %
XXXI	H	H	C_6H_5	CH_3	80—82	0,41	68,1	8,3	9,2	$C_{18}H_{26}N_2O_3$	67,9	8,2	8,8	68
XXXII	CH_3	H	C_6H_5	CH_3	85—87	0,49	68,8	8,5	8,3	$C_{19}H_{28}N_2O_3$	68,6	8,5	8,4	74
XXXIII	H	H	CH_3	CH_3	97—99	0,59	61,0	9,6	10,7	$C_{13}H_{24}N_2O_3$	60,9	9,4	10,9	58
XXXIV	CH_3	H	CH_3	CH_3	99—101	0,62	61,8	9,5	10,5	$C_{14}H_{26}N_2O_3$	62,2	9,7	10,4	65
XXXV	H	CH_3	CH_3	CH_3	96—98	0,62	62,4	9,8	10,2	$C_{14}H_{26}N_2O_3$	62,2	9,7	10,4	64
XXXVI[c]	H	H	C_6H_5	C_6H_5	216—217	0,88	69,6	6,6	—	$C_{27}H_{28}N_2O_3 \cdot HCl$	69,7	6,2	—	56
XXXVII[c]	CH_3	H	C_6H_5	C_6H_5	222—223	0,93	—	—	5,6	$C_{28}H_{30}N_2O_3 \cdot HCl$	—	—	5,8	60
XXXVIII[c]	H	H	C_6H_5	$CH{=}CH{-}C_6H_5$	213—214	0,91	71,8	6,5	5,2	$C_{31}H_{32}N_2O_3 \cdot HCl$	72,0	6,4	5,4	54

[a]From hexane. [b]On KSK silica gel in a 25% ammonia—96% ethanol system (1:10). [c]Obtained in the form of the hydrochloride and recrystallized from alcohol—acetone; the composition was also confirmed by analysis for chlorine.



XXI–XXV XXVI–XXX XXXVI–XXXVIII XXXI–XXXV

$R^1, R^2 = H, CH_3$; $R^3 = CH_3, C_6H_5$; $R^4 = C_6H_5, CH{=}CHC_6H_5$

O,N-Diacyl derivatives XXXI-XXXVIII were obtained in 60-70% yields by acylation of amino alcohols XXVI-XXX with acetic anhydride and amino alcohols I-V with benzoyl and cinnamoyl chlorides (Table 5). Two characteristic absorption bands of the stretching vibrations of amide (ν 1630-1670 cm^{-1}) and acyloxy (ν 1710-1750 cm^{-1}) carbonyl groups are observed in their IR spectra.

The anesthetizing activity of the synthesized compounds was found to be low during a pharmacological investigation of the synthesized compounds. The duration of terminal anesthesia reaches 30-60 min/60-90 min (the numerator refers to deep anesthesia, and the denominator pertains to incomplete anesthesia) only in the case of amino ester XVII when applied in a 1% concentration to the mucous membrane of a rabbit's eye, as compared with 15-30 min/30-60 min for XVI. These values do not exceed 10-15 min/15-30 min in the case of all of the remaining amino esters.

EXPERIMENTAL

The IR spectra of solutions of the compounds in CCl_4 (for amino acid concentrations of $5 \cdot 10^{-3}$ M, which excludes intermolecular interactions) were recorded with a UR-10 spectrometer with an LiF prism. The degree of completion of the reactions and the individuality of the compounds were monitored by thin-layer chromatography (TLC) on a loose layer of KSK silica gel in a 25% ammonia–96% ethanol system (1:10). The hydrochlorides were obtained by the addition of a saturated solution of dry hydrogen chloride in anhydrous ether to a solution of the base in ether.

cis-1-Methyl-4-phenyl-3-aminomethyl-4-hydroxypiperidine (I). A) A 47.6-g (0.22 mole) sample of 1-methyl-4-phenyl-3-cyano-4-hydroxypiperidine was added in small portions with stirring to a suspension of 30 g (0.77 mole) of LAH in 1 liter of anhydrous ether at such a rate that the ether boiled evenly, after which the mixture was heated at 38-40°C for 6 h. At the end of the reaction, the mixture was cooled with ice water, and 60 ml of water was added dropwise. The precipitated aluminum hydroxide was removed by filtration and washed on the filter with ether. The combined ether solutions were dried with magnesium sulfate, and the ether was removed by distillation to give 26 g (54%) of crystalline amino alcohol I.

B) A solution of 78.5 g (1.0 mole) of acetyl chloride in 50 ml of acetone was added to a solution of 100 g (0.46 mole) of cyanopiperidol in 200 ml of anhydrous acetone in the presence of 1 g of fine magnesium turnings, and the mixture was maintained at room temperature for 2 days. The precipitate was removed by filtration and dissolved in water, and the solution was treated with sodium carbonate and extracted with ether. The ether was removed from the extract by distillation to give 110 g (93%) of cyanopiperidol acetate.

A 56.8-g (0.22 mole) sample of cyanopiperidol acetate was added to a suspension of 30 g (0.77 mole) of LAH in 1 liter of ether, and the mixture was treated as in method A. Workup gave 35.5 g (68% based on the cyanopiperidol and 74% based on its acetate) of amino alcohol I.

Amino alcohols II-V were similarly obtained (Table 1).

cis-1-Methyl-4-phenyl-3-dimethylaminomethyl-4-hydroxypiperidine (VI). An 11-g (0.05 mole) sample of amino alcohol I was added in portions with stirring to a mixture of 12 ml (0.12 mole) of 30% formalin and 12 ml (0.25 mole) of 85% formic acid, during which the mixture became warmer. It was then refluxed for 8 h, after which it was cooled and made alkaline with 40% NaOH solution. The base was extracted with ether, and the extract was dried with potassium carbonate. The ether was removed by distillation, and the residue was recrystallized from benzene–hexane (1:1) to give 10.8 g (87%) of amino alcohol VI.

The same method was used to obtain amino alcohols VII-X (Table 2).

cis-1-Methyl-4-phenyl-3-dimethylaminomethyl-4-hydroxypiperidine Benzoate (XI). A solution of 5 g (0.02 mole) of amino alcohol VI and 7 g (0.05 mole) of benzoyl chloride in 30 ml of benzene was refluxed in the presence of 0.3 g of magnesium turnings for 1 h (or was maintained at room temperature for 2 days), after which 30 ml of dilute (1:1) hydrochloric acid was added, and the organic layer was separated. The aqueous layer was washed with ether, cooled with ice water, and saturated with sodium carbonate. The base was extracted repeatedly with ether, and the extract was dried with magnesium sulfate and filtered. The base was converted to 6.5 g (77%) of the dihydrochloride of benzoate XI.

Amino esters XII-XX were obtained in the same way as benzoate XI (Table 3), except that in the case of cinnamates XVI-XX equimolar ratios of amino alcohols VI-X and cinnamoyl chloride were used.

cis-7-Methyl-10-phenylperhydropyrido[3,4-e][1,3]oxazine (XXI). A mixture of 22 g (0.1 mole) of amino alcohol I, 50 ml (0.5 mole) of 30% formalin, 150 ml of ethanol, and 14 g (0.1 mole) of potassium carbonate was heated on a boiling-water bath for 10 h. At the end of the reaction, the alcohol and excess formalin were removed by vacuum distillation, and the condensation product was extracted with ether. The ether extracts were washed with a saturated solution of sodium bisulfite and filtered. The ether was removed by distillation, and the residue crystallized to give 13.5 g (58%) of piperidooxazine XXI.

Piperidooxazines XXII-XXV were similarly obtained (Table 4).

cis-1-Methyl-4-phenyl-3-methylaminomethyl-4-hydroxypiperidine (XXVI). A solution of 10 g (0.04 mole) of piperidooxazine XXI in 20 ml of dry ether was added dropwise to a suspension of 8 g (0.2 mole) of LAH in 200 ml of dry ether, and the mixture was refluxed for 7 h. Water (16 ml) was then added with stirring and cooling (with ice water), and the precipitate was removed by filtration and washed with ether. The combined ether solutions were dried with magnesium sulfate, and the ether was removed by distillation to give 9.2 g (92%) of amino alcohol XXVI.

Amino alcohols XXVII-XXX were obtained by the method used to prepare amino alcohol XXVI (Table 2).

cis-1-Methyl-4-phenyl-3-methylacetamidomethyl-4-acetoxypiperidine (XXXI). Acetic anhydride [4 ml (0.04 mole)] was added to a solution of 3.4 g (0.015 mole) of amino alcohol XXVI in 10 ml of dry benzene, and the mixture was refluxed for 3 h. The benzene and excess acetic anhydride were removed by vacuum distillation, and the residue was dissolved in water. The cooled aqueous solution was saturated with sodium carbonate in the presence of ether, and the base was extracted with ether. The extract was dried with magnesium sulfate, and the ether was removed by distillation to give 3.3 g (68%) of amido ester XXXI.

Amido esters XXXII-XXXV were similarly obtained (Table 5). In the preparation of benzoates XXXVI and XXXVII and cinnamate XXXVIII the acylation of amino alcohols I and II was carried out in benzene in the presence of benzoyl and cinnamoyl chlorides in a threefold molar excess with respect to the amino alcohols.

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REACTION OF ISOPROPYLIDENE MALONATE WITH N-ARYLIDENE-1(OR 2)-NAPHTHYLAMINES

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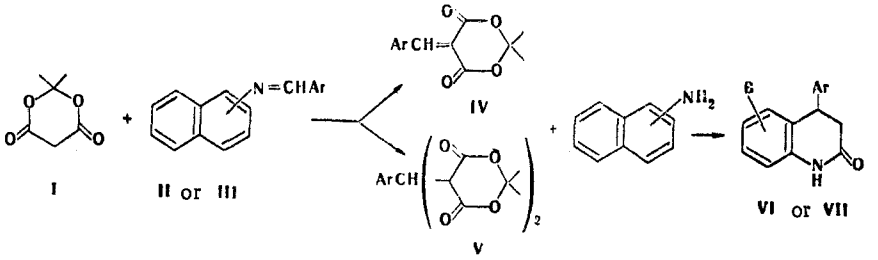
UDC 547.841'832.2:542.954

The initial step in the reaction of isopropylidene malonate with N-arylidene-1(or 2)-naphthylamines is cleavage of the latter. The reaction gives isopropylidene 2-arylidene malonates, which subsequently react with α(or β)-naphthylamines to give 4-aryl-2-oxo-1,2,3,4-tetrahydro-7,8(or 5,6)-benzoquinolines. The latter are also obtained in the reaction of arylbis(isopropylidenemalonatyl)methanes with α(or β)-naphthylamines. Indane-1,3-dione and dimedone also cleave N-arylidene-1(or 2)-naphthylamines, and 2-arylideneindane-1,3-diones or arylbis(dimedonyl)methanes are obtained.

The reaction of isopropylidene malonate (I) with N-arylidene-1(or 2)-naphthylamines (II or III) gives [1, 2] 4-aryl-2-oxo-1,2,3,4-tetrahydro-7,8(or 5,6)-benzoquinolines (VI or VII).

When a mixture of isopropylidene malonate (I) was refluxed with arylidenenaphthylamines IIa or IIIa in ethanol for 1 h, the reaction product was unexpectedly isopropylidene 2-(4-N,N-dimethylaminobenzylidene)malonate (IVa). An increase in the reaction time to 12 h led to benzoquinolines VIa or VIIa. The latter were also obtained by reaction of isopropylidene arylidenemalonate IVa with α(or β)-naphthylamines. This indicates that the initial step is cleavage of amines IIa or IIIa to give IVa, which subsequently reacts with naphthylamines to give VIa or VIIa. It was felt that it was necessary to ascertain whether this sort of reaction occurs in all of the investigated cases.



II = α-$C_{10}H_7$; III = β-$C_{10}H_7$; VI B = 7,8-benzo; VII B = 5,6-benzo; a Ar = 4-$(CH_3)_2NC_6H_4$; b Ar = 4-$(C_2H_5)_2NC_6H_4$; c Ar = 3,4-$(CH_3O)_2C_6H_3$; d Ar = 4-$CH_3OC_6H_4$; e Ar = 4-$O_2NC_6H_4$; f Ar = C_6H_5; g Ar = H

Cleavage products IV are isolated in good yields in the reaction of arylidenenaphthylamines II or III with electron-donor substituents. The absorption of arylidenenaphthylamine IId vanishes in the UV spectrum of the reaction mixture of isopropylidene malonate (I) with N-(4-methoxybenzylidene)-1(or 2)-naphthylamine (IId), and absorption characteristic for isopropylidene arylidenemalonate IVd appears; the spectrum contains two isobestic points (255 and 330 nm) in which the sum of the extinction coefficients of starting I and IId is equal to the sum of the extinction coefficients of products IVd and α-naphthylamine. This indicates that the cleavage reaction takes place exclusively. The UV spectrum of the reaction mixture of I and IIId does not contain isobestic points, but a decrease in the intensity of the absorption of product IVd is observed, and this indicates the occurrence of a subsequent reaction. Overlapping of the absorption bands of the starting compounds and the cleavage products is observed for the reaction mixtures of other arylidenenaphthylamines II or III

Riga Polytechnic Institute, Riga 226828. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1369-1372, October, 1978. Original article submitted May 23, 1977; revision submitted February 27, 1978.

