Synthesis of annulated oxazolidinones as potential precursors of cyclic *cis*-β-amino alcohols

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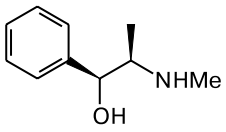
A simple method for the synthesis of annulated 1,3-oxazolidin-2-ones from accessible ketones, acetylene, and carbon dioxide was developed. If their molecules contain arylalkyl substituents, intramolecular cyclization in acidic media gave rise to fused heterocyclic systems in high yields. The effects of the substituents in positions 3 and 5 of the oxazolidine ring on the regioselectivity of this cyclization were studied. The possibilities of converting oxazolidinones into cyclic *cis*-β-amino alcohols were studied.

Key words: chiral auxiliary reagents, β-amino alcohols, carbonates, dioxolanones, 1,3-oxazolidin-2-ones, amidoalkylation, tetrahydronaphthalenes, tetrahydroisoquinolines, cyclization.

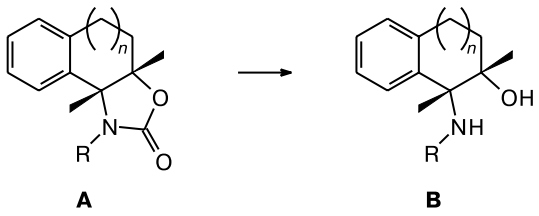
cis-β-Amino alcohols such as ephedrine and its derivatives are known to be efficient chiral auxiliary reagents for asymmetric synthesis and resolution of racemates into enantiomers. They are prepared both from natural compounds and by resolution of synthetic analogs of the types **A** and **B** into enantiomers.[1,2] However, many of them are not easily accessible.



Ephedrine

The goal of the present work was to search for simpler routes to racemic polycyclic oxazolidinones of the type **A**, in which a five- or six-membered carbocyclic ring is simultaneously fused with an aromatic and oxazolidine rings (Scheme 1).

Scheme 1

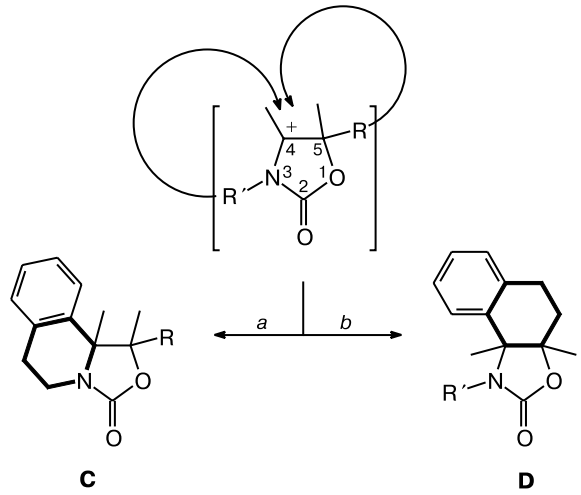


n = 0, 1

It is known that their hydrolysis gives racemates of type **B**, which can be efficiently resolved into enantiomers by crystallization of salts with optically active acids. Enantiomers **B** can be very effective in asymmetric synthesis because of the fixed *cis*-orientation of hydroxy and amino groups, while two methyl groups exert the steric effect on the environment of chiral centers, thus making subsequent transformations more stereoselective.[3]

We have shown[4] that oxazolidinones can be suitable precursors of *cis*-β-amino alcohols since the *cis*-arrangement of the hydroxy and amino groups is predetermined by the configuration of the five-membered oxazolidine ring **A**. For instance, intramolecular amidoalkylation of *N*-arylethyl-4-hydroxyoxazolidin-2-ones results in closure of a six-membered ring to give 1,5,6,10b-tetrahydrooxazolo[4,3-*a*]isoquinolin-3-ones (Scheme 2, struc-

Scheme 2



a: R′ = $ArCH_2CH_2$; *b*: R = $ArCH_2CH_2$

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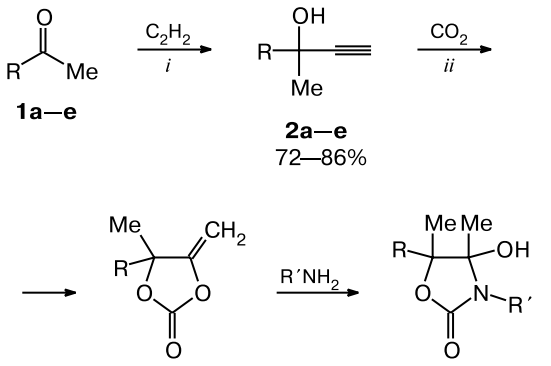
ture **C**).[4,5] Here we studied the abilities of various arylalkyl substituents in position 5 to participate in such cyclization yielding structures of the type **D**.

Results and Discussion

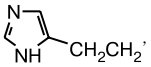
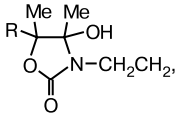
First we planned a synthetic strategy leading, according to previous data,[4,5] through compounds **1**—**3** to key oxazolidin-2-ones **4**—**8** (Scheme 3).

Scheme 3



i. Liquid NH_3, KOH. *ii*. *p*, Δ, catalyst

Compound	R	Compound	R´
1a—3a, 4	$Ph(CH_2)_2$	**4a**, **5a**, **7a**	H
		4b, **5b**, **7b**	Me
		4c, **5c**,	Et
		6a, **7c**	Et
1b—3b, 5	$PhCMe_2CH_2$	**4d**, **5d**,	$PhCH_2$
		6b, **7d**	$PhCH_2$
1c—3c, 6	$PhCH_2$	**4e**, **5e**	$Ph(CH_2)_2$
1d—3d, 7	$Fur(CH_2)_2$	**4f**, **5f**	$3,4\text{-}(MeO)_2C_6H_4(CH_2)_2$
1e—3e, 8	Me	**4g**, **5g**, **6c**	Oxn
		4h, **5h**, **6d**	CH_2COONa
		4i, **5i**,	Hyst
		6f, **8a**	Hyst

Note. Hyst =  , Oxn =  ,

Fur = 2-furyl.

Earlier unknown α-hydroxyalkynes **2** have been obtained by ethynylation of the respective ketones with acetylene in liquid ammonia in the presence of KOH. The ^{1}H NMR spectra of all hydroxyalkynes in DMSO-d_6 show singlets for the hydroxy group at δ 2—2.5 (1 H), singlets for the methyl group at δ 1.2—1.4 (3 H), and singlets for the acetylene proton at δ 3.3—3.5 (1 H). Their mass spectra contain molecular ion peaks.

Reactions of alkynols with CO_2 (see Ref. 6) gave the corresponding dioxolan-2-ones **3** (cyclic carbonates). The reactions were carried out at a pressure of 160—220 atm and at 80—100 °C in the presence of catalytic amounts of triethylamine, CuBr, and phase-transfer catalysts. The ^{1}H NMR spectra of carbonates **3** contain two doublets for the methylidene protons at δ 4.5—5.0 (1 H each, $J \approx 4$ Hz) and a singlet for the methyl group at δ 1.40—1.65 (3 H).

In most cases, the synthesis of oxazolidinones by the action of primary aliphatic amines on carbonates **3** occurred under mild conditions in acetonitrile or water at 40—80 °C. Difficulties sometimes arose during crystallization of products initially formed as oils. Because of the presence of two chiral centers in compounds **4**—**7**, their ^{1}H NMR spectra show a double set of signals for all protons, which complicates their assignment. In reality, all oxazolidinones but **8** (R = Me) consist of two pairs of diastereomers (with the *cis*- or *trans*-orientation of the methyl groups at the oxazolidine ring).

The reactions of carbonates **3a**—**c** with ethylenediamine yielded bisoxazolidinones **4g**, **5g**, and **6c** (see Ref. 7). Even with a tenfold excess of ethylenediamine used as a 10% aqueous solution, no asymmetric product containing the $CH_2CH_2NH_2$ fragment was obtained.

We have found[4] that 4-hydroxyoxazolidin-2-ones in acidic media eliminate the hydroxy group and the resulting electrophilic acyliminium species can attack the aromatic ring (see Scheme 2) to give the tetrahydroisoquinoline system **C**. Such an intramolecular amidoalkylation occurs best upon heating in polyphosphoric acid (PPA). In the present work, we used 4-hydroxy-5-phenethyl- (**4**) and 4-hydroxy-5-(2-methyl-2-phenylpropyl)oxazolidin-2-ones (**5**). Intramolecular cyclization (amidoalkylation) gave products **9** and **10** containing the tetrahydronaphthalene system (Scheme 4).

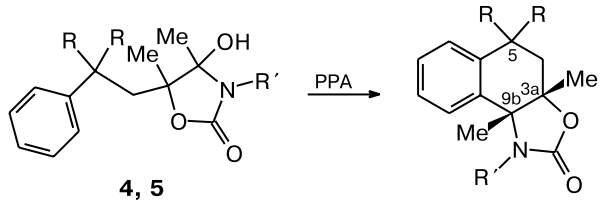
It should be noted that the methyl groups in positions 3a and 9b of structures **9** and **10** are strictly *cis*-oriented, which is due to the planar geometry of the five-membered oxazolidine ring and the steric control of the intramolecular electrophilic attack by the planar acyliminium species (see Scheme 2). This was exemplified by NOESY data for compound **9e**. We believe that this method may afford optically active diastereomerically pure derivatives **9** and **10** from scalemic starting alcohols **2a**—**e** (asymmetric ethynylation techniques are known[8]).

In the case of bisderivatives **4g** and **5g**, the cyclization involves both the benzene rings to give products **9g** and **10g** containing two tricyclic fragments in high yields.

The ^{1}H NMR spectra of cyclization products show signals for the *ortho*-disubstituted benzene ring, two singlets for the methyl groups (3 H each), and signals for the methylene groups (four multiplets (1 H each) for compound **9** and two multiplets (1 H each) and two singlets (3 H each) for compound **10**.

We studied the possibility of cyclization of dioxolanones **3a,b** under the same conditions as for oxazolidinones

Scheme 4



4, 5

9a—e,g,h, 10a—g

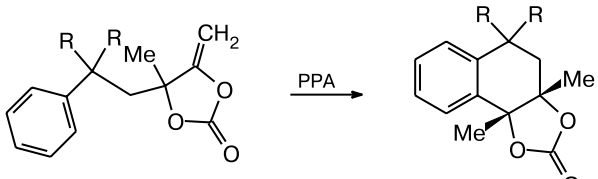
56—85%

R = H (**9**), Me (**10**)

9	10	R′	9	10	R′
a	**a**	H	—	**f**	3,4-$(MeO)_2C_6H_4(CH_2)_2$
b	**b**	Me			
c	**c**	Et			
d	**d**	$PhCH_2$			
e	**e**	$Ph(CH_2)_2$			
h	—	CH_2CO_2H	**g**	**g**	

(by heating in PPA). The resulting compounds **11a,b** obtained in high yields are potential precursors of *cis*-diols (Scheme 5). These compounds are inert toward amines even under drastic conditions (benzylamine, boiling acetonitrile).

Scheme 5



3a,b

11a,b

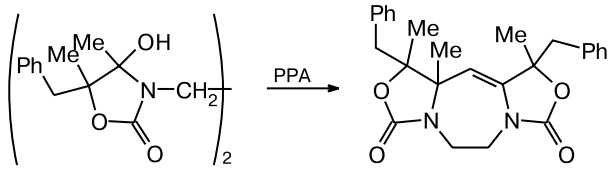
>90%

R = H (**3a, 11a**), Me (**3b, 11b**)

We attempted closure of a five-membered ring by intramolecular amidoalkylation like that in Scheme 4. However, the action of PPA on oxazolidinones **6a,b** and dioxolanone **3c** under standard conditions did not result in the desired cyclization and the starting compounds were recovered unchanged (checking by TLC and melting point determination). An increase in the temperature resulted in resinification and intense evolution of carbon dioxide. This result agrees with a theory stating that *exo-trig* cyclization into such five-membered rings is hindered.[9] Bisoxazolidinone **6c** yielded product **12** with the seven-membered ring (Scheme 6). As noted above, homologous bisderivatives **4g** and **5g** underwent no transformation of this type.

Intramolecular amidoalkylation that can follow competitive pathways is of particular interest (Scheme 7).

Scheme 6



6c

12, 82%

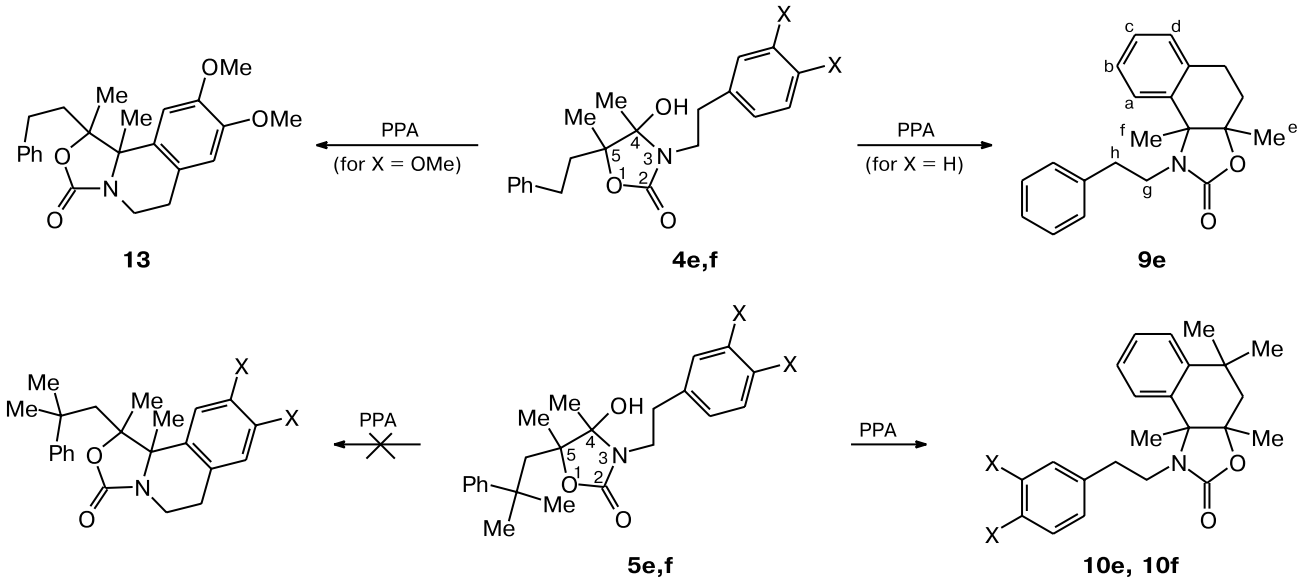
When compound **4e** with two unsubstituted benzene rings was heated in PPA, an intramolecular electrophilic attack occurred only at the benzene ring of the phenethyl substituent in position 5 of the oxazolidine ring to give tetrahydronaphthalene compound **9e** (X = H). For compound **4f** (X = OMe) under analogous conditions, only the benzene ring activated by two methoxy groups in the N-phenethyl substituent is under electrophilic attack leading to tetrahydroisoquinoline compound **13** (*cf.* Scheme 4).

Heating in PPA of compounds **5e,f** containing two geminal methyl groups in the side chain of the phenethyl substituent in position 5 of the oxazolidine ring yielded exclusively tetrahydronaphthalene compounds **10e,f** (although the benzene ring of the phenethyl fragment at the N atom in compound **5f** is activated by two methoxy groups). Apparently, the presence of these two geminal Me groups in compound **5f** (compared to compound **4f**) favors the conformation in which the benzene ring of the C-phenethyl fragment comes close to the reactive site. In both cases, the intramolecular amidoalkylation gave the only product in high yield.

Both tetrahydronaphthalene and tetrahydroisoquinoline products formed according to Scheme 7 must have equal molecular masses and similar NMR spectra. All tetrahydronaphthalene compounds were obtained as one diastereomer (with the *cis*-orientation of the methyl groups at the five-membered oxazolidine ring), while tetrahydroisoquinoline systems allows two diastereomers with the *cis*- and *trans*-orientations of the methyl groups. Indeed, the ^{1}H NMR spectra of all compounds **9** and **10** contain one set of signals, while those of tetrahydroisoquinoline compounds (*e.g.*, **13**) show a double set of signals. Structure determination for the cyclization products containing methoxy groups (**13**, **10f**) was not difficult: the aromatic protons of the dimethoxybenzene fragment are easy to distinguish since their signals are characteristically shifted upfield. According to ^{1}H NMR data, the number of the aromatic protons in the products is lower by one than that in the starting compounds; disappearance of a particular proton from one or the other benzene ring is indicative of the cyclization pathway.

The structure of compound **10e** was determined from the presence of two characteristic separate low-field doublets (1 H each) for the aromatic protons, which is typical

Scheme 7

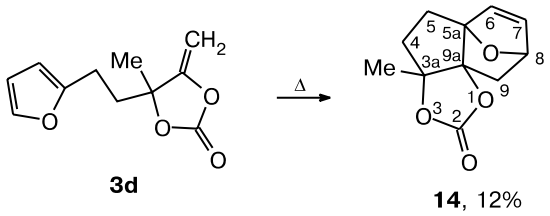


X = H (**4e**, **5e**, **10e**), OMe (**4f**, **5f**, **10f**); the yields are 80—90%

of the ^{1}H NMR spectra of all compounds **10**. Structure **9e** was strictly proven by a homonuclear 2D NOESY experiment. Its spectrum shows distinct cross peaks between the aromatic proton H_a (δ 7.67) (Scheme 7) and the methyl protons H_f (δ 1.46) and between the same proton H_a (δ 7.67) and the methylene protons H_g (δ 3.12 and 3.35). The alternative tetrahydroisoquinoline system (analogous to **13**) contains no aromatic proton that is simultaneously close to both the methyl group and the methylene group at the N atom and manifests itself by analogous cross peaks. The NOESY spectrum also confirmed the *cis*-arrangement of the methyl groups, which is evident from the respective cross peaks between the H_e (δ 1.32) and H_f protons (δ 1.46).

Many physiologically active natural and synthetic substances include a furan ring. It was of interest to obtain furan-containing dioxolanones and oxazolidinones and study their properties. However, it is known that the furan ring is chemically reactive and that furan-containing compounds are unstable in acidic media. As expected, carbonate **3d** we obtained was prone to various transformations during its synthesis and distillation. The major product of these transformations was isolated from tar materials upon the distillation of compound **3d** (Scheme 8). This product was assigned structure **14** from ^{1}H and ^{13}C NMR and mass spectra and elemental analysis data. The ^{1}H NMR spectrum shows signals for the olefin protons at δ 6.47 (d, 1 H, C(7)H, J = 5.8 Hz) and 6.63 (dd, 1 H, C(6)H, J_1 = 5.8 Hz, J_2 = 1.5 Hz). The formation of this compound can be attributed to the intramolecular Diels—Alder reaction between the double bond of dioxolanone and positions 2 and 5 of the furan ring acting as a diene. Such transformations have not been documented for 4-methylidenedioxolan-2-ones. Attempted cyclization of furan-containing dioxolanone **3d** and oxazolidinones **7** under the action of acid agents (PPA and TsOH in toluene) resulted only in rapid resinification of the reaction mixture and intense evolution of carbon dioxide. On storage, these compounds darkened and became resinified and new products were detected by TLC analysis.

Scheme 8



Tetrahydronaphthooxazolidinones **9** and **10** were interesting objects for hydrolytic opening of the oxazolidine ring since such a transformation should give rise to multipurpose chiral β-amino alcohols.

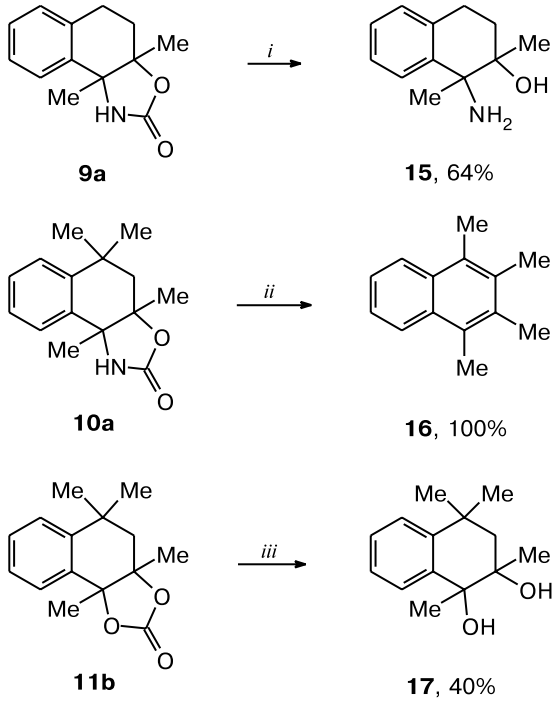
Nevertheless, oxazolidinones **9a**—**c** and **10a,b** proved to be very resistant to hydrolysis: they were recovered unchanged upon refluxing in 70% H_3PO_4 (160 °C, 8 h) and underwent resinification when heated at 100 °C in 60% H_2SO_4. In 60% H_2SO_4, carbonate **11a** converted quantitatively into 1,2-dimethylnaphthalene, while its

homolog **11b** was recovered unchanged. Nor were compounds **9b,c** and **10b** converted into the corresponding *cis*-β-amino alcohols with $LiAlH_4$ in $MeOBu^t$ as described earlier.[10] Compounds **9a—c** and **10a,b** did not react with $NaBH_4$ in aqueous ethanol.

The desired result was attained only in DMSO—water—KOH according to the earlier[11] proposed method. Heating of compound **9a** for 100 h gave the target *cis*-β-amino alcohol **15** (Scheme 9) isolated as oxalate in 64% yield.

Treatment of compound **10a** with $LiAlH_4$ in $MeOBu^t$ at 40 °C quantitatively yielded 1,2,3,4-tetramethylnaphthalene (**16**) probably formed *via* opening of the oxazolidine ring, rapid elimination of the hydroxy and amino groups, bond rearrangement, migration of the methyl group, and final aromatization. The same result was reached by treatment of this compound with KOH in aqueous methanol.

Scheme 9



i. KOH—H_2O, DMSO; *ii*. $LiAlH_4$—$MeOBu^t$ or KOH—MeOH, H_2O; *iii*. $LiAlH_4$, dioxane.

Treatment of compound **11b** with $LiAlH_4$ in boiling dioxane gave the corresponding diol **17**. The ^1H NMR spectrum of this compound shows a single set of signals for each group (*i.e.*, the mutual *cis*-arrangement of the methyl groups was retained during the reaction). 1,2,3,4-Tetramethylnaphthalene (**16**) was obtained as a minor product (~20%).

The results obtained open up a route to pure enantiomers of the β-amino alcohols under study. For instance,

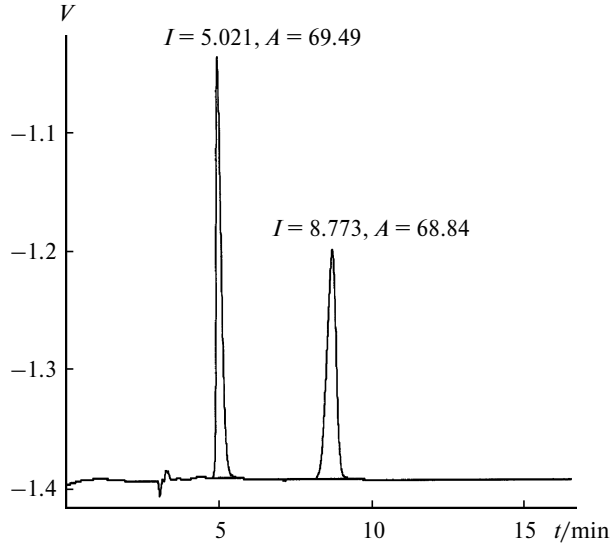


Fig. 1. Chromatographic resolution of the enantiomers of compound **9a**.

compound **9a** was completely resolved into the enantiomers on an optically active Chiralpak AD column (4.6×250 mm, Amylose tris(3,5-dimethylphenyl) carbamate as an optically active phase) (Fig. 1). The efficiency of this column (~4 mg of the resolved substance in a single run) will allow preparative resolution of such compounds on larger columns.

Experimental

NMR spectra were recorded on a Bruker DRX-500 instrument (500.13 MHz) in DMSO-d_6 (unless otherwise specified). Mass spectra were recorded on a Kratos MS-30 instrument (direct inlet probe, EI, 70 eV, ionization chamber temperature 250 °C). The course of the reactions was monitored by TLC on Silufol UV-254 plates. The yields and physicochemical characteristics of the compounds obtained are given in Tables 1—7.

Ketones **1a** (see Ref. 12), **1b** (see Ref. 13), **1c** (see Ref. 14), and **1d** (see Ref. 15) were prepared as described earlier.

Alkynols 2. Ammonia (1 kg) and acetylene (130 g) were added at −6 °C to an appropriate ketone (2 mol) in a 3.5-L shaking autoclave. Then a solution of KOH (11.2 g) in anhydrous ethanol (50 mL) was added for 20 min and the reaction was carried out at 20 °C for 15—40 h. The reaction was continued until a conversion of 90—95% was reached (GLC). The acetylene—ammonia mixture was evaporated and the residue was neutralized with 25% H_2SO_4. The organic part was separated and the product from the residue was additionally extracted with benzene. The product was isolated by microfractionation *in vacuo*.

Following the above procedure, we obtained for the first time 3-methyl-5-phenylpent-1-yn-3-ol (**2a**), 3,5-dimethyl-5-phenylhex-1-yn-3-ol (**2b**), 2-methyl-1-phenylbut-3-yn-2-ol (**2c**), and 5-(2-furyl)-3-methylpent-1-yn-3-ol (**2d**).

Dioxolanones 3. A rotating 1.3-L autoclave with a heating unit was charged with an appropriate alkynol (1 mol), triethylamine (2 mL), tetraethylammonium bromide (0.42 g), and

Table 1. Constants and yields of compounds **2** and **3**

Compound	B.p./°C (Torr) or m.p./°C	Yield (%)	Found / Calculated (%)		Molecular formula
			C	H	
2a	93—95 (1.5)	72	82.70 82.72	8.12 8.10	$C_{12}H_{14}O$
2b	91—92 (1)	71	83.13 83.12	8.96 8.97	$C_{14}H_{18}O$
2c	81—83 (1)	78	82.44 82.46	7.57 7.55	$C_{11}H_{12}O$
2d	78—84 (1)	86	73.14 73.15	7.37 7.37	$C_{10}H_{12}O_2$
3a	132 (0.5)	82	71.53 71.54	6.48 6.47	$C_{13}H_{14}O_3$
3b	42—43[a]	76	73.14 73.15	7.37 7.37	$C_{15}H_{18}O_3$
3c	86—87[b]	80	70.53 70.58	5.91 5.92	$C_{12}H_{12}O_3$
3d	117—120 (0.5)	75	63.46 63.45	5.80 5.81	$C_{11}H_{12}O_4$

[a] From light petroleum.
[b] From acetone.

CuBr (0.4 g). Carbon dioxide was pumped until the initial pressure at 100 °C was 220 atm. The reaction was carried out for 20—30 h; the conversion was 95—98% (GLC). The reaction mixture was diluted with an equal volume of acetone, the catalyst was filtered off, and the solvent was removed. Compounds **3a,d** were purified by distillation *in vacuo*, while compounds **3b,c**, by crystallization (see Table 1).

Following this procedure, we obtained for the first time 4-methyl-5-methylidene-4-phenethyl-1,3- (**3a**), 4-methyl-5-methylidene-4-(2-methyl-2-phenylpropyl)-1,3- (**3b**), 4-benzyl-4-methyl-5-methylidene-1,3- (**3c**), and 4-[2-(2-furyl)ethyl]-4-methyl-5-methylidene-1,3-dioxolan-2-ones (**3d**).

Oxazolidinones 4a—h, 5a—h, 6a—e, and 7a—d. A dioxolanone **3** (10 mmol) was dissolved in acetonitrile (7 mL) and an appropriate amine (10 mmol) was added (ammonia, methylamine, ethylamine, and ethylenediamine were used as aqueous solutions; sodium glycinate was predissolved in a minimum amount of water). The reaction mixture was left at 45 °C and then concentrated. Most oxazolidinones were isolated as yellow oils crystallized from MeOBu^t—light petroleum. The yields of the products were 80—100%.

Following this procedure, we obtained for the first time 4-hydroxy-4,5-dimethyl-5-phenethyl-1,3- (**4a**), 4-hydroxy-3,4,5-trimethyl-5-phenethyl-1,3- (**4b**), 3-ethyl-4-hydroxy-4,5-dimethyl-5-phenethyl-1,3- (**4c**), 3-benzyl-4-hydroxy-4,5-dimethyl-5-phenethyl-1,3- (**4d**), 4-hydroxy-4,5-dimethyl-3,5-diphenethyl-1,3- (**4e**), and 3-[2-(3,4-dimethoxyphenyl)ethyl]-4-hydroxy-4,5-dimethyl-5-phenethyl-1,3-oxazolidin-2-ones (**4f**), 1,2-bis(4-hydroxy-4,5-dimethyl-2-oxo-5-phenethyl-1,3-oxazolidin-3-yl)ethane (**4g**), sodium (4-hydroxy-4,5-dimethyl-2-oxo-5-phenethyl-1,3-oxazolidin-3-yl)acetate (**4h**), 4-hydroxy-4,5-dimethyl-5-(2-methyl-2-phenylpropyl)-1,3- (**5a**), 4-hydroxy-3,4,5-trimethyl-5-(2-methyl-2-phenylpropyl)-1,3- (**5b**), 3-ethyl-4-hydroxy-4,5-dimethyl-5-(2-methyl-2-phenylpropyl)-1,3- (**5c**), 3-benzyl-4-hydroxy-1,3-dimethyl-5-(2-methyl-2-phenylpropyl)-1,3- (**5d**), 4-hydroxy-4,5-dimethyl-5-(2-methyl-2-phenylpropyl)-3-phenethyl-1,3- (**5e**), and 3-[2-(3,4-dimethoxyphenyl)ethyl]-4-hydroxy-4,5-dimethyl-5-(2-methyl-2-phenylpropyl)-1,3-oxazolidin-2-ones (**5f**), 1,2-bis[4-hydroxy-4,5-dimethyl-5-(2-methyl-2-phenylpropyl)-2-oxo-1,3-oxazolidin-3-yl]ethane (**5g**), sodium [4-hydroxy-4,5-dimethyl-5-(2-methyl-2-phenylpropyl)-2-oxo-1,3-oxazolidin-3-yl]acetate (**5h**), 5-benzyl-3-ethyl-4-hydroxy-4,5-dimethyl-1,3- (**6a**) and 3,5-dibenzyl-4-hydroxy-4,5-dimethyl-1,3-oxazolidin-2-ones (**6b**), 1,2-bis(5-benzyl-4-hydroxy-4,5-dimethyl-2-oxo-1,3-oxazolidin-3-yl)ethane (**6c**), sodium (5-benzyl-4-hydroxy-4,5-dimethyl-2-oxo-1,3-oxazolidin-3-yl)acetate (**6d**), 3-anilino-5-benzyl-4-hydroxy-4,5-dimethyl-1,3-oxazolidin-2-one (**6e**), and 5-[2-(2-furyl)ethyl]-4-hydroxy-4,5-dimethyl-1,3- (**7a**), 5-[2-(2-furyl)ethyl]-4-hydroxy-3,4,5-trimethyl-1,3- (**7b**), 3-ethyl-5-[2-(2-furyl)ethyl]-4-hydroxy-4,5-dimethyl-1,3- (**7c**), and 3-benzyl-5-[2-(2-furyl)ethyl]-4-hydroxy-4,5-dimethyl-1,3-oxazolidin-2-ones (**7d**).

Oxazolidinones 4i, 5i, 6f, and 8a. An appropriate dioxolanone **3** (10 mmol) was dissolved in acetonitrile (10 mL) and histamine hydrochloride (10 mmol) was added. Triethylamine (15 mmol) was added at 60 °C to the stirred mixture and stirring was continued at the same temperature for 1 h. The reaction mixture was cooled, the resulting precipitate of triethylamine hydrochloride was filtered off, the solvent was removed, and the residue was crystallized from MeOBu^t. The yields of the products were 25—60%.

Following this procedure, we obtained for the first time 4-hydroxy-3-[2-(imidazol-5-yl)ethyl]-4,5-dimethyl-5-phenethyl-1,3- (**4i**), 4-hydroxy-3-[2-(imidazol-5-yl)ethyl]-4,5-dimethyl-5-(2-methyl-2-phenylpropyl)-1,3- (**5i**), and 5-benzyl-4-hydroxy-3-[2-(imidazol-5-yl)ethyl]-4,5-dimethyl-1,3-oxazolidin-2-ones (**6f**) and 4-hydroxy-3-[2-(imidazol-5-yl)ethyl]-4,5,5-trimethyl-1,3-oxazolidin-2-one (**8a**).

Synthesis of compounds 9—13 (general procedure). Polyphosphoric acid (30-fold amount, w/w) was added to oxazolidinone **4a—h**, **5a—g**, or **6c**. The reaction mixture was stirred at 80 °C for 30 min, cooled, and diluted with a tenfold volume of ice water. In the case of compounds **9a—d**, **10a,b**, and **11**, the resulting precipitate was filtered off and washed with water to pH 7. In the other cases, the reaction mixture was carefully neutralized with 40% NaOH so that the temperature did not increase above 30 °C and the product was extracted three times with AcOEt (the volume of AcOEt was ~1/3 that of the aqueous phase). For products **9g,h**, **10g**, and **12**, $CHCl_3$ was used as an extractant. The extracts were combined, dried with Na_2SO_4, and concentrated. The cyclization products were crystallized from MeOBu^t or MeOBu^t—AcOEt.

Following this procedure, we obtained for the first time 3a,9b-dimethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**9a**), 1,3a,9b-trimethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**9b**), 1-ethyl-3a,9b-dimethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**9c**), 1-benzyl-3a,9b-dimethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1H)-one (**9d**), 3a,9b-dimethyl-1-phenethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**9e**), 1,2-bis(3a,9b-dimethyl-2-oxo-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-1(2*H*)-yl)ethane (**9g**), (3a,9b-dimethyl-2-oxo-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-1(2*H*)-yl)acetic acid (**9h**), 3a,5,5,9b-tet-

Table 2. Constants and yields of compounds **4—16**

Compound	R_f	Eluent[a]	M.p. /°C[b]	Yield (%)	Found / Calculated (%)			Molecular formula
					C	H	N	
4a	0.64	A	162	91	66.34 66.36	7.30 7.28	5.96 5.95	$C_{13}H_{17}NO_3$
4b	0.35	A	124	95	67.49 67.45	7.65 7.68	5.61 5.62	$C_{14}H_{19}NO_3$
4c	0.38	A	151	80	68.40 68.42	8.04 8.04	5.34 5.32	$C_{15}H_{21}NO_3$
4d	0.45	A	135	89	73.77 73.82	7.16 7.12	4.31 4.30	$C_{20}H_{23}NO_3$
4e	0.62	A	120	78	74.37 74.31	7.40 7.42	4.09 4.13	$C_{21}H_{25}NO_3$
4f	0.22	A	129	95	69.16 69.15	7.33 7.32	3.49 3.51	$C_{23}H_{29}NO_5$
4g	0.64	D	155	46	67.69 67.72	7.32 7.31	5.66 5.64	$C_{28}H_{36}N_2O_6$
4h	0.28	C[c]	132	74	—	—	—	$C_{15}H_{18}NNaO_5$
4i	0.70	D	185	62	65.64 65.63	7.03 7.04	12.76 12.76	$C_{18}H_{23}N_3O_3$
5a	0.07	A	222	92	68.36 68.42	8.05 8.04	5.36 5.32	$C_{15}H_{21}NO_3$
5b	0.22	A	203	94	69.34 69.29	8.34 8.36	5.02 5.05	$C_{16}H_{23}NO_3$
5c	0.28	A	140	93	70.02 70.07	8.68 8.65	4.83 4.81	$C_{17}H_{25}NO_3$
5d	0.22	B	100	75	74.71 74.76	7.73 7.70	3.98 3.96	$C_{22}H_{27}NO_3$
5e	0.21	B	108	87	75.13 75.17	7.98 7.95	3.82 3.81	$C_{23}H_{29}NO_3$
5f	0.48	A	190	75	70.21 70.23	7.81 7.78	3.27 3.28	$C_{25}H_{33}NO_5$
5g	0.64	A	218	38	69.54 69.54	8.04 8.02	5.05 5.07	$C_{32}H_{44}N_2O_6$
5h	0.37	C[c]	195	47	—	—	—	$C_{17}H_{22}NNaO_5$
5i	0.69	D	179	35	67.13 67.20	7.63 7.61	11.81 11.76	$C_{20}H_{27}N_3O_3$
6a	0.35	A	145	82	67.40 67.45	7.70 7.68	5.65 5.62	$C_{14}H_{19}NO_3$
6b	0.61	A	161	80	73.34 73.29	6.78 6.80	4.46 4.50	$C_{19}H_{21}NO_3$
6c	0.37	D	156	82	66.66 66.65	6.87 6.88	5.98 5.98	$C_{26}H_{32}N_2O_6$
6d	0.25	C[c]	145	68	—	—	—	$C_{14}H_{16}NNaO_5$
6e	0.54	A	166	63	69.14 69.21	6.47 6.45	9.02 8.97	$C_{18}H_{20}N_2O_3$
6f	0.61	D	82	60	64.67 64.74	6.71 6.71	13.40 13.32	$C_{17}H_{21}N_3O_3$
7a	0.14	A	133	86	58.66 58.66	6.72 6.71	6.21 6.22	$C_{11}H_{15}NO_4$
7b	0.31	A	75	83	60.21 60.24	7.19 7.16	5.85 5.85	$C_{12}H_{17}NO_4$
7c	0.29	B	76	79	61.64 61.64	7.57 7.56	5.52 5.53	$C_{13}H_{19}NO_4$

(*to be continued*)

Table 2 (*continued*)

Compound	R_f	Eluent[a]	M.p. /°C[b]	Yield (%)	Found / Calculated (%)			Molecular formula
					C	H	N	
7d	0.48	A	94	81	68.60 68.55	6.68 6.71	4.43 4.44	$C_{18}H_{21}NO_4$
8a	0.59	D	145	30	55.16 55.22	7.18 7.16	17.60 17.56	$C_{11}H_{17}N_3O_3$
9a	0.32	A	166	77	71.85 71.87	6.96 6.96	6.46 6.45	$C_{13}H_{15}NO_2$
9b	0.51	A	95	87	72.72 72.70	7.41 7.41	6.04 6.06	$C_{14}H_{17}NO_2$
9c	0.65	A	Oil	68	73.42 73.44	7.80 7.81	5.74 5.71	$C_{15}H_{19}NO_2$
9d	0.74	A	82	82	78.14 78.15	6.89 6.89	4.56 4.56	$C_{20}H_{21}NO_2$
9e	0.79	A	112	85	78.45 78.47	7.21 7.21	4.38 4.36	$C_{21}H_{23}NO_2$
9g	0.34	A	205	56	72.98 73.02	7.04 7.00	6.08 6.08	$C_{28}H_{32}N_2O_4$
9h	0.34	C	138	61	65.48 65.44	6.21 6.22	5.05 5.09	$C_{15}H_{17}NO_4$
10a	0.31	A	204	84	73.41 73.44	7.83 7.81	5.71 5.71	$C_{15}H_{19}NO_2$
10b	0.27	B	139	64	74.07 74.10	8.18 8.16	5.42 5.40	$C_{16}H_{21}NO_2$
10c	0.41	B	97	62	74.65 74.69	8.48 8.48	5.16 5.12	$C_{17}H_{23}NO_2$
10d	0.55	B	115	67	78.79 78.77	7.51 7.51	4.16 4.18	$C_{22}H_{25}NO_2$
10e	0.72	B	114	81	79.08 79.05	7.78 7.79	3.99 4.01	$C_{23}H_{27}NO_2$
10f	0.59	A	152	83	73.29 73.32	7.66 7.63	3.43 3.42	$C_{25}H_{31}NO_4$
10g	0.66	A	193	77	74.33 74.39	7.83 7.80	5.45 5.42	$C_{32}H_{40}N_2O_4$
11a	0.8	A	132	97	71.53 71.54	6.48 6.47	—	$C_{13}H_{14}O_3$
11b	0.59	B	134	91	73.12 73.15	7.39 7.37	—	$C_{15}H_{18}O_3$
12	0.62	A	176	57	75.23 75.32	7.05 7.02	6.57 6.51	$C_{27}H_{30}N_2O_3$
13	0.28	B	175	92	72.44 72.42	7.13 7.13	3.65 3.67	$C_{23}H_{27}NO_4$
14	0.62	B	127	12	63.44 63.45	5.82 5.81	—	$C_{11}H_{12}O_4$
15	0.14	E	157	64	75.40 75.35	8.93 8.96	7.30 7.32	$C_{12}H_{17}NO$
17	0.44	D	Oil	40	74.94 74.97	8.41 8.39	—	$C_{12}H_{16}O_2$

[a] The eluents: A is AcOEt—benzene (1 : 2), B is AcOEt—benzene (1 : 5), C is AcOEt, D is AcOEt—EtOH (1 : 1), and E is Pr^iOH—AcOEt—12% NH_3 (aq) (7 : 9 : 4).

[b] The melting points of all the compounds given in Table 2 were determined after their crystallization from $MeOBu^t$—light petroleum.

[c] After acidification with 2 *N* HCl followed by microextraction with $CHCl_3$.

Table 3. Mass spectra of the compounds obtained

Compound	M /g mol^{-1}	m/z (I_{rel} (%))
3a	218	218(9); 174(45); 159(47); 146(35); 141(39); 131(64); 117(61); 104(68); 91(100)
3d	208	208(5); 164(7); 121(19); 106(13); 94(26); 91(20); 81(100)
4b	249	249(33); 232(8); 174(8); 149(54); 127(100); 105(46); 91(83); 56(84)
4c	263	263(2); 246(6); 174(22); 149(40); 141(100); 105(33); 91(65); 70(52)
4d	325	325(5); 261(2); 203(73); 149(19); 105(18); 91(100); 65(20)
4e	339	339(29); 217(34); 175(16); 104(31); 100(40); 91(100); 43(57)
4f	399	399(10); 164(100); 151(18); 91(21)
4g	496	243(2); 230(18); 186(22); 149(10); 134(38); 91(100)
4i	329	329(2); 207(23); 148(33); 94(69); 91(100); 61(19)
5a	263	263(4); 119(100); 91(44); 84(17); 77(11)
5b	277	259(10); 203(21); 127(55); 119(74); 91(100)
5c	291	291(2); 141(24); 119(86); 91(60); 72(18); 43(100)
5d	353	353(4); 290(8); 203(28); 177(22); 119(72); 91(100)
5e	367	367(11); 217(17); 119(90); 105 (100); 91(62); 43(50)
5f	428	427(8); 164(100); 151(14); 119(12); 91(13)
5g	552	271(6); 258(12); 214(13); 177(16); 162(13); 119(100); 91(32)
5i	357	339(3); 235(19); 207(28);148(41); 94(63); 91(100)
6a	249	249(2); 140(15); 91(36); 87(69); 72(40); 43(100)
6b	311	311(4); 91(100); 43(32)
6c	468	450(6); 273(24); 172(15); 158(16); 135(17); 91(96); 43(100)
6e	312	312(7); 294(21); 204(23); 152(46); 135(77); 91(100); 57(38)
6f	315	315(6); 225(11); 148(24); 94(40); 91(100); 43(72)
7a	225	225(4); 207(15); 164(16); 113(100); 94(64); 80(85)
7b	239	221(2); 166(2); 127(100); 94(24); 81(74); 56(74)
7c	253	253(2); 235(4); 192(20); 141(43); 112(55); 94(88); 80(100)
7d	315	297(8); 254(18); 206(56); 185(43); 94(100); 91 (76); 81(57)
8a	239	221(18); 137(52); 94(95); 80(100); 59(73); 54(51)
9a	217	217(1); 156(100); 146(50); 131(79); 115(25)
9b	231	231(7); 216(59); 172(46); 160(79); 156(100); 141(53); 131(84); 115(45); 91(66)
9c	245	245(3); 216(6); 157(100); 131(82); 115(55); 91(53)
9d	307	307(1); 158(76); 143(32); 115(16); 91(100)
9e	321	321(33); 230(71); 186(97); 157(100); 145(76); 131(49); 91(61)
9g	460	460(11); 243(67); 186(31); 157(100); 143(67); 131(83); 115(40); 91(50)
9h	275	275(16); 231(21); 158(78); 156(100); 143(41); 131(34); 115(30); 91(18)
10a	245	245(22); 230(76); 186(100); 179(95); 171(65); 144(39); 91(35)
10b	259	259(15); 244(93); 200(51); 187(57); 159(59); 128(41); 115(34); 91(42); 56(100)
10c	273	273(8); 244(100); 186(54); 159(66); 128(38); 91(76)
10d	335	335(1); 186(100); 171(78); 156(16); 128(16); 91(97)
10e	349	349(22); 258(60); 214(100); 185(81); 158(37); 131(37); 117(29); 91(45)
10f	409	409(9); 214(8); 185(11); 164(100); 151(12); 117(7)
10g	516	516(1); 271(79); 214(33); 186(100); 171(35); 156(16); 68(28)
11a	218	218(34); 174(13); 159(70); 146(78); 141(78); 131(100); 115(51); 91(70); 77(28)
11b	246	246(37); 231(47); 187(100); 172(55); 156(35); 145(54); 129(43); 115(19); 91(30)
12	432	432(1); 270(83); 179(65); 115(10); 91(100); 65(21)
13	381	381(4); 366(12); 219(60); 104 (52); 91(100); 43(48)
14	208	208(5); 164(19); 136(54); 121(65); 107(76); 94(85); 81(100); 69(44); 53(55)
15	191	191(3); 174(8); 156(38); 133(100); 118(89); 91(25)
17	220	220(4); 203(11); 132(100); 91(34)

ramethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**10a**), 1,3a,5,5,9b-pentamethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**10b**), 1-ethyl-3a,5,5,9b-tetramethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**10c**), 1-benzyl-3a,5,5,9b-tetramethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**10d**), 3a,5,5,9b-tetramethyl-1-phenethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-2(1*H*)-one (**10e**), 1,2-bis(3a,5,5,9b-tetramethyl-2-oxo-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]oxazol-1(2*H*)-yl)ethane (**10g**), 3a,9b-dimethyl-3a,4,5,9b-tetrahydronaphtho[1,2-*d*][1,3]dioxol-2-one (**11a**), 3a,5,5,9b-tetramethyl-3a,4,5,9b-tetrahydronaph-

Table 4. ^{1}H NMR spectra of dioxolanones **3**

Compound	5-Me (s, 3 H)	4-CH_2= (d, 1 H)	—CH_2—	Ar	Me_2
3a	1.66	4.59, 4.83 (J = 4.0)	2.05—2.25, 2.58—2.73 (both m, 2 H each)	7.11—7.28 (m, 5 H)	—
3b	1.39	4.50, 4.63 (J = 4.0)	2.29, 2.44 (both d, 1 H each)	6.17 (t, 1 H); 7.28 (t, 2 H); 7.39 (d, 2 H)	1.27, 1.31 (both s, 3 H each)
3c	1.64	4.71, 4.82 (J = 3.9)	3.16 (dd, 2 H)	7.17—7.33 (m, 5 H)	—
3d	1.65	4.57, 4.81 (J = 3.9)	2.16—2.23, 2.67—2.73 (both m, 2 H each)	6.05, 6.25, 7.34 (all s, 1 H each)	—

Table 5. ^{1}H NMR spectra of oxazolidinones **4**—**8**

Compound*	4-Me, 5-Me	4-OH	—CH_2—; CMe_2	Ar	Other signals
4a (1 : 2)	1.31, 1.34 (both s, 3 H); 1.37 (s, 3 H)	5.60, 5.67 (both s, 1 H)	1.70—2.19, 2.60—2.80 (both m, 2 H each)	7.10—7.27 (m, 5 H)	7.75 (s, 1 H, N<u>H</u>)
4b (4 : 7)	1.31, 1.33 (both s, 3 H); 1.36, 1.38 (both s, 3 H)	5.76, 5.81 (both s, 1 H)	1.75—1.84, 1.90—2.18 (both m, 1 H each); 2.62—2.80 (m, 2 H)	7.10—7.29 (m, 5 H)	2.70, 2.71 (both s, 3 H, N<u>CH_3</u>)
4c (1 : 0)	1.29, 1.37 (both s, 3 H each)	5.59 (s, 1 H)	1.85—2.02 (m, 2 H); 2.56—2.65, 2.68—2.77 (both m, 1 H each)	7.18 (t, 1 H); 7.22 (d, 2 H); 7.29 (t, 2 H)	1.11 (t, 3 H, NCH_2<u>CH_3</u>); 3.14 (q, 2 H, N<u>CH_2</u>CH_3)
4d (2 : 5)	1.15, 1.18 (both s, 3 H); 1.35, 1.42 (both s, 3 H)	5.93, 5.97 (both s, 1 H)	1.71—2.15, 2.65—2.82 (both m, 2 H each)	7.09—7.33 (m, 10 H)	4.18, 4.51 (both d, 2 H, N<u>CH_2</u>Ph, J = 12)
4e (2 : 3)	1.06, 1.12 (both s, 3 H); 1.20, 1.32 (both s, 3 H)	5.97, 5.99 (both s, 1 H)	1.58—1.71, 1.83—2.02 (both m, 2 H); 2.55—2.75 (m, 2 H)	7.12—7.34 (m, 10 H)	2.78—2.91, 3.17—3.40 (both m, 2 H each, N<u>CH_2</u>—C<u>H_2</u>Ph)
4f (1 : 2)	1.12, 1.20 (both s, 3 H); 1.24, 1.34 (both s, 3 H)	5.92, 5.95 (both s, 1 H)	1.61—1.76, 1.86—2.05 (both m, 2 H); 2.56—2.69 (m, 2 H)	6.67—6.90 (m, 3 H); 7.16—7.33 (m, 5 H)	2.72—2.85, 3.20—3.40 (both m, 2 H each, N<u>CH_2</u><u>CH_2</u>Ar); 3.65, 3.73 (both s, 3 H, O<u>Me</u>); 3.68, 3.76 (both s, 3 H, O<u>Me</u>)
4g**	1.28—1.49 (m, 12 H)	5.97—6.09 (m, 2 H)	1.74—2.08, 2.59—2.81 (both m, 4 H each)	7.14—7.33 (m, 10 H)	3.21—3.40 (m, 4 H, N<u>CH_2</u><u>CH_2</u>N)
4h (1 : 1)	1.22, 1.24 (both s, 3 H); 1.31, 1.38 (both s, 3 H)	No signal	1.70—1.79 (m, 1 H); 2.58—2.80 (m, 2 H)	7.12—7.31 (m, 5 H)	3.38—3.47, 3.76—3.82 (both m, 2 H, N<u>CH_2</u>COONa)
4i (2 : 3)	1.25, 1.27 (both s, 3 H); 1.35 (s, 3 H)	5.95, 6.37 (both s, 1 H)	1.71—1.82, 5.59—2.71 (both m, 2 H each)	7.16—7.32 (m, 5 H)	2.72—2.86, 3.27—3.40 (both m, 2 H each, N<u>CH_2</u><u>CH_2</u>—); 6.66, 6.86 (both s, 1 H), 7.50 (s, 1 H), C<u>H</u> imidazole); 11.73, 11.84 (both s, 1 H, N<u>H</u>)
5a (1 : 0)	0.60, 1.45 (both s, 3 H each)	5.69 (s, 1 H)	2.17 (s, 2 H); 1.15, 1.26 (both s, 3 H each)	7.15 (t, 1 H); 7.30 (t, 2 H); 7.92 (d, 2 H)	7.86 (s, 1 H, N<u>H</u>)
5b (1 : 0)	0.60, 1.46 (both s, 3 H each)	5.82 (s, 1 H)	2.13—2.26 (m, 2 H); 1.17, 1.27 (both s, 3 H each)	7.15 (t, 1 H); 7.31 (t, 2 H); 7.93 (d, 2 H)	2.61 (s, 3 H, NC<u>H_3</u>)
5c (1 : 0)	0.56, 1.46 (both s, 3 H each)	5.84 (s, 1 H)	2.13, 2.23 (both d, 2 H each); 1.17, 1.26 (both s, 3 H each)	7.16 (t, 1 H); 7.31 (t, 2 H); 7.93 (d, 2 H)	1.05 (t, 3 H, NCH$_2$<u>CH_3</u>); 3.04—3.13 (m, 2 H, N<u>CH_2</u>CH_3)

(*to be continued*)

Table 5 (*continued*)

Compound*	4-Me, 5-Me	4-OH	—CH_2—; CMe_2	Ar	Other signals
5d (3 : 4)	0.64, 0.76 (both s, 3 H); 1.49 (s, 3 H)	5.93, 6.03 (both s, 1 H)	1.26, 2.11 (both d, J = 16); 2.23 (s, 2 H); 1.04, 1.16 (both s, 3 H); 1.29, 1.30 (both s, 3 H)	7.11—7.48 (m, 10 H)	4.17, 4.42 (both d, 2 H, N$\underline{CH_2}$Ph, J = 16.2)
5e (2 : 3)	0.47, 0.65 (both s, 3 H); 1.44, 1.46 (both s, 3 H)	5.76, 5.87 (both s, 1 H)	1.67, 1.93, 2.13, 2.19 (all d, 2 H, J = 14); 0.95, 1.05 (both s, 3 H); 1.24, 1.26 (both s, 3 H)	7.13—7.45 (m, 10 H)	2.76—2.93, 3.13—3.39 (both m, 2 H each, N$\underline{CH_2}\underline{CH_2}$Ph)
5f (1 : 0)	0.50, 1.45 (both s, 3 H each)	5.86 (s, 1 H)	2.14, 2.20 (both d, 2 H, J = 16); 1.00, 1.26 (both s, 3 H each)	6.68 (d, 1 H); 6.79 (s, 1 H); 6.83 (d, 1 H); 7.17 (t, 1 H); 7.31 (t, 2 H); 7.42 (d, 2 H)	2.73 (t, 2 H, N$\underline{CH_2}\underline{CH_2}$Ar); 3.13—3.35 (m, 2 H, N$\underline{CH_2}\underline{CH_2}$Ar); 3.70, 3.72 (both s, 3 H each, O$\underline{CH_3}$)
5g**	0.55—0.74, 1.40—1.50 (both m, 6 H each)	5.74—5.95 (m, 2 H)	1.83—2.26 (m, 4 H); 1.17—1.39 (m, 12 H)	7.11—7.20 (m, 2 H); 7.25—7.33, 7.37—7.46 (both m, 4 H each)	3.09—3.36 (m, 4 H, N$\underline{CH_2}\underline{CH_2}$N)
5h (5 : 3)	0.52, 0.72 (both s, 3 H); 1.44, 1.46 (both s, 3 H)	No signal	1.77—1.81, 2.02—2.23 (both m, 2 H); 1.12 (s, 3 H); 1.24, 1.26 (both s, 3 H)	7.11—7.19 (m, 1 H); 7.26—7.33, 7.38—7.46 (both m, 2 H each)	3.29—3.39, 3.70—3.81 (both m, 2 H, N$\underline{CH_2}$COONa)
5i (1 : 0)	0.54, 1.48 (both s, 3 H each)	6.18 (br.s, 1 H)	2.14—2.21 (m, 2 H); 1.05, 1.27 (both s, 3 H each)	7.16 (t, 1 H); 7.30 (t, 2 H); 7.41 (d, 2 H)	6.76 (s, 1 H); 7.50 (s, 1 H, $\underline{CH}$ imidazole); 11.71 (br.s, 1 H, N$\underline{H}$); 2.71 (t, 2 H); 3.19—3.32 (m, 2 H, N$\underline{CH_2}\underline{CH_2}$—)
6c (1 : 2)	1.06, 1.19 (both s, 3 H); 1.31, 1.45 (both s, 3 H)	5.74, 5.91 (2 d, 1 H, J = 2.5)	2.53, 2.66, 2.87, 3.15 (all d, 2 H, J = 13.5)	7.17—7.33 (m, 5 H)	1.13—1.21 (m, 3 H, N$CH_2\underline{CH_3}$); 3.16—3.25 (m, 2 H, N$\underline{CH_2}CH_3$)
6d (1 : 1)	1.08, 1.21 (both s, 3 H); 1.13, 1.26 (both s, 3 H)	5.97, 6.14 (both d, 1 H, J = 2.5)	2.66, 3.21 (both d, 1 H, J = 13.8); 2.85—2.93 (m, 1 H)	7.18—7.33 (m, 10 H)	4.21, 4.25 (both s, 1 H, N$\underline{CH_2}$Ph); 4.55, 4.56 (both d, 1 H each, N$\underline{CH_2}$Ph, J = 2)
6g**	1.04—1.56 (m, 12 H)	6.12 (br.s, 2 H)	2.56—3.52 (m, 8 H, all CH_2 groups)	7.11—7.35 (m, 10 H)	—
6h (5 : 2)	0.99, 1.15 (both s, 3 H); 1.24, 1.38 (both s, 3 H)	No signal	2.65, 2.97 (both d, 1 H, J = 13.8); 2.83, 3.17 (both d, 1 H, J = 13.8)	7.17—7.35 (m, 5 H)	3.42—3.52, 3.81—3.90 (both m, 1 H each, N$\underline{CH_2}$COONa)
6i (1 : 0)	1.24, 1.31 (both s, 3 H each)	6.52 (s, 1 H)	2.98, 3.22 (both d, 1 H each, J = 13.8)	7.24—7.38 (m, 5 H)	6.74 (t, 1 H, NH—$\underline{Ph}$); 6.84 (d, 2 H, NH—$\underline{Ph}$); 7.16 (t, 2 H, NH—$\underline{Ph}$); 7.69 (br.s, 1 H, N$\underline{H}$)
6k (1 : 0)	0.57, 1.47 (both s, 3 H each)	6.23 (br.s, 1 H)	3.22—3.33 (m, 2 H)	7.17 (t, 1 H); 7.31 (t, 2 H); 7.43 (d, 2 H)	6.83, 7.49 (both s, 1 H each, $\underline{CH}$ imidazole); 11.70 (br.s, 1 H, N$\underline{H}$); 2.13—2.24, 2.64—2.80 (both m, 2 H, N$\underline{CH_2}\underline{CH_2}$—)

(*to be continued*)

Table 5 (*continued*)

Compound*	4-Me, 5-Me	4-OH	—CH_2—; CMe_2	Ar	Other signals
7a (1 : 2)	1.23, 1.26 (both s, 3 H); 1.28, 1.31 (both s, 3 H)	5.89, 5.92 (both s, 1 H)	1.73—2.06, 2.58—2.78 (both m, 2 H each)	6.10, 6.14 (both d, 1 H); 6.32—6.36, 7.49—7.52 (both m, 1 H each)	8.09, 8.12 (both s, 1 H, N<u>H</u>)
7b (3 : 8)	1.28, 1.31 (both s, 3 H); 1.35 (s, 3 H)	5.79, 5.84 (both s, 1 H)	1.77—2.21, 2.66—2.76 (both m, 2 H each)	6.00—6.03, 6.22—6.28, 7.30—7.36 (all m, 1 H each)	2.70, 2.91 (both s, 3 H, N<u>C</u>H$_3$)
7c (2 : 3)	1.24, 1.30 (both s, 3 H); 1.34, 1.36 (both s, 3 H)	5.99, 6.02 (both s, 1 H)	1.75—2.08, 2.61—2.80 (both m, 2 H each)	6.10—6.15, 6.33—6.36, 7.48—7.53 (all m, 1 H each)	1.06—1.13 (m, 3 H, NCH$_2$<u>C</u>H$_3$); 3.08—3.17 (m, 2 H, N<u>C</u>H$_2$CH$_3$)
7d (3 : 4)	1.16, 1.17 (both s, 3 H); 1.31, 1.36 (both s, 3 H)	5.95 (br.s, 1 H)	1.76—2.26, 2.66—2.81 (both m, 2 H each)	6.01, 6.06 (both d, 1 H); 6.22—6.28 (m, 1 H); 7.17—7.35 (m, 6 H)	4.16, 4.20 (both s, 1 H, N<u>C</u>H$_2$Ph); 4.47, 4.51 (both d, 1 H each, N<u>C</u>H$_2$Ph, J = 2)
8a	1.20 (s, 6 H), 1.30 (s, 3 H)	6.24 (br.s, 1 H)	2.77, 3.31 (both t, 2 H each, J = 7.3)	—	6.81, 7.52 (both s, 1 H each, C<u>H</u> imidazole); 11.83 (br.s, 1 H, N<u>H</u>)

* The diastereomer ratio is given in parentheses.
** The mixture of four diastereomers.

Table 6. ^{1}H NMR spectra of cyclization products **9—14**

Compound	4-Me, 5-Me (s)	—CH_2—; CMe_2	Ar	Other signals
9a	1.48, 1.53 (3 H each)	1.87—1.96, 2.10—2.17, 2.65—2.73, 2.90—2.98 (all m, 1 H each)	7.06 (d, 1 H); 7.10—7.24 (m, 2 H); 7.49 (d, 1 H)	7.91 (s, 1 H, N<u>H</u>)
9b	1.45, 1.60 (3 H each)	1.73—1.81, 2.15—2.22, 2.64—2.71, 2.85—2.94 (all m, 1 H each)	7.12—7.26 (m, 3 H); 7.44—7.50 (m, 1 H)	2.56 (s, 3 H, N<u>C</u>H$_3$)
9c	1.43, 1.62 (3 H each)	1.65—1.72, 2.16—2.24, 2.64—2.72, 2.85—2.95 (all m, 1 H each)	7.13—7.19, 7.21—7.26, 7.48—7.52 (all m, 1 H each)	0.77 (t, 3 H, N<u>C</u>$_2$<u>H</u>$_5$); 3.01—3.11 (m, 2 H, N<u>C</u>$_2$<u>H</u>$_5$)
9d	1.45, 1.49 (3 H each)	1.66—1.74, 2.17—2.24, 2.57—2.65, 2.77—2.86 (all m, 1 H each)	7.02 (d, 2 H); 7.07 (d, 1 H); 7.12—7.27 (m, 5 H); 7.50 (d, 1 H)	4.01, 4.23 (both d, 2 H, N<u>C</u>H$_2$Ph)
9e	1.33, 1.47 (3 H each)	1.69—1.76, 2.02—2.09, 2.20—2.28, 2.75—2.83 (all m, 1 H each)	7.02 (d, 2 H); 7.16—7.34 (m, 6 H); 7.68 (d, 1 H)	2.61—2.70 (m, 2 H); 3.09—3.17, 3.32—3.40 (both m, 1 H each, N<u>C</u>H$_2$<u>C</u>H$_2$Ph)
9g	1.38, 1.49 (6 H each)	1.67—1.75, 2.05—2.13, 2.73—2.82, 2.84—3.07 (all m, 2 H each)	7.09—7.47 (m, 8 H)	2.61—2.73 (m, 4 H, N<u>C</u>H$_2$<u>C</u>H$_2$N)

(*to be continued*)

Table 6 (*continued*)

Compound	4-Me, 5-Me (s)	—CH_2—; CMe_2	Ar	Other signals
9h	1.49, 1.58 (6 H each)	1.80—1.88, 2.16—2.24, 2.64—2.70, 2.86—2.96 (all m, 1 H each)	7.14—7.19 (m, 1 H); 7.21—7.27 (m, 2 H); 7.58—7.62 (m, 1 H)	3.72, 3.93 (both d, 2 H, NCH_2COOH, J = 18.0); 12.46 (br.s, 1 H, $COOH$)
10a	1.38, 1.48 (3 H each)	1.31, 1.33 (both s, 3 H each); 1.92, 2.03 (both d, 1 H each, J = 15.2)	7.22—7.27 (m, 2 H); 7.36—7.41, 7.46—7.51 (both m, 1 H each)	8.17 (s, 1 H, NH)
10b	1.38, 1.59 (3 H each)	1.30, 1.34 (both s, 3 H each); 1.93, 2.05 (both d, 1 H each, J = 15.0)	7.26, 7.31 (both t, 1 H each); 7.47, 7.52 (both d, 1 H each)	2.78 (s, 3 H, NCH_3)
10c	1.37, 1.58 (3 H each)	1.29, 1.33 (both s, 3 H each); 1.89, 2.04 (both d, 1 H each, J = 14.9)	7.24, 7.30 (both t, 1 H each); 7.44, 7.60 (both d, 2 H each)	0.96 (t, 3 H, NC_2H_5); 3.15—3.24, 3.34—3.43 (both m, 1 H each, NC_2H_5)
10d	1.38, 1.52 (3 H each)	1.28, 1.29 (both s, 3 H each); 1.92, 2.05 (both d, 1 H each, J = 14.7)	7.15—7.33 (m, 7 H); 7.44, 7.68 (both d, 1 H each)	4.41, 4.53 (both d, 1 H each, NCH_2Ph)
10e	1.32, 1.41 (3 H each)	1.23, 1.27 (both s, 3 H each); 1.86, 1.99 (both d, 1 H each, J = 14.8)	7.17—7.34 (m, 7 H); 7.45, 7.64 (both d, 1 H each)	2.59—2.59, 2.80—2.88, 3.31—3.39, 3.56—3.64 (all m, 1 H each, NCH_2CH_2Ph)
10f	1.32, 1.42 (3 H each)	1.25, 1.28 (both s, 3 H each); 1.86, 1.99 (both d, 1 H each, J = 14.7)	6.67 (d, 1 H); 6.77 (s, 1 H); 6.86 (d, 1 H); 7.27, 7.32 (both t, 1 H each); 7.45, 7.64 (both d, 1 H each)	2.43—2.50, 2.72—2.80 3.28—3.36, 3.53—3.62 (all m, 1 H each), (m, 1 H, NCH_2CH_2Ar); 3.72, 3.76 (both s, 3 H each, $ArOCH_3$)
10g	1.40, 1.41 (6 H); 1.54, 1.57 (6 H)	1.29, 1.30 (both s, 6 H); 1.34, 1.35 (both s, 6 H); 1.88—1.94, 2.04—2.11 (both m, 2 H each)	7.19—7.36, 7.39—7.51 (both m, 4 H each)	3.18—3.31, 3.38—3.47 (2 m, 4 H, NCH_2CH_2N)
11a	1.56, 1.75 (3 H each)	2.03—2.11; 2.17—2.23; 2.73—2.80; 2.90—3.00 (all m, 1 H each)	7.16 (d, 1 H); 7.24—7.32 (m, 2 H); 7.54 (d, 1 H)	—
11b	1.50, 1.75 (3 H each)	1.34 (s, 6 H); 2.07, 2.18 (both d, 2 H, J = 15.5)	7.32, 7.38 (both t, 1 H each); 7.46, 7.53 (both d, 1 H each)	—
12	0.96, 1.40, 1.53 (3 H each)	2.91—3.01 (m, 2 H); 3.53, 3.71 (both d, 2 H, J = 14)	7.20—7.37 (m, 10 H)	2.72—2.80 (t, 1 H, NCH_2CH_2N); 3.08—3.24 (m, 3 H, NCH_2CH_2N); 4.78 (s, 1 H, CH)
13, 2 : 3	0.92, 1.68 (3 H); 1.48, 1.51 (3 H)	2.18—2.37, 2.47—2.58, 2.66—2.88 (three m, 6 H); 3.06—3.15, 3.82—3.88 (both m, 1 H each)	6.65, 6.67 (both s, 1 H); 6.74, 6.78 (both s, 1 H); 6.95—6.98, 7.08—7.13, 7.17—7.24, 7.31—7.37 (four m, 5 H)	3.72, 3.76 (both s, 3 H, $ArOCH_3$); 3.75, 3.77 (both s, 3 H, $ArOCH_3$)

tho[1,2-*d*][1,3]dioxol-2-one (**11b**), 1,10-dibenzyl-1,10,10a-trimethyl-5,6,10,10a-tetrahydro-1*H*-bis[1,3]oxazolo[3,4-*d*:4′,3′-*g*][1,4]diazepine-3,8-dione (**12**), and 8,9-dimethoxy-1,10b-dimethyl-1-phenethyl-1,5,6,10b-tetrahydro[1,3]oxazolo[4,3-*a*]isoquinolin-3-one (**13**).

3a-Methyl-5a,8-epoxy-3a,4,5,5a,8,9-hexahydroindano[1,7*a*-*d*][1,3]dioxol-2-one (14). Crude dioxolanone **3d** obtained from compound **2d** (130 g) (see above) was distilled *in vacuo* (1 Torr, 170 °C (oil bath), distillation rate ~1 drop/s). The tar material was dissolved in ethyl acetate and passed through a silica gel layer. The solution containing compound **14** as the major product was concentrated and the residue was crystallized from benzene—light petroleum to give pure compound **14** (10 g, 12%) as a white powder. ^{1}H NMR, δ: 1.59 (s, 3 H, CH_3-C(3a)); 1.64 (d, 1 H, HC(4), J = 12.8 Hz); 2.00—2.09 (m, 1 H); 2.14—2.21 (m, 2 H); 2.33—2.40 (m, 1 H); 2.51 (dd, 1 H, HC(5),

Table 7. ^{1}H NMR spectra of hydrolysis products **15** and **17**

Compound	4-Me, 5-Me	—CH_2—; CMe_2	Ar	Other signals
15	1.24 (s, 3 H); 1.50 (s, 3 H)	1.77—1.86 (m, 1 H); 1.91—1.99 (m, 1 H); 2.68—2.77 (m, 1 H); 2.89—2.98 (m, 1 H)	7.11—7.17 (m 1 H); 7.21—7.28 (m 2 H); 7.60—7.67 (m 1 H)	4.5—6.5 (br.s, 7 H, $N\underline{H}_2$, O<u>H</u>, oxalate, water)
17	1.24 (s, 3 H); 1.39 (s, 3 H)	1.20 (s, 6 H); 1.82 (s, 2 H)	7.09—7.16 (m, 2 H); 7.25, 7.56 (both d, 1 H each)	3.91, 4.35 (both s, 1 H each, O<u>H</u>)

J = 12.8 Hz, J = 4.8 Hz); 5.00 (dd, 1 H, HC(5a), J = 4.7 Hz, J = 1.4 Hz); 6.47 (d, 1 H, HC(7), J = 5.8 Hz); 6.63 (dd, 1 H, HC(6), J = 5.8 Hz, J = 1.5 Hz). ^{13}C NMR, δ: 23.20 (CH_3C(3a)); 23.88 (C(9)); 35.90, 38.97 (C(4), C(5)); 78.55 (C(8)); 90.66, 95.66, 95.96 (C(3a), C(5a), C(9a)); 133.57, 139.4 (C(6), C(7)); 152.68 (C(2)).

1-Amino-1,2-dimethyl-1,2,3,4-tetrahydronaphthalen-2-ol (15). Compound **9a** (0.75 g, 3.5 mmol) was dissolved in DMSO (3.5 mL) and a solution of KOH (1.96 g, 35 mmol) in water (3.5 mL) was added. The mixture was heated to 80 °C and stirred at this temperature for ~100 h. Water (15 mL) was added and the mixture was neutralized with 25% H_2SO_4 and cooled. The organic material was extracted with $CHCl_3$ (2×10 mL) and the extract was dried with Na_2SO_4 and concentrated. The residue was dissolved in boiling MeOBu^t (15 mL) and cooled. The resulting crystals of the unreacted starting oxazolidinone were filtered off (conversion ~80%). A solution of anhydrous oxalic acid (0.27 g, 3 mmol) in MeOBu^t was added to the filtrate. The resinous precipitate that formed was separated and washed with hot MeOBu^t. Recrystallization from a minimum amount of acetonitrile gave the target amino alcohol as white crystals of its oxalate salt, m.p. 157 °C.

1,2,3,4-Tetramethylnaphthalene (16). ***A.*** Compound **10a** (0.735 g, 3 mmol) was dissolved in hot anhydrous MeOBu^t (20 mL) and $LiAlH_4$ (0.56 g, 15 mmol) was added. The reaction mixture was refluxed for 3 h. On cooling, ethyl acetate (10 mL) was gradually added. The mixture was filtered, the filtrate was concentrated, and the residue was crystallized from MeOH. The yield of compound **16** was quantitative. The melting point[16] (107 °C) and ^{1}H NMR spectrum[17] agree with the literature data.

B. Compound **10a** (0.44 g, 1.8 mmol) was dissolved in hot methanol (10 mL) and a solution of KOH (2.8 g, 50 mmol) in water (4 mL) was added. The reaction mixture was refluxed for 10 h and then neutralized with 30% H_2SO_4. The product was extracted with MeOBu^t. The extract was concentrated and the residue was crystallized from MeOH. The yield of compound **16** was quantitative.

1,2,4,4-Tetramethyl-1,2,3,4-tetrahydronaphthalene-1,2-diol (17). Compound **11b** (1.09 g) was dissolved in dioxane (15 mL) and $LiAlH_4$ (1.14 g) was added. The reaction mixture was refluxed for 8 h (conversion ~90%). Ethyl acetate (20 mL) and, after 30 min, ice (5 g) were added. After the reaction with $LiAlH_4$ was completed, the reaction mixture was filtered and concentrated. Unreacted dioxolanone **11b** was crystallized from ethanol—water and the crystals were filtered off. The filtrate was concentrated, dissolved in ethanol—ethyl acetate (1 : 1), and passed through a silica gel layer. Concentration gave a yellow oil.

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References

1. K. Saigo, Yu. Khashimoto, and A. Sudo, *Zh. Org. Khim.*, 1996, **32**, 249 [*J. Org. Chem. USSR*, 1996, **32** (Engl. Transl.)].
2. K. Maruoka, S. Saito, and H. Yamamoto, *J. Am. Chem. Soc.*, 1995, **117**, 1165.
3. S. Sugiyama, K. Morishita, M. Chiba, and K. Ishii, *Heterocycles*, 2002, **57**, 637.
4. I. Yu. Titov, Yu. B. Chudinov, N. B. Chernysheva, A. A. Bogolyubov, and V. V. Semenov, *Izv. Akad. Nauk, Ser. Khim.*, 2006, 548 [*Russ. Chem. Bull., Int. Ed.*, 2006, **55**, No. 3].
5. N. B. Chernysheva, A. A. Bogolyubov, V. V. Murav´ev, V. V. Elkin, and V. V. Semenov, *Khim. Geterotsikl. Soedin.*, 2000, 1409 [*Chem. Heterocycl. Compd.*, 2000, **36** (Engl. Transl.)].
6. Germ. Pat. 1.098.953; *Chem. Abstrs*, 1962, **56**, 2453.
7. N. B. Chernysheva, A. A. Bogolyubov, and V. V. Semenov, *Khim. Geterotsikl. Soedin.*, 1999, 241 [*Chem. Heterocycl. Compd.*, 1999, **35** (Engl. Transl.)].
8. H. Huang, *J. Org. Chem.*, 2004, **24**, 1388.
9. F. M. Menger, *Tetrahedron*, 1983, **39**, 1013.
10. A. M. Moiseenkov, V. A. Dragan, V. V. Veselovskii, B. A. Cheskis, N. A. Shpiro, and A. S. Shashkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 1361 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 1226 (Engl. Transl.)].
11. V. Arivo, R. York, and R. F. Polany, *Can. J. Chem.*, 1977, **55**, 24.
12. A. G. Sakhabutdinov and A. G. Usmanova, *Zh. Org. Khim.*, 1988, **24**, 1691 [*J. Org. Chem. USSR*, 1988, **24** (Engl. Transl.)].
13. A. Hoffman, *J. Am. Chem. Soc.*, 1929, **51**, 2542.
14. O. Yu. Magidson and G. A. Garkusha, *Zh. Obshch. Khim.*, 1941, **11**, 339 [*J. Gen. Chem. USSR*, 1941, **11** (Engl. Transl.)].
15. A. A. Ponomarev and Z. V. Til´, *Zh. Obshch. Khim.*, 1957, **27**, 1075 [*J. Gen. Chem. USSR*, 1957, **27** (Engl. Transl.)].
16. C. L. Hewett, *J. Chem. Soc.*, 1940, 293.
17. J. Rigaudy and M. Lachgar, *Bull. Soc. Chim. Fr.*, 1994, **131**, 177.

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